APPENDIX A. SEARCH STRATEGIES

Table 1. Ovid (MEDLINE) Search Strategy

	Search Terms
1	exp Veterans/
2	veteran$.mp.
3	exp Veterans Health/
4	(active duty or military or service member$ or soldier$ or national guard or reserv$).mp.
5	1 or 2 or 3 or 4
6	exp Iraq War, 2003-2011/
7	exp Afghan Campaign 2001-/
8	(Operation Enduring Freedom or Operation Iraqi Freedom or Operation New Dawn).mp.
9	6 or 7 or 8
10	5 or 9
11	(TBI or mTBI or traumatic brain injur$).mp.
12	exp Brain Injuries, Traumatic/
13	((mild adj2 traumatic) or (m adj2 TBI) or (mild adj2 TBI)).mp.
14	11 or 12 or 13
15	10 and 14
16	exp Stress Disorders, Post-Traumatic/
17	(((post-traumatic or posttraumatic) adj2 stress) or PTSD).mp.
18	exp Depressive Disorder/ or exp Depressive Disorder, Treatment-Resistant/ or exp Depressive Disorder, Major/
19	depression.mp.
20	exp Substance-Related Disorders/
21	suicide.mp. or exp Suicide/ or exp Suicide, Attempted/
22	exp Suicidal Ideation/
23	exp Anxiety Disorders/

24	((problem adj2 (alcohol or drink$ or drug$ or substance)) or (substance adj2 abuse) or (substance adj2 disorder) or ((alcohol or drug or tobacco) adj2 (abuse or addiction or disorder))).mp
25	(general adj2 anxiety).mp.
26	16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25
27	15 and 26
28	limit 27 to (English language and humans and yr="2000 -Current")

Table 2. PsycINFO Search Strategy

1	exp Military Personnel/ or exp MILITARY VETERANS/ or Veteran$.mp.
2	(soldier$ or "service member$" or "national guard" or "active duty" or reserves).mp.
3	exp Military Deployment/
4	exp Combat Experience/
5	(Operation Enduring Freedom or Operation Iraqi Freedom or Operation New Dawn).mp.
6	exp Traumatic Brain Injury/
7	("traumatic brain injur$" or TBI or mTBI).mp.
8	1 or 2 or 3 or 4 or 5
9	6 or 7
10	8 and 9
11	posttraumatic stress disorder.mp. or exp Posttraumatic Stress Disorder/
12	exp Major Depression/ or depressive disorder.mp.
13	depression.mp.
14	exp Treatment Resistant Depression/
15	exp "Substance Use Disorder"/ or exp Drug Abuse/
16	problem drinking.mp. or exp Alcohol Abuse/
17	("substance abuse" or "substance disorder" or "tobacco abuse").mp.
18	suicidal ideation.mp. or exp Suicidal Ideation/
19	exp ATTEMPTED SUICIDE/ or exp SUICIDE/ or Suicide.mp.
20	exp Anxiety Disorders/ or exp Generalized Anxiety Disorder/ or anxiety.mp.

21	11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22	10 and 21
23	limit 22 to (human and English language and yr="2000 -Current")

APPENDIX B. PEER REVIEW COMMENTS/AUTHOR RESPONSES

Question Text	Reviewer Comment	Author Responses
1) Are the objectives, scope, and methods for this review clearly described?	Yes	Thank you.
	Yes	
	Yes	
	Yes	
	Yes	
	No: Concerned about: Key question 1: suicide attempt and death not being included; key question 2: efficacy not explored	Please see responses under Question 4) below.
2) Is there any indication of bias in our synthesis of the evidence?	No	Thank you.
	No	
	No	
	No	
	No	
	No	
3) Are there any published or unpublished studies that we may have overlooked?	No	
	Yes - The report lists only 1 study that examined HBOT for combat-associated TBI and PTSD. The study cited is uncontrolled and not worthy of inclusion while there are results from the 3 military HBOT trials that examine an effect in PTSD. These are RCT's and worthy of discussion.	The military HBOT trials included service members with a history of TBI and persistent postconcussion symptoms, not PTSD. Our KQ2 was focused on whether treatments for 5 specific psychiatric conditions are effective in individuals who have both the condition and a history of TBI or does the presence of a TBI history limit or moderate treatment effectiveness. Therefore, the military HBOT studies would not have been eligible because participants did not have one of the 5 pre-defined psychiatric conditions of interest for our review. We clarified in the Introduction that the focus of our review is on the specific psychiatric conditions.
	No	
	Yes - The authors say there have been no RCTs of treatment for mental health conditions in TBI. However, there are three that reported PTSD Checklist outcomes following HBOT: Miller, Cifu,	Please see the comment above regarding eligibility of these trials. We reviewed the Portland ESP Evidence Brief on HBOT and cite the report in the

Question Text	Reviewer Comment	Author Responses
	and Wolf. Overall, I think the section on treatment could benefit from discussion with the Portland ESP center that did the recent review on HBOT. That review also cites a 4th RCT that was published only as a conference proceeding.	Discussion section. We also modified the statements about no RCTs of treatment to specify the psychiatric conditions of interest for our review.
	No	
	No	
4) Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.	Adequate to outstanding	Thank you.
	1) The introduction cites that there is an increase in TBI in wars as a result of improvements in IEDs - is this actually true or simply a continuation of the myth of OEF/OIF? There were significant percentages of TBI in WWII and Vietnam that were unreported, but likely higher than OEF/OIF given the numbers of troop involved, the amount of large ammunition utilized and the high rate of mines/IEDs (in Vietnam). Since >50% of all the TBI's in OEF/OIF were related to motor vehicle trauma, this would seem to be important to emphasize, not include as an afterthought. 2) I don't believe the use of the term "psychiatric" disorders and diagnoses is the preferred adjective and would prefer either mental health or psychologic diagnoses/disorders, 3) While it may be a premise of this review, I'm believe that the overwhelming majority of TBI clinicians actually feel that the standard treatments for mental health conditions are safe and effective even in the face of a TBI (given their practice patterns). Again, I am concerned with this report spreading the same misleading myths that the DoD (and certain researchers) have perpetuated. Clinicians that I work with feel comfortable with these treatments, and this review was an attempt to support that practice.	1) We appreciate the reviewer's comments. We modified the introduction in both the Executive Summary and full report. 2) In accordance with the Diagnostic and Statistical Manual of Mental Disorders we choose to use the term psychiatric disorders. 3) The purpose of our review was to identify and report on the evidence. We do not make recommendations for treatment. At present, there is limited evidence on which clinicians can base treatment decisions.
	Please remove all text and table occurrences, as well as the reference for the Harch Hyperbaric oxygen study.	We have added text to emphasize that this is a small, uncontrolled, pre-post study. However, it does meet our eligibility criteria and therefore it would be selective reporting were we to remove it.
	The review is well done in many ways, so these comments are meant to help strengthen a good report. 1. In the reviews of prevalence, to what extent is there a problem with the same VA admin data being used in different studies. The data included in two studies focused differently enough to be	Thank you. 1. There is clearly overlap. "Study Periods" are reported in column one of Table 2 and in the description of the Sampling Method in Appendix C,

Question Text	Reviewer Comment	Author Responses
	independent papers could still be non-independent, but appear as two different studies. This would be a much greater problem in meta-analysis in which the Ns were being used for weighting, but it is also a potential problem here in the sense that there may appear to be more supportive evidence than is actually the case if the same people are contributing to findings across studies. 2. As mentioned specifically in response to the question about excluded studies, I believe there are 3 or 4 excluded RCTs of HBOT. The failure to include the RCTs seems to have resulted in a misstatement about the evidence for HBOT, e.g., p. 10. I cannot see how the inclusion/exclusion criteria would have led to these studies being excluded. If the criteria in fact are responsible, this is a more significant problem. 3. Should RCTs that examined TBI status as an effect modifier be summarized differently than studies that simply compare TBI/no TBI in a pre-post design? 4. P. 12, although 10 points on the CAPS-IV has been validated in multiple studies (e.g., Schnurr & Lunney, 2016), 8 points on the PCL is not an agreed-upon MCID for the PCL. Monson et al (2008), for example, found 10 points to be a good number, and Shiner et al. (2011) found 5 points to be a good number. 5. Is the method of PTSD assessment (clinical admin diagnosis, structured clinical interview, self-report) important in its relation to outcome? 6. On p. 12, the suggestion to create further study fails to account for ongoing longitudinal studies that could be used to answer important questions TBI and its comorbidities. These studies include the Neurocognition Deployment Health Study (Vasterling), VALOR (Marx & Keane), Mil Cohort Study, and the Marine Resiliency Study. 7. P. 15, re the possible reasons for the comorbidity of PTSD and TBI, one additional one is that the same event that could cause a TBI could cause PTSD. I think this is the view that is more predominant in the field.	Table 1. The population-based studies provide information on the population of VA users within the identified time period (*ie*, the VA as a population rather than a sample). We comment on the overlap in the Executive Summary and full report. 2. Please see note above regarding the exclusion of these studies. We also clarified the Study Selection sections in the Executive Summary and full report. 3. The text and tables for Key Question 2 have been rearranged to emphasize the studies with TBI as an effect modifier. 4. Thank you for this information. We modified the statement about the PCL to include a range of values and added the suggested citations to the full report. 5. Yes. We now describe the method of assessment for all of the mental health outcomes with greater detail on the Appendix tables. 6. Thank you for the suggestion. We added this information In the Discussion/Future Research sections of the Executive Summary and full report. 7. We modified the Introduction to remove information about reasons for the comorbidity of PTSD and TBI given that this is not the focus of our review.

Question Text	Reviewer Comment	Author Responses
	Overall, I found this to be an excellent review of the current literature relating mTBI to mental health conditions, including, PTSD, depression, substance abuse, anxiety disorders and suicidal ideation (attempt). I found the criteria for inclusion of the studies to be sound and feel that the literature assembled accurately represents the literature.	Thank you.
	As a general comment, I question the use of the phrase “combat-deployed mTBI”. There is no other kind of combat TBI if not incurred during deployment. If this phrase is to refer to either combat-related mTBI OR deployment-related mTBI, I would simply use the latter phrase (deployment-related, as it is almost never specified if the injury was incurred in a combat situation).	We replaced “combat-deployed” with deployment-related. Our study inclusion criteria required that at least 75% of the TBIs were experienced while deployed (not necessarily in a combat role).
	Also, where specific clinical assessment scores are reported, especially for PTSD (CAPS or PCL), it would be helpful to note whether the assessment was for the DSM IV or 5 diagnostic criteria. The scores are not comparable (e.g., scores on CAPS IV ≠ CAPS 5), so it is important to note from which they are derived so the score you report can be put into the proper context.	We verified that all references to the CAPS or PCL include the version (if reported).
	The following are both editorial and content suggestions throughout the manuscript:	
	1. Page 1: The paragraph beginning “The focus of our review”. I would suggest that the fact that the review is focused on mTBI be moved up to the first paragraph and the methodology for presuming mTBI in studies where the severity of the TBI is unspecified be explained only in the methods section. The rationale for this decision as described in this paragraph is unclear.	1) We revised the Introduction in the Executive Summary and the full report. We agree with including the details of study selection in the Methods section.
	2. Page 2, first paragraph. I assumed that the outcomes were for current diagnoses, meaning that the Veterans and SM included in the studies had active psychological conditions.	2) Yes,
	3. Page 2 Study Selection. I tried to follow the inclusion and exclusion criteria reported here with the flow diagram on page 20 (this is also the case for the main study description). The n’s reported for the various exclusions noted in the figure do not match up with the actual exclusionary criteria. There are more exclusionary criteria on Page 20 than are noted on Page 2. Also,	3) Thank you for pointing this out. We revised the descriptions of the Inclusion and Exclusion criteria in the Executive Summary and main report. They now are aligned with Figure 1.

