APPENDIX A. SEARCH STRATEGIES

Database: Ovid MEDLINE(R) and Ovid OLDMEDLINE(R) <1946 to September Week 3 2012>, Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations <October 02, 2012>

Search Strategy:

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1 exp Brain edema/ (11605)
2 exp cerebrovascular trauma/ (4960)
3 exp craniocerebral trauma/ (113847)
4 exp coma/ (17150)
5 exp glasgow outcome scale/ (1042)
6 exp glasgow coma scale/ (6068)
7 ((brain* or capitis or cerebr* or crani* or hemispher* or inter-crani* or intra-crani* or skull*) adj4 (contusion* or damag* or fractur* or injur* or trauma* or wound*)).ab,ti. (77042)
8 ((brain or crani* or cerebr* or head or inter-cran* or intra-cran*) adj4 (bleed* or haematoma* or haemorrhag* or hematoma* or hemorrhag* or pressure)).ti,ab. (23995)
9 (Glasgow adj (coma or outcome) adj (scale* or score*)).ab,ti. (7439)
10 'Rancho Los Amigos Scale'.ti,ab. (31)
11 diffuse axonal injur*.ti,ab. (755)
12 ((brain or cerebral or intracranial) adj3 (edema or oedema or swell*)).ab,ti. (11389)
13 ((coma* or concuss* or unconscious* or 'persistent vegetative state') adj2 (damag* or fractur* or injur* or trauma* or wound*)).ti,ab. (1686)
14 (mtbi or "mild trauma* injur*").tw. or "minor trauma* injur*".mp. (639)
15 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 (209513)
16 exp cohort studies/ (1212058)
17 exp prognosis/ (967036)
18 exp morbidity/ (328065)
19 exp mortality/ (255922)
20 exp survival analysis/ (158174)
21 exp models, statistical/ (230839)
22 prognos*.tw. (324957)
23 course*.tw. (428896)
24 diagnosed.tw. (303319)
25 cohort*.tw. (221535)
26 death.tw. (417341)
27 predict*.tw. (808663)
28 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 (3743025)
29 diagnosed.tw. (303319)
30 cohort:.mp. (281196)
31 (predictor: or death).tw. (578864)
32 exp models, statistical/ (230839)
33 prognosis/ (327999)

34 29 or 30 or 31 or 32 or 33 (1494750)
35 28 or 34 (3743144)
36 15 and 35 (67135)
37 exp rehabilitation, vocational/ (8852)
38 exp employment/ (49891)
39 exp work/ (12406)
40 sick leave/ (3365)
41 absenteeism/ (6861)
42 exp occupational health/ (23070)
43 exp occupational medicine/ (21574)
44 exp disabled persons/ (43220)
45 "recovery of function"/ (25824)
46 exp human activities/ (291441)
47 exp self care/ (36358)
48 activities of daily living.tw. (13206)
49 (dressing or feeding or eating or toilet$ or bathing or mobil$ or driving or public transport$).tw. (409253)
50 ((daily or domestic or house or home) adj5 (activit$ or task$ or skill$ or chore$)).tw. (34321)
51 ("work status" or "work capacity").tw. (4948)
52 (unemployment or re-employment or underemployment or "job retention").ti,ab. (6217)
53 (return* adj2 school).tw. (428)
54 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 (884984)
55 15 and 54 (12268)
56 exp dementia/ (109281)
57 Delirium/ or exp Delirium, Dementia, Amnestic, Cognitive Disorders/ (165121)
58 dement*.mp. or alzheimer*.tw. (137451)
59 exp Parkinsonian Disorders/ (53442)
60 parkinson*.tw. (67897)
61 56 or 57 or 58 or 59 or 60 (263117)
62 15 and 61 (10666)
63 36 or 55 or 62 (80547)
64 animals/ not (humans/ and animals/) (3693774)
65 63 not 64 (72473)
66 limit 65 to (danish or english or french or norwegian or spanish or swedish) (62699)
67 limit 66 to yr="2001 -Current" (36478)
68 exp "Outcome Assessment (Health Care)"/ (605282)
69 (intervention* adj3 stud*).tw. (23915)
70 68 or 69 (626005)
71 15 and 70 (12781)
72 71 not 64 (12055)
73 limit 72 to (yr="2001 -Current" and (danish or english or french or norwegian or swedish)) (8537)
74 67 or 73 (36658)

75 randomized controlled trial.pt. (337763)
76 Randomized controlled trial/ (337763)
77 Randomized Controlled Trials as Topic/ (83241)
78 Double-Blind Method/ (117191)
79 clinical trial.pt. (474276)
80 "double blind:".mp. (143695)
81 placebos/ (31353)
82 placebo:.mp. (158293)
83 random:.mp. (788646)
84 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 (1069355)
85 15 and 84 (10248)
86 review/ (1739065)
87 (medline or medlars or pubmed or grateful med or CINAHL or scisearch or psychinfo or psycinfo or psychlit or psyclit or handsearch* or hand search* or manual* search* or electronic database* or bibliographic database* or embase or lilacs or scopus or web of science).mp. (74569)
88 86 and 87 (48085)
89 meta-analysis.mp. (59484)
90 meta-analysis as topic/ (12450)
91 meta-analysis/ (36480)
92 systematic review*.tw. (38103)
93 cochrane database*.jn. (9039)
94 88 or 89 or 90 or 91 or 92 or 93 (112607)
95 15 and 94 (1435)
96 exp brain neoplasms/ (111650)
97 (cancer* or neoplasm* or tumor* or malign*).mp. and brain.tw. (75605)
98 exp Glioma/ (55756)
99 96 or 97 or 98 (164154)
100 15 and 99 (9656)
101 exp pain/ (283152)
102 exp chronic disease/ (210066)
103 101 and 102 (20005)
104 (chronic* adj3 pain*).mp. (32890)
105 103 or 104 (40897)
106 15 and 105 (366)
107 exp sports/ (100542)
108 exp recreation/ (116143)
109 (return* adj3 play*).tw. (803)
110 107 or 108 or 109 (116607)
111 15 and 110 (3782)
112 exp mental disorders/ (880032)
113 15 and 112 (15929)
114 exp disability evaluation/ (35932)
115 exp "Outcome Assessment (Health Care)"/ (605282)
116 disab:.tw. (119042)

117 114 or 115 or 116 (728782)
118 15 and 117 (17459)
119 74 or 85 or 95 or 100 or 106 or 111 or 113 or 118 (68980)
120 limit 119 to (english language and yr="2001 -Current" and (danish or english or french or norwegian or swedish)) (43016)
121 animals/ not (humans/ and animals/) (3693774)
122 120 not 121 (39793)
123 exp "United States Department of Veterans Affairs"/ or exp Veterans Health/ or exp Hospitals, Veterans/ or exp Veterans Disability Claims/ or exp Veterans/ (15311)
124 veteran.mp. (2331)
125 veterans.mp. (23349)
126 VA.mp. (16805)
127 VA.in. (58986)
128 VAMC.mp. (285)
129 VAMC.in. (2086)
130 exp Military Medicine/ or exp "United States Department of Defense"/ or exp Naval Medicine/ (30814)
131 exp Hospitals, Military/ (3861)
132 exp Military Facilities/ (3901)
133 (army or navy or air force or marines or coast guard).mp. [mp=title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier] (15842)
134 military.mp. or exp Military Personnel/ (22947)
135 soldier.mp. (1480)
136 soldiers.mp. (5245)
137 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134 or 135 or 136 (151164)
138 122 and 137 (1170)
139 traumatic brain injury.mp. or exp Brain Injuries/ (48119)
140 tbi.mp. (10831)
141 139 or 140 (51178)
142 137 and 141 (1468)
143 138 or 142 (1977)
144 from 143 keep 1-1977 (1977)

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The above search strategy was applied to two additional databases on Oct. 3, 2012, with the following yield:
PsycINFO=961
Cochrane Register of Controlled Trials (OVID)=46

APPENDIX B. STUDY SELECTION FORM

1. Language: Is the full text of the article in English?
   Yes.....Proceed to #2
   No.....Code **X1**. STOP

2. Population: Is the population adult, human participants who are Veterans or members of the military from any country? Studies that do not differentiate between adult and child populations, or between Veteran/military and civilian populations, will be excluded.
   Yes.....Proceed to #3
   No.....Code **X2.** Add code **B** if retaining for background/discussion. STOP

3. Publication type: Does the article present original study data, or is it a systematic-review or meta-analysis? Narrative or non-systematic reviews, letters, editorials, and commentaries will be excluded.
   Yes.....Proceed to #4
   No.....Code **X3**. Add code **B** if retaining for background/discussion. STOP

4. Case definition: Does the article stratify/examine mTBI separately from moderate to severe TBI cases? Participants can consist of a mixed group of TBI severity (mild, moderate or severe) only if the results are stratified by severity and the mTBI subjects can be clearly identified. Studies that include mixed groups of TBI severity and do not differentiate between mild, moderate and severe TBI in their analysis will be excluded. Patients must be clearly described as having mTBI, Post-Concussive Syndrome, or concussion; if none of these terms are used, patients must be clearly defined as falling within the definition of mTBI from the VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury (2009) listed below.
   Yes.....Proceed to #5
   No.....Code **X4**. Add code **B** if retaining for background/discussion. STOP

5. Systematic review: Is the article a systematic review or meta-analysis of primary studies?
   Yes..... Code **ISR (systematic review).** STOP
   No.....Proceed to #6

6. Sample size: Is the article a primary study with a sample size of at least 30 mTBI cases?
   Yes…….Proceed to #7
   No ……Code **X6**. Add code **B** if retaining for background/discussion. STOP

7. Applicability: Does the study report outcomes addressed in our Key Questions (e.g., health, cognitive, etc. for KQ1; or factors *associated* with outcomes in KQ1; or cost/utilization)?
   Yes.....Proceed to #8
   No.....Code **X7**. Add code **B** if retaining for background/discussion. STOP

8. Intervention studies: Is the study an intervention study?
   Yes.....Proceed to #9
   No.....Proceed to #10

9. Intervention outcomes: Does the intervention study report outcomes not influenced by intervention participation (e.g., baseline and/or control group outcome data)?
   Yes.....Proceed to #10
   No.....Code **X8**. Add code **B** if retaining for background/discussion. STOP

10. VA/DoD mTBI definition: Does the study define mTBI participants as meeting the VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury (2009) definition of mTBI (listed below) with the exception of including/excluding/not reporting positive imaging results? Studies may use a different mTBI definition, but all criteria with the exception of positive imaging must fall within the VA/DoD definition.
    Yes.....Code **IPS (primary study)**. STOP
    No.....Code **X10.** Add code **B** if retaining for background/discussion. STOP

APPENDIX C. DEFINITION OF MTBI FROM THE VA/DOD CLINICAL PRACTICE GUIDELINE FOR MANAGEMENT OF CONCUSSION/MILD TRAUMATIC BRAIN INJURY (2009)

1.1 Definition of Traumatic Brain Injury

A traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs, immediately following the event:

- Any period of loss of or a decreased level of consciousness (LOC)
- Any loss of memory for events immediately before or after the injury (post-traumatic amnesia[6])
- Any alteration in mental state at the time of the injury (confusion, disorientation, slowed thinking, etc.) (Alteration of consciousness/mental state[5])
- Neurological deficits (weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia, etc.) that may or may not be transient
- Intracranial lesion

External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, a foreign body penetrating the brain, forces generated from events such as a blast or explosion, or other forces yet to be defined.

The above criteria define the event of a TBI. Not all individuals exposed to an external force will sustain a TBI, but any person who has a history of such an event with immediate manifestation of any of the above signs and symptoms can be said to have had a TBI.

1.2 Severity of Brain Injury Stratification

TBI is further categorized as to severity into mild, moderate, or severe based on the length of LOC, AOC, or PTA (see Table A-1). Acute injury severity is determined at the time of the injury.

- The patient is classified as mild/moderate/severe if s/he meets any of the criteria in Table A-1 within a particular severity level. If a patient meets criteria in more than one category of severity, the higher severity level is assigned.
- If it is not clinically possible to determine the brain injury level of severity because of medical complications (e.g., medically induced coma), other severity markers are required to make a determination of the severity of the brain injury.
- Abnormal structural imaging (e.g., Magnetic Resonance Imaging or Computed Tomography Scanning) attributed to the injury will result in the individual being considered clinically to have greater than mild injury.

In addition to traditional imaging studies, other imaging techniques such as functional magnetic resonance imaging, diffusion tensor imaging, positron emission tomography scanning; electrophysiological testing such as electroencephalography; and neuropsychological or other standardized testing of function have been used in the evaluation of persons with TBIs, but are

not considered in the currently accepted criteria for measuring severity at the time of the acute injury outlined in Table A -1.

The severity level has prognostic value, but does not necessarily predict the patient's ultimate level of functioning. There is substantial evidence that the epidemiology, pathophysiology, natural history, and prognosis for concussion/mTBI are different than for moderate and severe TBI. For example, moderate and severe TBI are often associated with objective evidence of brain injury on brain scan or neurological examination (e.g., neurological deficits) and objective deficits on neuropsychological testing, whereas these evaluations are frequently not definitive in persons with concussion/mTBI. The natural history and prognosis of moderate and severe TBI are much more directly related to the nature and severity of the injury in moderate and severe TBI, whereas factors unrelated to the injury (such as co-existing mental disorders) have been shown to be the strong predictors of symptom persistence after a concussion/mTBI.

Table A-1. Classification of TBI Severity

Criteria	Mild	Moderate	Severe
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0–30 min	> 30 min and < 24 hrs	> 24 hrs
Alteration of consciousness/ mental state (AOC)	a moment up to 24 hrs	> 24 hours. Severity based on other criteria	
Post-traumatic amnesia (PTA)	0-1 day	> 1 and < 7 days	> 7 days
Glasgow Coma Scale (best available score in first 24 hours)	13-15	9-12	< 9

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APPENDIX D. EXCLUDED STUDIES THAT DID NOT MEET MTBI DEFINITION CRITERIA

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Adams, Larson, Corrigan, et al., 2012[1]	Length of LOC classified as < 1 minute, 1-20 minutes, or > 20 minutes. Used the Health Related Behaviors Among Active Duty Military Personnel Survey response categories: "The HRB Survey symptom response groups permit recoding LOC as up to 20 minutes and greater than 20 minutes. This provides insufficient information to code LOC using the American Congress of Rehabilitation Medicine's definition of mild TBI."	NR	Kay, Harrington, Adams, et al., 1993	Self-report survey
Arbisi, Polusny, Erbes, et al., 2011[2]	Adapted from the Defense and Veterans Brain Injury Center screening tool: yes to last item "dazed, confused, see stars, get knocked out or lose consciousness" classified as mTBI. No participants reported "receiving treatment while in Iraq for a TBI or were removed from assigned duties as a result of exposure to blast or other form of head trauma."	NR	Schwab et al., 2007	Self-report mailed questionnaire
Armistead-Jehle, 2010[3]	"Screened positive on the VHA TBI screens" for "possible mTBI." "All patients suffered at most a mild TBI…, as none reported loss of consciousness of more than 30 minutes or posttraumatic amnesia of 24 hours or more."	NR	US Department of Veterans Affairs, 2007	Self-report
Bazarian, Donnelly, Peterson, et al., 2012[4]	"Mild TBI diagnosis was determined by in-person interview using a 22-item questionnaire developed to establish the nature, probability, and severity of deployment-related TBI among OEF/OIF veterans. The interview followed previously published TBI diagnostic criteria, which include confirmation of a possible TBI event, confirmation of alteration of consciousness, and confirmation of postconcussion symptoms. On the basis of the standardized clinical interview, interviewers rated the likelihood of mild TBI according to a 6-point scale: "not at all likely," "very unlikely," "somewhat unlikely," "somewhat likely," "very likely," and "almost certainly." These likelihood categories were used in all analyses. However, for descriptive purposes, subjects were defined as having mild TBI if interviewers rated them "very likely" or "almost certainly.""	NR	Lew, Poole, & Vanderploeg, 2007	Clinical interview

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Booth-Kewley, Highfill-McRoy, Larson, et al., 2012[5]	"Mild TBI symptoms were assessed using a set of questions that asked participants whether they had received an injury to the head during their most recent deployment that involved 'being dazed, confused, or 'seeing stars" or 'not remembering the injury, or losing consciousness (knocked out).' A participant was classified as having a positive TBI screen if any of the three questions elicited a positive response."	NR	Centers for Disease Control and Prevention & World Health Organization definitions adapted by the Defense and Veterans Brain Injury Center working group for military use	Self-report survey
Brenner, Terrio, Homaifar, et al., 2010[6]	Warrior Administered Retrospective Casualty Assessment Tool (WARCAT) and Brief Trauma Brain Injury Screen. "All 45 participants whose test scores were included in analyses had a history of blast exposure with alteration of or loss of consciousness (LOC)." "The nature of the most serious mTBIs reported were: $n = 30$, altered consciousness only; $n = 12$, up to 1-min LOC; and $n = 3$, one to 20-min LOC."	NR	Soldier Readiness Process, 2007; Schwab et al., 2007	Chart review, self-report survey, and clinical interview
Brenner, Ivins, Schwab, Warden, Nelson, Jaffee, & Terrio, 2010[7]	As described in Terrio et al., 2009: Warrior Administered Retrospective Casualty Assessment Tool (WARCAT) and Brief Trauma Brain Injury Screen	NR	Soldier Readiness Process, 2007; Schwab et al., 2007	Chart review, self-report survey, and clinical interview
Cameron, Marshall, Sturdivant, & Lincoln, 2011[8]	"Incident cases of mTBI were operationally defined according to the administrative case definition proposed by the Centers for Disease Control and Prevention (CDC) for research purposes… and include ICD-9-CM codes for skull fracture (800.00, 800.5, 801.0, 801.5, 803.0, 803.5, 804.0, and 804.5), concussion (850.0, 850.1, 850.5, and 850.9), intracranial injury of unspecified nature (854.0), and head injury unspecified (959.01). In addition to the four digit codes listed, all subordinate five-digit codes were also included."	NR	Centers for Disease Control and Prevention, 2003	Chart review
Carlson, Kehle, Meis, et al., 2011[9]	"Included studies must have assessed participants for a "probable" TBI (identified using self-report screening instruments) or diagnosed TBI history."	NR	NR	NA
Clement & Kennedy, 2003[10]	LOC<60 minutes with no neurological findings	Excluded	NR	Chart review

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Dougherty, MacGregor, Han, et al., 2011[11]	International Classification of Diseases, 9th Revision (ICD-9) codes 800.0-801.9, 803.0-804.9, 850.0-854.1. "The Abbreviated Injury Scale (AIS) was used to describe the severity of brain injury… Due to a small number of TBI observations with scores of 4 (severe injury) and 5 (critical injury) in the present study, TBI severity was classified as follows: 0 = No TBI, 1 = minor, 2 = moderate and 3-5 = serious to critical. Service members with AIS scores of 6 were not eligible for inclusion in the study."	NR	Gennarelli & Wodzin, 2005	Chart review
Drake, Gray, Yoder, et al., 2000[12]	"Subjects were consecutive MTBI patients… meeting specific inclusion criteria… a documented TBI classified by accepted criteria as a mild TBI." No specific mTBI definition noted.	NR	NR	Self-report and chart review
Eskridge, 2011[13]	"Clinical diagnosis codes from the International Classification of Diseases, 9th Revision (ICD-9) were assigned to each injury… In addition to the assigning of diagnosis codes, severity of each injury is accessed with two different standardized measures of injury severity; the Abbreviated Injury Scale (AIS) and the Injury Severity Scale (ISS)… The ISS for each blast episode was documented and categorized into one of four severity levels; mild (ISS 1-3), moderate (ISS 4-8), serious (ISS 9-15) and severe (ISS 16 and higher)."	NR	NR	Chart review
Fear, Jones, Groom, et al., 2009[14]	"Criteria for identification include confusion or disorientation, loss of consciousness lasting less than 30 min or post-traumatic amnesia lasting less than 24 h." However, description of population studied only states, "we have examined the prevalence of symptoms thought to be a consequence of mTBI," with unclear description of how mTBI was determined.	NR	Holm, et al., 2005	Chart review
Ferrier-Auerbach, Erbes, Polusny, et al., 2009[15]	"Three items adapted from the Defense and Veterans Brain Injury Center (DVBIC) Blast Exposure Screening Questionnaire… (1) Were you ever so close to a blast that you could feel the blast wave (such as heat or pressure) or afterward had trouble hearing or problems with attention or memory?... (2) Did you have any injuries from a blast, vehicle crash, bullet/shrapnel or fall?... (3) Did any injury cause you to be dazed/confused, 'see stars,' get knocked out, or lose consciousness?"	NR	Schwab et al., 2007	Self-report survey

