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Prevalence and Epidemiology of Combat Blast Injuries from the Military Cohort 2001-2014

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PREFACE

Quality Enhancement Research Initiative's (QUERI) Evidence-based Synthesis Program (ESP) was established to provide timely and accurate syntheses of targeted healthcare topics of particular importance to Veterans Affairs (VA) clinicians, managers and policymakers as they work to improve the health and healthcare of Veterans. The ESP disseminates these reports throughout the VA, and some evidence syntheses inform the clinical guidelines of large professional organizations.

QUERI provides funding for four ESP Centers and each Center has an active university affiliation. The ESP Centers generate evidence syntheses on important clinical practice topics, and these reports help:

- develop clinical policies informed by evidence;
- guide the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- set the direction for future research to address gaps in clinical knowledge.

In 2009, the ESP Coordinating Center was created to expand the capacity of HSR&D Central Office and the four ESP sites by developing and maintaining program processes. In addition, the Center established a Steering Committee comprised of QUERI field-based investigators, VA Patient Care Services, Office of Quality and Performance, and Veterans Integrated Service Networks (VISN) Clinical Management Officers. The Steering Committee provides program oversight, guides strategic planning, coordinates dissemination activities, and develops collaborations with VA leadership to identify new ESP topics of importance to Veterans and the VA healthcare system.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP Coordinating Center Program Manager, at Nicole.Floyd@va.gov.

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EXECUTIVE SUMMARY

INTRODUCTION

Combat blast injuries are typically categorized by the mechanism of injury. Primary blast injuries result from the over-pressurization wave and typically affect gas-filled body structures (*eg*, lungs, gastrointestinal tract, middle ear) resulting in injuries such as blast lung, tympanic membrane rupture, abdominal hemorrhage, and concussion. Secondary blast injuries result from flying debris propelled by the blast wind and may affect any body part. Blunt force or penetrating injuries are possible. Tertiary blast injuries occur when the body is accelerated by the blast wind or pressure gradients. Any body part may be affected and typical injuries include fracture and traumatic amputation, closed and open brain injuries, and crush injuries. Quaternary blast injuries are due to other products of the explosion (*eg*, heat, light) and exposure to toxins and gases. Any body part may be affected and injuries include burns, blindness, and respiratory problems from inhaled toxic gases. Quinary blast injuries include illnesses, injuries, and diseases resulting from post-explosion environmental contaminants (*eg*, bacteria, radiation).

Despite recognition of greater use of improvised and other explosive devices in the Afghanistan and Iraq War counter-insurgency operations relative to prior conflicts, the scientific literature regarding the incidence and prevalence of explosive device-induced injuries is limited. Additionally, the consequences of experiencing a traumatic brain injury (TBI) related to blast exposure versus a TBI due to other mechanisms of injury may be different. Accurate assessment of the incidence and prevalence of blast- and non-blast-related injuries as well as their long-term outcomes is a critical first step in injury prevention, treatment, and health system resource management. The purpose of this report is to systematically review the literature on 1) incidence and prevalence of combat blast injuries sustained during Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) 2001 through 2014 and 2) the outcomes (*eg*, pain, vision loss, cognitive function, quality of life) following blast versus non-blast TBI.

We developed the following Key Questions with input from stakeholders and Technical Expert Panel (TEP) members:

Key Question #1: What is the incidence of combat blast injuries associated with OEF, OIF, and OND as reported in the literature or in published reports from Department of Defense (DoD) and VA databases during the period 2001-2014?

> **Key Question #1a:** What is the incidence by blast characteristics (*ie*, primary, secondary, tertiary, quaternary, and quinary), injury site, and injury outcome?

Key Question #2: What is the prevalence of combat blast injuries associated with OEF, OIF, and OND as reported in the literature or in published reports from Department of Defense (DoD) and VA databases during the period 2001-2014?

> **Key Question #2a:** What is the prevalence of blast injury by blast characteristics, injury site, and injury outcome?

Key Question #3: What are the short-term (up to 30 days), mid-term (30 days to one year) and long-term (greater than one year) injury outcomes (*ie,* pain, burns, limb loss, vision loss, hearing loss, vestibular dysfunction, mental health/PTSD, cognitive function, quality of life, functional status/employment, other-organ system-specific) among US military personnel (2001-2014) who have sustained a blast-related TBI versus a non-blast TBI or a combined blast/non-blast TBI?

> **Key Question #3a:** What are the short-term (up to 30 days), mid-term (30 days to one year) and long-term (greater than one year) injury outcomes among US military personnel (2001-2014) who have sustained a blast-related TBI according to blast characteristics?

METHODS

Data Sources and Searches

We searched MEDLINE (Ovid) for articles published in English from 2000 through April 2015 using separate search strategies for Key Questions 1 and 2 and Key Question 3. Our searches were designed to identify studies of combat injuries in US military personnel during OEF, OIF, and OND. The full search strategies are presented in Appendix A. We obtained additional articles by hand-searching the table of contents of Journal of Trauma-Injury Infection & Critical Care and reference lists of systematic reviews and other reports, and from references suggested by stakeholders, TEP members, and peer reviewers.

Study Selection

Abstracts from the MEDLINE searches were reviewed in duplicate by investigators and research associates and abstracts from the table of contents search were reviewed by a single investigator. We identified for full-text review studies of any design potentially relevant to the key questions. Two investigators or research associates independently reviewed full-text articles excluding the following:

- Studies not including US military personnel from OEF, OIF, or OND (2001-2014);
- Studies not involving combat injuries;
- Modeling studies (*eg,* mechanical/engineering models, animal studies);
- Studies not relevant to the key questions;
- Studies of treatment outcomes;
- Imaging studies or studies reporting changes in tissue (*eg,* white matter);
- Case reports;
- Studies for Key Questions 1 and 2 where the denominator was not the number deployed during the study period (*ie,* reports of injuries at a medical facility were excluded); and
- Studies for Key Question 3 that did not report outcomes of interest for blast-related TBI and non-blast TBI groups (*ie,* studies only reporting on blast-related TBI were excluded).

Data Abstraction and Risk of Bias Assessment

Study characteristics and outcomes were extracted onto evidence tables by one investigator or research associate and verified by another. We did not assess the risk of bias of the included studies although risk of bias for each study was likely moderate or high due to the study design used, selective population studied, and failure to control for potential confounding factors.

Data Synthesis and Analysis

We created summary tables for incidence and prevalence data (Key Questions 1 and 2). We organized evidence tables for Key Question 3 by outcome and time since exposure (< 30 days, 30 days to 1 year, > 1 year, or not specified). Pooled analyses were not possible due to heterogeneity of the study populations and outcome measures.

We did not formally rate the overall strength of evidence for outcomes. The typical approach to assessing strength of evidence considers consistency, precision, directness, and risk of bias of the included studies. However, because included studies were observational and there was limited reporting of outcomes of interest (*ie,* most outcomes reported in only a few studies and often using different measures), it is unlikely that strength of evidence would be anything above low. Many outcomes had insufficient evidence.

RESULTS

Results of Literature Search

Our literature searches yielded 1,146 abstracts. We identified 324 articles for full-text review and excluded 290. We identified an additional 8 articles by hand-searching, resulting in a total of 42 included articles (6 for Key Questions 1 and 2, 36 from 34 studies for Key Question 3).