Question Text	Reviewer Comment	Author Responses
	on Page 3, it would be helpful if paragraph beginning on Line 30 describing the exclusions referred to the figure on page 20.	
	4. The Executive Summary Tables (page 6 & 9) should use the same legends (page 9 more informative).	4) We made the suggested change.
	5. Page 7 Executive Summary Table 2. Under the comments section, 2nd bullet, “Type of TBI”. Should this be severity of TBI? Type can be confused with etiology.	5) Thank you – we meant severity.
	6. Page 8 Line 12. I do not think that “one reporting similar severity in the groups with a history of mTBI and no TBI” is reported in Table 3.	6) This was an error on Table 3 – now corrected.
	7. Page 11 Line 50 insert either “combat” or “deployment-related” between that and mTBI.	7) We added ”deployment-related”.
	8. Page 12 Line 10. “changed” should be “changes”.	8) This has been corrected
	9. The important issue of reintegration is first mentioned on Page 11 in the discussion. It feels like it comes out of the blue there because it has not been motivated prior to this. I would suggest moving the issue of reintegration to Page 12 in the Research Gaps/Future Research section. It is critically important that no studies to date have looked at this issue and the need for treatment studies to include this as an outcome measure should be stressed.	9) Thank you for the suggestion. We deleted the mention of reintegration in the Discussion section and added to the Research Gaps/Future Research section that outcomes should include both functioning and quality of life measures in addition to symptom measures. Reintegration reflects both functioning and quality of life (and more), but in a very specific population during a set period of time. Also, only one study looked at mental health quality of life, so we need more information in this area.
	10. Page 16, Line 45. It doesn’t make sense to have Timing be “Any time post-TBI” because the studies include non-TBI. I am not sure where that time point should be anchored (post-deployment?).	10) We agree and changed “Timing” to post-deployment
	11. Page 17, Line 35. “abstract” should be “abstracts” and “were” should be inserted between that and eligible (on next line).	11) We corrected this sentence.
	12. Page 18, again the exclusion criteria do not follow information on Page 20.	12) As noted above, we revised the text to align with Figure 1
	13. Thought the tables reporting the Prevalence and Severity data were great.	13) Thank you
	14. Page 36. Sentence on Line 54 is incomplete. “The rate of binge drinking….”	14) We corrected this sentence.
	15. Page 39 there is reference again to assessment of health status at “varying times post injury”. Relating #10 above.	15) We changed this to post-deployment.
	16. Page 40. I believe there should be a reference to Figure 2 in the paragraph describing findings for CPT.	16) Thank you – we modified the KQ2 text and this figure is no longer included.

Question Text	Reviewer Comment	Author Responses
	17. Page 51-52. Here I feel that you take a step back in the innovation department by simply referring back to current VA/DoD guidelines for the management of PTSD and the other comorbidities, given the limited evidence on the effectiveness of treatments for mental health conditions. These guidelines don't take advantage of what has been learned through this review. Given that this is the discussion section, I would much rather see some thoughtful, albeit speculative, recommendations regarding the treatment of the common comorbidities. I also don't believe that TBI should be listed here as a mental health condition because it is the base condition forming the comorbidities as far as this report is concerned.	17) Thank you for the suggestion. We removed the section on the VA/DoD guidelines. We comment that the studies showed no indication of harms for evidence-based treatments for treatment of PTSD in service members and Veterans with and without a history of TBI.
	1) Summaries in executive summary do not sufficiently couch findings in the context of risk of bias findings. At times findings seem to stray from key questions - particularly pertaining to Key Question 2 2) Was there a reason why suicide attempts or death were not included in key questions? (this seems like a major weakness) - nonetheless some data is reported on SA (pg. 5) - this is confusing 3) Some concern re: inclusion of up to 25% moderate to severe - as results could certainly be skewed - same with those in which % were not reported 4) Further articulation of the purpose of the studies included - Key Question #1 (particularly if it was not to measure prevalence) would be useful 5) In terms of Key Question 1 - would be helpful to report throughout if symptoms reported were above clinical cutoffs - see page 5 final bullet (line 46) - this is great 6) In terms of Key Question 2 - would be helpful to report throughout if symptoms were "clinically significant" a. Why was simple efficacy not explored?	1) We modified summary paragraphs in the Executive Summary and moved the strength of evidence tables closer to the summary text. 2) Suicidal ideation was identified by the operational partners as the psychiatric condition of interest for the review. One study reported suicide attempts so we did extract and include that outcome. A review of studies excluded from our review did not find additional reports of "attempts." 3) Studies typically enroll a mixed population and in evidence reviews we often use 75% as the threshold. Had we required strict reporting of 100% mTBI, we would have few, if any, eligible studies. 4) We noted this in the Overview of Studies for Key Question 1. 5) In Appendix C, Tables 1 and 2 we provide information on clinical cut-offs from the KQ1 studies although we note that there is disagreement on clinical cut-offs. 6) In Appendix C, Table 5 we provide information on clinical cut-offs for the KQ2 studies. a. We considered the included studies to be "effectiveness" studies – evaluating the interventions in "real world" settings. We did not

Question Text	Reviewer Comment	Author Responses
	b. Would suggest that the lack of RCTs needs to be further emphasized 7) Believe that the word effectiveness is used when efficacy would likely be more correct (see page 10) a. same page - term TBI status is confusing 8) Unclear why the team included outcome associated with negative psychiatric outcomes (page 11) - Pugh 2018 9) With low to no evidence - unclear how team can suggest that therapies are effective and safe - page 11 (this seem like a major weakness) 10) Tables are useful; however, would suggest adding citations in those where they are not provided 11) Research gaps - what other models besides cohort might be appropriate?	exclude any studies of interventions based on whether they were efficacy or effectiveness studies. b) We note the need for RCTs in the Discussion and Future Research sections. 7) We believe that effectiveness is correct – the studies are testing efficacy in “real world’ settings a) We modified and rearranged these statements. We replaced TBI status with “history of TBI” 8) We removed the text referred to in this comment. 9) We modified the Discussion and Applicability section but note that we did find clinically significant differences in outcomes and no reported harms. 10) Thank you. Citations are added in the final report version. 11) We noted that existing registries may contain relevant information.

APPENDIX C. EVIDENCE TABLES

Table 1. Prevalence and/or Severity of Psychiatric Conditions – National Samples (KQ1)