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
French, Lange, Iverson, Ivins, et al., 2012[16]	LOC < 15 mins; PTA < 24 hours; absence of intracranial abnormality on computed tomography or magnetic resonance imaging scan	Excluded	Used VA/DoD criteria, but data limited to LOC < 15 minute categories.	Chart review
Gottshall, Gray, Drake, et al., 2007[17]	Definition: GCS 13-15. One patient identified as having an open head injury. LOC categorized as 31-60 (1 patient), and > 60 minutes (one patient), and up to 20 minutes (all remaining patients).	NR	American Academy of Neurology, 1997	Clinical presentation (to ED or Battalion Aid Station)
Helfer, Jordan, Lee, et al., 2011[18]	ICD-9CM codes 850.0, 850.11, 850.12, 850.2, 850.3, 850.4, 850.5, 850.9, 959.01, V15.52	NR	US Dept of Health and Human Services, 2008	Chart review
Heltemes, Dougherty, MacGregor, & Galarneau, 2011[19]	International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes 800.0-801.9, 803.0-804.9, 850.0-854.1.	NR	Centers for Disease Control and Prevention, 2003	Chart review
Hoffer, Balaban, Gottshall, et al., 2010[20]	"Definitive diagnosis of mild traumatic brain as defined by the 2007 Joint Service Surgeon General's Definition"	NR	Assistant Secretary of Defense: Memorandum on Traumatic Brain Injury: Definition and Reporting. Available at http://www.pdhealth.mil/TBI.asp	In theater clinical evaluation
Hoffer, Donaldson, Gottshall, et al., 2009[21]	No specific mTBI definition listed.	NR	NR	Clinical interview
Hoge, McGurk, Thomas, et al., 2008[22]	Positive response to three questions: LOC, being dazed and confused, seeing stars or not remembering the injury. However, "four Soldiers reported LOC lasting longer than 30 minutes. Although technically they were considered to have a moderate TBI they were not excluded because the number was low and it was not possible to verify the self-report data on any of the subjects".	NR	DVBIC, 2006; CDC, 2003	Self-report
Ivins, Schwab, Baker, & Warden, 2003[23]	"Head injury for which any LOC or any alteration of mental state without LOC was reported." Reports rates of concussion grades separately, though the categories are divided by LOC < 20 minutes and LOC between 20-59 minutes.	NR	Kay et al., 1993	Chart review
Ivins, Schwab, Baker, & Warden, 2006[24]	ICD-9CM codes 800.00-801.99, 803.00-804.99, and 850.0-854.19 and AIS severity codes of minor or moderate.	NR	Kay et al., 1993; Thurman & Guerrero, 1999	Chart review

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Ivins, Kane, & Schwab, 2009[25]	Brief Traumatic Brain Injury Screen (BTBIS); LOC criteria < 20 mins. Additional computerized survey administered; however, it appears that only those with LOC < 20 minutes were included in the further assessment. Brief Traumatic Brain Injury Screen (BTBIS); Patients who screened positive for TBI and had LOC< = 20 minutes and/or possible PTA< = 24 hours were identified as having MTBI with LOC or possible PTA	NR	Kay et al., 1993; Thurman & Guerrero, 1999	Chart review
Ivins, 2010[26]	Mapped ICD-9 CM diagnoses to the Abbreviated Injury Scale (AIS): ICD-9CM codes 800.00-801.99, 803.00-804.99, and 850.0-854.19 and AIS severity codes of minor or moderate. Combines mild and moderate into one category.	NR	Kay et al., 1993; Thurman & Guerrero, 1999	Chart review
Lange, Pancholi, Bhagwat, et al., 2012[27]	"PTA < 24 hours and LOC < 15 minutes." "It was our preference to use a LOC criterion of < 30 minutes, consistent with commonly used diagnostic criteria… However, the available information regarding LOC was limited to categorical data that did not allow us to differentiate between LOC greater or lower than 30 min."	Included	Carroll et al., 2004; Management of Concussion/mTBI Working Group, 2009; ACRM, 1993	Chart review
Lange, Pancholi, Brickell, et al., 2012[28]	LOC < 15 mins; PTA < 24 hours	Included	Used VA/DoD criteria, but data limited to LOC < 15 minute categories.	Chart review and clinical interview
Lange, Brickell, French, et al., 2012[29]	Uncomplicated: PTA<24 hours, LOC < 15 mins, negative imaging; complicated: positive imaging. "It was our preference to use an LOC criterion of 30 min to classify MTBI consistent with commonly used military and civilian diagnostic criteria. However, the available information regarding LOC was limited to categorical data that did not allow us to differentiate between LOC greater or less than 30 min (i.e., available data = LOC < 15 min and LOC 16–60 min)."	Excluded	Used VA/DoD criteria, but data limited to LOC < 15 minute categories.	Routine comprehen-sive clinical evaluation
Lew, Garvert, Pogoda, et al., 2009[30]	Mild TBI was defined as an initial GCS score of 13 to 15, PTA duration of <1 day, or LOC duration of <1 hour	NR	NR	Chart review and clinical evaluation

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Luis, Venderploeg, & Curtiss, 2003[31]	"During the interview, participants were asked, among many others, the following three questions: 1) since your discharge from active duty, have you been injured in a MVA? 2) Since your discharge from active duty have you injured your head (HI)? and (3) Did you lose consciousness as a result of the head injury?" Analysis by LOC group but time of LOC not specified.	NR	NR	Self-report
MacGregor, 2007[32]	"An ICD-9 code in the following ranges was defined as a TBI (n = 124): 800.0-801.9 (fractures of the vault or base of the skull); 803.0-804.9 (other and unqualified and multiple fractures of the skull); and 850.0-854.1 (intracranial injury, including concussion, contusion, laceration, and hemorrhage)… Severity of TBI was indicated with the Abbreviated Injury Scale (AIS). The AIS ranges from 1 (relatively minor) to 6 (currently untreatable), and is determined separately for each different body region. Severity of TBI was determined by maximum AIS score for the head region – head AIS 1-2 indicated mild TBI, head AIS 3-5 indicated moderate-severe TBI. A majority of TBI identified via CHAMPS did not have a head AIS score present; in this case the TBI was assumed to be of mild severity due to a closed head injury."	NR	ICD-9-CM, 2005	Chart review
MacGregor, Dougherty, & Galarneau, 2011[33]	International Classification of Diseases, 9th Revision (ICD-9) codes 800.0-801.9, 803.0-804.9, 850.0-854.1. "The AIS was used to describe the severity of these injuries and the injuries were scored according to the following scale: 0, no injury; 1 minor; 2, moderate; 3, serious; 4, severe; 5, critical; 6, fatal injury. As per previous literature, each participant was categorized by the severity of their highest (or maximum) AIS Head score as mild (AIS score = 1-2), moderate (AIS score = 3), or severe (AIS score = 4-6).	NR	Ommaya, Ommaya, Dannenberg, et al., 1996	Chart review
MacGregor, Dougherty, Morrison, et al., 2011[34]	"A concussion was defined by the ICD-9-CM code of 850.0-850.9. Severity of concussion was defined using the AIS."	NR	NR	Chart review
MacGregor, Shaffer, Dougherty, et al. 2010[35]	ICD-9 codes 800-801.9, 803-804.9, and 850-854.1; Abbreviated Injury Scale (AIS) score 1-2 = "mild," 3-5 = "moderate to severe"	NR	Ommaya et al., 1996	Chart review

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
McGuire, Marsh, Sowin, & Robinson, 2012[36]	"LOC less than 30 min or amnesia less than 60 min"	NR	Annegers et al., 1998	NR
Mora, Ritenour, Wade, et al., 2009[37]	"Consciousness status to determine mTBI was queried using both codes from ICD and Abbreviated Injury Scale for indications of trauma to the head, concussive injuries, and indications of consciousness at the time of injury. A loss of consciousness served as the definition for mTBI.	NR	NR	Chart review
Morgan, Lockwood, Steinke, et al., 2012[38]	No clear mTBI definition.	NR	NR	Self-report screening and clinical interview
Nelson, Weiser, Giford, et al., 2011[39]	"The Brief Traumatic Brain Injury Screen was used to identify cases (probable mTBl) and controls (no mTBI). Individuals were placed in the "probable mTBl" group if they endorsed an injury (reported at least one injury on the BTBIS) and indicated that they had lost consciousness for a defined period of time (ranging from less than 1 minute to longer than 20 minutes) following the injury. Those who did not report an injury or a loss of consciousness (LOC) for any amount of time following an injury acted as the control group."	NR	Defense and Veterans Brain Injury Center (DVBIC)	Chart review
Olson-Madden, Forster, Huggins, & Schneider, 2012[40]	"Injury severity data were coded as either mild (alteration in consciousness or loss of consciousness </ = 30 minutes) or moderate/severe (loss of consciousness > 30 minutes)."	NR	Kay et al., 1993	Clinical interview
Ommaya, Ommaya, Dannenberg, et al., 1996[41]	"Head-injury-related discharge diagnosis (800.00-801.99, 803.00-804.99, and 850.0-854.19)." Injury Severity Scale and Abbreviated Injury Scale were calculated.	NR	NR	Chart review
Ommaya, Salazar, Dannenberg, et al., 1996[42]	"Records with a head-injury hospital-related discharge diagnosis (800.00-801.99, 803.00-804.99, and 850.0-854.19) were identified as described in a previous study." "Maximum Abbreviated Injury Score (AIS) head and Injury Severity Score (ISS) were computed using the ICD-9 map. Mild TBI was defined as maximum AIS head equal to 1 or 2"	NR	NR	Clinical records
Pietrzak, Johnson, Goldstein, Malley, Southwick 2009[43]	"Positive mTBI screen" based on endorsement of all 4 items on the DVBIC questionnaire	NR	GAO, 2008 & DVBIC, 2006	Self-report survey

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Plassman, Havlik, Steffens, et al., 2000[44]	"1) mild injury = loss of consciousness or posttraumatic amnesia for less than 30 minutes, with no skull fracture; 2) moderate injury = loss of consciousness or post-traumatic amnesia for more than 30 minutes but less than 24 hours, and/or a skull fracture; and 3) severe injury = loss of consciousness or post-traumatic amnesia for more than 24 hours."	NR	Frankowski, Annengers, & Whitman, 1985	Chart review
Polusny, Kehle, Nelson, Erbes, Arbisi, Thuras, 2011[45]	Injury with altered mental status or LOC (items 1-3 on DVBIC screen)	NR	Schwab et al., 2007	Self-report in theater, 1 month prior to return home
Roebuck-Spencer, Vincent, Twille, et al., 2012[46]	"Although data on recency and severity of injury were not available in this dataset, TBIs reported in this study are presumed to be mild in nature given that Service Members were still on active duty. Mild TBI was defined as such when individuals reported an injury event accompanied by an alteration of consciousness. This included endorsement of at least one of the following: feeling dazed or confused, experiencing loss of consciousness (LOC), or experiencing loss of memory for the injury or posttraumatic amnesia (PTA) for the event."	NR	NR	Self-report screening tool
Romesser, Shen, Reblin, Kircher, Allen, Roberts, & Marchand, 2011[47]	"History of military-related concussion during a VHA TBI secondary evaluation." Excluded if "self-report suggested a history of a moderate or severe TBI (i.e., if they endorsed loss of consciousness more than 30 minutes)."	NR	NR	Clinical interview
Rona, Jones, Fear, et al., 2012[48]	"Possible mTBI was assessed using a modified version of the BTBIS… A second item asked about possible symptoms associated with the injury. These were losing consciousness; being dazed or confused; not remembering the injury; concussion (e.g., headache, dizziness); head injury, and none of these. Participants were asked to tick all that applied. Self-report of the duration of any loss of consciousness was also obtained, we eliminated one participant from the analysis who reported prolonged loss of consciousness… Participants who endorsed at least one of these symptoms were classified as having mTBI."	NR	Iverson, Langlois, McCrea, & Kelly, 2009	Self-report question-naire

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Rona, Jones, Fear, et al., 2012[49]	"Possible mTBI was assessed using a modified version of the BTBIS, which included an item exploring possible causes of injury (blast, shrapnel fragments, bullet, fall, and vehicle accident and other). Participants could state that they had not suffered an injury during deployment. A second item asked about possible symptoms associated with the injury. These were losing consciousness; being dazed or confused; not remembering the injury; concussion (e.g., headache, dizziness); head injury; and none of these. Participants were asked to tick all that applied. Self-report of the duration of any loss of consciousness was also obtained, we eliminated 1 participant from the analysis who reported prolonged loss of consciousness (which would be classified traumatic brain injury, not mTBI). Participants who endorsed at least one of these symptoms were classified as having mTBI."	NR	Iverson, Langlois, McCrea, & Kelly, 2009	Self-report question-naire
Schneiderman, Braver & Kang, 2008[50]	Three-item Brief Traumatic Brain Injury Screen	NR	Defense and Veterans Brain Injury Center	Self-report survey
Skopp, Trofimovich, Grimes, et al., 2012[51]	mild TBI (subset of all TBI codes): 310.2, 800.00-800.02, 800.06, 800.09, 800.50, 800.52, 801.00, 801.01,801.02, 801.06, 801.09, 801.50, 801.51, 801.52, 803.00-803.02, 803.06, 803.09, 803.50, 803.51, 803.52, 804.00, 804.01, 804.02, 804.06, 804.09, 804.50, 804.51, 804.52, 850.0, 805.1, 850.11, 850.9, 959.01, V15.52, V15.5_7, V15.5_C, V15.52_2, V15.52_2,V15.52_7, V15.52_C	NR	DoD standard TBI surveillance case definition to ascertain TBI status and severity	Chart review

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Theeler, Flynn, & Erickson, 2010[52]	"2-question screen followed by a 10-question screen… The first question asks if, while deployed, the soldier was exposed to or near a blast, improvised explosive device (IED) explosion, car bomb, suicide explosion, or exposed to any other combat event or resulted in a blow or jolt to the head. The second question asks if the soldier was involved in a motor vehicle accident, a fall, a sports accident, or any other event that caused a blow to the head or resulted in a neck whiplash. If the soldier answers yes to either question 1 or 2, 10 more questions asking about loss of consciousness, dazed sensation after the event, and neurologic or behavioral sequelae following the event are administered. This questionnaire is scored in a standardized manner from 0 to 39.The case definition for concussion constituted a score of 5 or greater on the 2-plus-10 questionnaire."	NR	NR	Self-report survey
Theeler, Flynn, & Erickson, 2012[53]	No specific criteria: 2-question followed by a 10-question screen if the soldier answers yes to either of the first 2 questions. This questionnaire is scored in a standardized manner from 0 to 39; the score from the 2-plus-10 questionnaire will herein be called the TBI Score	NR	Theeler, Flynn, & Erickson, 2010	Self-report survey
Vanderploeg, Belanger, & Curtiss, 2009[54]	"Have you injured your head?… Did you lose consciousness as a result of the head injury?" "those individuals who required hospitalization after their head injury (n = 40) were excluded." "head injury with altered consciousness" were classified as mild TBI.	NR	NR	Clinical interview
Vanderploeg, Curtiss & Belanger, 2005[55]	"During the interview, participants were asked, among many others, the following three questions: 1) Since your discharge from active duty, have you been injured in a MVA? 2) Since your discharge from active duty have you injured your head (HI)? and 3) Did you lose consciousness as a result of the head injury?"	NR	NR	Self-report
Vanderploeg, Curtiss, Duchnick, Luis, 2003[56]	Positive responses to following questions: "Since discharge from active duty, have you been injured in a MVA?"; "Since discharge from active duty, have you injured your head (from any cause)?"; and "Did you lose consciousness as a result of the head injury?"	NR	NR	Self-report survey

Author, Year	Definition	Patients with Abnormal Imaging	Citation	How Assessed
Vasterling, Brailey, Proctor, et al., 2012[57]	"Congruent with reports showing stronger associations between clinical outcomes and TBI following loss of consciousness v. altered consciousness, only those pre- to post-deployment interval injuries resulting in loss of consciousness were queried."	NR	NR	Self-report survey
Wilk, Herrell, Wynn, Riviere, & Hoge, 2012[58]	"Injury resulted in being dazed, confused, or seeing stars, not remembering the injury, or losing consciousness (knocked out)."	NR	DoD/VA Brain Injury Center Brief Traumatic Brain Injury Screen	Self-report survey
Wilk, Thomas, McGurk, et al., 2010[59]	"Injury resulted in being dazed, confused, or seeing stars, not remembering the injury, or losing consciousness (knocked out)."	NR	DoD/VA Brain Injury Center Brief Traumatic Brain Injury Screen	Self-report survey
Yurkiewicz, Lappan, Neely, et al., 2012[60]	"Defense and Veterans Brain Injury Center (DVBIC) assesses TBI severity after a blast event or motor vehicle accident, answers questions about evacuation and in-theater clinical care and medication, and provides recommendations on headache management and vision, hearing, vestibular, and neurologic issues. Successes of the program include a stratified headache protocol for primary care providers and an early management protocol for mild TBI and posttraumatic headache stratified headache protocol." "We reviewed consults sent to the neurology group from October 2006 to December 2010 and consults sent to the TBI group from March 2008 to December 2010. Microsoft Excel spreadsheets were constructed to organize and analyze data regarding number of consultations, response times, location of origin, branch of service, clinical images transmitted, anatomic location of complaint, type of injury, workup recommended, and treatment and evacuation recommendations."	NR	DVBIC Brief Traumatic Brain Injury Screen	Chart review

Note. None of the studies reported information on assessor blinding of study hypotheses when assessing mTBI.

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APPENDIX E. RESULTS OF INCLUDED STUDIES

Cognitive Functioning

Table 1a. Language abilities and general fund of verbal knowledge measures in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	WTAR scaled score	---	106.7 (10.1)	105.4 (5.7)	"NS"	NR
		WAIS-III	Information scaled score	12.8 (1.7)	11.8 (2.1)	"NS"	NR
	Forensic context	WAIS-III	Information scaled score	11.97 (1.92)	11.58 (1.82)	"NS"	NR
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposed	RBANS	Language	97.43 (12.42)	92.81 (14.10)	p = 0.187	NR
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	Shipley Institute of Living Scale	Vocabulary Subtest	49.15 (7.50)	49.15 (6.20)	NR	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	Mental Health Diagnosis other than PTSD	WTAR	---	96.8 (10.8)	101.7 (12.3)	NR	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	PTSD Diagnosis	WTAR	---	96.8 (10.8)	99.0 (11.2)	NR	NR
Belanger, Kretzmer, Venderploeg, & French, 2010[10]	Same population with moderate/severe TBI	WTAR	Estimated Full Scale IQ (FSIQ)	98.3 (9.3)	97.6 (9.1)	p = .67	NR
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Same population with moderate/severe TBI	WTAR	Estimated Full Scale IQ (FSIQ)	98.1 (14.6)	96.1 (12.8)	p = .35	NR
Cooper, Mercado-Couch, Critchfield, et al., 2010[18]	Same population without mTBI	RBANS	Language	92.90 (15.586)	93.66 (11.873)	p = 0.732	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Same population without mTBI; none with poor effort	WAIS-III	Information scaled score	12.21 (2.01)	12.26 (2.25)	"NS"	d = .22
Nelson, Hoelzle, Doane, et al., 2012[29]	Same population without mTBI; none have Axis I	WAIS-III	Information scaled score	12.8 (1.7)	11.9 (2.6)	"NS"	NR
		WTAR	scaled score	106.7 (10.1)	106.0 (9.2)	"NS"	NR

Table 1b. Visuospatial function in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Spencer, et al., 2010[36]	NA	RCFT	Figure Copy	33.6 (2.9)	NA	NA	NA
			Figure Orientation	3.6 (1.7)	NA	NA	NA
			Time to Copy	158.7 (63.5)	NA	NA	NA
Cooper, Mercado-Couch, Critchfield, et al., 2010[18]	Same population without mTBI	RBANS	Visuospatial/ Constructional	104.06 (13.382)	109.29 (10.47)	p = 0.007	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Same population without mTBI; none have Axis I	RCFT	Figure Copy	31.3 (3.2)	32.0 (2.1)	"NS"	NR
		WAIS-III	Block Design scaled score	12.2 (2.6)	13.0 (2.9)	"NS"	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	RCFT	Figure Copy	31.3 (3.2)	31.5 (3.0)	"NS"	NR
		WAIS-III	Block Design scaled score	12.2 (2.6)	12.2 (3.1)	"NS"	NR
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposed	RBANS	Visuospatial/ Constructional	112.11 (9.70)	108.09 (11.80)	p = 0.159	NR
Drag, Spencer, Walker, et al., 2012[20]	HADS Anxiety	Visual Organization/ Processing Factor	---	NR	NR	p > .05	r = -.12
	HADS Depression	Visual Organization/ Processing Factor	---	NR	NR	p < .001	r = -.25
	LOC and/or PTA	Visual Organization/ Processing Factor	---	49.08 (9.98)	50.46 (10.12)	p = .30	NR
		RCFT	Figure Copy	33.72 (2.64)	33.78 (2.38)	NR	NR
			Organization	3.64 (1.74)	3.99 (1.81)	NR	NR
			Time to Copy	170.51 (63.07)	166.17 (74.91)	NR	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	Mental Health Diagnosis other than PTSD	RCFT	Figure Copy	32.6 (4.9)	32.7 (4.7)	NR	NR
Drag, Spencer, Walker, et al., 2012[20]	PCL-M score	Visual Organization/ Processing Factor	---	NR	NR	p < .05	r = -.18
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	PTSD Diagnosis	RCFT	Figure Copy	32.6 (4.9)	32.1 (6.0)	NR	NR
Spencer et al., 2010[36]	Self-reported slowed thinking/organization	RCFT	Figure Copy	NR	NR	"NS"	r = -.13
			Figure Orientation	NR	NR	"NS"	r = -.02
			Time to Copy	NR	NR	"NS"	r = -.14
Drag, Spencer, Walker, et al., 2012[20]	Service connected	Visual Organization/ Processing Factor	---	NR	NR	p = .57	NR