Summary of Results for Key Questions

Key Questions 1 and 2

We identified 6 studies meeting inclusion criteria for Key Questions 1 or 2 (incidence and prevalence of combat blast injuries). These studies included data from 2001 to 2011; 5 used the Joint Theater Trauma Registry (JTTR) and one used Department of Defense tabular reports. Three of the JTTR studies were based on the same cohort of deployed service members (described by Belmont et al, 2012) with one reporting overall casualties, one reporting musculoskeletal casualties, and one reporting spinal injuries. The JTTR (now the Department of Defense Trauma Registry [DoDTR]) was established in 2004 and contains information on all casualties (individuals lost to the theater of operations due to illness or injury) treated at US military medical facilities in and outside the combat zone. All but one study, which focused on the troop surge in Iraq, included casualties from both Iraq and Afghanistan. The mean ages of service members in the study cohorts ranged from 26 to 30 years, and 92% to 99% were male (k = 5 reporting). In the 4 studies that reported branch of service and rank, 78% to 100% were from the Army and the large majority (up to 93%) were from enlisted ranks. None of the studies provided information on deployment details including assigned or actual duties. Additional details are presented in Appendix C, Tables 1 and 2.

Key Question 1. Incidence

The National Institute of Mental Health defines incidence as the number of new cases of a condition, symptom, death, or injury that develop during a specific time period. We included registry studies that reported incidence of combat blast injuries for the deployed population (Executive Summary Table 1).

Belmont et al (2012) reported incidence of explosion (*ie*, improvised explosive device, mortar, and rocket-propelled grenade) injuries for the years 2005 to 2009. Soldiers killed in action or sustaining non-battle injuries were not included in the analysis. The number of service members deployed and years of service were obtained through the Defense Manpower Data Center. The incidence was 4.5 blast injuries per 1,000 deployed in 2005, 3.5 per 1,000 in 2006, 4.0 per 1,000 in 2007, 1.7 per 1,000 in 2008, and 1.7 per 1,000 in 2009. The slight increase in 2007 corresponded to the troop surge.

A second report detailed all combat explosion injuries in a US Army Brigade Combat Team (n = 4,122) deployed during the 2007 troop surge in Iraq. The cohort was followed for 6 months following the 15-month deployment. The incidence of explosion injuries was 83 per 1,000 deployed soldiers.

Executive Summary Table 1. Incidence Data

Outcome	2005	2006	2007	2008	2009	2010
Explosion injuries (*any*) per 1,000 deployed (Belmont 2010)			83[a]			
Explosion injuries (*any*) per 1,000 deployed (Belmont 2012)	4.5	3.5	4.0	1.7	1.7	
Explosion-related *musculoskeletal injuries* per 1,000 deployed[b] (Belmont 2013)	3.5	2.7	3.1	1.3	1.3	
Explosion-related *spinal injuries* per 1,000 deployed[b] (Schoenfeld 2013)	0.4	0.4	0.4	0.2	0.3	
Blast-related *thoracolumbar burst* fractures per 10,000 soldier years (Freedman 2014)				0.45[c]	0.60[c]	2.08[c]

[a] All explosion injuries for a US Army Brigade Combat Team (n = 4,122) deployed during the 2007 troop surge
[b] Additional analysis of cohort described by in Belmont 2012
[c] Data from August of preceding year to August of specified year

Key Question 1a

No study reported incidence by blast characteristics (*ie*, primary, secondary, *etc*) or injury outcomes (*eg*, pain, amputations, vision loss, cognitive function, functional status, quality of life). Three reported incidence by injury site (*ie*, body location or system injured) (Executive Summary Table 1).

Two of the studies provided information about specific injury types for the service members deployed to Afghanistan and Iraq and included in the cohort described by Belmont et al 2012. One study identified explosion-related musculoskeletal injuries (upper and lower extremity, spine, and pelvis wounds including fractures, soft tissue injuries, joint dislocations, neurologic injuries, and traumatic amputations) during a 5-year period. The incidence values (per 1,000 deployed soldiers) were 3.5 in 2005, 2.7 in 2006, 3.1 in 2007, 1.3 in 2008, and 1.3 in 2009. The other study reported on explosion-related spinal injuries finding 0.4 per 1,000 deployed soldiers in 2005, 2006, and 2007; 0.2 per 1,000 soldiers in 2008; and 0.3 per 1,000 soldiers in 2009. The injuries included fractures, dislocations, disk displacements, nerve root injuries, and spinal cord injuries.

Another study looked specifically at combat thoracolumbar burst fractures, a pattern of injury that occurs as a result of vertical forces imparted by an explosion beneath an armored vehicle. The analysis included service members injured in Afghanistan and Iraq. The incidence of thoracolumbar burst fractures increased from 0.45 per 10,000 soldier-years in the one-year period August 2007-2008, to 0.60 per 10,000 soldier-years in August 2008-2009, and 2.08 per 10,000 soldier-years in August 2009-2010. The increase in 2009-2010 was largely among soldiers serving in Afghanistan and authors attributed this to increased use of powerful improvised explosive devices against newer, up-armored vehicles. Authors speculated that with the newer military vehicles, explosives that might have caused deaths in the past were now associated with non-fatal burst fracture injuries.

Key Question 2. Prevalence

The National Institute of Mental Health has defined prevalence as the proportion of a population who have (or had) a specific condition in a given time period regardless of when they first acquired the condition. For this review, we report cumulative data as prevalence (Executive Summary Table 2).

Explosion-related injuries over a 5-year period (2005-2009) were reported for the Belmont et al cohort. Among 1,992,232 soldiers deployed to Afghanistan or Iraq during that time period, there were 5,862 explosion injuries, or 0.29% of deployed soldiers experienced an explosion-related injury. Explosion injuries accounted for 74% of injuries.

Key Question 2a

No studies reported prevalence by blast characteristic or injury outcome.

Four studies reported specific injury sites (Executive Summary Table 2). Two studies were additional analyses of the Belmont et al cohort. The study of musculoskeletal injuries reported 4,563 soldiers with explosion-related injuries (0.23% of deployed soldiers). Of all musculoskeletal injuries, 82% were explosion-related. Another analysis reported there were 650 soldiers with explosion-related spinal injuries (0.03% of deployed soldiers). Of all spinal injuries, 75% were explosion-related. Among the 650 with explosion-related spinal injuries, 31% (n = 204) had injuries to more than one spinal region. Associated head and neck injuries were noted in 57% (n = 132) of soldiers with an explosion-related cervical spine injury.

The study of thoracolumbar burst fractures reported that over the period 2007-2010, the rate of blast-related fractures was 2.02 per 10,000 soldier-years. A Congressional Budget Office Working Paper reported major amputations (loss of a limb proximal to the wrist or ankle). The prevalence was 38 per 100,000 troop-years in OEF and OND and 88 per 100,000 troop-years in OEF.

Executive Summary Table 2. Prevalence Data

Outcome	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Explosion-related injuries *(any)* (Belmont 2012)					74% of injuries 0.29% of 1,992,232 deployed (30.5 per 10,000 deployed)						
Blast-related *thoraco-lumbar burst fractures* (Freedman 2014)							2.02 per 10,000 soldier-years				
Explosion-related *musculo-skeletal injuries* (Belmont 2013)					82% of musculoskeletal wounds (14,158 wounds) 0.23% of 1,992,232 deployed (22.9 per 10,000 deployed)						
Explosion-related *spinal injuries* (Schoenfeld 2013)					75% of spinal casualties 0.03% of 1,992,236 deployed (3.3 per 10,000)						
Improvised explosive device *major amputations* (Goldberg 2014)	Iraq (OEF, OND): 38.3/100,000 troop-years Afghanistan (OEF): 87.8/100,000 troop-years										

Key Question 3

We included 34 studies (in 36 papers). Executive Summary Table 3 provides an overview of the studies. The majority of reports were clinical cohort studies with patient injury outcomes (*eg*, post-traumatic stress disorder [PTSD], pain, limb loss, vision impairment, cognitive function loss) assessed at a medical facility in the US. Many studies did not report the time from blast exposure to assessment. Of those that did, most assessments took place 30 days to one year post-exposure. Eighteen of the 34 studies included only patients with mild TBI.