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Adams, 2017[10] National, data from the Substance Use and Psychological Injury Combat Study National Institute of Drug Abuse (NIDA) Sampling method: Subsample of Army active duty members who completed both initial and follow	Sample size: 267,100 (TBI: 19,240, No TBI: 247,860) Mean age: NR, 46% age 17-24 y, 24% age 25-29 y, 23% age 30-39 y, 6% age 40+ y Male (%): 90 Race/ethnicity (%): White, non-Hispanic 53; Black, non-Hispanic 18; Asian/Pacific Islander 15; American Indian/Alaskan Native 1, Hispanic 11 Time since TBI: NR Time since discharge: NA Method of TBI diagnosis: self-report	**PTSD**	NR	NR	NR	NR
		Depressive Disorders	NR	NR	NR	NR
		Substance Use Disorders, frequent binge drinking	PDHRA (6+ drinks per occasion) 28% (5312/19,240) *TBI only (by gender*) 26% M/8% F *TBI+mental health problems* 34% M/16% F	PDHRA (6+ drinks per occasion) 19% (47,478/247,860) *Mental health problems only (by gender)* 29% M/12% F *No TBI or mental health problems* 20% M/7% F	NR	NR
		Suicidal Ideation	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
up questionnaires (DoD post-deployment heath surveillance program FY2008-2011)	Multiple TBI: NR TBI etiology: NR Eligibility: OEF/OIF service members who completed questionnaires within 30–300 days of the end date of deployment (>90% within 3–9 months)	**Anxiety Disorders**	NR	NR	NR	NR
Cifu, 2013[11] National VA HSR&D Sampling method: VA FY2009-2011 National Patient Care Database	Sample size: 613,391 (TBI: 58,885 "majority likely mild", No TBI: 554,506) Mean age: 32 Male (%): 88 Race (%): White 58, non-White 20, unknown 22 Ethnicity (%): Hispanic 10, non-Hispanic 71, unknown 19 Time since TBI: NR	**PTSD**	ICD-9 76% (44,777/58,885)	ICD-9 24% (135,559/554,506)	NR	NR
		Depressive Disorders	NR	NR	NR	NR
		Substance Use Disorders	NR	NR	NR	NR
		Suicidal Ideation	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
	Time since discharge: NR Method of TBI diagnosis: unclear, captured TBI diagnoses at any point in medical care received at a VA facility Multiple TBI: NR TBI etiology: NR Eligibility: OIF/OED/OND Veterans, diagnosed with TBI, PTSD, and/or common head, neck, or back pain (by ICD-9-CM codes) and receiving inpatient or outpatient VHA care	**Anxiety Disorders**	NR	NR	NR	NR
Fonda, 2017[12] National Study performed without financial support Sampling method: National VA electronic	Sample size: 273,591 (TBI: 42,392 mild 88%, No TBI: 231,199) Mean age: 29 Male (%): 84 Race/ethnicity (%): White 65, Black 14, Unknown/missing 16 Time since TBI: NR Time since discharge: NR	**PTSD**	ICD-9 63% (26,781/42,392)	ICD-9 10% (22,365/231,199)	NR	NR
		Depressive Disorders	ICD-9 Mood Disorder 31% (13,068/42,392)	ICD-9 Mood Disorder 12% (27,362/231,199)	NR	NR
		Substance Use Disorders	ICD-9 *Alcohol* 13% (5,631/42,392) *Other* 7% (2,739/42,392)	ICD-9 *Alcohol* 4% (8,894/231,199) *Other* 2% (4,462/231,199)	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
medical records databases April 2007-September 2012	Method of TBI diagnosis: VA CTBIE Multiple TBI: NR TBI etiology: blast 74%, other injuries 47%, motor vehicle accidents 40%, falls 39% Eligibility: US Veterans deployed in support of OEF/OIF/OND after 9/11/2001; received VA health care 4/2007 to 9/2012, aged 18–40 years at time of first VA care *Excluded* diagnoses of bipolar disorder; schizophrenia or related psychiatric disorder (except psychosis due to trauma-related hallucinations); inconclusive TBI data	**Suicidal Ideation**	ICD-9 Attempted Suicide[d] 0.5% (227/42,392)	ICD-9 Attempted Suicide[d] 0.1% (318/231,199)	NR	NR
		Anxiety Disorders	ICD-9 17% (7,326/42,392)	ICD-9 8% (17,728/231,199)	NR	NR
Grossbard, 2017[13] National VA PTBRI QUERI, VA Center of	Sample size: 358,147 (TBI: 30,197 % mild NR, No TBI: 327,950) Mean age: NR, 35% <30 years, 33% 30-39 years, 32% ≥40 years Male (%): 87	**PTSD**	ICD-9 73% overall (22,107/30,197) 74% M/64% F	ICD-9 33% overall (106,752/327,950) 34% M/26% F	NR	NR
		Depressive Disorders	ICD-9 43% overall (13,047/30,197) 43% M/52% F	ICD-9 26% overall (85,382/327,950) 25% M/33% F	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Excellence in Substance Abuse Treatment and Education, VA Clinical Sciences R&D Career Development Award, and National Institute on Alcohol Abuse and Alcoholism Sampling method: VA Corporate Data Warehouse, 2012	Race (%): Black 16, White 68, missing 11 Ethnicity (%): Hispanic 11, non-Hispanic 82, missing 7 Time since TBI: NR Time since discharge: NR Method of TBI diagnosis: unclear (ICD-9 code in medical record); TBIs diagnosed outside VA and not documented in medical record were not captured Multiple TBI: NR TBI etiology: NR Eligibility: Veterans age ≥18; received alcohol screening (AUDIT-C) in 2012, documented OEF/OIF service (VA Decision Support System), used outpatient or inpatient VA services (≥1 visit) in year before AUDIT-C	**Substance Use Disorders**	ICD-9 *Alcohol (AUDIT-C ≥5)* 19% overall (5,879/30,197) 20% M/11% F *Drug* 12% overall (3,570/30,197) 12% M/6% F *Tobacco* 25% overall (7,660/30,197) 26% M/16% F	ICD-9 *Alcohol (AUDIT-C ≥5)* 11% overall (34,473/327,950) 11% M/5% F *Drug* 5% overall (17,389/327,950) 6% M/3% F *Tobacco* 19% overall (60,899/327,950) 19% M/13% F	Moderate alcohol misuse (AUDIT-C 5-7) 11% overall (3,387/30,197) 12% M/5% F Severe alcohol misuse (AUDIT-C 8-12) 8% overall (2,516/30,197) 9% M/2% F	Moderate alcohol misuse (AUDIT-C 5-7) 9% overall (30,684/327,950) 10% M/4% F Severe alcohol misuse (AUDIT-C 8-12) 6% overall (18,291/327,950) 6% M/2% F
		Suicidal Ideation	NR	NR	NR	NR
		Anxiety Disorders	ICD-9 26% overall (7,994/30,197) 26% M/32% F	ICD-9 16% overall (53,549/327,950) 16% M/19% F	NR	NR
Jaramillo, 2015[14] National	Sample size: 303,716 (TBI: 42,520, No TBI: 261,196)	**PTSD**	ICD-9 77% (32,800/42,520)	ICD-9 33% (85,951/26,1196)	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
VA HSR&D Sampling method: 1) Identified individuals deployed in Afghanistan or Iraq using the OEF/OIF roster file 2) Selected Veterans who received care at VA in FY2010 and FY2011 3) Linked inpatient and outpatient data	Mean age: 35 Male (%): NR Race/ethnicity (%): NR Time since TBI (days): NR Time since discharge: NR Method of TBI diagnosis: ICD-9 codes Multiple TBI: NR TBI etiology (%): NR Eligibility: received inpatient or outpatient care at least once each year	**Depressive Disorders**	ICD-9 50% (21,259/42,520)	ICD-9 28% (73,195/26,1196)	NR	NR
		Substance Use Disorders	NR	NR	NR	NR
		Suicidal Ideation	NR	NR	NR	NR
		Anxiety Disorders	NR	NR	NR	NR
Johnson, 2015[15] National Funding NR	Sample size: 162,898 (TBI: 11,122 mild 83%, No TBI: 151,776) Mean age: NR, 47% age 17-24 y, 21% age 25-29 y, 22% age 30-39 y, 9% age 40+ y	**PTSD**	NR	NR	NR	NR
		Depressive Disorders	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Sampling method: 1) Retrospective cohort; active service members with electronic health records in Defense Medical Surveillance System (2008-2010); includes military and civilian inpatient and outpatient encounters; additional data from Theater Medical Data Store 2) Exposed = all incident TBI; unexposed = 10% random sample of any other medical encounter diagnosis	Male (%): 85 Race/ethnicity (%): White 63, Black 16, Hispanic 11, American Indian/Alaskan Native 0.4, Asian/Pacific Islander 4 Time since TBI: NR Time since discharge: NA Method of TBI diagnosis: ICD-9 codes meeting DoD case definition, diagnosed while deployed or within 30 days of return Multiple TBI: NR TBI etiology: NR Eligibility: service members with ≥365 days of continuous active service from start of study, no prior TBI, AUD, or ODUD diagnoses	**Substance Use Disorders**	ICD-9-CM AUD 4% (452/11,122) ODUD 2% (176/11,122) AUD and ODUD 0.7% (82/11,122)	ICD-9-CM AUD 2% (2,726/151,776) ODUD 0.6% (858/151,776) AUD and ODUD 0.3% (435/151,776)	NR	NR
		Suicidal Ideation	NR	NR	NR	NR
		Anxiety Disorders	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Kontos 2013[16] National US Special Operations Command Biomedical Initiatives Steering Committee Sampling methods: web-based baseline evaluation of all available US Army Special Operations Command (USASOC) personnel (11/2009-12/2011); 82% eligible after exclusions	Sample size: 22,203 (mTBI: 2,813, No mTBI 19,390) Mean age: 30 Male (%): 96 Race/ethnicity (%): NR Time since TBI: NR Time since discharge: NA Method of TBI diagnosis: mTBI defined as head injury with a Glasgow Coma Scale score of 13-15 and no associated pathology on neuroimaging Multiple TBI: NR TBI etiology: 60% blunt trauma, 31% blast-related, 9% blast-blunt combination Eligibility: no history of moderate to severe TBI, brain surgery, major psychiatric disorder, or neurological disorder; neurocognitive assessment deemed invalid	**PTSD**	NR	NR	PCL (range 17-85)* Blunt: 20.3 (7.1) Blast: 22.6 (8.8) Blast-blunt: 24.3 (10.7) *Version not reported	PCL (range 17-85) 18.4 (5.3)
		Depressive Disorders	NR	NR	NR	NR
		Substance Use Disorders	NR	NR	NR	NR
		Suicidal Ideation	NR	NR	NR	NR
		Anxiety Disorders	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Macera 2012[17] National US Navy Bureau of Medicine and Surgery Sampling method: Navy and Marine Corps who completed the PDHA and PDHRA (2008-2009)	Sample size: 9,902 (TBI: 473, TBI&PTSD 644, No TBI and No PTSD: 8,785) Mean age: 27 Male (%): 100 Race/ethnicity (%): NR Time since TBI: NR Time since discharge: NA Method of TBI diagnosis: self-report of injury in blast or explosion with alteration/loss of consciousness or posttraumatic amnesia Multiple TBI: NR TBI etiology: blast-related Eligibility: Navy sailors and Marines deployed to Iraq, Afghanistan, or Kuwait in 2008-2009; completed PDHA within 30 days of deployment and PDHRA 30 to 365 days later; responded "yes" to at least 1 of 3 combat experience items; excluded women and non-blast TBI	**PTSD**	NR	NR	NR	NR
		Depressive Disorders	PHQ-2 items *TBI Only* 11% (52/473) *TBI & PTSD* 48% (309/644)	PHQ-2 items *No TBI & No PTSD* 11% (978/8785)	NR	NR
		Substance Use Disorders	NR	NR	NR	NR
		Suicidal Ideation	NR	NR	NR	NR
		Anxiety Disorders	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Pogoda, 2016[18] National Sampling method: 1) Retrospective analysis of data from OEF/OIF Veterans who completed VA CTBIE (10/2007 to 6/2009) 2) Demographic, deployment and health data obtained from VA Patient Care	Sample size: 9,337 (mTBI: 6,352, No mTBI: 2,985)* Mean age: NR, 22% age 18-24 y, 34% age 25-29 y, 25% age 30-39, 20% age 40+ y Male (%): 94 Race/ethnicity (%): NR Time since TBI (days): NR Time since discharge: NR Method of TBI diagnosis: Clinician rating based on CTBIE Multiple TBI: NR	**PTSD**	CTBIE checklist 74% (4,711/6,352)	CTBIE checklist 54% (1,602/2,985)	NR	NR
		Depressive Disorders	CTBIE checklist 40% (2,562/6,352)	CTBIE checklist 35% (1,053/2,985)	NR	NR
		Substance Use Disorders	CTBIE checklist *Alcohol* 8% (483/6,352) *Drugs* 2% (133/6,352)	CTBIE checklist *Alcohol* 7% (209/2,985) *Drugs* 2% (51/2,985)	NR	NR
		Suicidal Ideation	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
Services and DoD Manpower Data Management Center **NOTE: Prevalence data obtained from author**	TBI etiology (%): Non-blast only 20; Blast only 39; Non-blast + blast 41 Eligibility: completed CTBIE; sufficient data to determine TBI status and severity; TBI status agreement between CTBIE and VA/DoD criteria; no pre-or-post deployment TBI(s); known employment status *Demographics for full study population, including 1,481 individuals with moderate/severe TBI	**Anxiety Disorders**	CTBIE checklist 24% (1,544/6,352)	CTBIE checklist 26% (760/2,985)	NR	NR
Seal 2016[19] National VA HSR&D Sampling method: VA CTBIE database (enrolled in VA	Sample size: 66,089 (mTBI: 38,556, No mTBI: 27,533) Median age: 28 Male (%): 94 Race/ethnicity (%): White 54, Non-White 46 Time since TBI: NR	**PTSD**	ICD-9[e] 74% (28,532/38,556)	ICD-9 64% (17,706/27,533)	NR	NR
		Depressive Disorders	ICD-9[f] 47% (17,943/38,556)	ICD-9 45% (12,348/27,533)	NR	NR
		Substance Use Disorders	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
healthcare, at least one first-level TBI screen since 4/14/2007); other sources include VA OIF/OEF/OND Roster, VA National Patient Care Database, VA Decision Support System	Time since discharge: NR Method of TBI diagnosis: CTBIE Multiple TBI: NR TBI etiology: NR Eligibility: OIF/OEF Veterans; completed Level 1 TBI screen (positive) and CTBIE with determinate diagnosis	**Suicidal Ideation**	NR	NR	NR	NR
		Anxiety Disorders	NR	NR	NR	NR
Taylor 2015[20] National VA HSR&D Sampling method: All Iraq and Afghanistan War Veterans who used VHA inpatient or outpatient care in FY2014 and had records in the Planning Services and Support Group	Sample size: 684,133 (TBI: 47,845, No TBI: 636,288) Mean age: 36 Male (%): 87 Race/ethnicity (%): White 67, Black 17, Native American/ Alaska Native 1, Asian 2, Native Hawaiian/Pacific Islander 1, Multiracial 2 Ethnicity (%): Non-Hispanic 83, Hispanic 11 Time since TBI: NR	**PTSD**	ICD-9 73% (34,927/47,845)	ICD-9 28% (178,161/636,288)	NR	NR
		Depressive Disorders	ICD-9 48% (22,966/47,845)	ICD-9 24% (152,709/636,288)	NR	NR
		Substance Use Disorders	ICD-9 38% (18,181/47,845) Nicotine dependence 25% (11,961/47,845)	ICD-9 21% (133,620/636,288) Nicotine dependence 14% (89,080/636,288)	NR	NR
		Suicidal Ideation	NR	NR	NR	NR

Study, year (ref) Location Funding Sampling Method	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)		Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)	
			mTBI	No mTBI	mTBI	No mTBI
FY2014 enrollment files; other data sources included patient geocode files, VETSNET, Corporate Data Warehouse	Time since discharge: NR Method of TBI diagnosis: ICD-9 codes Multiple TBI: NR TBI etiology: NR Eligibility: Iraq and Afghanistan War Veterans; used VHA care with records in Planning Services and Support Group FY2014 enrollment files	**Anxiety Disorders**	ICD-9 31% (14,832/47,845)	ICD-9 16% (101,806/636,288)	NR	NR

AUDIT-C=Alcohol Use Disorders Identification Test-Consumption Questions; BAI=Beck Anxiety Inventory; BDI-II=Beck Depression Inventory-II; CAGE=Cutting down, Annoyance by criticism, Guilty feeling, and Eye openers; CAPS=Clinician Administered PTSD Scale for DSM-IV; CESD=Center for Epidemiologic Studies Depression; CTBIE-Comprehensive TBI Evaluation (VA); FY=fiscal year; GAD-7=Generalized Anxiety Disorders Questionnaire; HAM-A=Hamilton Rating Scale for Anxiety; HSR&D=Health Services Research and Development; ICD-9=*International Classification of Diseases, Ninth Revision*; IQR= interquartile range; NA=not applicable; NR=not reported; OEF=Operation Enduring Freedom; OIF=Operation Iraqi Freedom; OND=Operation New Dawn; PCL-C=PTSD Checklist-Civilian Version; PCL-M= PTSD Checklist-Military Version; PDHA=Post-Deployment Health Assessment; PDHRA=Post-Deployment Health Reassessment; PHQ=Patient Health Questionnaire; PNS=Polytrauma Network Sites; PTBRI=Polytrauma and Blast-Related Injury; PTSD=Post Traumatic Stress Disorder; QUERI=Quality Enhancement Research Initiative; R&D=Research and Development; STDI=Structured TBI Diagnostic Interview; TBI=traumatic brain injury; mTBI=mild traumatic brain injury; VA=Veterans Affairs

[a]Calculated (not reported in manuscript)
[b]At 1 year post-deployment
[c]Lenient criteria (CAPS-IV): score of "yes" for at least 1 re-experiencing symptom, at least 3 avoidance and numbing symptoms, and at least 2 hyperarousal symptoms
[d]Resulting in emergency department visit or hospitalization
[e]With or without comorbid depression
[f]With or without comorbid PTSD

Table 2. Prevalence and/or Severity of Psychiatric Conditions – Geographically Diverse Samples (KQ1)

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
Baldassarre, 2015[21] 3 VA Polytrauma Network Sites: Kentucky Arizona Illinois VA HSR&D Sampling method: 1) OEF/OIF registries at 3 PNSs (Veterans could opt-out) (Aug 2010-Sept 2011) 2) OEF/OIF Veterans presenting for care at any clinic at the PNSs	Sample size: 398 (mTBI: 210, No mTBI: 188) Mean age: 32 Male (%): 89 Race/ethnicity (%): Caucasian/white 75 Time since TBI: 4.8 years Time since discharge: NR Method of TBI diagnosis: STDI Multiple TBI: NR TBI etiology: NR Eligibility: Veterans, age ≥18 years, deployed in OEF or OIF conflicts, no treatment for concussion in 30 days preceding study enrollment	**PTSD**	CAPS-IV (lenient)[c] 56% (117/210)	CAPS-IV (lenient)[c] 28% (52/188)	<.0001	NR	NR	
		Depressive Disorders	BDI-II (≥17) 49% (103/210)	BDI-II (≥17) 21% (40/188)	<.0001	NR	NR	
		Substance Use Disorders	AUDIT (≥4 [M] or ≥3 [F]) 50% (105/210) probable alcohol use disorder	AUDIT (≥4 [M] or ≥3 [F]) 44% (83/188) probable alcohol use disorder	.0013	NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	BAI (≥8) 63% (132/210)	BAI (≥8) 35% (65/188)	<.0001	NR	NR	
Brenner, 2010[22] Fort Carson, Colorado, USA Sampling Method: 1) Retrospective analysis; US	Sample size: 1247 (mTBI: 878, No mTBI: 369) Age group (%): 51% age 18-24 y, 24% age 25-29 y, 21% age 30-39 y, 4% age 40-53 y	**PTSD**	PDHA survey-4 (+ on ≥ 2 questions) 37% (323/878)	PDHA survey-4 (+ on ≥ 2 questions) 22% (82/369)	<.0001[d]	NR	NR	
		Depressive Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
Army Brigade Combat Team returning from 1 year deployment in Iraq (date NR) 2) Soldiers participated PDHA, completed WARCAT and were interviewed by clinicians 3) Military and demographic characteristics from Army Medical Surveillance Activity	Male (%): 99 Race/ethnicity (%): NR Time since TBI (days): NR Time since discharge: NA Method of TBI diagnosis: WARCAT and clinician interviews Multiple TBI: NR TBI etiology (%): NR Eligibility: Self-reported injury during deployment (full-duty status at time of assessment); complete demographic and PTSD data	**Substance Use Disorders**	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
Bryan, 2013, Bryan, 2013[23,24] Iraq (US Army base) No funding Sampling Method: 1) Referred to outpatient TBI clinical at combat	Sample size: 158 (mTBI: 135, No mTBI: 23) Mean age: 28 Male (%): 93 Race/ethnicity (%): White 72, Black 15, Hispanic 10, Asian/ Pacific 3 Time since TBI (days): 2 (median)	**PTSD**	NR	NR		PCL-M (cut point ≥ 50) 32.7 (14.5)	PCL-M (cut point ≥ 50) 20.5 (5.1)	<.001
		Depressive Disorders	NR	NR		BHM-20 Depression (clinical range: >1.38) 1.0 (0.9)	BHM-20 Depression (clinical range: >1.38) 0.2 (0.3)	<.001
		Substance Use Disorders	NR	NR		NR	NR	NR