Table 1c. Memory functioning in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	CVLT-II	Long Delay Free Recall z-score	0.5 (0.9)	-0.1 (1.1)	"Significant"	NR
			Trials 1-5 z-score	0.6 (0.9)	0.1 (1.0)	"NS"	NR
		RCFT	Delayed Recall z-score	-0.1 (1.3)	-0.5 (.98)	"NS"	NR
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Blast exposure	BVMT-R	Delayed Recall t score	48.6 (12.8)	50.7 (10.7)	"NS"	NR
			Total Recall t score	45.2 (12.3)	50.1 (10.1)	"NS"	NR
		CVLT-II	Long Delay Free Recall t-score	48.3 (9.1)	50.5 (11.4)	p = .38	NR
			Total Trials 1-5 t-score	52.8 (10.5)	54.0 (8.1)	p = .38	NR
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposure	RBANS	Immediate Memory	91.70 (11.0)	91.81 (15.67)	P = 0.994	NR
			Delayed Memory	96.96 (16.59)	95.12 (16.04)	P = 0.664	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Forensic context	CVLT-II	Long Delay Free Recall z-score	0.03 (0.99)	-0.73 (1.12)	"NS"	NR
			Trials 1-5 t-score	52.82 (8.61)	46.33 (9.23)	"NS"	NR
Drag, Spencer, Walker, et al., 2012[20]	HADS Anxiety	Memory Factor	---	NR	NR	p < .001	r = -.29
Drag, Spencer, Walker, et al., 2012[20]	HADS Depression	Memory Factor	---	NR	NR	p > .05	r = -.15
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	Memory Factor	---	49.22 (9.89)	49.61 (10.36)	NR	NR
		RBANS	Story Memory Immediate Recall	44.99 (10.19)	48.10 (10.36)	NR	NR
			Story Memory Delayed Recall	45.41 (10.49)	44.98 (10.71)	NR	NR
		RCFT	Immediate Recall	44.43 (12.72)	44.50 (13.65)	NR	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	Mental Health Diagnosis other than PTSD	CVLT-II	Long Delay Free Recall	8.9 (3.7)	8.9 (3.9)	NR	NR
			Short Delay Free Recall	8.3 (3.5)	8.6 (3.9)	NR	NR
		CVLT-II	Total Trials 1-5	43.7 (12.0)	44.6 (13.7)	NR	NR
		RCFT	Immediate Recall	16.4 (7.7)	17.4 (7.2)	NR	NR
			Delayed Recall	16.0 (7.9)	17.4 (7.2)	NR	NR

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Spencer, et al., 2010[36]	No comparison group	RBANS	Story Memory Immediate Recall	17.2 (3.4)	NA	NA	NA
			Story Memory Delayed Recall	8.4 (2.3)	NA	NA	NA
		RCFT	Immediate Recall	19.9 (6.2)	NA	NA	NA
			MSP subtest	Baseline: 51 (43-53) ≤ 72 hours: 44 (38.5-51)	Baseline: 50 (45-55) ≤ 72 hours: 50 (44-56)	Baseline: p = .57 ≤ 72 hours: p <.001	NR
Drag, Spencer, Walker, et al., 2012[20]	PCL-M score	Memory Factor	---	NR	NR	p < .05	r = -.34
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	PTSD Diagnosis	CVLT-II	Long Delay Free Recall	8.9 (3.7)	7.6 (3.2)	NR	NR
			Short Delay Free Recall	8.3 (3.5)	7.0 (3.4)	NR	NR
			Total Trials 1-5	43.7 (12.0)	38.7 (11.1)	NR	NR
		RCFT	Immediate Recall	16.4 (7.7)	15.7 (8.5)	NR	NR
			Delayed Recall	16.0 (7.9)	16.1 (7.1)	NR	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Same population of research participants, none with poor effort	CVLT-II	Long Delay Free Recall z-score	0.27 (0.91)	0.45 (0.81)	"NS"	d = 0.21
			Trials 1-5 t-score	54.43 (8.95)	57.16 (8.04)	"NS"	d = 0.32
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Same population with moderate/ severe TBI	BVMT-R	Delayed Recall	NR	NR	"NS"	NR
		BVMT-R	Total Recall	NR	NR	"NS"	NR
		CVLT-II	Long Delay Free Recall	NR	NR	p < .05	NR
			Total Trials 1-5	NR	NR	p < .01	NR
Schiehser, Delis, Filoteo, et al., 2011[35]	Same population with moderate/ severe TBI	Memory Composite Score	---	9.0 (2.4)	7.7 (2.8)	p = .04	NR
Coldren, Russell, Parish, et al., 2012[15]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	ANAM	CDD subtest	Baseline: 42.5 (36.5-50) 5+ days: 49.5 (40-56) 10+ days: 49.5 (40.1-53.1)	Baseline: 44 (37-52) 5+ days: 50.3 (44.1-57.8) 10+ days: 50.3 (44.1-57.8)	Baseline: p = 0.47 5+ days: p = 0.07 10+ days: p = 0.17	NR
			MSP subtest	Baseline: 51 (43-53) 5+ days: 50.5 (44-58) 10+ days: 51.8 (43.5-57.9)	Baseline: 52 (44.5-57.8) 5+ days: 51.5 (44.5-57.6) 10+ days: 51.5 (44.5- 57.6)	Baseline: p = 0.29 5+ days: p = 0.47 10+ days: p = 0.77	NR
Cooper, Mercado-Couch, Critchfield, et al., 2010[18]	Same population without TBI	RBANS	Immediate Memory	95.14 (14.181)	96.49 (14.445)	p = .589	NR

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Kelly, Coldren, Parish, et al., 2012[24]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	ANAM	CDD subtest	Baseline: 42.5 (35-50) ≤ 72 hours: 42 (35-49.5)	Baseline: 45 (38-52) ≤ 72 hours: 44.75 (39-51)	Baseline: p = .20 ≤ 72 hours: p = .04	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Same population without mTBI; none have Axis I	CVLT-II	Long Delay Free Recall z-score	0.5 (0.9)	0.6 (0.8)	"NS"	NR
			Trials 1-5 z-score	0.6 (0.9)	0.8 (0.8)	"NS"	NR
		RCFT	Delayed Recall z-score	-0.1 (1.3)	-0.3 (1.3)	"NS"	NR
			Delayed Memory	96.48 (12.998)	100.42 (12.854)	p = 0.072	NR
Spencer et al., 2010[36]	Self-reported memory deficits	RBANS	Story Memory Immediate Recall	NR	NR	"NS"	r = -.05
			Story Memory Delayed Recall	NR	NR	p < .05	r = -.20
		RCFT	Immediate Recall	NR	NR	"NS"	r = .08
Drag, Spencer, Walker, et al., 2012[20]	Service connected	Memory Factor	---	NR	NR	p = .17	NR

Table 1d. Attention/concentration measures in studies of U.S. Veterans and members of the U.S. military with mTBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	WAIS-III	Digit Span scaled score	9.9 (2.8)	9.9 (2.1)	"NS"	NR
	Forensic context	WAIS-III	Digit Span scaled score	9.61 (2.55)	8.42 (2.77)	"NS"	NR
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposure	RBANS	Attention	98.89 (16.64)	94.78 (14.51)	p = 0.311	NA
Drag, Spencer, Walker, et al., 2012[20]	HADS Anxiety	Verbal Attention Factor	---	NR	NR	p < .05	r = -.24
		Visual Attention Factor	---	NR	NR	p > .05	r = -.12
	HADS Depression	Verbal Attention Factor	---	NR	NR	p < .05	r = -.24
		Visual Attention Factor	---	NR	NR	p > .05	r = -.13
	LOC and/or PTA	Verbal Attention Factor	---	49.69 (10.91)	49.87 (9.69)	p = .91	NR
		Visual Attention Factor	---	50.67 (9.61)	49.61 (10.36)	p = .50	NR
	LOC and/or PTA	WAIS-IV	Digit Sequencing	9.30 (2.76)	9.41 (2.27)	NR	NR
			Digit Span Backward	9.23 (2.54)	8.92 (2.18)	NR	NR
			Digits Forward	8.39 (2.63)	8.64 (2.70)	NR	NR
Spencer et al., 2010[36]	No comparison group	WAIS-IV	Digit Sequencing	8.0 (1.9)	NA	NA	NA
			Digits Backward	7.8 (2.1)	NA	NA	NA
			Digits Forward	9.6 (2.1)	NA	NA	NA
Drag, Spencer, Walker, et al., 2012[20]	PCL-M score	Verbal Attention Factor	---	NR	NR	p < .05	r = -.21
		Visual Attention Factor	---	NR	NR	p < .05	r = -.20
			Digit Span scaled score	9.9 (2.8)	10.9 (2.4)	"NS"	NR
Coldren, Russell, Parish, et al., 2012[15]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	ANAM	Mathematical Processing (MTH) subtest	Baseline: 51 (42-57.3) 5+ days: 50.5 (43-56) 10+ days: 50.8 (46.3-55.8)	Baseline: 50 (42-55) 5+ days: 52 (44-59.8) 10+ days: 52 (44-59.8)	Baseline: p = 0.71 5+ days: p = 0.29 10+ days: p = 0.51	NR
Cooper, Mercado-Couch, Critchfield, et al., 2010 [18]	Same population without mTBI	RBANS	Attention	84.06 (15.013)	89.74 (14.898)	p = 0.026	NR

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Kelly, Coldren, Parish, et al., 2012[24]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	ANAM	Mathematical Processing (MTH) subtest	Baseline: 47 (42-57) ≤ 72 hours: 46.7 (40.5-52.5)	Baseline: 52 (42-55) ≤ 72 hours: 50 (44-56.6)	Baseline: p = .57 ≤ 72 hours: p = .03	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Same population without mTBI; none with poor effort	WAIS-III	Digit Span scaled score	10.50 (2.29)	10.65 (2.37)	"NS"	d = .06
Spencer, et al., 2010[36]	Self-reported attention deficits	WAIS-IV	Digit Sequencing	NR	NR	"NS"	r = -.15
			Digits Backward	NR	NR	"NS"	r = -.11
			Digits Forward	NR	NR	"NS"	r = -.15
			Digit Sequencing	NR	NR	"NS"	r = .00
			Digits Backward	NR	NR	"NS"	r = -.14
Drag, Spencer, Walker, et al., 2012[20]	Service connected	Verbal Attention Factor	---	NR	NR	p = .42	NR
		Visual Attention Factor	---	NR	NR	p = .17	NR

Table 1e. Cognitive processing speed in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	Stroop Color and Word Test	Color t-score	49.5 (6.9)	45.8 (7.8)	"NS"	NR
			Word t-score	49.4 (9.8)	46.2 (8.6)	"NS"	NR
		Trail Making Test	Part A t-score	50.0 (11.7)	50.5 (9.7)	"NS"	NR
		WAIS-III	Digit Symbol Coding scaled score	10.9 (2.0)	9.8 (2.4)	"NS"	NR
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Blast exposure	Trail Making Test	Part A t-score	45.8 (14.8)	46.2 (11.6)	all p values > .10	NR
		WAIS-III	Digit Symbol Coding scaled score	8.3 (2.7)	8.9 (2.5)	all p values > .10	NR

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, McGuire, et al., 2010[30]	Forensic context	Stroop Color and Word Test	Color t-score	45.29 (8.60)	40.04 (7.00)	"NS"	NR
			Word t-score	45.47 (9.01)	39.12 (7.54)	"NS"	NR
		Trail Making Test	Part A t-score	48.71 (10.44)	39.96 (9.78)	"Significant"	NR
		WAIS-III	Digit Symbol Coding scaled score	9.92 (2.53)	7.12 (2.53)	"Significant"	NR
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	Trail Making Test	Part A	48.93 (10.83)	47.99 (11.04)	NR	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	Mental Health Diagnosis other than PTSD	Stroop Color & Word Test	Color	58.8 (12.1)	54.1 (11.2)	NR	NR
			Word	76.2 (16.5)	77.0 (17.7)	NR	NR
		Trail Making Test	Part A	41.8 (15.8)	41.9 (19.1)	NR	NR
Spencer et al., 2010[36]	No comparison group	Trail Making Test	Part A	29.6 (13.1)	NA	NA	NA
			Procedural Reaction Time (PRT) subtest	Baseline: 52 (43-53) ≤ 72 hours: 46 (34.5-54.5)	Baseline: 50 (47-58) ≤ 72 hours: 52.5 (46.5-59)	Baseline: p = .60 ≤ 72 hours: p < .001	NR
			Simple Reaction Time (SRT) subtest	Baseline: 53 (48-55) ≤ 72 hours: 44.5 (34.5-52)	Baseline: 52 (47-55) ≤ 72 hours: 52 (47-55.5)	Baseline: p = .24 ≤ 72 hours: p < .001	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	PTSD Diagnosis	Stroop Color & Word Test	Color	58.8 (12.1)	60.8 (15.3)	NR	NR
			Word	76.2 (16.5)	79.6 (18.2)	NR	NR
		Trail Making Test	Part A	41.8 (15.8)	40.1 (15.0)	NR	NR
Coldren, Russell, Parish, et al., 2012[15]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	ANAM	Code Substitution (CDS) subtest	Baseline: 46 (39.5-48.5) 5+ days: 52.5 (46.5-58) 10+ days: 53 (47-60)	Baseline: 48 (43-55) 5+ days: 57 (50-63) 10+ days: 57 (50-63)	Baseline: p = 0.04 5+ days: p = 0.03 10+ days: p = 0.14	NR
			Procedural Reaction Time (PRT) subtest	Baseline: 52 (43-57) 5+ days: 52 (44.5-58.5) 10+ days: 48.8 (42-62.1)	Baseline: 52 (47-58) 5+ days: 54 (47-62.5) 10+ days: 54 (47-62.5)	Baseline: p = 0.77 5+ days: p = 0.13 10+ days: p = 0.20	NR
			Simple Reaction Time (SRT) subtest	Baseline: 53 (52-55) 5+ days: 54 (48-56.5) 10+ days: 54.5 (46.6-57.6)	Baseline: 52 (47-58) 5+ days: 53.5 (48.8-56.5) 10+ days: 53.5 (48.8-56.5)	Baseline: p = .23 5+ days: p = .97 10+ days: p = .71	NR
Kelly, Coldren, Parish, et al., 2012[24]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	ANAM	Code Substitution (CDS) subtest	Baseline: 44 (37-50) ≤ 72 hours: 44 (38.5-51)	Baseline: 48 (43-55) ≤ 72 hours: 52 (45-57)	Baseline: p = .02 ≤ 72 hours: p < .001	NR

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or Median (IQR)	Comparison group Mean (SD) or Median (IQR)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, McGuire, et al., 2010[30]	Same population without mTBI; none with poor effort	Stroop Color and Word Test	Color t-score	46.00 (8.88)	47.26 (6.90)	"NS"	d = 0.16
			Word t-score	46.29 (9.10)	48.58 (8.64)	"NS"	d = 0.26
		Trail Making Test	Part A t-score	48.89 (9.89)	49.61 (11.66)	"NS"	d = 0.10
		WAIS-III	Digit Symbol Coding scaled score	10.46 (2.52)	10.35 (2.47)	"NS"	d = 0.04
Nelson, Hoelzle, Doane, et al., 2012[29]	Same population without mTBI; none have Axis I	Stroop Color and Word Test	Color t-score	49.5 (6.9)	48.9 (6.7)	"NS"	NR
Swick, Honzel, Larsen, et al., 2012[37]	Same population without mTBI; participants had PTSD	Reaction time on a Go/NoGo task	---	NR	NR	p > .7	NR
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Same population with moderate/severe TBI	Trail Making Test	Part A	NR	NR	all p values > .10	NR
		WAIS-III	Digit Symbol Coding	NR	NR	all p values > .10	NR
			Word t-score	49.4 (9.8)	48.3 (6.6)	"NS"	NR
		Trail Making Test	Part A t-score	50.0 (11.7)	51.8 (12.1)	"NS"	NR
		WAIS-III	Digit Symbol Coding scaled score	10.9 (2.0)	11.1 (2.7)	"NS"	NR
Spencer, et al., 2010[36]	Self-reported attention deficits	Trail Making Test	Part A	NR	NR	"NS"	r = -.03
Spencer, et al., 2010[36]	Self-reported slowed thinking/organization	Trail Making Test	Part A	NR	NR	"NS"	r = -.09

Table 1f. Executive functioning in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Blast exposure	Trail Making Test	Part B t-score	49.1 (15.0)	45.6 (9.4)	all p values > .10	NR
	Same population with moderate/severe TBI	Trail Making Test	Part B	NR	NR	all p values > .10	NR
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	Trail Making Test	Part B t-score	49.96 (8.35)	48.80 (8.65)	NR	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	Mental Health Diagnosis other than PTSD	Stroop Color & Word Test	Color Word	32.9 (7.9)	30.3 (9.0)	NR	NR
		Trail Making Test	Part B	93.0 (38.8)	106.1 (73.2)	NR	NR
	PTSD Diagnosis	Stroop Color & Word Test	Color Word	32.9 (7.9)	30.5 (8.5)	NR	NR
		Trail Making Test	Part B	93.0 (38.8)	95.2 (34.5)	NR	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	COWA t-score	---	46.4 (11.0)	42.7 (9.5)	"NS"	NR
		Stroop Color and Word Test	Color-Word t-score	51.1 (9.5)	48.3 (9.5)	"NS"	NR
		Trail Making Test	Part B t-score	51.0 (12.1)	48.4 (10.8)	"NS"	NR
	Same population without mTBI; none have Axis I	COWA t-score	---	46.4 (11.0)	48.9 (9.7)	"NS"	NR
		Stroop Color and Word Test	Color-Word t-score	51.1 (9.5)	52.6 (7.0)	"NS"	NR
		Trail Making Test	Part B t-score	51.0 (12.1)	53.6 (7.5)	"NS"	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Forensic context	COWA t-score	---	44.79 (10.43)	42.83 (8.52)	"NS"	NR
		Stroop Color and Word Test	Color-Word t-score	46.95 (9.09)	43.78 (8.10)	"NS"	NR
		Trail Making Test	Part B t-score	51.45 (10.25)	44.71 (10.22)	"NS"	NR
	Same population without mTBI; none with poor effort	COWA t-score		47.04 (8.94)	46.97 (9.69)	"NS"	d = 0.01
		Stroop Color and Word Test	Color-Word t-score	48.86 (9.35)	50.52 (9.22)	"NS"	d = 0.18
		Trail Making Test	Part B t-score	52.21 (10.20)	52.77 (5.83)	NS	d = 0.07
Schiehser, Delis, Filoteo, et al., 2011[35]	Same population with moderate/severe TBI	Executive Function Composite Score	---	10.4 (2.2)	9.5 (3.0)	p = .13	NR
Spencer, et al., 2010[36]	None	Trail Making Test	Part B	72.8 (34.8)	NA	NA	NA
	Self-reported attention deficits	Trail Making Test	Part B	NR	NR	"NS"	r = -.01
	Self-reported slowed thinking/organization	Trail Making Test	Part B	NR	NR	"NS"	r = -.01

Table 1g. Effort and motivation measures in a study of U.S. Veterans with mild TBI evaluated in a research versus forensic context

Author, year	Outcome measure	Portion or subscale	Research context Mean (SD)	Forensic context Mean (SD)	p value for comparison	Magnitude of effect
Nelson, Hoelzle, McGuire, et al., 2010[30]	CVLT-II	Forced Choice	15.87 (0.41)	15.50 (1.18)	"NS"	NR
	Effort Failures raw score	---	0.32 (0.58)	1.17 (0.87)	"Significant"	NR
	Rey FIT	Combination	28.84 (2.06)	26.13 (3.72)	"Significant"	NR
	VSVT	Easy Items	23.90 (0.31)	22.92 (2.00)	"Significant"	NR
		Difficult Items	22.11 (2.87)	15.63 (6.25)	"Significant"	NR
		Total Items	46.00 (3.08)	38.54 (7.43)	"Significant"	NR
	WAIS-III	Reliable Digit Span	9.63 (1.98)	8.38 (1.71)	"NS"	NR

Table 1h. Total and cross-domain composite scores in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposure	RBANS	Total Score	98.61 (9.33)	94.88 (12.92)	p = 0.211	NR
Cooper, Mercado-Couch, Critchfield, et al., 2010[18]	Same population without mTBI	RBANS	Total Score	92.16 (11.932)	96.71 (11.672)	p = 0.023	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Same population without mTBI; none with poor effort	Overall Test Battery Mean z-score	---	0.00 (0.55)	0.11 (0.42)	"NS"	d = 0.22
Nelson, Hoelzle, Doane, et al., 2012[29]	Same population without mTBI; none have Axis I	Overall Test Battery Mean z-score	---	0.14 (0.69)	0.26 (0.38)	"NS"	d = .23
Schiehser, Delis, Filoteo, et al., 2011[35]	Same population with moderate/severe TBI	Attention/Processing Speed Composite Score	---	9.8 (1.9)	8.5 (2.0)	p < .01	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	Overall Test Battery Mean z-score	---	0.14 (0.69)	-.14 (.45)	"NS"	NR
Nelson, Hoelzle, McGuire, et al., 2010[30]	Forensic context	Overall Test Battery Mean z-score	---	-0.15 (0.55)	-0.75 (0.52)	"Significant"	NR
Ruff, Ruff, & Wang, 2009[34]	Headache intervention involving sleep hygiene, Prazosin, headache and pain education, and group therapy	MOCA	---	24.50 (.49)	28.60 (.59)	p < .001	NR
Ruff, Riechers, Wang, et al., 2012[32]	LOC	MOCA	---	28.9 (.32)	25.1 (.18)	p < .001	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	Mental Health Diagnosis other than PTSD	WAIS-III (73 participants administered); WAIS-IV (9 participants administered)	WAIS-III Vocabulary, Information, Matrix Reasoning, Block Design Subscales; WAIS-IV: all subtests	97.4 (11.0)	100.2 (15.4)	NR	NR
Ruff, Ruff, & Wang, 2008[33]	Positive neurological and/or neuropsychological findings	Number of blast exposures associated with LOC or AOC	---	2.65 (.18)	4.42 (.23)	p < .001	NR
		Number of blast exposures associated with LOC only	---	1.46 (.09)	3.91 (.20)	p < .001	NR
Gordon, Fitzpatrick, Hilsabeck, 2011[22]	PTSD Diagnosis	WAIS-III (73 participants administered); WAIS-IV: (9 participants administered)	WAIS-III Vocabulary, Information, Matrix Reasoning, Block Design Subscales; WAIS-IV: all subtests	97.4 (11.0)	95.6 (13.3)	NR	NR