Injury outcomes are summarized in Executive Summary Table 4. In studies of injury outcomes among military personnel sustaining a blast or non-blast TBI, blast and non-blast groups had similar rates of mortality, pain, vision loss, vestibular dysfunction, functional ability, depression, sleep disorders, alcohol misuse, and post-concussive symptoms. Results were consistent across studies despite the fact that the studies varied in sample size, location where assessment took place, time from exposure to assessment (< 30 days, 30 days to one year, or > one year), and level of TBI severity.

Findings were less consistent for PTSD, hearing loss, cognitive function loss, and headache, with some studies finding increased levels in the blast-related TBI groups and some finding blast and non-blast groups to be similar. Burn injuries, limb loss, and quality of life were infrequently reported (3, 2, and one study, respectively).

We found little data on outcomes according to blast characteristics. One study failed to find a difference in hearing outcomes by primary versus secondary blast injuries. Three studies that defined blast injury as due to primary blast force reported few differences between their blast injury group and non-blast injury comparator groups.

Executive Summary Table 3. Overview of Study Characteristics – Key Question 3

Number of Studies	Data Source		Sample Size	Characteristics									
				Location of Assessment[a]			Time Since Exposure[b]				TBI Severity[c]		
	Registry/ Database	Clinical Cohort		Combat Zone	After Deployment	DoD, VA or Other Medical Facility	< 30 days	30 days to 1 year	> 1 year	Any or Unclear	Mild	Moderate/ Severe	Mixed (results not reported separately)
34	6	28	18 to 12,521	3	2	26	3	10	5	14	18	1	12

[a] 2 additional studies: 1 completed in combat zone and at end of deployment; 1 unclear
[b] 2 additional studies: both with outcomes at <30 days and 30 days to 1 year post exposure
[c] 3 additional studies; 2 included mild and moderate/severe TBI with results reported separately; 1 included all severity levels reporting some results separately

Executive Summary Table 4. Overview of Outcomes According to Blast versus Non-blast TBI – Key Question 3

Number of Studies	Data Source		Outcomes Reported[a]												
	Registry/ Database	Clinical Cohort	Mortality	PTSD	Pain	Burn	Limb Loss	Vision Impairment	Hearing Impairment	Vestibular Dysfunction	Cognitive Function Loss	Quality of Life	Functional Status/ Employment	Other
34	6	28	↔2	**- 7 ↔8 1 MIXED**	**↔3**	**- 1 ↔1 ?1**	**- 1 ↔1**	**- 1 ↔5 ¯1 1 MIXED**	**- 4 ↔3 2 MIXED**	**- 1 ↔4 1 MIXED**	**- 2 ↔5 3 MIXED**	**↔1**	**↔4 ¯1**	**Depression: ↔7 Sleep: - 1, ↔3, 1 MIXED Headache: ↔2, 2 MIXED Alcohol misuse: ↔3 Post-concussive symptoms: - 1, ↔4 Injury severity: ↔1, ?1 TBI severity: - 1, ↔2, ?1**

[a] Number is number of studies reporting that outcome; symbol provides direction of statistically significant outcomes
- Higher prevalence or more severe in blast TBI group; ¯ Higher prevalence or more severe in non-blast TBI group; **↔** Blast and non-blast groups similar; **?** P value not reported
MIXED Multiple tests with mixed results

DISCUSSION

Key Findings

Key Questions 1 and 1a - Incidence

- The published literature provides limited information about the true incidence and prevalence of blast-related injuries experienced by US military personnel. Findings are likely influenced by assessment and reporting methods.

- The reported explosion injury incidence ranged from 4.5/1,000 deployed in 2005 to 1.7/1,000 deployed in 2009.

- During the Iraq troop surge (2007) explosion injury incidence was particularly high (83/1,000 deployed in a US Army Brigade Combat Team).

- Musculoskeletal explosion injury incidence (fractures, amputations, neurological injuries, joint dislocations, and soft tissue injuries) ranged from 3.5/1,000 deployed in 2005 to 1.3/1,000 deployed in 2009.

- Spinal injury incidence (fractures, dislocations, nerve root injuries, spinal cord injuries) ranged from 0.18/1,000 deployed in 2008 to 0.40/1,000 deployed in 2005.

- Thoracolumbar burst fracture incidence was low (0.45 to 2.1 per 10,000 soldier years between 2008 and 2010) but higher in Afghanistan than Iraq and increased over the study period.

- No study reported incidence by blast characteristics.

Key Question 2 and 2a - Prevalence

- Nearly three-quarters of all combat injuries over the period from 2005 to 2009 (31 per 10,000 deployed) were due to explosions.

- A high proportion of musculoskeletal injuries (82%; 23 per 10,000 deployed) and spinal injuries (75%; 3 per 10,000 deployed) between 2005 and 2009 were due to explosions. Of the musculoskeletal injuries, 80% of axial skeletal and extremity fractures, 94% of amputations, and 85% of soft tissue injuries were explosion-related. Another study reported explosion-related amputations in 4 per 10,000 troop-years (Iraq) and 9 per 10,000 troop-years (Afghanistan) over the period from 2001 to 2011.

- No study reported prevalence by blast characteristics.

Key Question 3

- The published literature provides limited information on outcomes associated with blast versus non-blast TBI experienced by US military personnel. Definitions of blast/non-blast injury, assessment of outcomes, and reporting methods vary and often are based on small selected groups.

- Blast and non-blast TBI groups had similar rates of pain, vision loss, vestibular dysfunction, functional ability, depression, sleep disorders, alcohol misuse, and post-concussive symptoms.

- Comparative outcomes in individuals with blast versus non-blast TBI were inconsistent across studies with regard to PTSD diagnosis or symptom severity, hearing loss, cognitive function, and headache in blast and non-blast TBI groups.

- Mortality, burn injuries, limb loss, and quality of life were infrequently reported in studies comparing blast versus non-blast TBI.

- Results were consistent across studies that varied by location of assessment (combat zone, medical facility), time from exposure to assessment (< 30 days, 30 days to one year, or > one year), and level of TBI severity, although the most studies were small, clinical cohort studies, with mTBI patients evaluated at a Department of Defense or Veterans Affairs medical facility.

- There is little data on outcomes among those with TBI according to blast characteristics.

Applicability

The findings of this review are highly applicable to military personnel and organizations that provide direct acute or chronic health care services including rehabilitation as well as employment to those either currently serving or of recent Veteran status. Additionally, an understanding of the incidence, prevalence, outcomes, and causal factors of blast and non-blast injuries may be used to help reduce these injuries in future combat operations.

However, many studies reported findings from individuals presenting to medical facilities and undergoing treatment for a specific combat injury. Patient and injury characteristics and subsequent health outcomes from these selected patients may differ in unknown ways from the broader group of individuals who had combat injuries. We also have little information on very long-term effects (*eg,* cognitive function decline over decades).

The Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans (released June 2015) reports that 1,906,754 OEF/OIF/OND Veterans have become eligible for VA health care since fiscal year 2002 (beginning October 1, 2001) and approximately 2.7 million troops (as of December 31, 2014) have served or are serving in the 2 theaters of operation since the beginning of the conflicts in Iraq and Afghanistan. OEF/OIF/OND Veterans who present for care at a VA facility undergo a screen for TBI which includes questions about exposure to physical trauma such as explosions. Veterans who screen positive for TBI undergo a comprehensive evaluation.