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
support hospital in 2009 2) Standardized intake evaluation including clinical interview	Time since discharge: NA Method of TBI diagnosis: Clinical interview using DOD and Department of VA criteria Multiple TBI: NR TBI etiology (%): NR Eligibility: Referred to TBI clinic; excluded if moderate or severe TBI	**Suicidal Ideation**	SBQ-R (≥7) *Ideation* 13% (18/135) *Ideation with plan* 1.4% (2/135)	SBQ-R (≥7) *Any suicidal behavior* 0% (0/23)	<.05[d]	SBQ-R (cut point ≥7) 3.5 (1.6)	SBQ-R (cut point ≥7) 0.0 (0.0)	<.001
		Anxiety Disorders	NR	NR		NR	NR	
Bryant, 2015[25] Iraq military combat theater hospital NR Sampling method: Military personnel serving in Iraq; received routine assessment for blast exposure at military combat theater hospital (2006-2007)	Sample size: 685 (mTBI: 567, No mTBI: 118) Mean age: 26 Male (%): NR Race/ethnicity (%): NR Time since TBI: 7.4 (21.3) days Time since discharge: NA Method of TBI diagnosis: Documented occurrence of injury to the head, loss of consciousness < 30 min, posttraumatic amnesia < 24 hr, normal CT findings with no focal	**PTSD**	PCL-M met criteria (unspecified) for PTSD without minimum 1-month duration 25% (142/567)	PCL-M met criteria (unspecified) for PTSD without minimum 1-month duration 11% (13/118)	0.001	NR	NR	
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
	neurological deficit or intracranial complications Multiple TBI: 13% reported prior blast-related TBI TBI etiology: 100% blast Eligibility: Exposed to explosive blast	**Anxiety Disorders**	NR	NR		NR	NR	
Carlson, 2010[26] Upper Midwest VA HSR&D, PT/BRI-QUERI Sampling method: 1) OEF/OIF Veterans screened for TBI in Upper Midwest VA integrated Service Network (VISN 23); Screened April 2007-Oct 2008	Sample size: 11,828 (TBI: 836, No TBI: 10,992) Mean age: 33 Male (%): 90 Race/ethnicity (%): Caucasian: 82 Time since TBI: NR Time since discharge (median): 430 days Method of TBI diagnosis: positive screen (VA TBI Screening Instrument) and assigned TBI-related ICD-9 codes in rehabilitation, neurology, mental health, or primary care clinics Multiple TBI: NR TBI etiology (%): Blast/explosion 90 Vehicular crashes 43 Falls 44	**PTSD**	ICD-9 codes 64% (534/836)	ICD-9 codes 18% (2,001/10,992)	<.05	NR	NR	
		Depressive Disorders	ICD-9 codes 46% (387/836)	ICD-9 codes 22% (2,367/10,992)	<.05	NR	NR	
		Substance Use Disorders	ICD-9 codes 26% (219/836)	ICD-9 codes 10% (1,056/10,992)	<.05	NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	ICD-9 codes 36% (298/836)	ICD-9 codes 13% (1,430/10,992)	<.05	NR	NR	NR

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
	Eligibility: Veterans screened for TBI in VISN 23							
Gaines, 2016[27] VA health centers, California VA of Greater Los Angeles Health Care System Sampling method: 1) Participants recruited through fliers and word of mouth at VA locations in California 2) Potential participants screened over the phone or in person to determine eligibility	Sample size: 114 (mTBI: 57, No mTBI: 57) Mean age: 30 Male (%): 100 Race/ethnicity (%): Caucasian 25, African American 9, Hispanic 43, Asian 12, Other 11 Time since TBI (days): NR Time since discharge: NR Method of TBI diagnosis: Criteria from American College of Rehabilitation and the American Congress of Rehabilitation Medicine Multiple TBI: NR TBI etiology (%): NR Eligibility: Served in Iraq or Afghanistan 2007-2012, history of learning disabilities or attention deficit hyperactivity disorder, no diagnoses of substance abuse or	**PTSD**	NR	NR		NR	NR	
		Depressive Disorders	NR	NR		BDI-II 22.4 (12.2)	BDI-II 12.9 (11.0)	.002
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
	dependence, and no major neurological or medical conditions							
Heltemes, 2011[28] OEF/OIF combat zone medical treatment facilities US Navy Bureau of Medicine & Surgery Sampling method: 1) All eligible injuries in US Expeditionary Medical Encounter Database (2004-2007) 2) Matched to alcohol abuse diagnoses from Standard Inpatient and Ambulatory Data Records	Sample size: 3,123 (mTBI: 1,413, No mTBI: 1,710) Median age: 23 Male (%): 100 Race/ethnicity (%): NR Time since TBI: Followed for 2 years from date of injury; Time since discharge: NA Method of TBI diagnosis: ICD-9 codes meeting CDC criteria Multiple TBI: excluded TBI etiology: 100% blast Eligibility: Male service members treated for combat-related blast injuries in combat zone medical facilities, single injury events, no alcohol abuse disorders prior to injury	**PTSD**	NR	NR		NR	NR	
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	ICD-9-CM Alcohol abuse diagnosis 6% (86/1,413)	ICD-9-CM Alcohol abuse diagnosis 5% (84/1,710)	.15	NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
Hoge, 2008[29] Maryland Washington, D.C. Military Operation Medicine Research Area Directorate Sampling Method: 1) US Army combat infantry brigades (active and reserve) after 1-year deployment were provided time to attend study recruitment briefing 2) Anonymous surveys conducted 3-4 months after deployment	Sample size: 2,525 (mTBI with LOC: 124, mTBI with altered state: 260, other injury: 435, no injury: 1,706) Age (% <30 years): 55 Male (%): 95 Race/ethnicity (%): NR Time since TBI: NR Time since discharge: NA Method of TBI diagnosis: Positive response to losing consciousness, being dazed and confused, or not remembering injury Multiple TBI: NR TBI etiology (%): Blast/explosion 75, Bullet 2, Fragment/ Shrapnel 21, Fall 29, Vehicle accident 22 Eligibility: recent return from deployment, attended recruitment briefing and completed questionnaire	**PTSD**	PCL (DSM-IV criteria and total score ≥50) *LOC* 44% (54/123) *Altered State* 27% (71/260)	PCL (DSM-IV criteria and total score ≥50) *Other Injury* 16% (70/433) *No Injury* 9% (155/1,701)	*LOC vs Other Injury* <.001 *Altered State vs Other Injury* <.001	PCL *LOC* 47 (19) *Altered State* 40 (16)	PCL *Other Injury* 35 (15) *No Injury* 29 (13)	*LOC vs Other Injury* <.001 *Altered State vs Other Injury* <.001
		Depressive Disorders	PHQ-9 (DSM-IV criteria and "very difficult" functioning) *LOC* 23% (27/118) *Altered State* 8% (21/250)	PHQ-9 (DSM-IV criteria and "very difficult" functioning) *Other Injury* 7% (28/423) *No Injury* 3% (55/1,673)	*LOC vs Other Injury* <.001 *Altered State vs Other Injury* .39 NS	NR	NR	
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
King, 2017[30] Five VA medical centers and one community-based outpatient clinic in Upstate New York VA HSR&D Sampling method: secondary analysis of data from longitudinal study of OEF/OIF Veterans recruited from clinical referrals for polytrauma or neuropsychology and VISN 2 registry; oversampling of women and minority backgrounds	Sample size: 291 (TBI: 153, no TBI: 138) Mean age: 31 Male (%): 92 Race/ethnicity (%): Caucasian 83, African American 7, Hispanic 5, Asian American 1, Native American 1 Time since TBI: NR Time since discharge: NR Method of TBI diagnosis: 22-item clinical interview Multiple TBI: NR TBI etiology: NR Eligibility: OEF/OIF Veterans intending to stay in Upstate New York for 18-month parent study who had sleep data available (58% of parent study participants)	**PTSD**	PCL-M Probable PTSD (≥50) 57% (87/153)	PCL-M Probable PTSD (≥50) 34% (47/138)	<0.001	PCL-M score 53 (15)	PCL-M score 42 (15)	<0.001
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	NR	NR		AUDIT-C score (≥3 (women) or ≥4 (men): hazardous drinking) 4.0 (3.2)	AUDIT-C score (≥3 (women) or ≥4 (men): hazardous drinking) 5.0 (3.1)	0.008
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
MacDonald, 2014[33] Landstuhl Regional Medical Center (LRMC), Germany	Sample size: 65 (mTBI: 47, No mTBI: 18) Median age: mTBI: 25, No mTBI: 32 Male (%): 100	**PTSD**	CAPS-IV 61% (29/47)	CAPS-IV 28% (5/18)	.01	CAPS-IV (from graph) ~60	CAPS-IV (from graph) ~40	.002
		Depressive Disorders	MADRS (>19) 51% (24/47)	MADRS (>19) 44% (8/18)	.63 (NS)	MADRS (from graph) 19 (11)	MADRS (from graph) 14 (10)	.05