Table 1i. Self-reported cognitive deficits in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI	Cognitive Cluster	10.01 (4.90)	6.88 (5.25)	p < 0.001	NR
			Concentration	2.16 (1.17)	1.40 (1.32)	p < 0.001	NR
			Decision-Making	1.74 (1.22)	1.04 (1.15)	p < 0.001	NR
			Memory	2.36 (1.16)	1.81 (1.34)	p < 0.001	NR
			Slowed Thinking/ Organization	1.89 (1.18)	1.11 (1.21)	p < 0.001	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	Memory	---	1 (5.6)	4 (11.8)	"NS"	NR
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	Blast exposure	NSI	Decision-Making	NR	NR	p > .002	NR
			Memory	NR	NR	p > .002	NR
			Slowed Thinking/ Organization	NR	NR	p > .002	NR
Drag, Spencer, Walker, et al., 2012[20]	HADS Anxiety	NSI	Concentration	NR	NR	p < .001	r = .56
			Decision-Making	NR	NR	p < .001	r = .52
			Memory	NR	NR	p < .001	r = .49
			Slowed Thinking/ Organization	NR	NR	p < .001	r = .58
	HADS Depression	NSI	Concentration	NR	NR	p < .001	r = .55
			Decision-Making	NR	NR	p < .001	r = .57
			Memory	NR	NR	p < .001	r = .51
			Slowed Thinking/ Organization	NR	NR	p < .001	r = .62
	LOC and/or PTA	NSI	Concentration	2.08 (1.21)	2.71 (1.12)	NR	NR
			Decision-Making	1.59 (1.365)	2.05 (1.36)	NR	NR
			Memory	2.17 (1.16)	2.86 (1.18)	NR	NR
			Slowed Thinking/ Organization	1.80 (1.32)	2.38 (1.29)	NR	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI	Concentration	2.31 (1.08)	NA	NA	NA
			Decision-Making	1.72 (1.12)	NA	NA	NA
			Memory	2.50 (1.04)	NA	NA	NA
			Slowed Thinking/ Organization	1.96 (1.18)	NA	NA	NA

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	PCL score > 50	NSI	Decision-Making	NR	NR	p < .002	NR
			Memory	NR	NR	p < .002	NR
			Slowed Thinking/ Organization	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI	Cognitive Cluster	3.04 (3.40)	13.32 (3.90)	p < .0001	NR
			Concentration	0.47 (0.79)	2.87 (0.88)	p < .0001	NR
			Decision-Making	0.33 (0.73)	2.28 (1.13)	p < .0001	NR
			Memory	0.95 (1.14)	3.00 (0.91)	p < .0001	NR
			Slowed Thinking/ Organization	0.42 (0.81)	2.57 (0.98)	p < .0001	NR
Drag, Spencer, Walker, et al., 2012[20]	PCL-M score	NSI	Concentration	NR	NR	p < .001	r = .59
			Decision-Making	NR	NR	p < .001	r = .63
			Memory	NR	NR	p < .001	r = .53
			Slowed Thinking/ Organization	NR	NR	p < .001	r = .68
Schiehser, Delis, Filoteo, et al., 2011[35]	Same population with moderate/severe TBI	FrSBe	Subjective Executive Dysfunction pre- to post-injury change	10.8 (14.2)	21.6 (18.3)	p = .01	NR
Drag, Spencer, Walker, et al., 2012[20]	Service connected	NSI	Concentration	NR	NR	p < .05	NR
			Decision-Making	NR	NR	p < .05	NR
			Memory	NR	NR	p < .001	NR
			Slowed Thinking/ Organization	NR	NR	p < .05	NR

Physical Health Outcomes

Table 2a. Headache outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group Mean (SD) or % of subjects	Comparison group Mean (SD) or % of subjects	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI: Headaches	2.71 (1.10)	1.45 (1.30)	p < 0.001	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	Headache	6 (33.3)	12 (35.3)	"NS"	NR
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	Blast exposure	NSI: Headaches	NR	NR	p < .002	NR
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposure	HIT-6	54.32 (9.44)	56.03 (9.54)	p = 0.489	NR
Ruff, Ruff, & Wang, 2009[34]	Headache intervention involving sleep hygiene, Prazosin, headache and pain education, and group therapy	Headache frequency (number per month)	12.40 (.94)	4.77 (.19)	p < .001	NR
		Headache pain level (scale 0-10)	7.28 (.27)	4.08 (.19)	p < .001	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI: Headaches	2.29 (1.04)	NA	NA	NA
Patil, St. Andre, Crisen, et al., 2011[31]	NA	Neurology referral for headaches	82/246 = 33.3%	NA	NA	NA
		Neurology referral for headaches, Chronic daily type	11/246 = 4.47%	NA	NA	NA
		Neurology referral for headaches, Cluster type	1/246 = 0.41%	NA	NA	NA
		Neurology referral for headaches, Migraine type	25/246 = 10.16%	NA	NA	NA
		Neurology referral for headaches, Mixed type	8/246 = 3.25%	NA	NA	NA
		Neurology referral for headaches, Other type	1/246 = 0.41%	NA	NA	NA
		Neurology referral for headaches, Post-traumatic type	4/246 = 1.63%	NA	NA	NA
		Neurology referral for headaches, Tension type	6/246 = 2.44%	NA	NA	NA
Theeler & Erickson, 2009[38]	NA	Headaches started < 1 week after trauma	12/33 = 36%	NA	NA	NA
		Headaches started > 1 month after trauma	3/33 = 9%	NA	NA	NA
		Headaches started 1 week to 1 month after trauma	1/33 = 3%	NA	NA	NA
		Unspecified onset of headache after trauma	5/33 = 15%	NA	NA	NA
		Worsening of pre-existing headaches	12/33 = 36%	NA	NA	NA
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	PCL score > 50	NSI: Headaches	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI: Headaches	1.01 (1.15)	2.79 (1.18)	p < .0001	NR

Author, year	Comparison group description	Outcome measure	mTBI group Mean (SD) or % of subjects	Comparison group Mean (SD) or % of subjects	p value for comparison	Magnitude of effect
Ruff, Ruff, & Wang, 2008[33]	Positive neurological and/or neuropsychological findings	Headache frequency: > 10 per month	0/0 = 0%	31/74 = 42%	p < .001	NR
		Headache frequency: > 4 per month	2/6 = 33%	71/74 = 96%	p < .001	NR
		Headache frequency: Daily	0/0 = 0%	10/14 = 14%	p < .001	NR
		Headache pain level (scale 0-10)	4.33 (.27)	7.28 (.27)	p < .001	NR
		Headache: Migraine type	0/0 = 0%	14/74 = 19%	p < .001	NR
		Headache: Mixed type	0/0 = 0%	30/74 = 41%	p < .001	NR
		Headache: Tension type	6/6 = 100%	30/74 = 41%	p < .001	NR
Patil, St. Andre, Crisen, et al., 2011[31]	Referral to Neurology clinic for headaches	NSI: Headache	1.97 (0.91)	2.87 (0.80)	p < .01	NR
Theeler & Erickson, 2009[38]	Same population without mTBI	Headache days per month after deployment (days/month)	11.9 (10.0)	10.3 (8.0)	NR	NR
		Headache days per month during deployment (days/month)	14.5 (11.7)	9.4 (9.4)	NR	NR
		Headache duration (hours)	8.8 (7.3)	7.5 (5.2)	NR	NR
		Headache NOS	7/33 = 21%	7/48 = 14%	NR	NR
		Headache severity (0-10 scale)	7.1 (1.5)	7.1 (1.2)	NR	NR
		Medication overuse headache	4/33 = 12%	0/48 = 0%	NR	NR
		MIDAS	30.8 (44.3)	26.8 (27.5)	NR	NR
		Migraine with aura	8/33 = 24%	3/48 = 6%	NR	NR
		Migraine without aura	15/33 = 45%	30/48 = 62%	NR	NR
		Multiple headache types	10/33 = 30%	16/48 = 33%	NR	NR
		Occipital headache	5/33 = 15%	3/48 = 6%	NR	NR
		Probable migraine	3/33 = 9%	5/48 = 10%	NR	NR
		Tension-type headache	5/33 = 15%	13/48 = 27%	NR	NR

Table 2b. Pain outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group	Comparison group	p value for comparison	Magnitude of effect
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	Pain (On a scale of 0 to 10, with 0 as no pain and 10 as the worst pain possible, how would you rate your current pain?)	Median = 3.5	Median = 2.0	p = .18	Cohen's d = .30
Lew, Pogoda, Hsu, et al., 2010[27]	Same population with moderate/severe TBI	Pain in the past 30-days	112/125 = 90%	6/6 = 100%	p = .53	NR

Table 2c. Vestibular outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	Blast exposure	NSI: Feeling Dizzy	NR	NR	p > .002	NR
		NSI: Loss of Balance	NR	NR	p > .002	NR
		NSI: Poor Coordination	NR	NR	p > .002	NR
	PCL score > 50	NSI: Feeling Dizzy	NR	NR	p < .002	NR
		NSI: Loss of Balance	NR	NR	p < .002	NR
		NSI: Poor Coordination	NR	NR	p < .002	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI: Feeling Dizzy	1.47 (.86)	NA	NA	NA
		NSI: Loss of Balance	1.32 (.92)	NA	NA	NA
		NSI: Poor Coordination	1.32 (.93)	NA	NA	NA
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI: Feeling Dizzy	0.52 (0.81)	1.88 (1.13)	p < .0001	NR
		NSI: Loss of Balance	0.45 (0.66)	1.89 (1.04)	p < .0001	NR
		NSI: Poor Coordination	0.30 (0.55)	1.98 (1.04)	p < .0001	NR
Gottshall, Drake, Gray, et al., 2003[23]	Control volunteer subjects without TBI. Not explicitly stated whether controls came from the same population as cases, but the controls were evaluated at the same time and place.	DHI	NR	NR	p < .01 for weeks 1, 2, 3, & 4 following injury	NR
	Control volunteer subjects without TBI. Not explicitly stated whether controls came from the same population as cases, but the controls were evaluated at the same time and place.	DVAT	NR	NR	p < .01 for week 1 p > .01 for week 4	NR
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI: Feeling Dizzy	1.44 (1.09)	0.94 (1.05)	p < 0.001	NR
		NSI: Loss of Balance	1.30 (1.08)	0.92 (0.98)	p = 0.002	NR
		NSI: Poor Coordination	1.71 (1.05)	0.92 (1.03)	p < 0.001	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	Disorientation	7 (38.9)	13 (38.2)	"NS"	NR
		Dizziness	5 (27.8)	8 (23.5)	"NS"	NR
		Imbalance	2 (11.1)	4 (11.8)	"NS"	NR

Table 2d. Vision outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group	Comparison group	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI: Sensitivity to Light	1.56 (1.26)	0.85 (1.22)	p < 0.001	NR
		NSI: Vision Problems	1.18 (1.16)	0.86 (1.16)	p = 0.022	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	Photophobia	4 (22.2)	6 (17.6)	"NS"	NR
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	Blast exposure	NSI: Sensitivity to Light	NR	NR	p > .002	NR
		NSI: Vision Problems	NR	NR	p > .002	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI: Sensitivity to Light	1.72 (1.17)	NA	NA	NA
		NSI: Vision Problems	1.51 (1.07)	NA	NA	NA
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	PCL score > 50	NSI: Sensitivity to Light	NR	NR	p < .002	NR
		NSI: Vision Problems	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI: Sensitivity to Light	0.65 (0.99)	2.06 (1.44)	p < .0001	NR
		NSI: Vision Problems	0.51 (0.99)	1.68 (1.23)	p < .0001	NR

Table 2e. Hearing outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description		Outcome measure	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	Blast exposure	NSI	Hearing Difficulty	NR	NR	p < .002	NR
			Sensitivity to Noise	NR	NR	p > .002	NR
	PCL score > 50	NSI	Hearing Difficulty	NR	NR	p < .002	NR
			Sensitivity to Noise	NR	NR	p < .002	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI	Hearing Difficulty	1.88 (1.06)	NA	NA	NA
			Sensitivity to Noise	1.85 (1.11)	NA	NA	NA
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI	Sensitivity to Noise	0.48 (0.87)	2.50 (1.09)	p < .0001	NR
			Hearing Difficulty	0.70 (1.02)	2.06 (1.11)	p < .0001	NR
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI	Sensitivity to Noise	1.86 (1.17)	1.29 (1.41)	p < 0.001	NR
			Hearing Difficulty	1.46 (1.12)	1.39 (1.28)	p = 0.620	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder		Tinnitus	8 (44.4)	13 (38.2)	"NS"	NR
			Phonophobia	4 (22.2)	4 (11.8)	"NS"	NR

Table 2f. Neurological outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group Mean (SD) or % of subjects	Comparison group Mean (SD) or % of subjects	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI: Numbness or Tingling	1.02 (1.08)	1.22 (1.32)	p = 0.157	NR
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	Blast exposure	NSI: Numbness or Tingling	NR	NR	p > .002	NR
Ruff, Riechers, Wang, et al., 2012[32]	LOC	Neurological deficits based on examination	0/16 = 0%	65/125 = 52%	p < .001	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI: Numbness or Tingling	1.61 (1.19)	NA	NA	NA
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	PCL score > 50	NSI: Numbness or Tingling	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI: Numbness or Tingling	0.76 (0.96)	1.83 (1.26)	p < .0001	NR

Table 2g. Nausea/appetite outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description		Outcome measure	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	Blast exposure	NSI	Change in Taste or Smell	NR	NR	p > .002	NR
			Loss of Appetite	NR	NR	p > .002	NR
			Nausea	NR	NR	p > .002	NR
	PCL score > 50	NSI	Change in Taste or Smell	NR	NR	p < .002	NR
			Loss of Appetite	NR	NR	p < .002	NR
			Nausea	NR	NR	p < .002	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI	Change in Taste or Smell	0.82 (1.03)	NA	NA	NA
			Loss of Appetite	1.53 (1.13)	NA	NA	NA
			Nausea	1.13 (1.01)	NA	NA	NA
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI	Change in Taste or Smell	0.15 (0.60)	1.14 (1.14)	p < .0001	NR
			Loss of Appetite	0.50 (0.84)	2.05 (1.10)	p < .0001	NR
			Nausea	0.31 (0.70)	1.57 (1.12)	p < .0001	NR
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI	Change in Taste or Smell	0.54 (0.92)	0.49 (0.90)	p = 0.681	NR
			Loss of Appetite	1.44 (1.11)	1.13 (1.16)	p = 0.026	NR
			Nausea	1.12 (1.07)	0.60 (0.94)	p < 0.001	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder		Nausea	3 (16.7)	4 (11.8)	"NS"	NR

Mental Health Outcomes

Table 3a. PTSD outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure		mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	PCL-C	Arousal With Reminder	3.02 (1.39)	2.17 (1.36)	p < 0.001	NR
			Avoid Activities	2.50 (1.39)	2.03 (1.28)	p = 0.004	NR
			Avoid Thoughts	2.92 (1.42)	2.31 (1.36)	p < 0.001	NR
			Avoidance Cluster	17.72 (7.54)	13.93 (6.61)	p < 0.001	NR
			Disturbing Dreams	3.10 (1.42)	2.74 (1.47)	p = 0.042	NR
			Disturbing Memories	3.32 (1.32)	3.03 (1.43)	p = 0.086	NR
			Feeling Distant	2.97 (1.43)	2.10 (1.22)	p < 0.001	NR
			Feeling Numb	2.31 (1.41)	1.85 (1.19)	p = 0.004	NR
			Future Cut Short	2.29 (1.40)	1.85 (1.24)	p = 0.006	NR
			Hyper-Arousal Cluster	17.47 (4.91)	13.65 (5.58)	p < 0.001	NR
			Irritability	3.18 (1.32)	2.51 (1.40)	p < 0.001	NR
			Jumpy, Easily Startled	3.34 (1.30)	2.72 (1.41)	p < 0.001	NR
			Loss of Interest	2.55 (1.41)	2.01 (1.19)	p = 0.001	NR
			Poor Sleep	4.11 (1.16)	3.36 (1.48)	p < 0.001	NR
			Re-experiencing Cluster	14.95 (5.74)	12.07 (5.92)	p < 0.001	NR
			Reliving Experience	2.54 (1.29)	1.99 (1.26)	p < 0.001	NR
			Super-Alert, Watchful	3.44 (1.28)	2.67 (1.39)	p < 0.001	NR
			Total Score	50.14 (16.66)	39.64 (16.72)	p < 0.001	NR
			Trouble Concentrating	3.41 (1.26)	2.46 (1.39)	p < 0.001	NR
			Trouble Remembering	2.48 (1.42)	2.05 (1.32)	p = 0.009	NR
			Upset When Reminded	2.98 (1.34)	2.42 (1.36)	p = 0.001	NR
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder		CAPS	9.8 (12.1)	54.2 (52.5)	"Significant"	NR
			SCID-I: PTSD	0 (0.0)	24 (70.6)	"NS"	NR
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	Blast exposure		PCL	37.3 (17.6)	41.5 (17.4)	p = .047	NR
Cooper, Chau, Armistead-Jehle, et al., 2012[16]	Blast exposure		PCL-M	36.29 (14.72)	37.88 (16.42)	p = .696	NR

Author, year	Comparison group description	Outcome measure		mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Kennedy, Leal, Lewis, et al., 2010[26]	Blast exposure	PCL-C	Avoidance	All: 15.6 (7.0) AOC: 14.8 (6.9) LOC: 16.1 (7.1)	All: 15.8 (7.4) AOC: 14.9 (7.1) LOC: 16.3 (7.5)	All: p = .826 AOC: "NS" LOC: "NS"	NR
			Hyper-Arousal	All: 14.5 (5.7) AOC: 14.0 (5.6) LOC: 14.8 (5.8)	All: 15.2 (5.6) AOC: 14.6 (5.4) LOC: 15.6 (5.7)	All: p = .202 AOC: "NS" LOC: "NS"	NR
			Re-experiencing	All: 12.0 (5.7) AOC: 11.8 (5.8) LOC: 12.2 (5.8)	All: 13.3 (5.9) AOC: 12.6 (5.7) LOC: 13.7 (5.9)	All: p = .020 AOC: "NS" LOC: "NS"	NR
			Total Score	All: 42.7 (16.9) AOC: 40.6 (17.0) LOC: 43.1 (17.0)	All: 44.3 (17.6) AOC: 42.0 (16.8) LOC: 45.7 (17.9)	All: p = .198 AOC: "NS" LOC: "NS"	NR
Lippa, Pasternik, Benge, & Thornton, 2010[28]	Blast exposure	PCL: Civilian and Military versions		49.75 (15.11)	54.45 (14.98)	p = .005	NR
Drag, Spencer, Walker, et al., 2012[20]	HADS Anxiety	PCL-M		NR	NR	p < .001	r = .76
	HADS Depression	PCL-M		NR	NR	p < .001	r = .76
Ruff, Riechers, Wang, et al., 2012[32]	LOC	PTSD diagnosis (based on PCL-M as well as clinical interview)		1/16 = 6.25%	83/125 = 66%	p < .001	NR
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	PCL-M		50.61 (16.24)	56.74 (14.61)	p < .05	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	PCL-C: Total Score		53.5 (15.6)	NA	NA	NA
Spencer et al., 2010[36]	NA	PCL-M		52.4 (15.0)	NA	NA	NA
Ruff, Ruff, & Wang, 2008[33]	Positive neurological and/or neuropsychological findings	PTSD diagnosis: (PCL score > 50 and meeting DSM-IV criteria)		11/46 = 24%	72/80 = 90%	p < .001	NR
Patil, St. Andre, Crisen, et al., 2011[31]	Referral to neurology clinic for headaches	PTSD (clinician confirmed or self-reported symptoms)		116/164 = 70.7%	66/82 = 80.5%	p = .10	NR
Belanger, Kretzmer, Venderploeg, & French, 2010[10]	Same population with moderate/ severe TBI	PCL		35.4 (16.8)	23.5 (13.7)	p < .0001	NR
Belanger, Kretzmer, Yoash-Gantz, Pickett, & Tupler, 2009[11]	Same population with moderate/ severe TBI	PCL		45.5 (17.2)	30.1 (15.5)	p < .0001	NR
Cooper, Nelson, Armistead-Jehle, & Bowles, 2011[19]	Same population with moderate/ severe TBI	PCL-M		42 (1)	37 (3)	NR	NR
Lew, Pogoda Hsu, et al., 2010[27]	Same population with moderate/ severe TBI	PTSD diagnosis		91/125 = 73%	5/6 = 83%	p = .49	NR
Cooper, Nelson, Armistead-Jehle, & Bowles, 2011[19]	Same population without mTBI	PCL-M		42 (1)	31 (4)	NR	NR
Gaylord, 2008[21]	Same population without mTBI	PCL-M: Score </= 44		14/31 = 45%	10/45 = 22%	p = .0345	NR
Theeler & Erickson, 2009[38]	Same population without mTBI	PCL-C		34.6 (13.3)	36.0 (14.0)	NR	NR

Author, year	Comparison group description	Outcome measure	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	CAPS: B – Re-experiencing Subscale	20.02 (7.03)	17.53 (6.06)	p = .08	Cohen's d = 0.38
		CAPS: Total Score	74.02 (16.21)	67.20 (13.21)	p = .03	Cohen's d = 0.46
		PCL-S	61.86 (11.04)	58.19 (12.89)	p = .17	Cohen's d = 0.30
Cooper, Nelson, Armistead-Jehle, & Bowles, 2011[19]	Same population, neurologic patients (tumor, stroke, electrical, subarachnoid hemorrhage, anoxia, encephalitis, Parkinson's disease, fronto-temporal dementia)	PCL-M	42 (1)	35 (5)	NR	NR
Spencer et al., 2010[36]	Self-reported attention deficits	PCL-M	NR	NR	p < .001	r = .60
	Self-reported memory deficits	PCL-M	NR	NR	p < .001	r = .48
	Self-reported slowed thinking/ organization	PCL-M	NR	NR	p < .001	r = .54