Research Gaps/Future Research

Accurately recording in a standardized fashion every injury to every individual who experiences a blast (including type of blast [*eg,* primary, secondary, *etc*], distance from the blast, *etc*) and then following those individuals to assess long-term outcomes would be ideal but not realistic. However, for those who have been determined to have received blast-related injuries additional information on the circumstances surrounding the injury should include: type of blast, distance from the blast, history of blast exposure, injury severity, assigned and actual duties, and military member's physical and psychosocial characteristics. Additional information gathered would be useful to evaluate methods to reduce combat-related blast injuries. Comparisons versus deployed controls may facilitate our understanding of the mechanisms and severity of blast-related injuries and the long-term health and social consequences of those injuries. This includes not only the treatments and health outcomes specific to the blast injury but also the long-term psychosocial, employment, and economic impact of blast injuries and the role and capacity needs for health care systems and the work force as these individuals reintegrate into the civilian society. Existing databases may already contain some of this information and future analyses should incorporate blast data where possible.

Conclusions

- The published literature provides limited information about the true incidence and prevalence of blast-related injuries experienced by US military personnel and the outcomes associated with blast versus non-blast TBI. We found no reports of incidence and prevalence of blast injuries associated with different combat roles.

- Few studies of incidence of blast-related injuries or outcomes associated with blast versus non-blast TBI report important characteristics of a blast injury: type of blast, how far the individual was from the blast, whether they experienced a blast wave, whether there was loss of consciousness or altered consciousness, whether there was amnesia (and length of time), and whether there was additional trauma.

- Only 6 studies, 3 of which were derived from the same data set, provide information about the incidence and prevalence of blast-related injuries in the deployed population at risk.

- Pain, vision loss, vestibular dysfunction, functional status, depression, sleep disturbance, alcohol misuse, and post-concussive symptoms were similar in groups of patients with blast and non-blast TBI. Findings were less consistent for PTSD, hearing loss, cognitive function, and headache. Few studies reported mortality, burn outcomes, limb loss, or quality of life.

- Reporting studies were often small and involved highly selected patients and thus may not be fully representative of all individuals with blast or non-blast TBI. There are few data on very long-term outcomes that may be particularly relevant to assessment of cognitive function and quality of life.

- Blast and blast injuries (including TBI) are often defined differently. Therefore, the incidence, prevalence, and patient outcomes may vary across studies in part due to differences in how blast injury is categorized.

- To more adequately address questions about consequences of blast exposure, future research efforts should focus on comprehensive and consistent documentation at the time of and following blast exposure and more complete analyses of databases that may already have captured blast exposure information.

ABBREVIATIONS TABLE

DoD	Department of Defense
DOW	Died of wounds
KIA	Killed in action
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OND	Operation New Dawn
PTSD	Post-traumatic Stress Disorder
RTD	Returned to duty
TBI (mTBI)	Traumatic brain injury (mild traumatic brain injury)
VA	Department of Veterans Affairs
VAMC	Veterans Affairs Medical Center
WIA	Wounded in action

EVIDENCE REPORT

INTRODUCTION

BACKGROUND

Combat blast injuries are typically categorized by the mechanism of injury.[1-5] Primary blast injuries result from the over-pressurization wave and typically affect gas-filled body structures (*eg*, lungs, gastrointestinal tract, middle ear) resulting in injuries such as blast lung, tympanic membrane rupture, abdominal hemorrhage, and concussion. Secondary blast injuries result from flying debris propelled by the blast wind and may affect any body part. Blunt force or penetrating injuries are possible. Tertiary blast injuries occur when the body is accelerated by the blast wind or pressure gradients. Any body part may be affected and typical injuries include fracture and traumatic amputation, closed and open brain injuries, and crush injuries. Quaternary blast injuries are due to other products of the explosion (*eg*, heat, light) and exposure to toxins and gases. Any body part may be affected and injuries include burns, blindness, and respiratory problems from inhaled toxic gases. Quinary blast injuries include illnesses, injuries, and diseases resulting from post-explosion environmental contaminants (*eg*, bacteria, radiation). Factors such as type of explosive, distance from the explosion, and body orientation relative to the explosion influence the impact of the explosion on the body.[4]

Despite recognition of greater use of improvised and other explosive devices in the Afghanistan and Iraq War counter-insurgency operations relative to prior conflicts, the scientific literature regarding the incidence and prevalence of explosive device induced injuries is limited. Additionally, the consequences of experiencing a traumatic brain injury (TBI) related to blast exposure versus a TBI due to other mechanisms of injury (*eg*, motor vehicle accident, fall) may be different.[3,4] Accurate assessment of the incidence and prevalence of blast and non-blast-related injuries as well as their long-term outcomes is a critical first step in injury prevention, treatment, and health system resource management. The purpose of this report is to systematically review the literature on 1) incidence and prevalence of combat blast injuries sustained during Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) 2001 through 2014 and 2) the outcomes (*eg*, pain, vision loss, cognitive function, quality of life) following blast versus non-blast TBI.

We developed the following key questions for this review with input from stakeholders and Technical Expert Panel (TEP) members:

Key Question #1: What is the incidence of combat blast injuries associated with OEF, OIF, and OND as reported in the literature or in published reports from Department of Defense (DoD) and VA databases during the period 2001-2014?

> **Key Question #1a:** What is the incidence by blast characteristics (*ie*, primary, secondary, tertiary, quaternary, and quinary),[1,2] injury site, and injury outcome?

Key Question #2: What is the prevalence of combat blast injuries associated with OEF, OIF, and OND as reported in the literature or in published reports from Department of Defense (DoD) and VA databases during the period 2001-2014?

Key Question #2a: What is the prevalence of blast injury by blast characteristics, injury site, and injury outcome?

Key Question #3: What are the short-term (up to 30 days), mid-term (30 days to one year) and long-term (greater than one year) injury outcomes (*ie*, pain, burns, limb loss, vision loss, hearing loss, vestibular dysfunction, PTSD, cognitive function, quality of life, functional status/employment, other) among US military personnel (2001-2014) who have sustained a blast-related TBI versus a non-blast TBI or a combined blast/non-blast TBI?

Key Question #3a: What are the short-term (up to 30 days), mid-term (30 days to one year) and long-term (greater than one year) injury outcomes among US military personnel (2001-2014) who have sustained a blast-related TBI according to blast characteristics?

PICOTS

The Population, Intervention, Comparator, Outcomes, Timing, and Setting (PICOTS) for the review are outlined below and displayed on analytic frameworks for Key Questions (KQ) 1 and 2 (Figure 1) and KQ 3 (Figure 2)

Population: Military cohort 2001-2014

Intervention: Combat blast injury (KQ1, KQ2) or blast-related TBI (KQ3)

Comparator: Non-blast or combined blast/non-blast TBI (KQ3)

Outcomes: Incidence and prevalence of combat blast injuries by blast characteristics, injury site, and injury outcome (KQ1, KQ2); injury outcomes for blast versus non-blast or combined TBI and injury outcomes by blast characteristics for blast-related TBI (KQ3)

Timing: Any duration from time of exposure (duration to be reported if available); injury outcomes categorized as short-term (up to 30 days after blast), mid-term (30 days to one year), and long-term (greater than one year)

Setting: Any active service setting (*ie*, training, deployment).