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
Congressionally Directed Medical Research Program, NIH Sampling method: Screened for TBI at LRMC (2008-2009)	Race/ethnicity (%): White 75, Hispanic/Latino 11, African American 11, Asian 3 Time since TBI: median 14 days (1-90) Time since discharge: NA Method of TBI diagnosis: Self-report of blast exposures with alterations of neurologic function Multiple TBI: NR TBI etiology (%): Blast plus other impact Eligibility: Screen for TBI at LRMC, injury from blast with or without additional mechanisms of injury within 90 days of enrollment, US military, no contraindications to MRI, no history of moderate to severe TBI, no history of major psychiatric disorder, agreement to complete study follow up	**Substance Use Disorders**	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
MacDonald, 2014[32] Landstuhl Regional Medical Center (LMRC), Germany Congressionally Directed Medical Research Program Sampling method: Screened for TBI at LRMC (2010-2013)	Sample size: 178 (mTBI plus impact: 53, non-blast mTBI: 29, No mTBI plus blast: 27, No TBI plus non-blast: 69) Median age: mTBI plus impact: 6 non-blast mTBI: 28, No mTBI plus blast: 34, No TBI plus non-blast: 31 Male (%): 93 Race/ethnicity (%): White 73, African American 17, Hispanic/Latino 8 Asian 2 Time since TBI (days): Blast plus impact TBI 12 (10), Non-blast TBI 14 (10) Time since discharge: NA Method of TBI diagnosis: Self-report of blast exposures with alterations of neurologic function Multiple TBI: NR TBI etiology (%): Blast plus impact 65 Non-blast 35 Eligibility: same as MacDonald 2014[33]	**PTSD**	CAPS-IV *Blast* 42% (22/53) *Non-blast* 48% (14/29)	CAPS-IV *Blast* 22% (6/27) *Non-blast* 6% (4/69)	*Blast* .09 NS *Non-blast* <.001	CAPS-IV (from graph) *Blast* ~48 *Non-blast* ~48	CAPS-IV (from graph) *Blast* ~31 *Non-blast* ~16	*Blast* .06 NS *Non-blast* <.001
		Depressive Disorders	NR	NR		MADRS (from graph) *Blast* ~15 *Non-blast* ~16	MADRS (from graph) *Blast* ~11 *Non-blast* ~9	*Blast* .24 NS *Non-blast* <.001
		Substance Use Disorders	NR	NR		MAST (from graph) *Blast* ~3 *Non-blast* ~2	MAST (from graph) *Blast* ~3 *Non-blast* ~2	NS
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
MacDonald, 2017[31] Kandahar Air Field or Camp Leatherneck, Afghanistan Congressionally Directed Medical Research Program, Defense Advanced Research Projects Agency, NIH Sampling method: 1) Screened for TBI at Kandahar Air Field or Camp Leatherneck (March 2012-Sept 2012) 2) Remained in-theater	Sample size: (blast mTBI: 38, No TBI/non-blast: 34) Median age: blast mTBI: 26, No TBI/non-blast: 28 Male (%): 87 Race/ethnicity (%): White 71, Hispanic/ Latino 19, African American 10, Asian 0 Time since TBI (days): All 0-7 days Time since discharge: NA Method of TBI diagnosis: Clinical diagnosis - criteria from American Congress of Rehabilitation Multiple TBI: NR TBI etiology (%): Blast +impact 100% Eligibility: Clinical diagnosis of TBI, US military, no contraindications to MRI, no history of moderate to severe TBI, no pre-deployment history of major psychiatric disorder, agreement to complete study follow up	**PTSD**	NR	NR		CAPS-IV (from graph) *Blast+impact* ~40	CAPS-IV (from graph) *Non-blast* ~23	<.0001
		Depressive Disorders	NR	NR		MADRS (from graph) *Blast+impact* ~15	MADRS (from graph) *Non-blast* ~8	<.0001
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
MacGregor, 2013[34] National US Navy Bureau of Medicine Sampling method: Queried Expeditionary Medical Encounter Database for personnel injured during OIF (March 2004-April 2008) who completed the PDHA and PDHRA	Sample size: 992 (mTBI: 334, No TBI/non-head injury: 658) Mean age: mTBI 23, no TBI 25, P<.001 Male (%): TBI 99.7, no TBI 93, P<.001 Race/ethnicity (%): NR Time since TBI: 255 days (for PDHRA) Time since discharge: NA Method of TBI diagnosis: TBI ICD-9-CM codes corresponding with AIS values of 1 or 2 Multiple TBI: NR TBI etiology (%): Battle, blast 89, Battle, non-blast 2, Non-battle 9 Eligibility: Minor to moderate injuries sustained during OIF March 2004 to April 2008, completed a PDHA and PDHRA within one year of injury	**PTSD**	PDHRA (PC-PTSD) (+ on ≥3 of 4 items) 28% (93/334)	PDHRA (PC-PTSD) (+ on ≥3 of 4 items) 17% (113/658)	<.001	NR	NR	
		Depressive Disorders	PDHRA (based on PHQ) (+ on ≥1 of 2 items) 21% (69/334)	PDHRA (based on PHQ) (+ on ≥1 of 2 items) 13% (87/658)	.002	NR	NR	
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
MacGregor, 2010[35] National	Sample size: 762 (mTBI: 105, No TBI/other head injury:	**PTSD**	ICD-9 codes 12% (13/105)	ICD-9 codes *Head Injury* 15% (40/273)	*mTBI vs Head Injury:* .62[d]	NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
US Navy Bureau of Medicine and Surgery Sampling method: 1) Identified in Expeditionary Medical Encounter Database 3) Registered in Career History Archival Medical and Personnel System (CHAMPS)	273, No TBI/non-head injury: 384) Mean age: 24 Male (%): 100 Race/ethnicity (%): NR Time since TBI: NR Time since discharge: NA Method of TBI diagnosis: TBI ICD-9-CM codes corresponding with AIS values of 1 or 2 Multiple TBI: NR TBI etiology (%): IED 72, Grenade 1, Blast 23, Gunshot wound 2, Fragment/shrapnel <1 Eligibility: Male OIF combatants, presented to forward deployment medical treatment facilities for battle injury Sept 2004-Feb 2005, registered in the EMED and CHAMPS databases, military discharge >90 days into follow-up period			*Non-head Injury* 19% (72/384)	*vs Non-head injury:* .15[d]			
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	ICD-9 codes 9 % (9/105)	ICD-9 codes *Head Injury* 4% (11/273) *Non-head Injury* 8% (31/384)	*mTBI vs Head Injury:* .12[d] *vs Non-head injury:* .84[d]	NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	ICD-9 codes 11% (11/105)	ICD-9 codes *Head Injury* 12% (32/273) *Non-head Injury* 15% (57/384)	*mTBI vs Head Injury:* .86[d] *vs Non-head injury:* .34[d]	NR	NR	
Mora, 2009[36]	Sample size: 110 (mTBI: 19, No mTBI: 91)	**PTSD**	PCL-M (≥44) 37% (7/19)	PCL-M (≥44) 21% (19/91)	.15	NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
US Army Institute of Surgical Research (USAISR) Burn Center, Texas Funding NR Sampling Method: 1) Retrospective review of clinical records of combat casualties injured in explosions and treated at USAISR (March 2003-March 2006) 2) Joint Theater Trauma Registry	Mean age: 26 Male (%): 93 Race/ethnicity (%): NR Time since TBI (days): 196 Time since discharge: NA Method of TBI diagnosis: Loss of consciousness based on ICD codes and AIS scores Multiple TBI: NR TBI etiology (%): Blast/explosion 100 Eligibility: OIF/OEF service members with explosion injury, PCL-M assessment 30 days post-injury	**Depressive Disorders**	NR	NR		NR	NR	
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
Pietrzak, 2009[37] Connecticut State of Connecticut, National Center for PTSD, Private donation Sampling Method: 1) Participants identified alphabetically by	Sample size: 277 (mTBI: 52, No TBI: 225) Mean age: 33 Male (%): 90 Race/ethnicity (%): White 80, Hispanic 6, Black 7, Other 7 Time since TBI: NR Time since last deployment (months): 23	**PTSD**	PCL-M (≥50) 65% (34/52)	PCL-M (≥50) 24% (55/225)	<.001	NR	NR	
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
to obtain 1000 names and addresses 2) Surveys mailed by CT Veterans Affairs to main confidentiality NOTE: 28.5% response rate	Method of TBI diagnosis: VA TBI screening instrument Multiple TBI: NR TBI etiology (%): NR Eligibility: Received and completed Wave 2 of Connecticut OEF/OIF Veterans Needs Assessment Survey, served Jan 2003-Mar 2007	**Anxiety Disorders**	NR	NR		NR	NR	
Polusny 2011[38] US National Guard Brigade Combat Team Veterans Health Administration Office of Research and Development Sampling Method: Recruited at redeployment transition briefings 1 month prior to return home from end of 16-month combat deployment (June	Sample size: 937 (mTBI: 86, No mTBI: 851) Mean age: 33 Male (%): 92 Race/ethnicity (%): white 87 Time since TBI: NR Time since discharge: NR Method of TBI diagnosis: self-report of closeness to blast, injuries, feeling dazed/confused Multiple TBI: NR TBI etiology (>1 answer allowed): Fragment 17%, Bullet 1%, Vehicular 21%,	**PTSD**	PCL-M (≥50) 30% (26/86)[b]	PCL-M (≥50) 12% (103/851)[b]	.0001	PCL-M *mTBI only* 34.3 (9.4)[b] *mTBI+PTSD* 63.1 (7.3)[b]	PCL-M *No mTBI/no PTSD* 29.3 (9.2)[b] *PTSD only* 62.5 (8.1)	<.0001[d] .73[d]
		Depressive Disorders (at 1 year)	NR	NR		BDI-II *mTBI only* 11.4 (8.5)[b] *mTBI+PTSD* 25.5 (8.7)[b]	BDI-II *No mTBI/no PTSD* 8.8 (7.2)[b] *PTSD only* 25.0 (8.9)	.008[d] .80[d]
		Substance Use Disorders (at 1 year)	NR	NR		AUDIT *mTBI only* 9.8 (7.1)[b] *mTBI+PTSD* 15.2 (9.3)[b]	AUDIT *No mTBI/no PTSD* 7.2 (5.4)[b] *PTSD only* 12.5 (9.6)	.0005[d] .20[d]

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
2007); invited to follow-up at 1 year after deployment NOTE: 50% response rate at 1 year	Fall 17%, Blast 73%, Other 17% Eligibility: member of US National Guard Brigade Combat Team completing 16-month combat deployment to Iraq; completed in-theater and post-deployment assessments	**Suicidal Ideation**	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
Tsai 2012[39] Hawaii VA HSR&D Sampling Method: Stratified sample from VA Hawaii Program Registry Nov-Dec 2010 NOTE: 52% response rate	Sample size: 233 (TBI: 79, No TBI: 158) Mean age: 37 Male (%): 87 Race/ethnicity (%): Asian/Pacific Islander 55%, Other 45% Time since TBI: NR Time since discharge: NR Method of TBI diagnosis: VA 4-item screen (history of combat-related concussion and persistent post-concussive symptoms) Multiple TBI: NR TBI etiology: NR Eligibility: Veterans Affairs Hawaii Program Registry,	**PTSD**	PCL-C (≥50) 57 (43/75)[a]	PCL-C (≥50) 18 (28/158)	<.001	NR	NR	
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	CAGE (≥2) 38% (27/75)[a]	CAGE (≥2) 17% (26/158)	<.01	NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
	served in Iraq or Afghanistan							
Vanderploeg 2015[40] Florida Veterans Health Administration, Defense and Veterans Brain Injury Center, 2 HSR&D grants Sampling Method: Survey of Florida National Guard 2009-2010; unselected, representative sample of respondents to invitation to participate in survey NOTE: 41% overall response rate **NOTE: Prevalence data obtained from author**	Sample size: 1443 (mTBI: 144, No mTBI: 1,299) Mean age: NR Male (%): 87 Race/ethnicity (%): Minority 34 Time since TBI: NR Time since deployment: 32 months (range 0-95) Method of TBI diagnosis: self-report Multiple TBI: 13% with prior mtBI TBI etiology: NR Eligibility: Florida National Guard members, reported at least 1 deployment, provided usable data and fully completed an anonymous on-line survey	**PTSD**	PCL (≥ 50 +DSM criteria) 25% (36/144)	PCL (≥ 50 +DSM criteria) 5% (64/1,299)	.0001[d]	NR	NR	
		Depressive Disorders	PHQ-9 (DSM-IV criteria and "very" difficult" functioning) 15% (22/144)	PHQ-9 (DSM-IV criteria and "very" difficult" functioning) 2% (25/1,299)	<.0001[d]	NR	NR	
		Substance Use Disorders	AUDIT-C (≥4 for men, ≥3 for women is hazardous 49% (71/144)	AUDIT-C (≥4 for men, ≥3 for women is hazardous 37% (483/1,299)	.005[d]	NR	NR	
		Suicidal Ideation	PHQ-9 (1 item) 20% (29/144)	PHQ-9 (1 item) 4% (51/1,299)	.0001[d]	NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
Walker 2017[41] Virginia and North Carolina (1 VA Medical Center Polytrauma Rehabilitation Center and 3 military bases) US Army Medical Research and Material Command Sampling Method: Recruited via letters, advertisements, and at ambulatory healthcare clinics	Sample size: 216 (mTBI: 40, No mTBI: 176) Mean age: 25 Male (%): 97 Race/ethnicity (%): White 78%, African American 15%, Other 6% Time since TBI: median 9 months (IQR 5-15) since most recent blast; all blast experiences within past 2 years Time since discharge: NR Method of TBI diagnosis: face-to-face interview (n=106) or algorithm based on Blast Experience Screening Questionnaire (n=110) Multiple TBI (blast TBI): 1 mTBI 45%, 2 mTBIs 22%, ≥3 mTBIs 15% TBI etiology: blast TBI prior to current deployment: NR Eligibility: Service Member of Veteran with one or more	**PTSD**	NR	NR		PCL (version not reported) *Baseline* mTBI with PTA: 49 (95%CI 46-52) mTBI w/o PTA: 49 (95%CI 45-52) *6 months* mTBI with PTA: 49 (95%CI 46-53) mTBI w/o PTA: 46 (95%CI 41-51) *12 months* mTBI with PTA: 47 (95%CI 43-50) mTBI w/o PTA: 46 (95%CI 42-51)	PCL (version not reported) *Baseline* 44 (95%CI 40-49) *6 months* 41 (95%CI 35-47) *12 months* 42 (95%CI 36-48)	*Baseline* mTBI with PTA vs no mTBI: .02[e] mtBI w/o PTA vs no mTBI: .04[e] *12 months* mTBI with PTA vs no mTBI: .03[e] mtBI w/o PTA vs no mTBI: .10[e]
		Depressive Disorders	NR	NR		CESD *Baseline:* mTBI with PTA: 19 (95%CI 17-21) mTBI w/o PTA: 18 (95%CI 15-20) *6 months:* mTBI with PTA: 18 (95%CI 16-21)	CESD *Baseline:* 16 (95%CI 13-19) *6 months:* 18 (95%CI 13-22)	*Baseline* mTBI with PTA vs no mTBI: .04[e] mtBI w/o PTA vs no mTBI: .17[e]