Table 3b. Measures of anxiety in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group Mean (SD)	Comparison group Mean (SD)	p value for comparison	Magnitude of effect
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	Blast exposure	NSI: Feeling Anxious	NR	NR	"NS"	NR
	PCL score > 50	NSI: Feeling Anxious	NR	NR	p < .002	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI: Feeling Anxious	2.58 (1.08)	NA	NA	NA
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI: Feeling Anxious	0.48 (0.82)	2.96 (0.91)	p < .0001	NR
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	HADS: Anxiety	11.56 (4.06)	13.16 (3.92)	p < .05	NR
	HADS Depression	HADS: Anxiety	NR	NR	p < .001	r = .56
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI: Feeling Anxious	1.99 (1.24)	1.49 (1.34)	p = 0.001	NR
Spencer, et al., 2010[36]	NA	HADS: Anxiety	11.9 (4.5)	NA	NA	NA
	Self-reported slowed thinking/organization	HADS: Anxiety	NR	NR	p < .001	r = .39
	Self-reported attention deficits	HADS: Anxiety	NR	NR	p < .001	r = .48
	Self-reported memory deficits	HADS: Anxiety	NR	NR	p < .001	r = .33

Table 3c. Measures of depression in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD) or % of subjects	Comparison group Mean (SD) or % of subjects	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI	Feeling Depressed or Sad	1.16 (1.26)	1.08 (1.19)	p = 0.566	NR
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	Blast exposure	NSI	Feeling Depressed or Sad	NR	NR	"NS"	NR
Drag, Spencer, Walker, et al., 2012[20]	LOC and/or PTA	HADS	Depression	7.95 (4.61)	10.34 (4.013)	p < .001	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI	Feeling Depressed or Sad	2.09 (1.20)	NA	NA	NA
Spencer et al., 2010[36]	NA	HADS	Depression	8.7 (4.3)	NA	NA	NA
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	PCL score > 50	NSI	Feeling Depressed or Sad	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI	Depression	0.30 (0.64)	2.44 (1.19)	p < .0001	NR
Swick, Honzel, Larsen, et al., 2012[37]	Same population without mTBI; all participants had PTSD.	BDI-II	---	20.0 (12.3)	20.8 (9.2)	NR	NR
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	BDI-II	---	31.56 (11.06)	29.17 (10.53)	p = .29	Cohen's d = 0.23
		Hopelessness (Who or what gives you strength and hope?)	---	6/46 = 13%	6/46 = 13%	NR	NR
		SCID-I	Major Depressive Disorder	25/46 = 54%	18/46 = 39%	p = .14	φ = .15
Spencer, et al., 2010[36]	Self-reported attention deficits	HADS	Depression	NR	NR	p < .001	r = .45
	Self-reported memory deficits	HADS	Depression	NR	NR	p < .001	r = .36
	Self-reported slowed thinking/organization	HADS	Depression	NR	NR	p < .001	r = .52

Table 3d. Substance use disorders in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group % of subjects	Comparison group % of subjects	p value for comparison	Magnitude of effect
Nelson, Hoelzle, Doane, et al., 2012[29]	Axis I disorder	SCID-I	Alcohol Abuse/Dependence	5/18 = 27.8%	12/34 = 35.3%	"Significant"	NR
	Same population without mTBI; none have Axis I		Alcohol Abuse/Dependence	5/18 = 27.8%	5/28 = 17.9%	"NS"	NR
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	SCID-I	Alcohol Problem	13/46 = 28%	17/46 = 37%	p = .37	φ = .09
			Drug Problem	4/46 = 9%	7/46 = 15%	p = .34	φ = .10

Table 3e. Suicide-related outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group % of subjects	Comparison group % of subjects	p value for comparison	Magnitude of effect
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	Suicidal ideation (Have you had thoughts about death or about killing yourself?)	11/44 = 25%	5/44 = 11%	p = .10	φ = .18
		Suicidal Intent (Have you ever intended to commit suicide?)	3/46 = 7%	1/46 = 2%	NR	NR
		Past Suicide Attempts (Have you ever attempted suicide?)	2/46 = 4%	2/46 = 4%	NR	NR

Table 3f. Other mental health outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group	Comparison group	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI	Affective Cluster	7.21 (4.21)	5.43 (4.54)	p < 0.001	NR
			Frustration	1.86 (1.22)	1.24 (1.29)	p < 0.001	NR
			Irritability	2.19 (1.23)	1.62 (1.32)	p < 0.001	NR
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	Blast exposure	NSI	Frustration	NR	NR	"NS"	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI	Frustration	2.41 (1.17)	NA	NA	NA
			Irritability	2.76 (1.06)	NA	NA	NA
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	PCL score > 50	NSI	Frustration	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI	Affective Cluster	2.97 (2.93)	14.64 (3.48)	p < .0001	NR
			Frustration	0.31 (0.68)	2.82 (0.95)	p < .0001	NR
			Irritability	0.63 (0.89)	2.95 (0.90)	p < .0001	NR
Schiehser, Delis, Filoteo, et al., 2011[35]	Same population with moderate/severe TBI	FrSBe	Apathy, pre- to post-injury change	14.7 (17.2)	27.8 (16.8)	p < .01	NR
			Behavioral Disinhibition, pre- to post-injury change	5.3 (7.8)	5.5 (11.2)	p = .98	NR
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	SCID-I	Any Co-Morbid Axis I Disorder	34/46 = 78%	29/46 = 63%	p = .14	φ = .12
Cooper, Mercado-Couch, Critchfield, et al., 2010[18]	Same population without mTBI	Psychiatric Diagnosis	---	25 (50.0%)	26 (22.2%)	p = 0.001	NR

Functional/Social Outcomes

Table 4a. Employment outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group % of subjects or OR (95% CI) compared to non-mTBI control	Comparison group % of subjects or OR (95% CI) compared to non-mTBI control	p value for comparison	Magnitude of effect
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	Unemployment (% who responded 'No' to 'Are you employed?')	9/45 = 20%	14/45 = 31%	p = .23	φ = .13
Toblin, Riviere, Thomas, et al., 2012[39]	LOC	Missed work: ≥2 missed workdays in the past month	1.8 (95% CI 0.9-3.5)	1.4 (95% CI 0.5-3.6)	NR	NR
		Occupational Impairment, Heavy Load: Difficulty carrying a heavy load in past month	2.2 (95% CI 1.3-3.5)	3.0 (95% CI 1.5-5.7)	NR	NR
		Occupational Impairment, Physical Training: Difficulty performing physical training (PT) in past month	1.9 (95% CI 1.2-2.9)	1.6 (95% CI 0.8-3.0)	NR	NR

Table 4b. Sleep outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	Subscale or test component	mTBI group Mean (SD), Median (IQR), or % of subjects	Comparison group Mean (SD), Median (IQR), or % of subjects	p value for comparison	Magnitude of effect
Kennedy, Cullen, Amador, et al., 2010[25]	At least one additional AIS code	NSI	Fatigue	1.85 (1.11)	1.51 (1.14)	p = 0.009	NR
			Sleep	2.73 (1.10)	2.15 (1.33)	p < 0.001	NR
Belanger, Proctor-Weber, Kretzmer, et al. 2011[12]	Blast exposure	NSI	Fatigue	NR	NR	p < .002	NR
Ruff, Ruff, & Wang, 2009[34]	Headache intervention involving sleep hygiene, Prazosin, headache and pain education, and group therapy	ESS	---	16.10 (0.28)	7.28 (0.34)	p < .001	NR
Benge, Pastorek, & Thornton, 2009[13]	NA	NSI	Fatigue	2.10 (1.11)	NA	NA	NA
			Sleep	2.72 (1.17)	NA	NA	NA
Coldren, Russell, Parish, et al., 2012[15]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	Sleep	hours per night < 4	6/47 = 13%	7/108 = 7%	p = 0.21 for sleep hours overall	NR
			hours per night ≥4	40/47 = 87%	99/108 = 93%	p = 0.21 for sleep hours overall	NR
		Sleep Change	< 2 hour loss	10/47 = 23%	4/108 = 6%	p = 0.02 for sleep change overall	NR
			> 2 hour loss	33/47 = 77%	62/108 = 94%	p = 0.02 for sleep change overall	NR
Kelly, Coldren, Parish, et al., 2012[24]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	Sleep	hours per night	Median = 6 (5-7)	Median = 6 (5-7)	p = .22	NR
		Sleep Change (negative value = hours lost)	---	Median = 0 (-2.5-0)	Median = 0 (0-0)	p < 0.001	NR
Belanger, Proctor-Weber, Kretzmer, et al., 2011[12]	PCL score > 50	NSI	Fatigue	NR	NR	p < .002	NR
Cooper, Kennedy, Cullen, et al., 2011[17]	PCL-C ≥60 (controls had PCL-C ≤30)	NSI	Fatigue	0.86 (0.91)	2.60 (1.04)	p < .0001	NR
			Sleep	1.24 (1.17)	3.45 (0.70)	p < .0001	NR
Ruff, Ruff, & Wang, 2008[33]	Positive neurological and/or neuropsychological findings	NSI	Sleep	5/46 = 11%	66/80 = 82.5%	p < .001	NR
Patil, St. Andre, Crisen, et al., 2011[31]	Referral to Neurology clinic for headaches	NSI	Sleep	2.53 (1.17)	2.78 (1.12)	p = .11	NR
Lew, Pogoda Hsu, et al., 2010[27]	Same population with moderate/severe TBI	Sleep disturbance in the past 30 days	---	2.72 (1.24)	3.17 (.75)	p = .38	NR

Table 4c. Social outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome measure	mTBI group % of subjects	Comparison group % of subjects	p value for comparison	Magnitude of effect
Barnes, Walter, & Chard, 2012[9]	Same population without mTBI	Lack of emotional support (% who responded 'No' to 'Do you have an emotional support system?')	9/35 = 26%	6/35 = 17%	p = .38	φ = .10
		Marital status (Are you married?)	NR	NR	p = .72	φ = .04

Service Utilization/Costs

Table 5. Service utilization outcomes in studies of U.S. Veterans and members of the U.S. military with mild TBI

Author, year	Comparison group description	Outcome Measure	mTBI group OR (95% CI) compared to non-mTBI control, % of subjects, or Mean (SD)	Comparison group OR (95% CI) compared to non-mTBI control, % of subjects, or Mean (SD)	p value for comparison	Magnitude of effect
Toblin, Riviere, Thomas, et al., 2012[39]	LOC	Medical utilization: ≥2 "sick call" visits in past month	2.0 (95% CI 1.3-3.1)	1.9 (95% CI 1.04-3.6)	NR	NR
Coldren, Russell, Parish, et al., 2012[15]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	Current Counseling	2/47 = 4%	4/108 = 4%	p >0.99	NR
		Current Mental Health Medication	2/47 = 4%	9/108 = 9%	p = 0.50	NR
Kelly, Coldren, Parish, et al., 2012[24]	Same population without mTBI; with minor traumatic injuries not involving the head and noninjured volunteers from same population	Current Counseling	4/66 = 6%	5/146 = 3%	p = .46	NR
		Current Mental Health Medication	3/66 = 5%	8/146 = 6%	p = .99	NR
Belanger, Kretzmer, Venderploeg, & French, 2010[10]	Same population with moderate/ severe TBI	Currently taking pain medications	24/44 = 55%	37/64 = 57%	p = .44	NR
Gaylord 2008[21]	Same population without mTBI	Length of Hospital Stay (days)	PTSD: 13.6 (9.8) No PTSD: 19.0 (20.9)	PTSD: 16.0 (26.6) No PTSD: 14.1 (22.2)	NR	NR
		Length of Intensive Care Unit Stay (days)	PTSD: 2.0 (6.7) No PTSD: 12.1 (12.1)	PTSD: 1.6 (3.9) No PTSD: 2.8 (8.9)	NR	NR
Swick, Honzel, Larsen, et al., 2012[37]	Same population without mTBI; all participants had PTSD.	Number of medications	18	5	NR	NR
Cooper, Mercado-Couch, Critchfield, et al., 2010[18]	Same population without mTBI	Pain Medication (Narcotic)	32 (64.0%)	85 (72.6%)	p = 0.264	NR

APPENDIX F. LIST OF EXCLUDED STUDIES GROUPED BY REASON FOR EXCLUSION

Population does not meet criteria for adult, human subjects who are Veterans or members of the military from any country
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APPENDIX G. PEER REVIEW COMMENTS AND RESPONSES

Reviewer	Comment	Response
Question 1: Are the objectives, scope, and methods for this review clearly described?		
1	No	Noted.
1	Suggest adding in the background of Executive Summary more rationale (e.g., purpose is understanding OEF/OIF cohort vis-à-vis mTBI for planning etc).	We have made this addition.
1	Also suggest adding the criteria that were used for inclusion/exclusion at the beginning of the document.	Due to space limitations, we have left reference to inclusion/exclusion criteria in the body of the report and appendices; however, this information will be presented earlier in the planned article publication of the results.
1	Suggest being more specific when mentioning comparison to controls (e.g., on page 4, were they injured controls, postdeployed controls?)	We have included this information in the data abstraction tables.
2	No	Noted.
2	Objectives of the review are clearly described. The scope of this review is clearly described.	Noted.
2	The methods lack detail. Expectations for reporting methodological detail have grown exponentially over the past few years, and although this would expand the methods section, I highly recommend that this be done.	Noted. We have expanded this discussion.
2	Specifically, I recommend that the report follow the most recent PRISMA guidelines for reporting systematic reviews. I recognize that this is not primarily an academic document. However, adherence to the PRISMA guidelines would enhance the credibility of the review.	Noted. We have expanded our reporting to be in line with PRISMA guidelines as you suggest.
2	1. I assume that no online protocol was published, but if so, that should be reported.	We have updated this information in the report.
2	2. Eligibility criteria: The study designs included were mentioned. I have a few questions. Case control studies are not listed in the inclusion criteria. Were case control studies excluded from the search? I assume that case series and case reports were excluded, but this is not explicit. Under the criteria "Timing: No limitations based on timing" – my question – timing of what? Please clarify	Noted. Case control studies were not excluded. Timing has been updated to reflect time since injury. The inclusion criteria have been updated accordingly.
2	3. Information Sources: This is well covered. However, if study authors were contacted for additional information, this information should be included. If they were not contacted, it is fine to leave the section as it is.	Correct – no authors were contacted for additional information about studies included in this review.

Reviewer	Comment	Response
2	4. Search: The electronic search is included in appendix A. This is very good. Also, it has become standard practice to clarify that the search was developed by a library scientist experienced in database searches of this sort. It has also recently become recommended practice for a search strategy to be peer reviewed by a second librarian. Was this done? What measures were taken to ensure that the search was comprehensive?	We have added this description of procedures.
2	5. Study selection: This section is nicely detailed. Including the study selection form is very useful. Other information to consider adding: What procedures were taken where the PI and the other reviewer disagreed on relevance at the point of abstract screening? What procedures were undertaken where the reviewers disagreed on relevance at the point of full article screening? A detailed definition of TBI is provided in Appendix C. This requires a Mild TBI to have normal CT/MRI. It might be noted in the methods section (or someplace else in the document) that this is not a universally agreed upon criteria – many definitions of MTBI allow for abnormalities on imaging, differentiating these by classifying them as complicated or uncomplicated mild TBI. Of course it is important to adhere to the VA/DoD criteria, but it is a possible point of discrepancy from other criteria that should be explicitly noted.	Thank you. We have included this additional information in the updated report.
2	6. Data abstraction: Good tables. It would be useful to have details about the data abstraction process. It has become the standard to have at least two independent data abstractors – was this done? Who did the data abstraction? How was this checked? Again, where data were missing or ambiguous in the report, were authors contacted? It would also be helpful to include study design in the tables.	We have updated the report with this additional information. We chose not to include study design in the tables because the designs were often inaccurately reported in the published studies and because all studies were observational in nature. Specific study design criteria related to quality/ potential for bias were abstracted in the tables (e.g., sample selection, comparison group, etc.)
2	7. Quality assessment: In this section, you state that case control and case series designs were included. This should be consistent with the statement of study design inclusion criteria. More details should be provided. Who did the quality assessment? It is standard practice to have two independent quality assessments on each paper, and to report the procedures undertaken when there is no consensus on quality. How (specifically) was the assessment of quality used in the data synthesis process? How specifically was this linked to rating the body of evidence? Who performed this linkage?	This discrepancy has been corrected. We have added this information.
2	8. Synthesis: You have provided a reasonable way of grouping the studies and no meta-analysis was conducted – I see this decision as appropriate. However, details about how the synthesis was conducted would be very good to add. This includes who conducted the synthesis, was this discussed in a larger group, were the conclusions agreed to by the working group, and what processes were used to reach agreement.	We have added this information.

Reviewer	Comment	Response
2	9. Results: I see a literature flow chart. This is very good.	Noted.
2	10. You provide well-formulated summary statements, and in your detailed results sections, you link findings to your citations. But it might also be useful to link findings to the particular studies in your summary statements as well. This is optional, but I present it as worth considering.	Due to the lengthiness of the report, we decided not to link findings to particular studies in the summary section. However, we linked findings in the results section to the citations of included studies should readers be interested in these specifics.
2	11. There is no linkage between particular studies and their study quality assessment – or more importantly, their assessed risk of bias. This does not necessarily imply the need for an overall score, and the use of an overall additive score has been widely criticized. But the reader should be able to see which studies have risk of which biases. There is some reference to overall study quality in the sections reporting summary of findings, but most recent standards recommend that this be reported in a more study-specific way. When you say "low quality" – what specifically do you mean? I also wonder whether studies with high risk of bias in their methodological quality can usefully contribute to our knowledge of TBI in the military?	We have updated our description of study quality and risk of bias to specifically describe each study as being of low quality due to the high risk of bias. We have also provided additional cautionary, interpretive statements in the summary section related to the strength of evidence from a body of low quality studies.
2	12. Were cross-sectional studies included in sections related to risk or prognostic factors. There is no information provided about the restriction of study designs for particular questions. Obviously, cross-sectional studies are appropriate for questions about prevalence of symptoms, but not for making causal inferences about these symptoms. Could this be clarified in the report?	We have clarified the inclusion of various types of study designs, highlighted findings from the only prospective study, and noted limitations of interpretation based solely on cross sectional studies reporting association rather than causal inferences.
2	13. The authors have done a good job in discussing limitations of the literature in the second last section. Would it be useful to be even more specific about biases in the Limitations and Recommendations section? E.g., providing concrete examples of recall bias; of incidence-prevalence bias (where it might exist), etc.	We have added additional discussion of these points.
3	Yes	Noted.
4	No	Noted.
4	1 The methods section of the Executive Summary is missing important information about inclusion/exclusion criteria and how quality and strength of evidence is rated. This latter point is particularly important as it makes it very difficult for the reader to understand why the authors consider the strength of the evidence to be low.	We have added this information to the executive summary section of the report.
4	It is also not clear when the authors state that no clear pattern of risk and protective factors emerge whether the studies were designed to look at risk and protective factors.	We have noted this in the discussion.

Reviewer	Comment	Response
4	2. In the Executive Summary Conclusions section (and elsewhere in the report) the authors refer to "objective results" (p.4). It would be helpful if they discussed which results were "objective" and what is meant by "objective".	We have updated this section to describe results not based on self-report.
4	3. It is not clear to me why the authors are including the headache intervention study. How is participating in a headache intervention a protective factor? What then is meant by protective factor? Do the authors mean that the sample referred for headache intervention was different than those not referred? Why is that relevant to the KQs? In general, the information presented on this particular study is confusing throughout the report and relevance is not clear.	We have clarified references to this intervention throughout the report.
4	4. It is not clear to me why studies focused on biomarkers are included. I do not see how biomarkers are "impairments" (KQ 1) according to any definition of impairment. I do not see how biomarkers address either KQ2A (pre-injury factors) or 2B (post injury factors) if they not include a focus on outcomes, given the way that KQ is worded. How does this study meet criteria for the outcomes listed on p.10?	We agree and have moved information from this section to the discussion rather than including it in the evidence synthesis.
4	5. Table 1: I find the mTBI definition column confusing. What do the authors mean by "citation". What do the authors mean when they list "LOC, AOC and PTA" given inclusion criteria requires DOD/VA/ACRM definition of mTBI? A note to the table may help clarify.	We have clarified this column label.
4	6. I did not finding tables summarizing strength of evidence per study. This information is particularly important given the conclusions. It would also make it easier for the reader to refer to specific studies when reviewing the report. In the absence of this information, it is difficult to interpret statements like, "Strength of the evidence was low because of ….". If I missed something that was included in the report, I apologize.	We have clarified this information in the text of the report. All included studies were rated as low quality due to high risk of bias, without exception.
4	7. Tables 2–6: I would have liked to see the pertinent studies referenced rather than or at least in addition to the number of studies listed in parentheses. Number may not be as important as quality, in my opinion. Question based on Table 2: Did 4 studies find that mean scores for processing speed were within normal limits with possible exceptions of those getting C&Ps and <10 days since injury (p.24)? This is what the Table suggests, unless I am not reading it correctly.	We have referenced individual citations in the text, and due to the low quality rating of all included studies, have not identified individual studies or study quality in the table for reasons of space. You are correct in your interpretation of the presented information in the table.