Figure 1. Analytic Framework for Key Questions 1 and 2

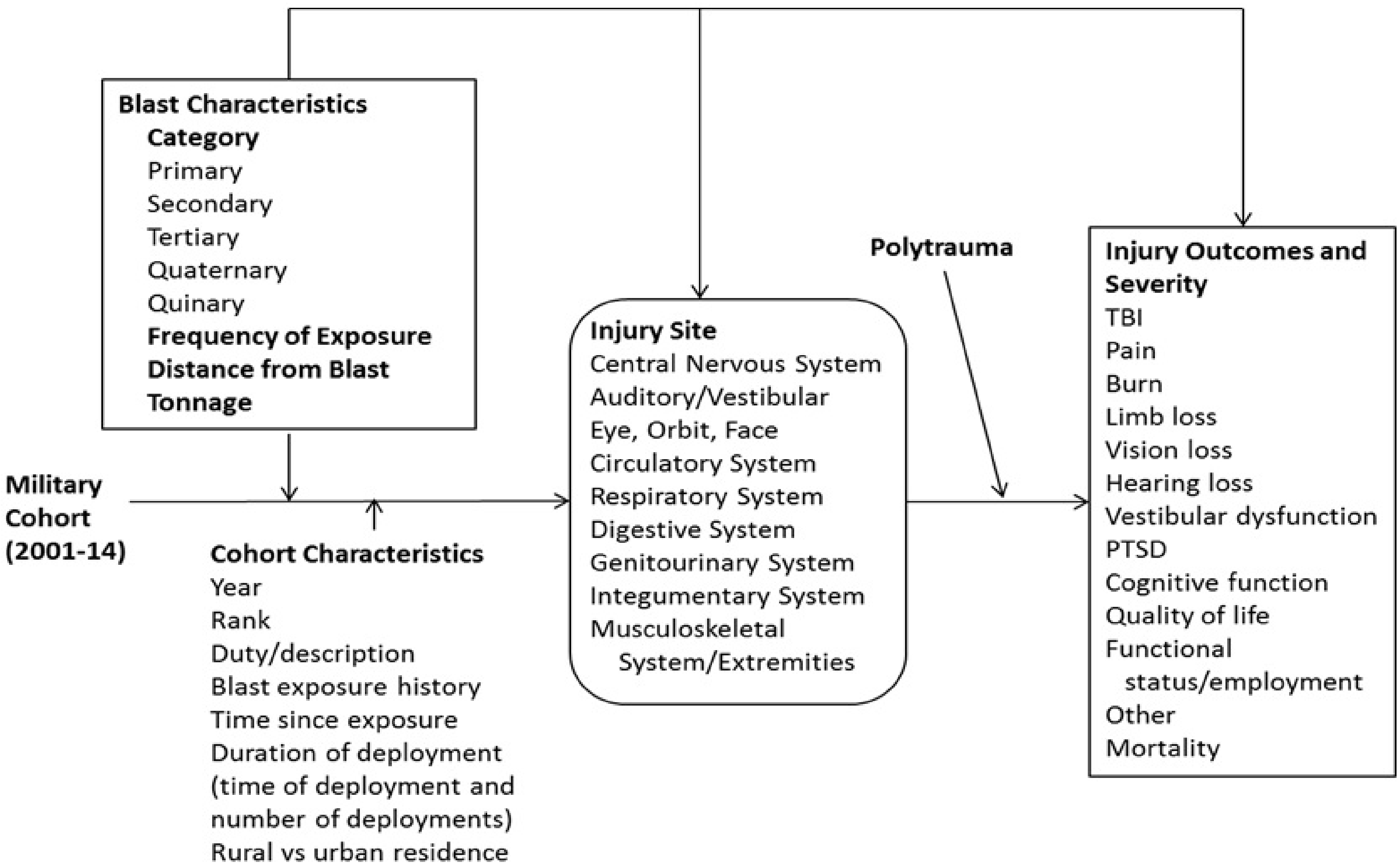
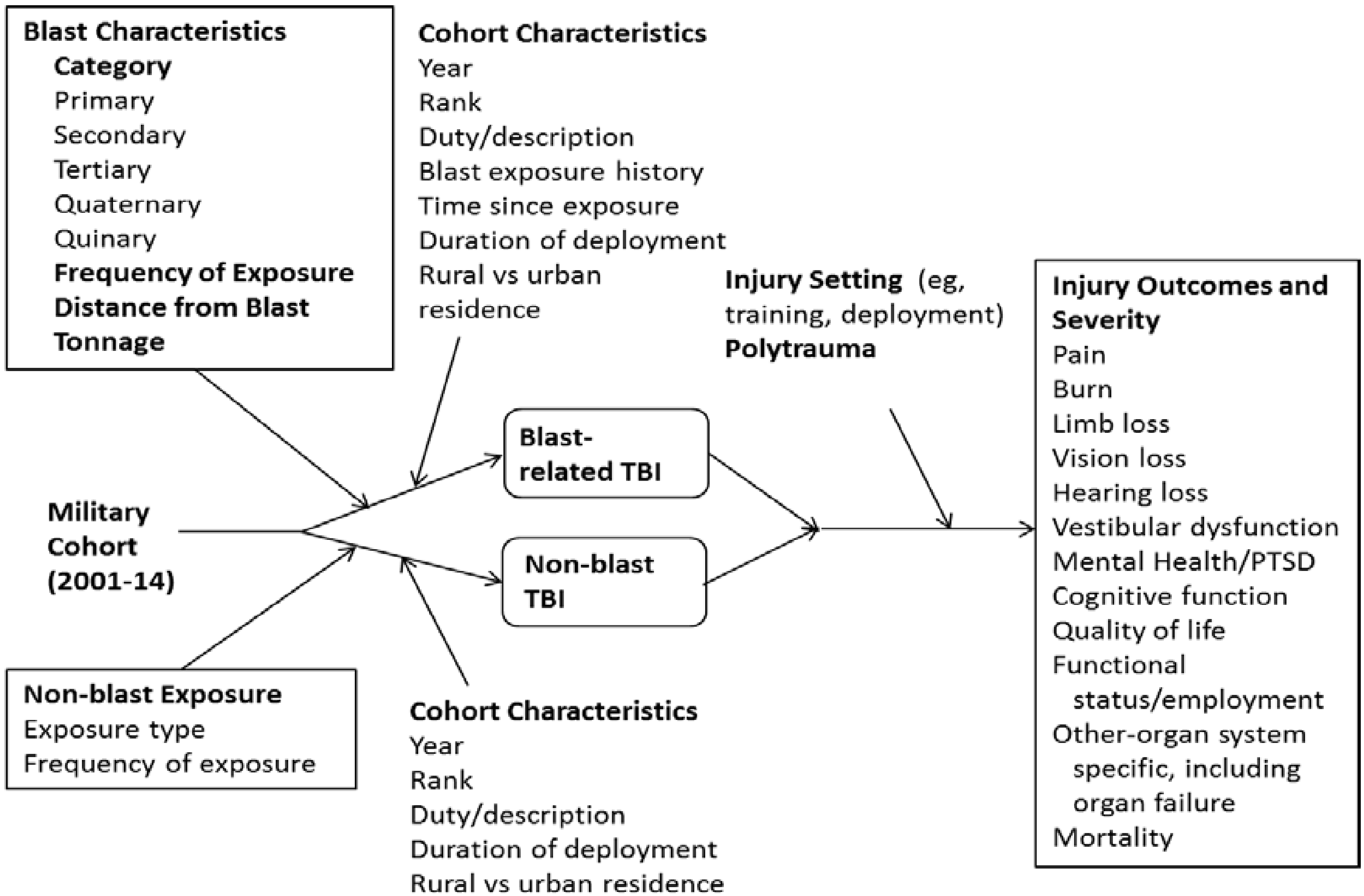


Figure 2. Analytic Framework for Key Question 3



METHODS

TOPIC DEVELOPMENT

This topic was nominated by Ralph DePalma, MD, Special Operations Office, Office of Research and Development. Additional stakeholders included: David Cifu, MD, Chair, VHA TBI Advisory Committee; Stuart Hoffman, PhD, Scientific Program Manager for Brain Injury, Rehabilitation Research and Development Service; and Col. Todd Rasmussen, MD, Director, Combat Casualty Care Research Program, US Army Medical Research and Materiel Command. Information on the incidence and prevalence of combat blast injuries and the outcomes of blast-related and non-blast TBI may be used to allocate research funding appropriately to improve care for Veterans with blast injuries and/or TBIs.