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
	blast experiences in past 2 years while deployed in OEF/OIF/OND; excluded severe and moderate TBI					mTBI w/o PTA: 17 (95%CI 13-20) *12 months* mTBI with PTA: 19 (95%CI 16-22) mTBI w/o PTA: 18 (95%CI 14-21)	*12 months* 16 (95%CI 12-20)	*12 months* mTBI with PTA vs no mTBI: .09[e] mtBI w/o PTA vs no mTBI: .40[e]
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
Wilk, 2012[42] Three brigade combat teams from one Active Component infantry division Sampling method: Unit commanders made Army soldiers available for group recruitment briefings (Nov	Sample size: 1502 (mTBI: 260, No mTBI: 1242) Mean age: NR (70% <30 yr) Male (%): 91 Race/ethnicity (%): NR Time since TBI: NR Time since return from deployment: 4-6 months Method of TBI diagnosis: DOD & VA	**PTSD**	PCL-17 (≥ 50) All 37% (96/260) With LOC 52% (45/86) With AOC 29% (51/174)	PCL-17 (≥ 50) All 12% (143/1242) Other injuries 17% (67/396) No injuries 9% (76/846)	<.05	NR	NR	
		Depressive Disorders	PHQ-9 (DSM-IV criteria and "very" or "extremely" difficult" functioning) All	PHQ-9 (DSM-IV criteria and "very" or "extremely" difficult" functioning) All	<.05	NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
2008-Dec 2008); soldiers voluntarily elected to complete the questionnaire packet NOTE: 86% of soldiers attending recruitment briefing consented to participate; approximately half randomly selected for different study	Brain Injury Center Brief TBI Screen Multiple TBI: 59% of those reporting concussion TBI etiology: blast/ explosion, bullet, fragment/shrapnel, fall, vehicle crash, or other means (% NR) Eligibility: Iraq or Afghanistan deployment experience, provided complete responses to injury and concussion-related questions		18% (48/260) With LOC 23% (20/86) With AOC 16% (28/174)	6% (70/1242) Other injuries 9% (36/396) No injuries 4% (34/846)				
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	
		Anxiety Disorders	NR	NR		NR	NR	
Yurgil 2014[43] Southern California VA HSR&D, Marine Corps, Navy Bureau of Medicine and Surgery Sampling method: Prospective longitudinal study; active duty Marine and Navy servicemen; data	Sample size: 1648 (TBI: 327 [87% mTBI] No TBI: 1321) Mean age: 22 Male (%): 100 Race/ethnicity (%): Hispanic 23%, White 85% Time since TBI: all within past 10 months Time since discharge: NA Method of TBI diagnosis: face-to-face interview Multiple TBI: NR TBI etiology: NR	**PTSD**	CAPS-IV (≥65) 6 (21/327)[a] CAPS-IV (40-64) 19 (61/327)[a]	CAPS-IV (≥65) 1 (18/1321) CAPS-IV (40-64) 6 (81/1321)	Both <.001	NR	NR	
		Depressive Disorders	NR	NR		NR	NR	
		Substance Use Disorders	NR	NR		NR	NR	
		Suicidal Ideation	NR	NR		NR	NR	

Study, year (ref) Location Funding	Study Characteristics	Condition	Prevalence of Psychiatric Conditions % (n/N)			Severity or Persistence Based on Symptom Scores (mean (SD) unless noted)		
			mTBI	No mTBI	P value	mTBI	No mTBI	P value
from assessments 1 week before 7-month deployment, 1 week and 3 months after deployment (June 2008-May 2012) NOTE: 671 lost to follow-up and 188 with missing data)	TBI prior to current deployment: 57% (66% of TBI group, 55% of No TBI group) Eligibility: Marine and Navy serviceman from 4 infantry battalions of the First Marine Division; excluded Officers	**Anxiety Disorders**	NR	NR		NR	NR	

AIS=Abbreviated Injury Scale; AOC=alteration of consciousness; AUD=alcohol use disorder; AUDIT-C=Alcohol Use Disorders Identification Test-Consumption Questions; BAI=Beck Anxiety Inventory; BDI-II=Beck Depression Inventory-II; BHM-20=Behavioral Health Measure-20; CAGE=Cutting down, Annoyance by criticism, Guilty feeling, and Eye openers; CAPS=Clinician Administered PTSD Scale; CBTIE=Comprehensive TBI evaluation; CESD=Center for Epidemiologic Studies Depression; CT=computerized tomography; FY=fiscal year; GAD-7=Generalized Anxiety Disorders Questionnaire; HAM-A=Hamilton Rating Scale for Anxiety; HSR&D=Health Services Research and Development; ICD-9-CM= International Classification of Diseases, Ninth Revision, Clinical Modification; IQR=interquartile range; ISS=Injury Severity Score; LOC=loss of consciousness; MADRS=Montgomery-Asberg Depression Rating Scale; MAST=Michigan Alcohol Screening Test; MDD=major depressive disorder; mTBI=mild traumatic brain injury; MVRI=Minnesota Veterans Research Institute; NA=not applicable; NR=not reported; ODOD=other drug use disorder; OEF=Operation Enduring Freedom; OIF=Operation Iraqi Freedom; OND=Operation New Dawn; PCL=PTSD Checklist; PCL-C=PTSD Checklist-Civilian Version; PCL-M= PTSD Checklist-Military Version; PC-PTSD=Primary Care PTSD screen; PDHA=Post-Deployment Health Assessment; PDHRA=Post-Deployment Health Reassessment; PHQ=Patient Health Questionnaire; PNS=Polytrauma Network Sites; PTSD=Posttraumatic Stress Disorder; SBQ-R=Suicide Behaviors Questionnaire-Revised; SCID= Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorder (DSM-IV-TR); STDI=Structured TBI Diagnostic Interview; TBI=traumatic brain injury; USAISR=United States Army Institute of Surgical Research; VA=Veterans Affairs; VISN=Veterans Integrated Service Network

[a]Any TBI
[b]At 1 year post-deployment
[c]Lenient criteria (CAPS): score of "yes" for at least 1 re-experiencing symptom, at least 3 avoidance and numbing symptoms, and at least 2 hyperarousal symptoms
[d]Calculated, not reported in manuscript
[e]Calculated, not reported in manuscript; n completing 12-month assessment not reported; baseline n used in calculations

Table 3. Risk of Bias for Prevalence Studies (KQ1)

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
Adams 2017[10]	Army only; included those who completed 2 post-deployment forms (61%); reported no large differences between those completing both questionnaires vs initial only	Adequate	Self-report (American Congress of Rehabilitation Medicine criteria)	Self-report (PC-PTSD, PDHRA)	N/A	**Moderate**
Baldassarre 2015[21]	Recruited via letter from OEF/OIF registries at 3 VA PNSs or presenting for care at the sites; study of sensitivity and specificity of mTBI screening measures	Limited information about service	STDI	Psychology technician administered (CAPS-IV, BDI-II, BAI, AUDIT-C)	25% of Veterans contacted consented and 71% of consented completed assessments; no information on *a priori* sample size estimation	**Moderate**
Brenner 2010[22]	US Army Brigade Combat Team from 1 military base in US; self-reported injury during recent deployment	Limited demographic information	Clinician confirmed based on interview, service member self-report, data from medical records	Self-report (PDHA)	N/A	**Moderate**
Bryan 2013, Bryan 2013[23,24]	Outpatient TBI clinic at combat support hospital in Iraq	Adequate	Licensed clinical psychologist using DoD and VA criteria	Self-report (SBQ-R, BHM-20, PCL-M)	N/A	**Moderate**
Bryant 2015[25]	Military combat theater hospital in Iraq	Limited demographic information	Documented injury to head, meeting LOC and PTA criteria; normal CT	Unclear if self-report (PCL-M)	N/A	**Moderate/high**

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
Carlson 2010[26]	VA administrative data for VISN23 including databases for demographics, diagnosis codes, clinic type	Limited demographic information	Assigned 1 or more ICD-9 codes for TBI in rehabilitation, neurology, mental health, or primary care clinics	ICD-9 codes	N/A	**Moderate**
Cifu 2013[11]	OEF/OIF/OND Veterans receiving VHA care FY2009-FY2011	Limited to information in Patient Care Database	ICD-9 codes	ICD-9 codes	N/A	**Moderate**
Fonda 2017[12]	OEF/OIF/OND Veterans receiving VHA care 2007-2012; excluded 44% due to inconclusive TBI data	Limited to information in VA electronic medical records databases	Confirmed diagnosis from VA CTBIE	ICD-9 code for suicide or self-inflicted injury recorded in emergency room visit or inpatient hospital admission (VA or facility reimbursed by VA)	N/A	**Moderate**
Gaines 2016[27]	Recruited at VA health care locations in California	Limited information about service	Unclear (prior diagnosis of mTBI or mild concussion)	Unclear if self-report (BDI-II)	N/A	**High**
Grossbard 2017[13]	Documented OEF/OIF service, AUDIT-C in 2012, used VA services in year before AUDIT-C	Limited to information in electronic medical record	ICD-9 code in EMR 365 days before to 30 days after AUDIT-C date	EMR (AUDIT-C administered by physician and ICD-9 codes)	N/A	**Moderate**

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
Heltemes 2011[28]	EMED; Navy, Marine Corps, & Army; treated for combat injury at forward-deployed medical facilities; excluded non-blast injuries	Adequate	ICD-9 codes	ICD-9 codes	N/A	**Moderate**
Hoge 2008[29]	Survey of Army soldiers from 2 combat infantry brigades (1 Active Component, 1 Reserve)	Adequate	Self-report of injury characteristics	Self-report (PHQ-15, PCL [version not reported])	59%; noted that some soldiers were transferred to other units or involved in training/military school	**Moderate**
Jaramillo 2015[14]	OEF/OIF Veterans receiving VHA care at least once per year in FY2010-FY2011	VA files plus OEF/OIF Roster Files for additional demographic data but limited reporting	ICD-9 codes	ICD-9 codes	N/A	**Moderate**
Johnson 2015[15]	Defense Medical Surveillance System data 2008-2010; active duty; all branches; 10% sample of those without TBI	Adequate	ICD-9 codes with DoD extender codes specific to military service	ICD-9 codes	N/A	**Low**
King 2017[62]	5 VA Medical Centers & 1 community-based outpatient clinic in Upstate NY; clinical referrals for polytrauma or neuropsychology and local OEF/OIF registry	Limited information about service	Clinical interview (developed for the study) administered by neuro-psychologists	Self-report (AUDIT-C, PCL-M)	N/A	**Moderate/high**

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
Kontos 2013[16]	Limited to US Army Special Operations Command personnel	Limited reporting	Unclear (self-report of post-concussion symptoms); no information on time since exposure	Self-report (PCL [version not reported])	N/A	**Moderate/high**
MacDonald 2014[33]	US military evaluated at medical center in Germany following evacuation from Iraq or Afghanistan	Adequate	Screened based on US military clinical criteria; medical record review	Clinician administered assessments (CAPS-IV, MADRS)	N/A	**Moderate**
MacDonald 2014[32]	US military evaluated at medical center in Germany following evacuation from Iraq or Afghanistan	Adequate	Self-report of alteration of neurological function	Clinician administered assessments (CAPS-IV, MADRS, MAST)	N/A	**Moderate**
MacDonald 2017[31]	Kandahar Air Field and Camp Leatherneck in Afghanistan	Adequate	US military clinical criteria including self-report of injury or clinical diagnosis based on criteria from American Congress of Rehabilitation 1993	Clinician administered assessments (CAPS-IV, MADRS)	N/A	**Moderate**
Macera 2012[17]	Navy/Marine Corps; PDHA and PDHRA forms completed 2008-2009; reported combat experience; excluded women and non-blast TBI	Adequate	Self-report of ≥1 injury item and ≥1 alteration/loss of consciousness or posttraumatic amnesia item on PDHA or PDHRA)	Self-report (PDHA)	N/A	**Moderate**

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
MacGregor 2013[34]	EMED; OIF, completed PDHA and PDHRA; minor to moderate injury	Adequate	ICD-9 codes with injury severity codes for minor injury	Self-report (PDHRA)	N/A	**Moderate**
MacGregor 2010[35]	EMED; OIF male combatants who presented to forward deployed medical treatment facility for battle injury	Adequate	ICD-9 codes and narrative completed by provider at point of injury	ICD-9 codes	N/A	**Moderate**
Mora 2009[36]	OEF/OIF combat casualties injured in explosions and treated at US Army Burn Center; records from Joint Theater Trauma Registry;	Limited reporting	ICD codes and Abbreviated Injury Scale scores	Self-report (PCL-M)	N/A	**Moderate**
Pietrzak 2009[37]	Survey of subset of Connecticut OEF/OIF Veterans	Adequate	Self-report; VA 4-question screen	Self-report (PCL-M)	28.5%; respondents were older than non-respondents	**High**
Pogoda 2016[18]	OEF/OIF Veterans completing CTBIE 2007-2009; deployment TBI and complete data; VA/DoD databases for demographics and health information	Adequate	Clinician administered CTBIE	Clinician rating on CTBIE	N/A	**Moderate**
Polusny 2011[38]	US National Guard Brigade Combat Team; 1 month prior to return from deployment and 1 year after deployment	Adequate	Self-report; 3-items from DVBIC screen (injury with altered mental status or LOC)	Self-report (PCL-M, BDI-II, AUDIT)	50.4% for follow-up questionnaire; some differences between returners/non-returners	**Moderate**