Reviewer	Comment	Response
4	8. When the authors make statements like "most research reported no significant risk or protective factors," it would be helpful to know the number/percent of studies were looking at risk/protective factors.	We have noted this information in the discussion as an overall commentary on the body of literature given that only one included study was prospective in nature, and the rest were not designed to assess risk/protective factors. We have also clarified these sentences in the report to reflect studies of association rather than implying that studies were designed to assess risk/protective factors.
4	9. I do not know that readers who are not neuropsychologists will understand how the authors are distinguishing between cognitive and physical health problems. For example, it may not be clear why visuospatial abilities falls in the cognitive domain but vision is in the physical health results section. It is not clear why the authors review "effort and motivation" at all. It is not clear why studies focused on sleep are in the functional/social outcomes section. I suggest that the authors explicitly describe the rationale for their groupings.	We have provided additional description of these decisions in the report.
4	10. In the Executive Summary Limitation section, the authors state that the studies included in the review relied on well-validated assessment tools. Are they classifying the NSI as well-validated? Perhaps this statement can be more precise.	We have made this statement more accurate and non-specific to individual tools. We refer to well-validated assessment tools being a strength of the overall body of literature, and report specific tools in the data abstraction. However, we did not to an individual literature search or other method of assessment to determine validation of each tool used in the included studies. We do also note limitations of some of the tools (e.g., the NSI) used to assess single-item, self-report outcomes.
4	11. Service Utilization and Costs: For this section, it does not make sense to me to collapse across Veteran and active duty samples given differences in the healthcare systems. I recommend that the authors clearly state which findings are specific to Veterans using VA and which are specific to active duty.	We have added a clarifying statement noting that all included studies investigated Veterans.
5	Yes	Noted.
6	Yes	Noted.
6	The objectives mention cognitive "disability" as an outcome, but based on the variables examined in the literature, cognitive "deficits" may be a better term. The language regarding mental health outcomes could also be clarified. The objectives mention "symptoms" but the operational definition is later given as diagnoses. However, examination of the measures in the studies included suggests that "symptoms" would be the more accurate term.	We have changed the wording to "deficits."
7	Yes	Noted.

Reviewer	Comment	Response
7	These are well described.	Noted.
8	Yes	Noted.
8	Methods and objectives clearly described, but missing some information. There was no discussion of how common features of mTBI, e.g. the presence of comorbidities and multiple TBIs, were handled in inclusion criteria.	We have clarified these criteria in the report.
8	"Study relevance" was a major factor in exclusion (p.14) but no further information provided on how this criterion was applied.	Study relevance simply implies that the study must provide information included in the KQs and meet inclusion/ exclusion criteria. No additional relevance criteria were applied.
8	Overall weakness in discussion of physical and neuroimaging outcomes. The scope as defined by the key questions does not include imaging or biomarkers as outcomes. It is not clear whether these topics were adequately searched according to the search strategy presented. However, I am not familiar with the abbreviations and formatting used to detail the search strategy, so this was a bit hard to follow. An explanation or reference would be helpful.	We agree and have moved the imaging/biomarker information to the discussion section and removed it from the results/evidence synthesis.
8	As a general comment, scope is very large and each element (e.g. cognitive effects) could be the subject of a report.	Noted.
9	Yes	Noted.
9	The key objectives and methodology are sound.	Noted.
10	Yes	Noted.
10	Consider rephrasing to: **Key Question # 1:** For Veterans/Service Members who suffer a mTBI and develop acute and or persistent sequale of mTBI symptoms what is the prevalence of health conditions (e.g. pain, headaches, insomnia, vertigo, or seizure disorder), functional limitations, (e.g. return to work/duty, marital status/family dynamics), cognitive impairment (e.g. attention, concentration or memory) and or associated mental health conditions (e.g. PTSD, depression or anxiety disorder). **Key Question # 2:** What factors affect outcomes for Veterans/service members with mTBI? **Key Question 2A:** For Veteran/military populations, are there pre-injury (premorbid) risk factors (e.g., pre-injury mental health factors, genetic factors, or prior concussions) or protective factors ??) that affect outcomes for mTBI? **Key Question 2B**: For Veteran/military populations, are there post-injury risk factors (e.g., PTSD, depression or anxiety) or protective factors that affect outcomes for mTBI?	We have changed the wording of the key questions slightly.
11	Yes	Noted.

Reviewer	Comment	Response
2. Is there any indication of bias in our synthesis of the evidence?		
1	No	Noted.
2	No	Noted.
2	I don't see an indication of bias, although it is always useful to discuss possible publication bias and how this might impact on the synthesis. However, a synthesis based on highly biased studies can bias a synthesis. Where studies were highly biased (low quality), can it be estimated what direction those methodological flaws would have biased the study's findings? (toward or away from the null, for example). This may impact on the interpretation of study findings.	Noted. We have added these points to the discussion.
3	No	Noted.
4	Yes	Noted.
4	1. The report states that TBI is THE leading cause of morbidity and disability in OEF/OIF. I do not believe that this is accurate. More important, one needs to distinguish between TBI history and TBI-related disability. The prevalence of TBI-related disability is unknown and some evidence suggests that persistent problems in many individuals who suffered TBI in OEF/OIF result from mental health comorbidities	Noted. We have changed the introductory paragraphs to better reflect these distinctions.
4	2. In Executive Summary Conclusions section, the authors state that "It is likely that the prevalence….is largely influenced by factors other than deployment rather than being uniquely associated with mTBI." They do NOT however describe a rationale for this conclusion. This reviewer suggests that the authors clearly build conclusions based on the literature reviewed otherwise the sentence reads like an opinion. The statement in the Executive Summary Conclusions that reads, "… the most likely exceptions are…evaluation linked with potential compensation" is particularly troubling as it seems to be based on the one study that looked at compensation effects (#34). In the Executive Summary Limitation section the authors state "…self-reported deficits are more likely to persist for individuals with mTBI particularly when associated with compensation (p.40." Again, this statement seems too strong if only one study (#34) reviewed looked at compensation effects unless that study was of very high quality	These conclusions are based on consistent findings across Veteran/military and civilian literature, though we agree that the conclusions could have been interpreted as basing conclusions on solely the Veteran/military literature, which would not have been warranted. These concluding statements have been tempered and clarified to more accurately reflect the results available from the body of literature.

Reviewer	Comment	Response
4	3. In the Summary and Discussion section the authors conclude, "The body of research …suggest that many health consequences resolve within the first few months following injury, if not sooner" (p.49). I am not clear about what evidence they are using the draw that conclusion given the design of the studies reviewed. To which specific studies/findings are the authors referring when they state, "Objective cognitive impairment most often resolves within a few weeks of initial injury."? I suggest that authors be very clear about the findings and studies they are using to make that claim. That claim also seems to be in direct contraction to their statement in the Background section that "TBI is the leading cause of morbidity and disability…" It also contradicts the statement in the Service Utilization/Costs that "The long-term resource needs of recent Iraq and Afghanistan War Veterans who sustained mTBI are likely substantial". (p.52). Why would that be the case?	We have clarified the studies on which these conclusions are based, as sometimes the quotes were in direct reference to the Carroll et al, 2004 review findings that we were summarizing. We have also tempered the introductory statements relating to the potential effects of TBI.
4	3. The authors also state in Summary and Discussion, "This report documents that litigation or evaluation for compensation as being a risk factor…(p.49)" Is this the finding based on one study referred to in multiple sections of this report (#34) or are there other studies? The basis for this statement was not clear to me.	This statement was in reference to findings from the Carroll et al, 2004 review, and this citation has been clarified.
5	Yes	Noted.
5	The bias has to do with studies included versus excluded. Your criteria are clear and stated on the bottom of page 9, of which the DoD/VA criteria are one operational definition of those criteria.	Noted.
5	However, the manuscript <u>includes</u> studies that don't meet that criteria because they:	Noted.
5	(a) include moderates and "unclassified" severity patients [Morrisette, Woodward, Kimbrel, et al, 2011[75], Schiehser, Delis, Filoteo, et al., 2011[35]] or,	Thank you for catching this error. Though this paper reports findings for the mTBI only group separately from those with moderate or unclassified TBI, the specific finding we reported in our review was a combined group finding; therefore, this study has been excluded.
5	(b) includes those where TBI was not verified ("probably TBI) [Ruff, Riechers, Wang, et al., 2012[32]], or	Though this paper reports some findings for a combined TBI group, the findings that we reported in this review are reported separately for the mTBI only group.
5	(c) at least as currently written in the tables, state criteria at variance to the DoD/VA criteria such as the GCS > 13 was used or GCS = 13 (when it should be ≥ 13) [Gaylord, Cooper, Mercado, et al., 2008[21], Cooper, Mercado-Couch, Richfield, et al., 2010 [18]].	You are correct that this was inaccurately stated in the table. It should be ≥ 13, as reported in the article, and therefore these studies remain included.

Reviewer	Comment	Response
5	Studies are excluded, that in my view meet the DoD/VA criteria at least as well, if not better, than some of the included studies. Of course I am biased, but I'm referring to my studies:	Noted. We have reviewed all the suggested studies and agree that they provide useful information; however, we have scoped the review to include a specific subset of papers meeting VA/DoD mTBI criteria, and the papers you suggest do not fit within those pre-specified criteria and are therefore not included in the review.
5	Luis CA, Vanderploeg RD, Curtiss G. Predictors of postconcussion symptom complex in community dwelling male veterans. *J Int Neuropsychol Soc.* Nov 2003;9(7):1001-1015.	Reviewed, not included due to not meeting inclusion criteria.
5	Vanderploeg RD, Belanger HG, Curtiss G. Mild traumatic brain injury and posttraumatic stress disorder and their associations with health symptoms. *Arch Phys Med Rehabil.* Jul 2009;90(7):1084-1093.	Reviewed, not included due to not meeting inclusion criteria.
5	Vanderploeg RD, Curtiss G, Belanger HG. Long-term neuropsychological outcomes following mild traumatic brain injury. *J Int Neuropsychol Soc.* May 2005;11(3):228-236.	Reviewed, not included due to not meeting inclusion criteria.
5	Vanderploeg RD, Curtiss G, Duchnick JJ, Luis CA. Demographic, medical, and psychiatric factors in work and marital status after mild head injury. *J Head Trauma Rehabil.* Mar-Apr 2003;18(2):148-163.	Reviewed, not included due to not meeting inclusion criteria.
5	Self-report for LOC is not reliable because individuals do not know if they actually had an LOC or simply a memory gap (i.e., PTA). Our studies used alteration of consciousness defined as "loss consciousness or 'black out'". That is, either a self-reported LOC or a self-reported Alteration of consciousness. It is possible, although unlikely, that my studies included a few folks who had moderate injuries. Unlikely because the data was collected in the 1970s at which time those with anything other than a mild TBI would be hospitalized overnight at least, and no subject was hospitalized. In addition, the bias come in because other studies were included that had moderate or "unclassified" TBI severity subjects.	See above comments; we have re-reviewed all noted studies and the inclusion/exclusion criteria have been appropriately applied. Thank you for noting the possible discrepancies as one of the studies was inappropriately included in the first draft of the report and has now been excluded (Morrisette).
5	None of this would change findings, but my studies do address things the manuscripts says have not been addressed – frequencies of different medical signs and symptoms and psychosocial outcomes, as well as frequencies of neuropsychological impairments, in addition to comparison with an injury control group (groups most other studies do not have) and controlling for comorbid or premorbid medical and mental health conditions.	See above response re: included studies.

Reviewer	Comment	Response
5	In addition, core findings of these studies have been replicated in a new sample using criteria that you would likely agree does meet the DoD/VA criteria for mild TBI. This study, also not included, is: Vanderploeg, R.D., Belanger, H.G., Horner, R.D., Spehar, A.M., Powell-Cope, G., Luther, S.L., Scott, S.G., (2012). Health Outcomes Associated With Military Deployment: Mild Traumatic Brain Injury, Blast, Trauma, and Combat Associations in the Florida National Guard. Archives of Physical Medicine and Rehabilitation, 93, 1887-1895.	We have reviewed this study and it does not quite meet VA/DoD criteria, and therefore is not included in the review.
6	No	Noted.
6	The selection of studies is straightforward, but given the large number excluded, it might be helpful to summarize in the table of excluded studies, the specific reasons for exclusion. Without knowing how close these studies came to being eligible for inclusion in the paper, it's difficult to assess whether the eligibility criteria themselves may have incidentally introduced a bias. For example, are war-zone samples more likely to be excluded than veteran samples due to contextual constraints that somehow limited the information gathered? I'm not suggesting altering the eligibility criteria, but instead suggesting assessing potential "sampling biases" (for inclusion in the review) based on the possible identification of variables consistently associated with failure to use the DoD/VA definition.	We had similar concerns, and this was the rationale for including a table of studies meeting all inclusion criteria except for VA/DoD mTBI definition so that we were transparent about exclusions and readers could examine the list for possible bias in the included/excluded studies. We have also added a table of all the full-text study citations and exclusion codes.
7	No	Noted.
7	The review was absent of bias, and was appropriately critical of the lack of rigorous methodology, TBI severity description, and appropriate controls that appear pervasive throughout the literature on TBI in U.S. service members and Veterans.	Noted.
8	Yes	Noted.
8	Inclusion criteria introduced biases that should be discussed. Use of VA/DoD criteria for mTBI could time-limit the literature to after 2007; indeed, all included studies were from within the last 3 years. These criteria may also limit to military and VA-affiliated researchers and to US researchers. It is possible that exclusion of studies based on reporting of LOC and PTA led to unnecessary loss of data, as the exact value of these is usually based on self-report and is unreliable.	We agree that any scoping decisions, this one included, introduce potential for bias. This decision was agreed upon by stakeholders for this review in order to obtain the most accurate description of a specific population of interest: Members of the US military/Veterans with mTBI meeting VA/DoD criteria. Therefore, though the report is limited in these ways, the stakeholders agreed that other, broader reports (e.g., the Carroll et al, 2004 WHO mTBI report) could address broader/different questions. In response to your comment, we have broadened the discussion of this point in the discussion.

Reviewer	Comment	Response
8	The requirement for an mTBI sample size of at least 30 will bias the type of outcome measures that are used. Because of expense and other limitations, few neuroimaging studies will fulfill this requirement. Large studies can be limited in the ability to perform in-depth testing, and so the report may be biased toward less sensitive questionnaire data and easier-to-administer testing protocols (e.g. RBANS is a screening measure designed for dementia). Large studies also may bias away from presentation of individual results, which as you note, can be informative. Few objective evaluations of physical outcomes (e.g. audiology) were included, which severely limits interpretation of this domain.	We agree, and have moved the neuroimaging information to the discussion section because of the likelihood that it is not comprehensive since we did not design the search to focus on these outcomes. We have also now added a table of excluded studies so that authors can review studies that were excluded based on sample size to gather additional information as needed.
8	Many studies served as sources across outcome domains (e.g. Nelson et al., 2012). This could potentially perpetuate any biases or limitations present in the single study across domains (e.g. recruitment setting, inadequate power).	We agree and have noted this limitation in the discussion.
9	No	Noted.
10	No	Noted.
11	No	Noted.
3. Are there any published or unpublished studies that we may have overlooked?		
1	Yes	Noted.
1	Cohen, Suri, Amick, & Yan, 2012 (published in Work)	This study does not meet our inclusion criteria because of unclearly reported definition of mTBI and because results are not reported separately for those with mTBI versus moderate/severe TBI.
2	No	Noted.
2	Not that I can think of.	Noted.
3	Yes	Noted.
3	Scholten et al, Analysis of US Veterans Health Administration comprehensive evaluations for traumatic brain injury in Operation Enduring Freedom and Operation Iraqi Freedom Veterans. Brain Inj 2012	We have reviewed this study and it does not meet inclusion criteria due to the mTBI definition used to define the cohort of participants.
4	Yes	Noted.
4	Have the authors reviewed the CBO report: The Veterans Health Administration's Treatment of PTSD and Traumatic Brain Injury Among Recent Combat Veterans?	We have reviewed this report and agree that though it provides important information and guidance, it does not meet our criteria for inclusion in this review.
5	Yes	Noted.

Reviewer	Comment	Response
5	Vanderploeg, R.D., Belanger, H.G., Horner, R.D., Spehar, A.M., Powell-Cope, G., Luther, S.L., Scott, S.G., (2012). Health Outcomes Associated With Military Deployment: Mild Traumatic Brain Injury, Blast, Trauma, and Combat Associations in the Florida National Guard. Archives of Physical Medicine and Rehabilitation, 93, 1887-1895.	We have reviewed this study and agree that though it provides important information, it does not meet VA/DoD mTBI definitional criteria and is therefore not included in this review.
6	Yes	Noted.
6	To my knowledge, the report captures all of the military/military veteran studies. However, in the discussion of meta-analytic studies from the civilian literature, it would be important to balance the discussion with the Pertab et al., meta-analysis that re-analyzes data from previous meta-analytic studies and reveals a potential qualification of prior findings.	This review has been added to the report.
7	Yes	Noted.
7	JRRD has recently come out with a TBI sensory and communications disorders edition (Vol. 49, Issue 7, 2012). Even though this journal is published after Oct. 3, 2012, these articles cover deployment-related experiences (e.g., blast, TBI), and associations with the following senses, conditions, and patterns: vestibular, visual, auditory, pain, PTSD, and referrals. This compendium fits well with the focus of the synthesis.	Thank you for this suggestion. We have reviewed all studies from this special issue none meet criteria for inclusion in this report.
7	Other published studies that were not included, though would be excluded for not meeting mTBI criteria, are: 1. Iverson, K. M., Hendricks, A., Kimerling, R., Krengel, M., Meterko, M., Stolzmann, K., Baker, E., Pogoda, T.K., Vasterling, J., & Lew, H.L. (2011). Psychiatric diagnoses and neurobehavioral symptom severity among OEF/OIF VA patients with deployment-related TBI. *Women's Health Issues, 2(4S),* S210-S217.	We have reviewed this study and agree that though it provides important information, it does not meet VA/DoD criteria and is therefore not included in this review.
7	2. Lew, H.L., Kraft, M., Pogoda, T.K., Amick, M.M., Woods, P., & Cifu, D.X. (2011). Prevalence and Characteristics of Driving Difficulties in Operation Enduring Freedom/Operation Iraqi Freedom Combat Returnees. *JRRD, 48*(8), 913-926.	We have reviewed this study and agree that though it provides important information, it does not meet VA/DoD criteria and is therefore not included in this review.
7	3. Lew, H. L., Pogoda, T.K., Baker, E., Meterko, M., Stolzmann, K.L., Cifu, D.X., Amara, J.H. & Hendricks, A.M. (2011*).* Prevalence of dual sensory impairment and its association with traumatic brain injury and blast exposure in OEF/OIF Veterans. *Journal of Head Trauma & Rehabilitation,* 26(6):489-96.	We have reviewed this study and agree that though it provides important information, it does not meet VA/DoD criteria and is therefore not included in this review.
7	4. Hendricks AM, Amara J, Baker E, Charns MP, Gardner JA, Iverson KM, et al. *(in press)* Screening for mild traumatic brain injury in OEF-OIF deployed US military: an empirical assessment of VHA's experience. *Brain Injury*	We were not able to obtain a copy of this study for review.
8	Yes	Noted.

Reviewer	Comment	Response
8	Luethcke et al. 2010. Comparison of Concussive Symptoms, Cognitive Performance, and Psychological Symptoms Between Acute Blast-Versus Nonblast-Induced Mild Traumatic Brain Injury. Journal of the International Neuropsychological Society (2011), 17, 36–45.	We reviewed this study and it did not meet inclusion criteria.
8	Terrio, et al. 2009 Traumatic Brain Injury Screening: Preliminary Findings in a US Army Brigade Combat Team. J Head Trauma Rehabil Vol. 24, No. 1, pp. 14–23.	We reviewed this study and it did not meet inclusion criteria.
8	Caplan et al. 2010 The Structure of Postconcussive Symptoms in 3 US Military Samples. *J Head Trauma Rehabil* Vol. 25, No. 6, pp. 447–458.	We reviewed this study and it did not meet inclusion criteria.
8	Cockerham, 2009. Eye and visual function in traumatic brain injury. J Rehab Research Dev Volume 46, Number 6, 2009 Pages 811–818.	We reviewed this study and it did not meet inclusion criteria.
8	Akin and Murnane, 2011. Head Injury and Blast Exposure: Vestibular Consequences. Otolaryngol Clin N Am 44 (2011) 323–334.	We reviewed this study and it did not meet inclusion criteria.
8	Pogoda et al., 2012. Multisensory Impairment Reported by Veterans with and without Traumatic Brain Injury History. J Rehab Research Dev Volume 49, Number 7 Pages 971–984.	This study has been included in the report. Thank you for the suggestion.
8	Vasterling, et al. 2012. Neuropsychological outcomes of mild traumatic brain injury, post-traumatic stress disorder and depression in Iraq-deployed US Army soldiers. Br J Psychiatry 201, 186-192	We reviewed this study and it did not meet inclusion criteria.
8	Schneibel et al., 2012 Altered brain activation in military personnel with one or more traumatic brain injuries following blast. J Int Neuropsychol Soc. 2012 Jan;18(1):89-100	We have moved the discussion of imaging and biomarkers to the discussion section of the report since it falls outside the scope of our key questions.
8	Morey et al., 2012 Effects of chronic mild traumatic brain injury on white matter integrity in Iraq and Afghanistan war veterans. Hum Brain Mapp. 2012 Jun 15	We have moved the discussion of imaging and biomarkers to the discussion section of the report since it falls outside the scope of our key questions.
8	Yurgelon-Todd, et al.,2011. Neuroimaging Correlates of Traumatic Brain Injury and Suicidal Behavior *J Head Trauma Rehabil* Vol. 26, No. 4, pp. 276–289	We reviewed this study and it did not meet inclusion criteria.
8	Sponheim, 2011. Evidence of disrupted functional connectivity in the brain after combat-related blast injury. NeuroImage 54 (2011) S21–S29	We have moved the discussion of imaging and biomarkers to the discussion section of the report since it falls outside the scope of our key questions.
8	Peskind et al., 2011. Cerebrocerebellar hypometabolism associated with repetitive blast exposure mild traumatic brain injury in 12 Iraq war Veterans with persistent post-concussive symptoms. NeuroImage 54 (2011) S76–S82.	We reviewed this study and it did not meet inclusion criteria.
9	Not aware of any that have been excluded that meet criteria for inclusion. Please see below regarding Vision data.	Noted.
10	Yes	Noted.