SEARCH STRATEGY

We searched MEDLINE (Ovid) for articles published in English from 2000 through April 2015 using separate search strategies for Key Questions 1 and 2 and Key Question 3. Our searches were designed to identify studies of combat injuries in US military personnel during OEF, OIF, and OND. The searches included the MeSH terms Brain Injuries; Wounds, Nonpenetrating; Wounds, Penetrating; Afghan Campaign 2001-; Iraq War, 2003-2011; and Military Personnel. The full search strategies are presented in Appendix A. We obtained additional articles by hand-searching the table of contents of Journal of Trauma-Injury Infection & Critical Care and reference lists of systematic reviews and other reports, and from references suggested by the topic stakeholders and TEP members.

STUDY SELECTION

Abstracts from the MEDLINE searches were reviewed in duplicate by investigators and research associates and abstracts from the table of contents search were reviewed by a single investigator. We identified for full-text review studies of any design potentially relevant to the key questions. Two investigators or research associates independently reviewed full-text articles excluding the following:

- Studies not including US military personnel from OEF, OIF, or OND (2000-2014);
- Studies not involving combat injuries;
- Modeling studies (*eg*, mechanical/engineering models, animal studies);
- Studies not relevant to the key questions;
- Studies of treatment outcomes;
- Imaging studies or studies reporting changes in tissue (*eg*, white matter);
- Case reports;
- Studies for Key Questions 1 and 2 where the denominator was not the number deployed during the study period (*ie*, reports of injuries at a medical facility were excluded); and
- Studies for Key Question 3 that did not report outcomes of interest for blast-related TBI and non-blast TBI groups (*ie*, studies only reporting on blast-related TBI were excluded).

DATA ABSTRACTION

For Key Questions 1 and 2, study characteristics (data source, inclusion/exclusion criteria, cohort characteristics) and outcomes (blast injury incidence, blast injury prevalence) were extracted into evidence tables by one investigator or research associate and verified by another. For Key Question 3, study characteristics (data source, inclusion exclusion criteria, cohort characteristics, outcome measures used) and outcomes (mortality, pain, burns, limb loss, vision loss, hearing loss, vestibular dysfunction, PTSD, cognitive function, quality of life, functional status/employment, other) for blast-related TBI and non-blast TBI patients were extracted into evidence tables by one investigator or research associate and verified by another.

RISK OF BIAS ASSESSMENT

We did not assess the risk of bias of the included studies, although risk of bias for each study was likely moderate or high due to the study design used, selective population studied, and failure to control for potential confounding factors.

DATA SYNTHESIS

We created summary tables with incidence and prevalence results (Key Questions 1 and 2). We organized evidence tables for Key Question 3 by outcome and time since exposure (<30 days, 30 days to 1 year, >1 year, or not specified). Pooled analyses were not possible due to heterogeneity of the study populations and outcome measures.

RATING THE BODY OF EVIDENCE

We did not formally rate the overall strength of evidence for outcomes. The typical approach to assessing strength of evidence considers consistency, precision, directness, and risk of bias of the included studies. However, because included studies were observational and there was limited reporting of outcomes of interest (*ie*, most outcomes reported in only a few studies and often using different measures), it is unlikely that strength of evidence would be anything above low. Many outcomes had insufficient evidence.

PEER REVIEW

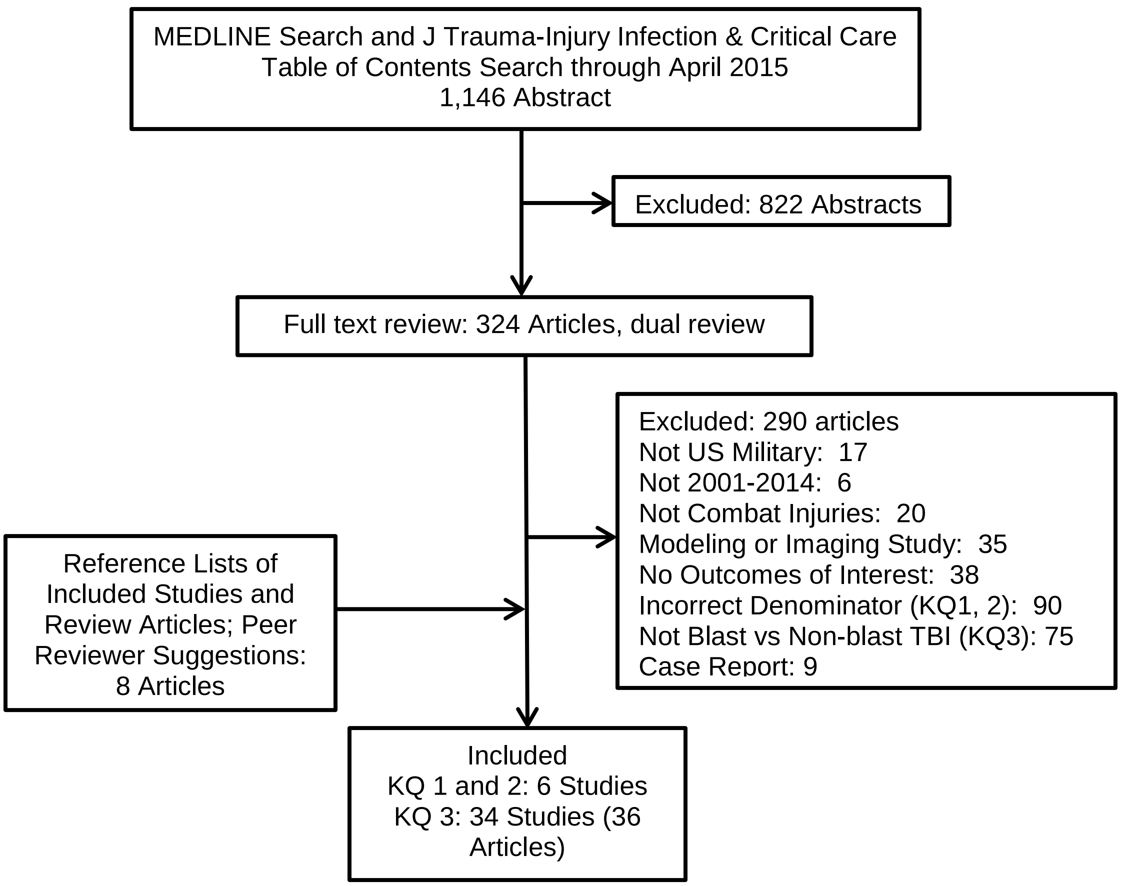
A draft version of this report was reviewed by content experts as well as clinical leadership. Reviewer's comments and our responses are presented in Appendix B and the report was modified as needed.

RESULTS

LITERATURE FLOW

Our literature searches yielded 1,146 abstracts (Figure 3). We identified 324 articles for full-text review and excluded 290. We identified an additional 8 articles by hand-searching resulting in a total of 42 included articles (6 for Key Questions 1 and 2, 36 from 34 studies for Key Question 3).

Figure 3. Literature Flow Chart



KEY QUESTION #1: What is the *incidence* of combat blast injuries associated with OEF, OIF, and OND as reported in the literature or in published reports from Department of Defense (DoD) and VA databases during the period 2001-2014?

KEY QUESTION #1A: What is the *incidence* by blast characteristics (*ie*, primary, secondary, tertiary, quaternary, and quinary), injury site, and injury outcome?

KEY QUESTION #2: What is the *prevalence* of combat blast injuries associated with OEF, OIF, and OND as reported in the literature or in published reports from Department of Defense (DoD) and VA databases during the period 2001-2014?