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
Seal 2016{Seal, 2016 #232	OEF/OIF Veterans in CTBIE database; definitive TBI finding; complete data; other databases for demographics and utilization	Adequate	Clinician administered CTBIE	ICD-9 codes	N/A	**Moderate**
Taylor 2015[20]	Iraq and Afghanistan War Veterans using VHA FY2014; other databases for demographics, utilization, and health information	Adequate	ICD-9 codes	ICD-9 codes	N/A	**Moderate**
Tsai 2012[39]	Survey of Veterans in VA Hawaii Program Registry for OEF/OIF/OND (stratified sample – rural/urban, proportion of female Veterans)	Adequate	Self-report; VA 4-item screen (combat-related concussion and persistent postconcussive symptoms	Self-report (PCL-C and CAGE)	52%; respondents similar to others in Hawaii Registry but some differences from national samples of OEF/OIF Veterans	**Moderate**
Vanderploeg 2015[40]	Survey of Florida National Guard (deployed group returned from deployment a mean of 2.7 yrs prior)	Adequate	Self-report of event(s) resulting in LOC, "blacking out," or memory gaps and duration of memory gaps	Self-report (PCL, PHQ-9, GAD-7, AUDIT-C)	41.3%; 22% of respondents excluded after validity checks on responses	**Moderate**
Walker 2017[41]	Recruited by letters, advertisements, and ambulatory clinics at 1 VA PRC and 3 military bases; ≥1 blast experiences in past 2 years	Adequate	~50% interviewed by research staff with data reviewed by physicians; ~50% extrapolated from BESQ information	Self-report (PCL [version not reported], CESD)	N/A	**Moderate**

Author, year	Sampling appropriate[a]	Subject/setting details[b]	TBI identification[c]	Psychiatric measures[d]	Response rate[e]	Overall risk of bias rating
Wilk 2012[42]	3 Brigade Combat Teams from 1 Active Component Infantry Division; 4-6 months post-deployment; randomly selected ~50% for inclusion	Limited demographic information	Self-report of injury event resulting in concussion-related items (*eg*, dazed, not remembering the injury) based in DOD and VA TBI Screen	Self-report (PCL-17, PHQ-9)	N/A	**Moderate/high**
Yurgil 2014[43]	Data from longitudinal study of Marine and Navy servicemen from 4 infantry battalions stationed in S California	Adequate	Interview about head injury history	Clinician administered (CAPS-IV)	N/A	**Low**

[a]Was the sampling appropriate to achieve a nationally representative population of Service Members and Veterans? [b]Were the study subjects and the setting described in sufficient detail? [c]Were valid, standard methods used for the identification of mTBI for all participants? [d]Were valid, standard methods used to assess the mental health conditions for all participants? [e]Was the response rate adequate, and if not, was the low response rate managed appropriately?

Adapted from JBI Critical Appraisal Checklist for Studies Reporting Prevalence Data (Available at: http://joannabriggs.org/research/critical-appraisal-tools.html) Munn Z, Moola S, Lisy K, Riitano D, Tufanaru C. Methodological guidance for systematic reviews of observational epidemiological studies reporting prevalence and incidence data. Int J Evid Based Healthc. 2015;13(3):147–153.

Shaded cells indicate nationally representative samples.

AUDIT-C=Alcohol Use Disorders Identification Test-Consumption Questions; BAI=Beck Anxiety Inventory; BDI-II=Beck Depression Inventory-II; BESQ=Blast Experience Screening Questionnaire; BHM-20=Behavioral Health Measure-20; CAGE=Cutting down, Annoyance by criticism, Guilty feeling, and Eye openers; CAPS-IV=Clinician Administered PTSD Scale for DSM-IV; CESD=Centers for Epidemiological Studies Depression scale; CT=computed tomography; CTBIE=Comprehensive TBI Evaluation; DVBIC=Defense and Veterans Brain Injury Center; EMED=Expeditionary Medical Encounter Database; EMR=electronic medical record; GAD-7=Generalized Anxiety Disorders Questionnaire; LOC=loss of consciousness; MADRS=Montgomery-Asberg Depression Rating Scale; MAST=Michigan Alcohol Screening Test; N/A=not applicable; OEF/OIF/OND=Operation Enduring Freedom/Operation Iraqi Freedom/Operation New Dawn; PCL=PTSD Checklist; PCL-M=PTSD Checklist-Military Version; PDHA=Post-Deployment Health Assessment; PDHRA= Post-Deployment Health Reassessment; PHQ-15 (-9)=Patient Health Questionnaire-15 item (-9 item); PNS=Polytrauma Network Site; PRC=Polytrauma Rehabilitation Center; PTA=posttraumatic amnesia; SBQ-R=Suicidal Behaviors Questionnaire-Revised; STDI=Structured TBI Diagnostic Interview; VHA=Veterans Health Administration

Table 4. Overview of Treatment Studies (KQ2)

Study, year (ref) Design Funding	Inclusion/Exclusion Criteria	Study Characteristics	Intervention 1 (describe)	Intervention 2 (describe)
Bomyea, 2017[44] Design: Secondary analysis of a randomized controlled trial Funding: Department of Defense	Inclusion: Veterans with ≥1 anxiety or depressive disorders (including PTSD) based on DSM-IV, psychiatric diagnoses (Mini-International Neuropsychiatric Interview) and cognitive impairment (Montreal Cognitive Assessment) screened Exclusion: Interfering neurocognitive impairments, psychosis, bipolar illness, imminent suicidality or self-injury, anticipated change in pharmacologic treatment, concurrent psychotherapy for presenting complaint, or anticipation of inability to complete all study procedures	N=129 Mean age: 35 Male (%): 78% (TBI+ 87% vs TBI- 63%, P<.01) Race/ethnicity: Caucasian/white 77%; African American 9%; Asian 7%; Native American 3%; Biracial/Other 4% History of TBI (%): 64 Time since TBI: NR Time since discharge: NR Multiple TBI: NR TBI etiology: NR PTSD: NR History of depression: NR	Patient centered therapy (PCT): 12 sessions of individual PCT treatment Duration: 1-hour weekly	Acceptance and commitment therapy (ACT): 12 sessions of individual ACT treatment Duration: 1-hour weekly

Study, year (ref) Design Funding	Inclusion/Exclusion Criteria	Study Characteristics	Intervention 1 (describe)	Intervention 2 (describe)
Chard, 2011[45] Design: Pre-post Funding: NR Psychiatric Condition: PTSD and depression	Inclusion: Veterans with current PTSD (CAPS-IV) using worst reported trauma, and history of TBI (severity definitions of TBI based on guidelines provided by DoD and VA; severity determined by examination of available medical records and patient interview) Exclusion: NR	N=28 mTBI, an additional 14 participants had moderate/ severe TBI Mean age: 34 Male (%): 100 Race/ethnicity: white 79% Time since TBI: ≥1 year Time since discharge: NR Multiple TBI (for all 47 – see note below): 81% TBI etiology (for all 47 – see note below): blast 62%, 36% motor vehicle accidents, 128% falls, other 47% (fights, sports) PTSD: 100% History of depression: 75%	Cognitive processing therapy-cognitive (CPT-C) in combined group and individual format as primary focus of active-trauma treatment; group held twice a week; individual CPT-C sessions a minimum of twice a week Duration: 7-weeks (residential) Note: Participants assessed posttreatment by independent evaluators who did not conduct their individual psychotherapy	NR

Study, year (ref) Design Funding	Inclusion/Exclusion Criteria	Study Characteristics	Intervention 1 (describe)	Intervention 2 (describe)
Harch, 2012[46] Design: Pre-post, proof-of-concept Funding: NR Psychiatric Condition: PTSD	Inclusion: Service members and Veterans;18–65 years, ≥1 mild/moderate TBI (loss of consciousness due to blast injury, ≥1 year old, occurred after 9/11/01); prior diagnosis of chronic TBI/PCS or TBI/PCS/PTSD by military or civilian specialists, no acute cardiac arrest or hemorrhagic shock at time of TBI; Disability Rating Scale score 0–3, negative urine screen for drugs of abuse, <90% on Percent Back to Normal Rating Scale Exclusion: Pulmonary disease precluding HBO_2, unstable medical conditions contraindicated in HBO_2, severe confinement anxiety, participation in another trial with active interventions, inability to complete protocol, history of hospitalization for past TBI, stroke, non-febrile seizures or seizure history outside of TBI, mental retardation, alcohol or drug abuse, or systemic illness impacting central nervous system	N=16 Mean age: 30 Male (%): 100 Race/ethnicity: NR Time since TBI: 2.8 years Time since discharge: NR, 8 were active duty Multiple TBI: average was 2.7 (range 1-7) TBI etiology: blast 100% PTSD: 100% (DSM-IV) History of depression: NR	Hyperbaric oxygen therapy (HBO_2) Patients compressed and decompressed at 1–2 pounds per square inch on 100% oxygen; rate depended on patient comfort and preference; depth of pressurization was 1.5 ATA; total dive time 60 min Duration: 40 sessions in 30 days; treatment twice/day, 5 days/week, with 3- to 4-h surface interval between treatments; protocol goal was 40 sessions.	

Study, year (ref) Design Funding	Inclusion/Exclusion Criteria	Study Characteristics	Intervention 1 (describe)	Intervention 2 (describe)
Ragsdale, 2016[47] Design: Pre-post, Retrospective data analysis Funding: NR Psychiatric Condition: PTSD	Inclusion: 41 OEF/OIF/OND Veterans, had completed either individual PE or individual CPT, assessed for PTSD by semi-structured interview based on DSM-IV, TBI status assessed by retrospective medical record reviews Exclusion: Veterans who received group therapy	N=41, 19 with TBI Mean age: 33 Male (%): 88 Race/ethnicity: Caucasian/white 85%; African American 7%; Hispanic/Latino 7% History of TBI (%): 46 Time since TBI: NR Time since discharge: NR Multiple TBI: NR TBI etiology: NR PTSD: 100% History of depression: NR, likely many also had depressive symptoms	Prolonged exposure (PE) therapy (n=21, 9 with TBI (43%)) Standard treatment in clinic provided by licensed psychologists or social workers (or trainees they supervised) who had completed or were engaged in VA certification for PE and CPT PE participants completed 6-15 (*mean*=10) sessions Duration: NR Note: Treatment providers were not necessarily blind to TBI status based on how TBI status was determined	Cognitive processing therapy (CPT**)** (n=20, 10 with TBI (50%)) CPT participants completed 7-16 (*mean*=12) sessions
Sripada, 2013[48] (Study 2) Design: Secondary data (post-hoc examination) from randomized controlled trial Funding: NR Psychiatric Condition: PTSD	Inclusion: Veterans in randomized trial diagnosed with PTSD using CAPS-IV Exclusion: NR	N=22, 8 (36%) with a TBI (most mild) Mean age: 33 Male (%): 91 Race/ethnicity: Caucasian/White 73; African American 23; Asian 4 History of TBI (%): 36 Time since TBI: NR Time since discharge: NR Multiple TBI: NR TBI etiology: NR PTSD (%): 100 History of depression (%): 57	Prolonged exposure (PE) therapy (a) psychoeducation (b) repeated in vivo exposure to commonly avoided trauma-related situations and cues (c) repeated imaginal exposure to traumatic memories and (d) subsequent discussion after imaginal exposures to facilitate emotional processing and corrective learning	Present centered therapy (PCT) Present centered and problem solving oriented approach to facilitate adaptive responses to ongoing stress and difficulties Duration: 10-12 sessions

Study, year (ref) Design Funding	Inclusion/Exclusion Criteria	Study Characteristics	Intervention 1 (describe)	Intervention 2 (describe)
Wolf 2015[49] Design: Pre-post, retrospective clinical data review Funding: James V. Haley and Durham VA Medical Centers Psychiatric Condition: PTSD	Inclusion: Veterans or active duty service members referred for clinical treatment of PTSD, history of TBI by CTBIE, ongoing cognitive deficits based on self-report and corroborated by medical observation following injury, and neuropsychologic or neuroimaging Exclusion: Psychosis, unstable bipolar disorder, imminent suicidal or homicidal ideation, and recent aggressive behavior, self-harm, or severe substance dependence	N=69 (complete data for 44) Active duty (%): 26, 36% for completers Mean age: 34 Male (%): 94 Race/ethnicity (%): Caucasian/White 67; African American 19; Hispanic/Latino 12; Other 3 History of TBI (%): 100, 75% with mTBI, 71% for completers Time since TBI (years): 4.7, 4.8 (3.1) for completers Time since discharge: NR Multiple TBI: mean 2.8, 2.6 for completers TBI etiology (%): Blast 51, 52% for completers Non-blast 48 PTSD: 100% History of depression: 83%, 86% for completers	Prolonged exposure (PE) therapy (a) psychoeducation (b) repeated in vivo exposure to commonly avoided trauma-related situations and cues (c) repeated imaginal exposure to traumatic memories and (d) subsequent discussion after imaginal exposures to facilitate emotional processing and corrective learning Modifications (*ie,* memory-enhancing strategies (phones, digital assistants) and increased structure) were incorporated Duration: Bi-weekly sessions for 6-8 weeks (inpatient program); weekly sessions for 3-6 months (residential polytrauma program)	