Reviewer	Comment	Response
10	Cooper DB et al. Relationship between mechanism of injury and neurocognitive functioning in OEF/OIF service members with mild traumatic brain injuries. Mil Med. 2012 Oct;177(10):1157-60.	This study has been included in the report. Thank you for the suggestion.
10	Scholten JD et al. Analysis of US Veterans Health Administration comprehensive evaluations for traumatic brain injury in Operation Enduring Freedom and Operation Iraqi Freedom Veterans. Brain Inj. 2012;26(10):1177-84.	We have reviewed this study and it does not meet inclusion criteria due to the mTBI definition used to define the cohort of participants.
10	Bryan CJ, et al. Loss of Consciousness, Depression, Posttraumatic Stress Disorder, and Suicide Risk Among Deployed Military Personnel With Mild Traumatic Brain Injury. J Head Trauma Rehabil. 2012 Oct 16.	This study has been added to the included studies for this report. Thank you for the suggestion.
11	Yes	Noted.
11	During an earlier call you had mentioned that another group (I believe IOM) was conducting a review of mTBI literature. It would be helpful to note this since non-Veteran studies were not included in the literature review and could have been aggregated to be the comparison to the Veteran based studies.	Agreed. The WHO group lead by Dr. Linda Carroll is updating the 2004 mTBI prognosis review, and we have included this information in our report for reader reference.
4. Please write additional suggestions or comments below. If applicable, please indicate the page and line numbers from the draft report.		
1	On page 26, please define "old learning." More specificity in general would be helpful (so for example, for 'memory studies', were delayed recall, trial-by-trial learning, recognition all examined? On page 48 in the summary of results, to what type of control groups were mTBI compared? On page 53, suggest adding the number of mTBI's as a future area for investigation. On page 54, suggest being judicious with the use of the word "persistent" since it is unclear if symptoms persist in the longitudinal sense.	We have changed "old learning" to be "language abilities and general fund of verbal knowledge." We have included additional information on specific tests and on comparison groups in the appendix tables. We have added a statement in the discussion relating to future research of the number of TBIs. We have clarified and limited use of the term persistent throughout the report.
2	Page 49, Where other reviews are cited, it would be useful to explicitly indicate what year they were published, since early systematic reviews might simply be outdated. The study citation is included, of course, but inclusion of the year of publication in the body of this section would highlight that point.	We have included the year in text in this section.
3	Overall, an excellent evidence review.	Noted. Thank you.
3	It should be emphasized for all domains that major shortcomings in the literature are the lack of non-mTBI comparison groups and lack of adequate pre-mTBI (premorbid) data.	Agreed, and we have added this point to the discussion.
3	In section on mental disorders, some controlled civilian studies do show higher rates of mental disorders after mTBI compared with non-TBI controls (e.g., Fann et al, Arch Gen Psychiatry 2004). Presence of prior psychiatric conditions is a major risk factor. Data from this same cohort showed higher health care utilization among those with mTBI compared with non-TBI controls (Rockhill et al, J Neurotrauma 2012).	We have clarified that some civilian literature indicates higher rates of mental disorders after mTBI, as noted in the Carroll et al 2004 review.

Reviewer	Comment	Response
4	Below I provide specific comments about organization and note some areas where the terms used where not clear to me. Please disregard if not helpful in efforts to finalize the report.	Thank you for the suggestions. Some will be included in this report, though some will be included in the planned article publication rather than in this full report.
4	1. I suggest that the authors orient the reader at the beginning to their overall approach to summarizing the findings. It took this reviewer a few reads to understand how the authors were presenting the material. It was a bit confusing to me to read the summary before the sections describing findings per domain (i.e., summary of cognitive functioning in general before description in each cognitive domain). Sometimes the summaries seem completely unnecessary because only one study is reviewed. In general, there was considerable repetition because of the structure of this report, which made the report difficult to read. It takes several reads to know what is new information versus a restating of what has already been summarized.	Because some parts of this report are purposely repetitive (e.g., the executive summary), we plan to make the suggested change for the published article.
4	2. This reviewer suggests the authors state reason time since injury is important rather than assuming the reader already has this information.	Noted, and this has been added.
4	3. To help the reader understand the "cognitive function" section, I suggest the authors tell the reader that x# studies are based on neuropsychological testing and briefly explain. It would be helpful to have an appendix in which the function each test assesses is described – otherwise, I am not sure how helpful it is to list measures/acronyms in Appendix E. I did not find it useful to have the names of the tests listed in the text – in fact, I think it makes the narrative harder to read.	We have made some of these changes, including shortening the acronyms listed in the results section of the report.
4	4. In the Summary of Findings for Cognitive Function Results the author state that "standardized scores are scores associated with impairment below a certain cutoff." This is not quite right and I do not think the sentence expresses what they intend it to.	We have corrected this sentence.
4	5. It is confusing when the authors state that risk factors include "LOC and PTA" or the like, given that they are using the DoD/VA/ACRM definition of mTBI. As opposed to what?	We have clarified that LOC and PTA were compared to just alteration of consciousness.
4	6. It would be more accurate on p.39 to state that the PCL scores suggest clinically significant *symptoms* rather than "impairment" as stated in the report	We have chosen to use the term impairment across measures to use similar terminology describing scores above a clinically significant cutoff.
4	7. The term "TBI sequelae" as used here is confusing. For example, on p. 28 the authors state that one study reported "…based on mTBI with LOC and PTA compared to those with mTBI who did not have these immediate sequelae." What does this mean? If these individuals did not have these "sequelae", how was mTBI determined? This is probably a matter of simple clarification.	We have changed this sentence to clarify.

Reviewer	Comment	Response
4	8. Summary and Conclusions: This section is largely devoted to discussion of the civilian literature. The subsection on Physical Health Outcomes (p.49) does not even discuss the Veteran/military studies. I suggest switching the focus so that the authors primarily discuss the literature they reviewed for this report.	Noted. We have updated the physical health section to focus the discussion on a comparison.
4	9. It seems to me that references are used inconsistently. Why are there no references for the summaries? Why are the "one study" referred to on p. 26 and the "single studies" on .34 not referenced What are the "some studies" (p.30 that found better cognitive function for those not evaluated in forensic settings? I thought there was just one study that examined this issue (#34). In some sections, it is very difficult to identify which studies are forming the basis of the authors' conclusions.	Noted. We have made the suggested corrections to text. The format for this report is such that summaries do not contain citations; however, citations will be used consistently throughout the published article.
4	10. Note that PTSD is an AXIS I disorder (p.35). I do not understand the statement, "Finally, though many individual studies…general association between specific mental health outcomes with other mental health diagnoses and symptoms".	We have clarified that some studies looked at only PTSD, some examined "any Axis I disorder" which would include PTSD. We have clarified the confusing sentence.
5	1. A statement is made without any supporting reference, that I do not believe the literature supports. Page 1: "TBI is the leading cause of morbidity and disability among OEF/OIF service members." I'm not sure about "morbidity" (but I think chronic pain and mental health are higher), but I'm quite sure there is no evidence to support the "disability" claim. This statement is repeated several times throughout the manuscript.	This has been corrected throughout the manuscript.
5	2. Page 2 bottom (and elsewhere) "One or more studies have found . . . [problems in those] experiencing loss or alteration of consciousness at the time of the injury." It seems to me that everyone included in every study meets this criteria because that is the criteria for TBI. So, that statement it seems problematic. If all studies had all subjects with an immediate event-related "loss or alteration of consciousness" how can "loss or alteration of consciousness at the time of injury" be a unique factor?	We have clarified that this refers only to patients who have PTA but not LOC or AOC, as described by the primary study authors.
5	3. Page 3 (an elsewhere): If you include my studies (or the one you inadvertently omitted because it was recently published), the statement "Similar to objective cognitive results, prevalence of self-reported cognitive deficits was not reported in the included studies" would be inaccurate.	We have updated all summary statements to reflect the final list of articles meeting inclusion criteria.

Reviewer	Comment	Response
5	4. Page 5: The statement ". . . self-reported deficits are more likely to persist for individuals with mTBI" is inaccurate. There is a difference between "persistence of symptoms" and "symptoms reported in the chronic phase" which may come-and-go or wax-and-wane. Studies have not demonstrated persistence. What they have demonstrated is problems/symptoms reported in the post-acute or chronic phase. The studies do not document that these began at the time of the mTBI and persisted over time to the time of assessment. Other civilian literature clearly documents that symptoms and problems are not persistent, but rather that they come-and-go or wax-and-wane, but are generally higher in frequency in mild TBI subjects. We don't know if they were also higher prior to the mild TBI but we do know that they are not persistent.	We have made this change throughout the report.
5	5. The term "Language and Old Learning" is a term no one uses, and as a result is confusing. Initially I thought you were referring to "Verbal Learning and Memory". I would suggest using the term "Language Abilities and General Fund of Verbal Knowledge" or something like that.	Thank you for this suggestion. We have made this change.
5	6. Throughout the review you refer to "statistical significance" or lack thereof. However, effect size would seem to better capture the important issue. If sample sizes are somewhat small (or there are is lot of variability across participants) a moderate effect size could be non-significant, but a moderate effect size would be clinically important.	We agree entirely. We report effect sizes in the tables whenever available; however, authors frequently did not report effect sizes or data with which effect sizes could be calculated.
5	7. A similar point to that above, is that studies may compare a mild TBI group to a non-mild TBI control group and find differences (as some studies did). However, those two groups may differ on other important factors as well that could explain group differences (e.g., education, race, age, degree of comorbid mental health or medical health conditions). It seems to me that you would want to address this issue if you can for those studies that reported group differences. An example of this is on the bottom of page 26.	Agreed. We highlighted any statistical adjustment or other adjustment for variation across groups in the text and tables; unfortunately, most studies did not provide this information, and this lack of adjustment for potential confounders is a contributing factor to the low study quality ratings for this body of literature.
5	8. Page 36: The term "associated with mTBI" is used in talking about mental health disorders and symptoms. This implies some actual association, when it is more likely that they are simply comorbid factors both due to deployment-related (or life-related) experiences that are risk factors for both mTBI and comorbid mental health conditions. -- I would suggest using the term "comorbid" rather than "associated".	We have made this change to the paper.

Reviewer	Comment	Response
6	Studies reporting mean cognitive performance scores are criticized within the report because they cannot provide prevalence estimates of impairment. However, the implication that report of percentage of participants scoring below an impairment cut-off or below a certain standard score would yield a good prevalence estimate of cognitive impairment does not take into account the premorbid cognitive abilities of participants. Clinically relevant cognitive impairment is typically thought of as an intra-individual decline. Scores normally thought of as below average may not indicate acquired impairment but instead reflect the innate potential of the individuals; similarly, above average scores may indicate a cognitive decline (i.e., impairment) in an individual with superior cognitive potential. Thus, the suggestion in the report does not go far enough. To best estimate the prevalence of cognitive impairment following a TBI, prospective, longitudinal measurement would be necessary. This is typically not feasible, but the report should nevertheless avoid implications that use of normative data without regard to the individual's baseline potential would yield accurate prevalence estimates of cognitive decline. The paper states this in the Summary and Discussion section, but it is also important to mention it earlier when discussion impairment cut-offs based on standardized scores.	Noted. We have included this discussion both within the section on cognitive outcomes, and within the discussion section.
7	Overall comments: The synthesis was very well written and took a comprehensive approach to examining the extant literature on mTBI in U.S. service members and military. The synthesis was inconsistent with respect to its use of citations in the text, and its repetition of acronyms and abbreviations. Other editorial and substantive comments (line numbers not included in reviewed drafts):	Noted. Thank you.
7	P. 1, Background: OEF/OIF should be defined. Also, what about OND?	This change has been made. No studies reported outcomes for OND Veterans and the information we describe in the background is specific to OEF/OIF Veterans.
7	P. 1 - Methods: Define WHO	This change has been made.
7	P. 3 - define LOC, PTA	This change has been made.
7	P. 3 – First introduction of NSI – Neurobehavioral Symptoms (no S) Inventory	This change has been made.
7	P. 3 – second to last paragraph, two instances of "reported that" – delete one	This change has been made.
7	P.3 – second to last paragraph – "mTBI)." ß no reference to an open parentheses, so delete the)	This change has been made.
7	P.4—define DTI, MRI	This change has been made.

Reviewer	Comment	Response
7	P.5 – last paragraph: the recommendation to include imaging results is noted; however, such a recommendation is not feasible in terms of equipment, manpower, participant willingness to participate (might lead to biased self-selection), timing, and costs. This recommendation also needs to be reconciled with the VA/DoD Clinical Practice Guidelines (see excerpt below). Though, the point is taken that if imaging studies, especially functional fMRI or DTI, were performed more frequently, then perhaps there would be notable distinctions between "normal" and "mild TBI" states. From: VA/DoD (p. 16)	Noted, and we have changed this recommendation slightly to be more consistent with this comment.
7	In addition to traditional imaging studies, other imaging techniques such as functional magnetic resonance imaging, diffusion tensor imaging, positron emission tomography scanning; electrophysiological testing such as electroencephalography; and neuropsychological or other standardized testing of function have been used in the evaluation of persons with TBIs, but are not considered in the currently accepted criteria for measuring severity at the time of the acute injury outlined in Table A -1	Noted, and the criteria presented are consistent with the VA/DoD criteria.
7	Abbreviations Table: There were some abbreviations throughout the text that were not "formally" defined before their first use, so these are included along with others: (a) AOC = Alteration of consciousness/mental state [5] (based on VA/DOD guidelines) p.5; (b) BAMC (last row) = Brooke Army Medical Center, p. 16; (c) C&P = Compensation & Pension , p. 21; (d) CTE = Chronic Traumatic Encephalopathy, p. 10; (e) EFP = Explosively formed penetrator (?) – used on p. 17 – define; (f) mBIAS – "symptoms" misspelled, p. 6; (g) NSI = I = Inventory, p. 6; (h) PI = Principal Investigator, p. 9 (or just say "Principal Investigator on p. 9); (i) VHA = Veterans Health Administration (like on p. 8), p. 7; (j) For SCID, indicate Axis I, not Axis 1, p. 7; (k) Define/include VACO and PM&R, as introduced on p. 8; (l) define WHO on p. 7 (mentioned on p. 8)	These changes have been made.
7	P. 8 – cite the studies from which the "12 to 23 percent" are derived. Also consider citing Hendricks et al. (in press, Brain Injuries), who examined VA comprehensive TBI evaluation (CTBIE) data and found: "In the study population, 21.6% screened positive for potential TBI and 54.6% of these had an electronic record of a CTBIE. Of those with CTBIE records, evaluators confirmed TBI in 57.7%, yielding a best estimate that 6.8% of all those screened were confirmed to have TBI."	This citation has been added.
7	P. 8 – second paragraph: "fame" should be "frame"	This change has been made.

Reviewer	Comment	Response
7	P.8 – second paragraph: "factors unique to combat deployments." I would take out "combat," (maybe replace with "military," but not sure if that's necessary), since deployment-related conditions (e.g., noise in the general military environment), separate from combat, may uniquely account for experiencing post-concussive symptoms. Plus, since women are restricted from some combat roles, the use of "combat" here may minimize what women potentially experience.	This change has been made.
7	P. 8 – misplaced semi-colon in second paragraph,	This change has been made.
7	P. 8 abbreviate "Veterans Health Administration" as VHA;	This change has been made.
7	P. 8 Define PM&R and VACO	This change has been made.
7	P. 9 Search strategy – can now call it "mTBI"	This change has been made.
7	P. 9 Last paragraph – why not include "post-traumatic amnesia" along with AOC, LOC?	This change has been made.
7	P. 9 – last paragraph, discussion about "severity of sequelae" gets a little confusing, because TBI sequelae can be defined as either AOC, LOC, or PTA (which the reader might be primed for, since there was just discussion about these in the previous sentence), or TBI residual symptoms (e.g., headache, vestibular, pain, auditory, visual, etc. impairment). I don't know if "the Severity of sequelae" sentence needs to be here, but I understand that it makes the point that very specific criteria are used to categorize TBI severity, and it's important to note that the severity of mental/physical symptoms following a TBI event are not used to classify severity. I would replace "sequelae" with "symptoms," and then provide a few NSI-22 symptoms to orient the reader. It might also be helpful to briefly state severity is based on the duration of LOC, AOC, or PTA. You can then list the criteria (e.g., LOC < 30 min), or refer to the reader to a more detailed description, as you currently do.	This change has been made.
7	P. 10 Identify DoD in first paragraph	This change has been made.
7	P. 10 – identify CTE in "Outcomes" paragraph	This change has been made.
7	P. 14, Figure 1: Bullet points in the last box to the right would help the criteria stand out more.	We left out bullet points for space reasons.
7	P. 15, Table 1: Barnes et al., spell out "medical"	We have corrected this mistake.
7	P. 16-17 Cooper, Mercado-Couch, et al. – BAMC should be defined earlier (e.g., in the Cooper et al. citation above it in the table); Should American "College" be "Congress?"; Was not clear about 10 participants excluded due to PTA suggesting a more severe TBI… Is it that the duration of PTA was longer than the criteria for mTBI, as specified by ACRM?	This change has been made.

Reviewer	Comment	Response
7	P. 17 Drag et al., define "C and P," also, in mTBI definition, why not just call it "AOC?"	This change has been made.
7	P. 17 Gaylord et al., American College or Congress?; defined "EFP," as previously noted.	This change has been made.
7	P. 18 Gordon et al., Time since Injury – define unit of time.	This change has been made.
7	P. 18, Kennedy, Leal et al., last column, just say MVA instead of spelling it out	This change has been made.
7	P. 19 MacDonald et al., use "TBI" consistently – sometimes it's spelled out (see first and last columns)	This is a quote so it is spelled out as in the original text.
7	P. 19 Morrisette et al., spell "through," not "thru."	This change has been made.
7	P. 19, Nelson et al., reference 34: define what "forensic" context is.	This change has been made.
7	P. 20, Patil et al., Based on "VA"/DoD Consensus definition (reversed as written).	This change has been made.
7	P. 20 Ruff, Riechers et al., "Department of CVAMC" needs editing; also, in description for three groups of Veterans, for the first two indicate "deployment-related" LOC? Not sure what "combat Veterans without "LOC" means – is this a control group or did they have AOC or PTA?; In the mTBI definition column, not sure what the definition is referring to – did Veterans have to have LOC or AOC following the TBI, PLUS PTA?	These changes have been made.
7	P. 21 Schiesher et al., mTBI definition column – delete ©	This change has been made.
7	P. 21 Spencer et al., C&P needs to be defined earlier	This change has been made.
7	P. 21 Swick et al., Combat Veterans diagnosed, not "diagnoses"	This change has been made.
7	P. 21 Theeler et al., mTBI definition column – use DVBIC acronym	This change has been made.
7	P. 23 Third from last paragraph – can abbreviate LOC and AOC – make clear, if this is the case, that participants demonstrated better overall cognitive functioning "post-intervention?"	This change has been made.
7	P. 23 – wasn't clear in 2nd to last paragraph – second line: Should this be "NOT" reported, or should "NOT" be deleted?	We have clarified this sentence.
7	P. 24, processing speed row, Key Question #1 column, not sure why "possible" exceptions is there – delete that word?	This change has been made.
7	P. 26, first paragraph – could you cite the 7 studies here?	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.

Reviewer	Comment	Response
7	P. 26, first paragraph, 2nd line, instead of "with" TBI, replace "with" with "experienced" or indicate "with mTBI history." Also make this correction in Key Question 2 paragraph, first line.	This change has been made.
7	P. 26, Visuospatial abilities, first sentence, cite the 5 studies here.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 26, last full paragraph: Just give the abbreviations/acronyms, no need to spell out the neuropsychological test names.	This change has been made.
7	P. 27, first paragraph, 3rd line: instead of saying "significant correlations," indicate directionality, since it seems like visuospatail abilities and MH conditions would be negatively correlated.	This change has been made.
7	P. 27, first "Memory" paragraph, mid-way through, again report direction of association.	This change has been made.
7	P. 27, Key Question 1 paragraph: just report abbreviations	This change has been made.
7	P. 27, Key Question 1 paragraph, 5th from last row, use "longer" instead of "much more."	This change has been made.
7	P. 27, second to last row, use (C&P) for compensation and pension, since this would have been introduced previously.	This change has been made.
7	P. 28, 1st paragraph, second from last row: Use LOC and PTA instead of spelling them out.	This change has been made.
7	P. 28, Attention/Concentration paragraph, cite the 7 studies after mentioning them.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 28, Attention/Concentration paragraph, last line can read "….OR PTSD was not consistently associated with outcomes."	This change has been made.
7	P. 28, Key Question 1 paragraph, do not spell out neuropsychological test names.	This change has been made.
7	P. 28, last paragraph, "forensic" mentioned a couple of times – define what exactly this setting is.	This change has been made.
7	P. 29, first paragraph, indicate direction of associations; do not spell out LOC, PTA	This change has been made.
7	P. 29, Key Question 1 paragraph (here the 9 studies are cited, very helpful!); , do not spell out neuropsychological test names.	This change has been made.