KEY QUESTION #2A: What is the *prevalence* of blast injury by blast characteristics, injury site, and injury outcome?

Overview of Studies

We identified 6 studies meeting inclusion criteria for Key Questions 1 or 2. These studies included data from 2001 to 2011; 5 used the Joint Theater Trauma Registry (JTTR)[6-10] and one used Department of Defense tabular reports.[11] Three of the JTTR studies were based on the same cohort of deployed service members with one reporting overall casualties,[8] one reporting musculoskeletal casualties,[7] and one reporting spinal injuries.[9] The JTTR (now the Department of Defense Trauma Registry [DoDTR]) was established in 2004 and contains information on all casualties (individuals lost to the theater of operations due to illness or injury) treated at US military medical facilities in and outside the combat zone. All but one study, which focused on the troop surge in Iraq,[6] included casualties from both Iraq and Afghanistan. The mean ages of service members in the study cohorts ranged from 26 to 30 years and 92% to 99% were male (k = 5 reporting). In the 4 studies that reported branch of service and rank, 78% to 100% were from the Army and the large majority (up to 93%) were from enlisted ranks. None of the studies provided information on deployment details including assigned or actual duties. Additional details are presented in Appendix C, Tables 1 and 2.

Key Question #1. Incidence

The National Institute of Mental Health has defined incidence as the number of new cases of a condition, symptom, death, or injury that develop during a specific time period.[12] We included registry studies that reported incidence of combat blast injuries for the deployed population (Table 1).

One study reported incidence of explosion (*ie,* improvised explosive device, mortar, rocket propelled grenade) injuries for the years 2005 to 2009.[8] Soldiers killed in action or sustaining non-battle injuries were not included in the analysis. The number of service members deployed and years of service were obtained through the Defense Manpower Data Center. The incidence was 4.5 explosion injuries per 1,000 deployed in 2005, 3.5 per 1,000 in 2006, 4.0 per 1,000 in 2007, 1.7 per 1,000 in 2008, and 1.7 per 1,000 in 2009. The slight increase in 2007 corresponded to the troop surge. Findings were also reported by country (Afghanistan versus Iraq).[8] In 2005 explosion injury incidence was higher in Iraq but beginning in 2008, the incidence was higher among soldiers deployed in Afghanistan.

A second report detailed all combat explosion injuries in a US Army Brigade Combat Team (n = 4,122) deployed during the 2007 troop surge in Iraq.[6] The cohort was followed for 6 months following the 15-month deployment. The incidence of explosion injuries was 83 per 1,000 deployed soldiers.

Table 1. Incidence Data

Outcome	2005	2006	2007	2008	2009	2010
Explosion injuries (*any*) per 1,000 deployed[6]			83[a]			
Explosion injuries (*any*) per 1,000 deployed[8]	4.5	3.5	4.0	1.7	1.7	
Explosion-related *musculoskeletal injuries* per 1,000 deployed[7]	3.5[b]	2.7[b]	3.1[b]	1.3[b]	1.3[b]	
Explosion-related *spinal injuries* per 1,000 deployed[9]	0.4[b]	0.4[b]	0.4[b]	0.2[b]	0.3[b]	
Blast-related *thoracolumbar burst* fractures per 10,000 soldier years[10]				0.45[c]	0.60[c]	2.08[c]

[a] All explosion injuries for a US Army Brigade Combat Team (n = 4,122) deployed during the 2007 troop surge
[b] Additional analysis of cohort described by in Belmont 2012
[c] Data from August of preceding year to August of specified year

Key Question #1a

No study reported incidence by blast characteristics (*ie*, primary, secondary, etc.) or injury outcomes (*eg*, pain, amputations, vision loss, cognitive function, functional status, quality of life). Three reported incidence by injury site (*ie*, body location or system injured) (Table 1).[7,9,10]

Two of the studies provided information about specific injury types for the service members deployed to Afghanistan or Iraq included in the cohort described by Belmont 2012.[8] One study identified explosion-related musculoskeletal injuries (upper and lower extremity, spine, and pelvis wounds including fractures, soft tissue injuries, joint dislocations, neurologic injuries, and traumatic amputations) during a 5 year period.[7] The incidence values (per 1,000 deployed soldiers) were 3.5 in 2005, 2.7 in 2006, 3.1 in 2007, 1.3 in 2008, and 1.3 in 2009. The other study reported on explosion-related spinal injuries finding 0.4 per 1,000 deployed soldiers in 2005, 2006, and 2007; 0.2 per 1,000 soldiers in 2008; and 0.3 per 1,000 soldiers in 2009.[9] The injuries included fractures, dislocations, disk displacements, nerve root injuries, and spinal cord injuries.

Another study looked specifically at combat thoracolumbar burst fractures, a pattern of injury that occurs as a result of vertical forces imparted by an explosion beneath an armored vehicle.[10] All soldiers who sustained this type of injury while deployed to Iraq or Afghanistan in 2007 to 2010 were identified through the JTTR and medical records from Landstuhl Regional Medical Center. The incidence increased from 0.45 per 10,000 soldier-years in the one-year period August 2007-2008, to 0.60 per 10,000 soldier-years in August 2008-2009, and 2.08 per 10,000 soldier-years in August 2009-2010. The increase in 2009-2010 was largely among soldiers serving in Afghanistan and the authors attributed to increased use of powerful improvised explosive devices against newer, up-armored vehicles. The authors speculated that with the newer military vehicles, explosives that might have caused deaths in the past were now associated with non-fatal burst fracture injuries.

Key Question #2. Prevalence

The National Institute of Mental Health has defined prevalence as the proportion of a population who have (or had) a specific condition in a given time period regardless of when they first acquired the condition.[12] For this review, we report cumulative data as prevalence. (Table 2)

Explosion-related injuries over a 5-year period (2005-2009) were reported for the Belmont et al cohort.[8] Among 1,992,232 soldiers deployed to Afghanistan or Iraq during that time period, there were 5,862 explosion injuries, or 0.29% of deployed soldiers experienced an explosion-related injury. Explosion injuries accounted for 74% of injuries.

Key Question #2a

No studies reported prevalence by blast characteristics (*ie,* primary, secondary, *etc*) or injury outcomes (*eg,* pain, amputations, vision loss, cognitive function, functional status, quality of life).

Four studies reported injuries to specific body sites or systems (Table 2). Two studies were additional analyses of the cohort reported by Belmont et al.[8] The study of musculoskeletal injuries reported 4,563 soldiers deployed to Afghanistan or Iraq with explosion-related injuries (0.23% of deployed soldiers).[7] Of all musculoskeletal injuries, 82% were explosion-related. By type of injury, 74% of axial skeleton fractures, 78% of upper extremity fractures, 84% of lower extremity fractures, 94% of amputations, 64% of neurologic injuries, 84% of joint dislocations, and 85% of soft tissue injuries were blast-related. Another analysis reported there were 650 soldiers with explosion-related spinal injuries (0.03% of deployed soldiers).[9] Of all spinal injuries, 75% were explosion-related. Among the 650 with explosion-related spinal injuries, 31% (n = 204) had injuries to more than one spinal region. Associated head and neck injuries were noted in 57% (n = 132) of soldiers with an explosion-related cervical spine injury.

The study of thoracolumbar burst fractures in Afghanistan or Iraq reported that over the period 2007-2010, the rate of blast-related fractures was 2.02 per 10,000 soldier years.[10] A Congressional Budget Office Working Paper reported major amputations (loss of a limb proximal to the wrist or ankle).[11] The prevalence was 38 per 100,000 troop years in OEF and OND and 88 per 100,000 troop years in OEF.