Study, year (ref) Design Funding	Inclusion/Exclusion Criteria	Study Characteristics	Intervention 1 (describe)	Intervention 2 (describe)
Wolf, 2012[50] Pilot study Design: Prospective observational study Funding: Minneapolis and James V. Haley VA Medical Centers Psychiatric Condition: PTSD	Inclusion: Veterans with current diagnosis of PTSD using CAPS-IV and PCL-M, documented history of TBI by CTBIE, ongoing cognitive deficits based on self-report and corroborated by medical observation following injury, and neuropsychologic or neuroimaging Exclusion: Active psychosis, un-medicated bipolar disorder, imminent suicidal or homicidal ideation or self-harm, and severe uncontrolled substance dependence	*Pilot study* N=10 Mean age: 33 Male (%): 100 Race/ethnicity (%): Caucasian/White 40; Hispanic/Latino 50; Asian 10 History of TBI (%): 100 Time since TBI: NR Time since discharge: NR Multiple TBI: NR TBI etiology: NR PTSD: 100% History of depression: 40% with a prior suicide attempt	Prolonged exposure (PE) therapy (a) psychoeducation (b) repeated in vivo exposure to commonly avoided trauma-related situations and cues (c) repeated imaginal exposure to traumatic memories and (d) subsequent discussion after imaginal exposures to facilitate emotional processing and corrective learning Modifications (*ie,* memory-enhancing strategies (phones, digital assistants), increased structure, and additional session time) were incorporated Duration: Average of 13 sessions (range 8-18) for 120 minutes NOTE: PE initiated after window of expected recovery for TBI was lapsed	

ATA=atmospheres absolute; CAPS-IV=Clinician-Administered PTSD Scale for DSM-IV; CTBIE=Comprehensive TBI Evaluation; DSM-IV=Diagnostic and Statistical Manual of Mental Disorders- 4th Edition; NR=not reported; PCL=PTSD checklist (M=Military version); PCS=post-concussive syndrome; PTSD=posttraumatic stress disorder; TBI=traumatic brain injury

Table 5. Outcomes from Treatment Studies (KQ2)

Study, year (ref) Treatment(s)	Outcome 1 (describe) (n) Mean (SD)	Outcome 2 (describe) (n) Mean (SD)	Outcome 3 (describe) (n) Mean (SD)	Outcome 4 (describe) (n) Mean (SD)
Bomyea, 2017[44] Present Centered Therapy and Acceptance and Commitment Therapy	NR	NR	*Present Centered Therapy* **BSI-18 (≥63=clinical elevation)** *Anxiety or depressive disorder and TBI (n=42)* Pre-treatment: 74.7 (7.7) Post-treatment: ~69 (figure) P NS *Without TBI* (n=25) Pre-treatment: 72.6 (7.6) Post-treatment: ~64 (figure)	*Acceptance and Commitment Therapy* **BSI-18 (≥63=clinical elevation)** *Anxiety or depressive disorder and TBI (n=41)* Pre-treatment: 73.3 (8.5) Post-treatment: ~68 (figure) P NS *Without TBI* (n=21) Pre-treatment: 72.5 (8.0) Post-treatment: ~65 (figure)
Chard, 2011[45] Cognitive Processing Therapy-Cognitive	**CAPS-IV** (n=28) **(cut-off NR)** Pre-treatment: 75.1 (5.9) Post-treatment: 49.0 (22.3) P<.01 vs baseline	**PCL (version not reported)** (n=28) **(cut-off NR)** Pre-treatment: 61.8 (10.3) Post-treatment: 46.5 (16.1) P<.01 vs baseline	**BDI-II** (n=28) **(cut-off NR)** Pre-treatment: 32.6 (10.7) Post-treatment: 23.7 (11.0) P<.01 vs baseline	NR
Harch, 2012[46] Hyperbaric oxygen therapy *Proof-of-concept study*	**PCL-M** (n=16) **(cut-off=50)** Pre-treatment: 67.4 (10.5) Post-treatment: 47.1 (16.0) Mean difference -20.3 [95%CI -30.4 to -10.2] P<.0001 vs baseline	NR	**PHQ-9 Depression** (n=16) **(cut-off NR)** Pre-treatment: 16.6 (4.9) Post-treatment: 8.2 (4.7) Mean difference -8.4 [95%CI -12.5 to -4.3] P<.0001 vs baseline	**GAD-7 Anxiety** (n=16) **(cut-off NR)** Pre-treatment: 12.7 (5.8) Post-treatment: 7.9 (5.3) Mean difference -4.8 [95%CI -8.0 to -1.6] P<.007 vs baseline

Study, year (ref) Treatment(s)	**Outcome 1 (describe) (n) Mean (SD)**		**Outcome 2 (describe) (n) Mean (SD)**	**Outcome 3 (describe) (n) Mean (SD)**		**Outcome 4 (describe) (n) Mean (SD)**
Ragsdale, 2016[47] Cognitive Processing Therapy and Prolonged Exposure Therapy	*Prolonged exposure therapy* **PCL-S (cut-off=50)** *PTSD+TBI* (n=9) Pre-treatment: 62.7 (11.4) Post-treatment: 32.9 (16.0) Change: -29.8 (13.7) *PTSD only* (n=12) Pre-treatment: 63.8 (8.4) Post-treatment: 29.2 (11.6) Change: -34.6 (10.3)	*Cognitive processing therapy* **PCL-S cut-off=50)** *PTSD+TBI* (n=10) Pre-treatment: 59.3 (12.1) Post-treatment: 42.9 (13.8) Change: -16.4 (8.8) *PTSD only* (n=10) Pre-treatment: 55.3 (11.5) Post-treatment: 43.8 (18.4) Change: -11.5 (14.1)	NR	*Prolonged exposure therapy* **BDI-II (clinical cut off NR)** *PTSD+TBI* (n=9) Pre-treatment: 28.3 (15.2) Post-treatment: 12.1 (14.6) Change: -16.2 (8.7) *PTSD only* (n=12) Pre-treatment: 30.1 (11.9) Post-treatment: 12.8 (13.8) Change: -17.3 (10.4)	*Cognitive processing therapy* **BDI-II (clinical cut off NR)** *PTSD+TBI* (n=10) Pre-treatment: 26.1 (11.1) Post-treatment: 19.8 (15.0) Change: -6.3 (7.9) *PTSD only* (n=10) Pre-treatment: 26.6 (7.4) Post-treatment: 19.8 (12.6) Change: -6.8 (10.0)	NR

Study, year (ref) Treatment(s)	**Outcome 1 (describe) (n) Mean (SD)**	**Outcome 2 (describe) (n) Mean (SD)**		**Outcome 3 (describe) (n) Mean (SD)**	**Outcome 4 (describe) (n) Mean (SD)**
Sripada, 2013[48] (Study 2) Present Centered Therapy and Prolonged Exposure Therapy	*Combined present centered and prolonged exposure therapy groups* **CAPS-IV** (n=22) **(reduction of 10 points=clinically significant reduction in PTSD)** Pre-treatment: 78.4 (11.3) Post-treatment: 41.4 (26.0) P<.001 vs pre-treatment **CAPS-IV (reduction of 10 points=clinically significant reduction in PTSD)** *TBI only* (n=8) Pre-treatment: 82.4 (11.7) Post-treatment: 45.5 (32.5) P<.001 vs pre-treatment *PTSD only* (n=14) Pre-treatment: 76.1 (10.8) Post-treatment: 39.1 (22.5) P NR	*Present centered therapy* **CAPS-IV (reduction of 10 points=clinically significant reduction in PTSD)** *PTSD+TBI* Pre-treatment: 82.0 (9.3) Post-treatment: 66.3 (27.3) P NS between treatments at either time point	*Prolonged exposure therapy* **CAPS-IV (reduction of 10 points=clinically significant reduction in PTSD)** *PTSD+TBI* Pre-treatment: 82.8 (15.3) Post-treatment: 24.8 (23.8)	NR	NR
Wolf 2015[49] Prolonged Exposure Therapy	**PCL (version not reported)** (n=69) **(cut-off=49)** Pre-treatment: 64.8 (10.1) Post-treatment: 43.5 (16.8) **PCL for completers** (n=44) Pre-treatment: 63.5 (9.2) Post-treatment: 34.8 (10.7)	NR		**BDI-II** (n=69) **(cut-off=14)** Pre-treatment: 29.6 (9.5) Post-treatment: 18.1 (12.6) **BDI-II for completers** (n=44) Pre-treatment: 29.1 (8.6) Post-treatment: 13.9 (10.3)	NR

Study, year (ref) Treatment(s)	Outcome 1 (describe) (n) Mean (SD)	Outcome 2 (describe) (n) Mean (SD)	Outcome 3 (describe) (n) Mean (SD)	Outcome 4 (describe) (n) Mean (SD)
Wolf, 2012[50] Prolonged Exposure Therapy *Pilot study*	**PCL-M** (n=10) **(cut-off=49.5)** Pre-treatment: 69.2 (8.1) Post-treatment: 38.0 (9.0) P<.001 Note: Based on a cut-off score of 49.5, 90% of participants achieved a clinically significant change	NR	**BDI-II** (n=10) **(cut-off=14.9)** Pre-treatment: 34.4 (9.7) Post-treatment: 17.7 (8.6) P<.001 Note: Based on a cut-off score of 14.9, 40% of participants achieved a clinically significant change	NR

AUDIT=Alcohol Use Disorders Identification Test; BDI-II=Beck Depression Inventory-II; BSI-18=Brief Symptom Inventory-18; CAPS=Clinician-Administered PTSD Scale; CPT=Cognitive Processing Therapy; GAD-7=Generalized Anxiety Disorder 7-item scale; EO=education only; PE=Prolonged Exposure Therapy; PCL=PTSD Checklist; PCL-M=PTSD Checklist-Military Version; PCL-S=PTSD Checklist-Specific; PCT=Present Centered Therapy; PHQ-9=9-item Patient Health Questionnaire; PST=problem-solving treatment; PTSD=posttraumatic stress disorder; TBI=traumatic brain injury

Table 6. Risk of Bias for Treatment Studies (KQ2)

Author, year	Sampling appropriate[a]	Follow-up complete[b]	Standard assessment methods[c]	Manual-based/fidelity monitored[d]	Independent outcome assessment[e]	Overall rating
Bomyea 2017[44]	Yes, secondary analysis of an RCT	Unclear, but the RCT notes all were analyzed	Yes, DSM-IV	Unclear, but the RCT notes fidelity was monitored independently	Unclear	Moderate
Chard 2011[45]	No control	Yes, completers only in analyses but reasons for non-completion stated	Yes, CAPS-IV	Yes/No, lack of treatment fidelity data	Yes, by "independent evaluators who did not conduct their individual psychotherapy"	Moderate
Harch 2012[46]	No control	Completers only, 1 (6%) withdrawal	Yes, DSM-IV	Not applicable	Unclear	Moderate
Ragsdale 2016[47]	No control, retrospective analysis	Unclear, completers only with no further details	Yes, interview based on DSM-IV diagnostic criteria	Yes/No, lack of treatment fidelity data	No, treatment providers were not necessarily blind to TBI status	Moderate/High
Sripada 2013[48]	No control (sample characteristics combined, post-hoc data from RCT)	Unclear, completers only with no further details	Yes, CAPS-IV	Yes/No, "treatment sessions were not coded for treatment fidelity"	Unclear, none noted	Moderate
Wolf 2015[49]	No control, retrospective analysis	Yes, differences between completers and non-completers addressed	Unclear ("evaluated by a psychiatrist or psychologist to confirm the diagnosis")	Yes/No, lack of treatment fidelity data ("no formal monitoring of the delivery of PE, and it was clear that there were nonstandard elements added for many participants")	Unclear, none noted	Moderate/High
Wolf 2012[50]	No control, possible selection bias	Yes, follow-up for all 10 participants	Yes, CAPS-IV	Yes/No fidelity data reported; noted that "very few modifications to the treatment manual were necessary …with exception of memory-enhancing strategies"	Unclear, none noted	Moderate/High

[a]Were the participants included in any comparisons similar at baseline? [b]Was follow up complete and if not, were differences between groups in terms of their follow up adequately described and analyzed? [c]Were standard methods used to assess the psychiatric conditions for all participants? [d]If applicable, was the therapy manual-based and was treatment fidelity monitored? [e]Were the outcomes of participants included in any comparisons measured by outcomes assessors independent of the intervention?

Adapted from JBI Critical Appraisal Tool for Quasi-Experimental Studies (experimental studies without random allocation) (Available at: http://joannabriggs.org/research/critical-appraisal-tools.html)

Tufanaru C, Munn Z, Aromataris E, Campbell J, Hopp L. Chapter 3: Systematic reviews of effectiveness. In: Aromataris E, Munn Z (Editors). Joanna Briggs Institute Reviewer's Manual. The Joanna Briggs Institute, 2017.