Reviewer	Comment	Response
7	P. 29, 30 Key Question 2 paragraphs for each page, can say C&P instead of spelling it out; on p. 30, no need to define what a C&P evaluation is here, define it when first introduced	This change has been made.
7	P. 30 Effort/Motivation paragraph – regarding "with mTBI," see comment #41	This change has been made.
7	P. 30, Key Question 2 paragraph, see comments #56, 58	This change has been made.
7	P. 31, Key Question 1 paragraph, do not spell out neuropsychological test names.	This change has been made.
7	P. 31, Key Question 1 paragraph: There is discussion about "non-mTBI" participants – are these participants who never experienced a TBI (non-mTBI history) or who do not currently have mTBI (symptoms resolved?)	This has been clarified
7	P. 31, Key Question 2 paragraph: compensation and pension evaluation can be abbreviated	This change has been made.
7	P. 31, Self-reported Cognitive Problems paragraph. I'm wondering if "service connection" should be considered a "risk factor," as it's really a proxy for a disabling injury that was sustained or aggravated during military service. The point is taken that "service connection" is a short-hand for the latter, so this might be a matter of semantics.	Agreed, and this is how it is described in the primary study.
7	P. 31 – last word – instead of saying "control," say "control group."	This change has been made.
7	P. 32 – summary of Physical health results first paragraph – it would be helpful to cite the 16 studies here.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 32 – summary of Physical health results first paragraph – to be consistent, remove dashes from time-since-injury.	This change has been made.
7	P. 32 – second from last paragraph, no need to spell out NSI – already introduced.	This change has been made.
7	P. 33 – Table 3 – first row, similar to comment 63, "referral to neurology clinic for headaches" is listed as a risk factor, but is likely a proxy for headache severity/frequency. Again, this might just be a matter of semantics and readers will understand the implication. Without reviewing the article, not sure if any specifics were given for why a patient might be referred to a neurology clinic, so I understand that this might be the only unit of measurement.	Agreed—and this is how it was described in the primary study.
7	P.33 – Table 3 – some articles from JRRD 49(7) would be relevant here (if you increase the time frame of your search)	We have added these articles.
7	P. 34 – First paragraph – when describing the pain level scale, please provide anchors, 0 (no pain at all?) to 10 (very severe pain?) scale.	This change has been made.

Reviewer	Comment	Response
7	P. 34 – first paragraph for "Headaches," last line about referral to neurology clinic for headaches, see comment #68.	Noted.
7	P. 34 – Key Question 1 paragraph – here, the 9 studies being alluded to are actually cited (good!). Can also just say "NSI" here, no need to spell it out.	This change has been made.
7	P. 34 – Key Question 2 paragraph: Provide more detail in the first sentence – describe all groups being compared	This change has been made.
7	P. 34 – Key Question 2 paragraph, last sentence – see comment #68.	Noted.
7	P. 35 – "Vision" paragraph: cite the one study being discussed	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 36 – "Nausea/Appetite" first paragraph - cite the specific studies you highlight, such as the study describing mild to moderate effects of mTBI population, PTSD studies, mixed results study	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	PP. 36-37 –Summary of Mental Health Results section – cite the studies where you describe 20 studies, two studies, PTSD, alcohol abuse, etc.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 38, Table 4, see comment #68	Noted.
7	For the PTSD sections, 17 studies are alluded to in the first paragraph, and then alluded to again in the Key Question paragraph, and then cited. Just make sure there is consistency between the sections throughout the report in terms of when you cite.	Noted.
7	P. 39 - for Key Question 2, could you add specifics? For example, for study #27, what was the association between the PCL re-experiencing cluster and blast-exposure?	This change has been made.
7	P. 39 – For the anxiety paragraph, cite the studies that are being alluded to.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 39—Key Question 1 – just say "NSI"	This change has been made.
7	P. 40 – Key Question 1 – abbreviations	This change has been made.

Reviewer	Comment	Response
7	P. 40 – Substance Use disorders first paragraph – cite studies alluded to	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 40 –Suicide first paragraph - cite studies alluded to	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 41 – Other Mental Health Outcomes first paragraph – cite studies alluded to	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 41 – Other Mental Health Outcomes first paragraph – aren't "frustration" and "irritability" in the NSI affective cluster (e.g., Meterko et al., 2012, Journal of Head Trauma Rehabilitation, 27(1), 55-62 Psychometric assessment of the Neurobehavioral Symptom Inventory-22: the structure of persistent postconcussive symptoms following deployment-related mild traumatic brain injury among veterans.)	Yes, and we would consider these part of the mental health related outcomes section for this report.
7	P. 41 - Key Question 1 – abbreviations	This change has been made.
7	P. 41 - Key Question 1, second to last sentence – period before 12,20 citations.	This change has been made.
7	P. 41 – Summary of functional/social outcome results: cite studies alluded to	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 41 – Summary of functional/social outcome results – make clear throughout the paragraph whether patients with mTBI, patients without mTBI, or results collapsed across both groups are being discussed.	This change has been made.
7	P. 43 – Sleep introduction paragraph – what are "positive neurological findings?"	This change has been made.
7	P. 43 – Sleep Key Question 1 – abbreviations	This change has been made.
7	P. 46 – In the "Results" paragraph: Throughout the paragraph, the word "obtaining" is used several times. I think a better word here would be "exhibiting."	This section has been removed and edited.
7	P. 46 –Key Question 1: Abbreviations	This section has been removed and edited.
7	P. 46 –Key Question 1: I found the first sentence difficult to follow – please add some additional punctuation and clarifying language.	This section has been removed and edited.
7	P. 46 – Key Question 2: the tense was different in this paragraph than in others. Use "exhibit" instead of "obtain."	This section has been removed and edited.

Reviewer	Comment	Response
7	P. 46— Summary of service utilization/costs results: Please cite studies alluded to.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 48 – Key Question 1: Table X = Table 7?	This change has been made.
7	P. 50 – For mental health outcomes, it's acknowledged that PTSD is a focus for researchers, but I'm wondering if this section could be rounded out by also examining a few other mental health conditions that are typically of interest: depression, non-PTSD anxiety, and substance use disorders? As a starting point, Thomas W. McAllister has published on mild TBI in civilian populations and its after effects (e.g., cognitive, mental health conditions; Silver JM, McAllister TW, Arciniegas DB. Depression and cognitive complaints following mild traumatic brain injury. Am J Psychiatry. 2009; 166: 653-61.)	Agreed, and due to space limitations, we provided an expanded discussion of PTSD at the request of our stakeholders, but have not provided an expanded discussion of other outcomes, instead referring readers to other reviews and studies.
7	P. 50—3rd paragraph of the MH Outcomes section: instead of "causal factors," maybe use the term "event-related?"	This change has been made.
7	P. 50—in the "Not Surprisingly" paragraph, cite the "aforementioned" literature base. Also, in the last sentence of this paragraph, it might be more clear to say, "….related to mTBI versus other factors, such as those that are deployment-related, are not clear."	This change has been made.
7	P. 51—first partial paragraph at top, "When individuals experience the mTBI as traumatic," consider replacing "experience" with "perceive," since, by definition, the experience of mTBI is traumatic, at least physiologically/functionally.	This sentence has been clarified.
7	P. 51-first full paragraph, starting with "The results," I think more detail could be added here, such as citations, especially when you cite specific figures. Consider rewording the last sentence as: However, these high prevalence estimates may differ from results observed in civilian populations, as they may be related to unique deployment-related factors, such as combat, rather than, specifically, to the presence of mTBI.	This change has been made.
7	P. 51 – Imaging/biomarkers paragraph: cite the one study here.	We are providing summary paragraphs without citations for each section, which are followed by the cited results sections by key question. This will be consolidated for the published article version of the report.
7	P. 51 – "Although biomarkers" sentence: Do you mean "as prognostic tools among those with… "severe" TBI or with "moderate to severe" TBI? (not sure if severe was being used as a category, or if this was meant as "not mild."	This change has been made.

Reviewer	Comment	Response
	P. 51 – "Although biomarkers" paragraph: after introducing chronic traumatic encephalopathy, put "(CTE)"	This change has been made.
7	P. 51 last paragraph, 2nd sentence, put "imaging" after "functional"; 5th sentence, use "DTI" instead of spelling it out; instead of "demonstrated" throughout this paragraph, use "observed;" Cite	This change has been made.
7	P. 52 – first paragraph, 2nd sentence; add "patients with" mTBI.	This change has been made.
7	P. 52 – first paragraph, 6th sentence, should be an "in" between "decreases memory"	This change has been made.
7	P. 52, first paragraph, 9th sentence, reword: differences between "individuals with mTBI" and "individuals without mTBI" or "individuals in the control group."	This change has been made.
7	P. 52, first paragraph, 9th sentence – reword, such as "fMRI studies found activation differences between individuals with mTBI and individuals in the control group during cognitive and behavioral tasks consistent with…."	This change has been made.
7	P. 52, first full paragraph, first sentence, reverse last two words so that it reads: mTBI neuroimaging; cite which studies found increased vs. decreased FA; instead of "controls," say "control participants."	This change has been made.
7	P. 54 – first paragraph, first sentence, say "universal" limitation (instead of across the board).	This has been re-worded.
7	P. 54 – first paragraph, what is the evidence that participants aren't blinded to study hypotheses? It's my sense that patients are told that the purpose of the study is to "examine differences," "observe," etc., and aren't informed about specific directional hypotheses until after study completion, if at all.	No studies reported that patients were blinded, and therefore we cannot assume that any were blinded.
7	P. 54 – second paragraph, 3rd-4th sentences; "wide variety of tools used to assess each outcome of interest."	This change has been made.
7	P. 54 –Conclusions, 2nd sentence, I would say, "The literature reviewed here,"	This change has been made.
7	P. 54 – Conclusions, 4th sentence, instead of saying "negative outcomes," consider: "Though a significant portion of individuals who have experienced an mTBI report long-term mental and physical health symptoms" ….."not significantly different from individuals who "did not experience mTBI" or "served as controls."	This section has been re-worded.
7	P. 54- Conclusions, 7th sentence, I would stay away from "outcomes," and say "self-reported symptoms," because we don't know whether symptoms/conditions are caused (i.e. an "outcome") by the mTBI.	This change has been made.
7	P. 54 –Conclusions, 8th sentence from last – instead of "do not have mTBI," I would say "who have not experienced mTBI" or "who do not have mTBI history"	This change has been made.

Reviewer	Comment	Response
7	P. 54 –Conclusions, 7th sentence from last, "instead of saying "is largely influenced by" I would say "can be accounted for" by other factors that are deployment-related, rather than…."	This change has been made.
7	P. 69 – Cameron et al., "five-difit", should be "five-digit"	This change has been made.
7	P. 72 – Hoge et al., "seeking starts" should be "seeing stars"	This change has been made.
7	P. 73- Luis et al., "loose" should be "lose"	This change has been made.
7	P. 87 & 96-Nelson et al. – why aren't the p-values listed?	We have listed results according to what was reported in the primary studies and have put labels used by study authors in quotes to indicate a direct quote in our tables.
8	Excellent that limitation of non-reporting of impaired subgroups is emphasized.	Noted. Thank you.
8	Text is somewhat repetitive and disorganized with regards to reporting of the conclusions reached. For example, conclusions are reported on p.13 within a paragraph on Literature Flow.	We have re-ordered the presentation of findings.
8	Presentation of results needs revision. Tables contain a great deal of text and no legends. Numbers are occasionally presented without units (e.g. p.18 Gordon et al; time since injury: 20.1 (weeks?)). Table 1 should include each study's outcome measures and preferably study hypothesis. It was good to see that effect sizes are reported in the tables in the appendices, but effect sizes are missing for most studies (if not reported, these can be calculated). Also, in cases where significance criteria have been corrected for multiple comparisons (e.g. Table 5), this should be indicated.	We have made these corrections to the table. For space reasons, we have presented some information in appendix tables rather than in text. We report the data as reported in the studies without calculating effect sizes when the authors did not provide this information; however, we are considering providing this calculated information in the article version of the report.
8	Discussion of imaging and biomarkers, p.51: it is mentioned twice that functional imaging studies have "failed" to show differences in performance along with differences in brain function, and this point would benefit from clarification. One explanation, supported by activation patterns, is that mTBI patients are able to accomplish similar test performance to uninjured controls through greater recruitment of neural resources. (e.g. McAllister, 2001, Neuroimage. 2001 Nov;14(5):1004-12.Differential working memory load effects after mild traumatic brain injury.)	We have moved all discussion of imaging results to the discussion due to searching limitations and refer readers to more comprehensive reviews of this literature.
8	p. 26 – Section title "Verbal and Old Learning" inappropriate as the tests described in this section measure vocabulary and knowledge, not learning (implies active learning and memory).	We have changed this title.
8	p. 26; paragraph 5: "…without mTBI on the RBANS Visuospatial/Constructional subscale." This sentence does not match information presented in table 1b for reference 33	We have made sure these results are correct and consistent with the table.

Reviewer	Comment	Response
8	Within Appendix E, some information in the "comparison group description column" does not appear to describe a comparison group, but rather a covariate (e.g. PCL score).	Yes, this indicates continuous variables rather than comparison groups, and as such, correlation results are presented for these studies.
8	Readability comments:	Noted as below.
8	p.1 paragraph 1: "…and its associated post-concussion symptoms is…" should be "are"	Refers to mTBI, not the symptoms, therefore left as "is."
8	p. 1 paragraph 1: "…a TBI while deployed)." The parenthesis does not have a partner.	This change has been made.
8	p.1 paragraph 2 and p.8 paragraph 2: "…balance problems) beyond this time fame;" should be "frame"	This change has been made.
8	p. 1 paragraph 2: "…often require the attention from a range of health care professionals…" should remove "the"	This change has been made.
8	p.3 paragraph 4: "lengthly" should be "lengthy"	This change has been made.
8	p. 3 paragraph 5: "…Veteran/military participants without mTBI)." The parenthesis does not have a partner.	This change has been made.
8	p. 9 paragraph 6: "disruption of brain function (e.g. altered of consciousness…)" should be "alteration"	This change has been made.
8	p. 28 paragraph 4: "six studies reporting…" Should be "reported"	This change has been made.
8	p. 41 paragraph 3: "Axis 1" should be "Axis I"	This change has been made.
8	p. 54 paragraph 3: "…we excluded many studies which proported to study mTBI" should be "purported"	This change has been made.
9	The work of Drs Cockerham and Goodrich might be beneficial in the section on Vision as it addresses occult visual deficits in this patient population. This can often be conflated with self-reported complaints, as previously established mechanisms of assessment were deemed not sensitive in detecting these abnormalities. Additionally, as this data is prospectively collected at all Polytrauma sites, could this data be incorporated in the analyses.	We have reviewed this literature and though it provides important information related to vision outcomes, we did not find studies meeting our inclusion criteria for this report due to the populations examined.
9	Would also recommend additional references regarding TBI incidence—pg #8 Introduction. The point could be substantiated by and WHO data or CDC Data.	We have re-worked the introduction for the report.

Reviewer	Comment	Response
10	In a significant number of veterans and service members who have incurred a blast or non-blast related mTBI have lead to persistent or chronic post-concussion syndrome (PCS). Multiple studies have reported PCS-like symptoms among Veterans many years after mTBI. Agree that published studies to date has been unable to identify all the potential risk factors and a major causative role other than mTBI. ICD-10 and DSM-4 criteria have been established for diagnosing PCS and differ somewhat. There continues to be a lack of consensus regarding PCS, ICD-10 guidelines limit the symptoms to within 4 weeks of injury, while DSM-4 criteria requires symptom onset shortly after injury, but persistence at least 3 months. Despite these diagnostic guidelines, evidence suggests that symptoms can appear immediately, or weeks to months after the initial injury (Ryan et al.2006) and recent studies have reported PCS-like symptoms among Veterans many years after mTBI. (Scholten et al.2012). While these persistent symptoms are known to complicate return to work/duty and negatively affect quality of life, their trajectories and time courses are not understood and diagnosis remains challenging and relies mostly on self-report of complex symptomatology rather than objective, quantitative or biological measures. The reasons why people recover slowly or fail to recover fully from mTBIs is not known and there are no current methodologies for diagnosis or prognosis of PCS. Identifying the cognitive, clinical, and serum biomarkers that accurately diagnose veterans or service members with persistent symptoms is critical to our understanding of long-term outcomes in this patient population and needs to explored further.	We have expanded the discussion section to include some of these ideas.
11	This was a challenging area with limited available published studies. I would suggest plainly stating in the early overview section that there are no prospective randomized RCTs.	We have stated this in the executive summary and the body of the report.
11	The overview also seems somewhat contradictory when you report that imaging findings are of low strength of evidence yet your recommendations indicate that prospective studies should be designed to report imaging findings.	We have rearranged and clarified the imaging findings and recommendations.
Optional Dissemination and Implementation Questions		
5. Are there any VA clinical performance measures, programs, quality improvement measures, patient care services, or conferences that will be directly affected by this report? If so, please provide detail.		
5	There really is no new information here. Conclusions are consistent with other reviews. However, making this available to national Polytrauma calls or conferences, and Mental Health/PTSD calls and conferences would help reinforce these findings.	Noted. We plan to make the report findings available in a variety of formats, including VA intranet, a published article, presentation at a national neuropsychology conference, and through a VA cyber-seminar. We will consider how to expand the audience as you recommend.

Reviewer	Comment	Response
6	Yes. The results raise the question of the context in which mTBI may be best treated within VA. The results also have implications for compensation and pension decisions regarding mTBI.	Noted, though we caution our readers not to make strong inferences based on the low quality literature available for synthesis in this report. Relying on these report findings in conjunction with related research on civilian populations with mTBI will provide the strongest available foundation for such weighty decisions.
7	Because "time since injury" was cited throughout the document as being related to impairment, but also noted to be missing in many studies, I think it would be very important to capture this variable in national VA databases, such as the Comprehensive TBI Evaluation database. If this information is available in any DoD databases, like Defense Manpower Data Center (DMDC), then a data exchange between DoD and VA would benefit studies by having these data located in one central source, thus reducing the risk of error through patient self-report.	We have added this to the discussion.
8	Given the limited nature and low quality of literature, it is not possible to reach firm conclusions. There is nothing to be implemented at this time.	Noted, and we encourage readers of this report to consider the results in conjunction with findings from civilian literature in order to make conclusions based on the best available evidence.
9	Vision Screening in the Inpatient/Polytrauma Units might be affected.	Noted.
10	Yes. Polytrauma/ TBI System of Care.	Noted.
11	Polytrauma System of Care, can be disseminated on one of the national calls and emailing providers with link to report	Noted.
6. Please provide any recommendations on how this report can be revised to more directly address or assist implementation needs.		
1	You might consider adding review of any studies that looked at multiple mTBI's. It is a common "complication" Also, on page 1, I'd suggest clearly delineating the difference between cognitive performance and symptom complaints. While it's true that the literature suggests complete cognitive performance recovery by 3 months (or even 7 days in sports literature), there is a difference between performance and symptoms. Furthermore, the civilian literature suggests that PCS symptoms in fact do not *persist* (See Meares et al) and such the use of the term 'persist' may be incorrect. "Presence" may be more accurate.	We have made these changes throughout the report.
5	There is no "So What" section. However, one could potentially make the suggestion that since outcomes do not differ following mTBI, that all the DoD/VHA time, energy, and attention devoted to this matter may be a less than ideal use of resources. For example: Do we really need to continue to screen for mTBI? Are the required Comprehensive TBI Evaluations following a positive TBI screen, really needed and a good use of resources?	Noted, and we have expanded our discussion of these points in the report.

Reviewer	Comment	Response
5	Are there better ways to meet the needs of those symptomatic returning service members and veterans than focusing on mTBI, when mTBI does not appear to be the factor explaining the symptoms and problems?	Noted, and we have expanded our discussion of this point in the report.
6	No recommendations. This is a thorough report with well-reasoned conclusions.	Noted. Thank you.
7	This report indicates that many of the mTBI studies performed with service members and Veterans are methodologically limited and provide low strength evidence. Because implementation should be based on strong evidence, it doesn't appear that this report should make any health services related recommendations on implementation, but should recommend that VA leaders prioritize research funding to ensure high quality research, and develop mechanisms (e.g., databases, standard communications between DoD and VA) that assist researchers in obtaining reliable data.	We agree that ideally, recommendations should be made based on strong evidence. However, in the absence of strong evidence, then the best available evidence should be the basis on which treatment and policy decisions are made. We have made cautious recommendations consistent with the best available evidence for treatment and policy as well as making strong recommendations for further high quality research as you suggest.
8	Readability and typographical errors should be addressed. Presentation of results should be revised. Consider other data presentation modes in addition to tables. Imaging and biomarkers could possibly be removed and examined in a separate report with selection criteria that are more appropriate for these kinds of studies.	Noted, and we have incorporated your suggested edits.
10	The current focus in the TBI clinics is the CHRONIC effects of mTBI 3-10 years post injury with retained sequale of the initial injury which does not completely follow the recovery pattern of the civilian mTBI population. In the civilian population the symptoms are transient and self-limiting, with apparent full recovery occurring from minutes to several weeks following injury (Levin et al., 1997) which is distinct from our veteran/service member population who have persistent symptoms and/or functional limitations (Iverson et al., 2006; Ruff et al., 1996). There needs to be further investigation into the etiology and treatment of these chronic/persistent PCS symptoms.	We agree and have expanded our discussion of treatment implications.
7. Please provide us with contact details of any additional individuals/stakeholders who should be made aware of this report.		
5	DCoE, DVBIC, VBA?	Noted.
6	No specific recommendations other than VA polytrauma staff.	Noted.
7	HSR&D/QUERI/RR&D leaders responsible for prioritizing funding, inclusive of and addition to: David X. Cifu, MD Nina A. Sayer, PhD Joel Scholten, MD Doug Bidelspach, MPT VA TBI/Polytrauma Clinic Directors	Noted.

Reviewer	Comment	Response
8	Katherine Helmick, Deputy Director, Defense and Veterans Brain Injury Center katherine.helmick@tma.osd.mil	Noted.
10	The following stakeholders should made aware of this report: VHA Polytrauma System of Care which include Polytrauma Rehabilitation Centers (PRC),Polytrauma Transitional Rehabilitation Programs (PTRP), Polytrauma Network Site (PNS), Polytrauma Support Clinic Team (PSCT), and Polytrauma Point of Contact (PPOC). In addition the Military Heath System's TBI clinics, Defense and Veterans Brain Injury Center (DVBIC) and National Intrepid Center of Excellence (NICoE) satellite TBI clinics.	Noted.