Table 2. Prevalence Data

Outcome	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Explosion-related injuries *(any)*[8]					74% of injuries 0.29% of 1,992,232 deployed (30.5 per 10,000 deployed)						
Blast-related *thoraco-lumbar burst fractures*[10]							2.02 per 10,000 soldier-years				
Explosion-related *musculo-skeletal injuries*[7]					82% of musculoskeletal wounds (14,158 wounds) 0.23% of 1,992,232 deployed (22.9 per 10,000 deployed)						
Explosion-related *spinal injuries*[9]					75% of spinal casualties 0.03% of 1,992,236 deployed (3.3 per 10,000)						
Improvised explosive device *major amputations*[11]	Iraq (OEF, OND): 38.3/100,000 troop-years Afghanistan (OEF): 87.8/100,000 troop-years										

Summary of Findings for Key Questions #1 and #2

One study reported explosion injury incidence from Afghanistan and Iraq, finding values ranging from 4.5/1,000 deployed in 2005 to 1.7/1,000 deployed in 2009. Another study reported data from the Iraq troop surge (2007), finding a high incidence of explosion injury (83/1,000 deployed in a US Army Brigade Combat Team). Three studies reported blast injury incidence by body location (musculoskeletal injuries, spinal injuries, or thoracolumbar burst fractures). No study reported incidence by blast characteristics.

Seventy-four percent of all combat injuries over the period from 2001 to 2011 were due to explosions. The prevalence was 30.5 per 10,000 deployed. The prevalence of explosion-related musculoskeletal injuries was 23 per 10,000 deployed; the prevalence of explosion-related spinal injuries was 3 per 10,000 deployed, the prevalence of blast-related thoracolumbar burst fractures was 2 per 10,000 soldier-years, and the prevalence of explosion-related major amputations ranged from 4 per 10,000 troop-years in Iraq to 9 per 10,000 troop-years in Afghanistan. No study reported prevalence by blast characteristics.

KEY QUESTION #3: What are the short-term (up to 30 days), mid-term (30 days to one year) and long-term (greater than one year) injury outcomes (*ie*, pain, burns, limb loss, vision loss, hearing loss, vestibular dysfunction, PTSD, cognitive function, quality of life, functional status/employment, other) among US military personnel (2001-2014) who have sustained a blast-related TBI versus a non-blast TBI or a combined blast/non-blast TBI?

Overview of Studies

We identified 34 studies (36 articles) reporting on outcomes associated with blast versus non-blast related TBI (Table 3). Six studies included data from registries or databases with sample sizes ranging from 604[13] to 12,521.[14] The remaining studies were clinical cohort studies with sample sizes ranging from 18[15] to 727.[16]

In 26 studies, patients were assessed at a medical facility (typically a DoD or VA hospital). Three studies assessed patients in combat zone facilities,[17-19] 2 included post-deployment assessment data,[20,21] one included both combat zone and post-deployment data,[22] one used a mailed questionnaire,[23] and location could not be determined for one study.[13]

The time from exposure to outcome assessment was less than 30 days for 3 studies[17,19,24] with another study including both an immediate assessment and a follow-up at 6 to 12 months.[18] One study assessed patients within 12 months of injury (50% within the first month).[25] Ten studies assessed outcomes between 30 days and one year from exposure and 5 at greater than one year. Fourteen studies included any time post-exposure or did not specify a time.

Eighteen studies included only patients with mild TBI (mTBI), one study included only patients with moderate or severe TBI,[13] 2 studies included patients with mild or moderate/severe TBI and reported results separately, 12 studies included any TBI (and did not report results by TBI severity), and one study reported some outcomes by TBI severity and some outcomes for the total sample.[20] Additional study characteristics are presented in Appendix C, Table 3.

Table 4 provides an overview of outcomes reported in these studies. The most frequently reported outcomes were PTSD, cognitive function, hearing impairment, and vision impairment. Few studies reported mortality, quality of life, limb loss, pain, or burn injuries. Findings for each outcome are reported below. More detailed outcome data are presented in Appendix C, Tables 4a to 4l.

Table 3. KQ3 Overview: Blast versus Non-blast TBI – Population and Study Characteristics

Author, year	Data Source		Sample Size	Characteristics									
				Location of Assessment			Time Since Exposure				TBI Severity		
	Registry/ Database	Clinical Cohort		Combat Zone	After Deployment	DoD, VA, or Other Medical Facility	< 30 days	30 days to 1 year	> 1 year	Any or Unclear	Mild	Moderate/ Severe	Mixed (results not reported separately)
Akin, 2011[15]		ü	18			ü				ü	ü		
Belanger, 2009[26]		ü	102			ü			ü		ü	ü	
Belanger, 2011[27]		ü	390			ü				ü	ü		
Brahm, 2009[28]		ü	192			ü				ü	ü	ü	
Clark, 2009[29]		ü	85			ü				ü			ü
Cockerham, 2013[30]		ü	53			ü		ü					ü
Collen, 2012[31]		ü	116			ü			ü				ü
Cooper, 2012[32]		ü	60			ü		ü			ü		
DuBose, 2011[13]	ü		604	?	?					ü		ü	
Fortier, 2014[33]		ü	56			ü			ü		ü		
French, 2014[25]		ü	579			ü		ü			ü		
Goodrich, 2013[34] Goodrich, 2014[35]		ü	100			ü		ü					ü
Hoffer, 2009[36]		ü	127			ü				ü	ü		
Kennedy, 2010[16]		ü	724			ü		ü			ü		
Kontos, 2013[22]	ü		2,813	ü	ü					ü	ü		
Lange, 2012[37]		ü	56			ü		ü			ü		
Lew, 2011[14]	ü		12,521			ü				ü			ü
Lew, 2007[38]		ü	150			ü				ü			ü
Lippa, 2010[39]		ü	194			ü			ü		ü		
Luethcke, 2011[17] Blast is primary blast; non-blast includes secondary, tertiary, quaternary, and non-blast		ü	82	ü			ü				ü		

Author, year	Data Source		Sample Size	Characteristics									
				Location of Assessment			Time Since Exposure				TBI Severity		
	Registry/ Database	Clinical Cohort		Combat Zone	After Deployment	DoD, VA, or Other Medical Facility	< 30 days	30 days to 1 year	> 1 year	Any or Unclear	Mild	Moderate/ Severe	Mixed (results not reported separately)
Mac Donald, 2014[18] Blast is blast plus other mechanism of head injury		ü	82[c]	ü[c]			ü[c]	ü[c]					ü
MacGregor, 2011[20]	ü		2,074		ü			ü			ü	ü	ü
Maguen, 2012[40]		ü	1,082 (968 for PTSD)			ü				ü			ü
Mendez, 2013[41] Mendez, 2013[42] Blast is primary blast only; non-blast is blunt injury		ü	24			ü			ü		ü		
Mora, 2009[43] Blast is IED exposure with primary blast injury; non-blast is IED exposure without primary blast injury		ü	19			ü		ü			ü		
Nakase-Richardson, 2013[44]		ü	106[b]			ü		ü					ü
Oleksiak, 2012[45]		ü	189			ü				ü	ü		
Pogoda, 2012[46]	ü		9,998			ü				ü	ü		
Reid, 2014[47]		ü	573			ü				ü	ü		
Sayer, 2008[48]		ü	188			ü		ü					ü
Schneiderman, 2008[23]		ü	275[e]					ü	ü		ü		
Wilk, 2010[21]		ü	574		ü			ü			ü		
Wojcik 2010[19]	ü		1,388[d]	ü			ü						ü

Author, year	Data Source		Sample Size	Characteristics									
				Location of Assessment			Time Since Exposure				TBI Severity		
	Registry/ Database	Clinical Cohort		Combat Zone	After Deployment	DoD, VA, or Other Medical Facility	< 30 days	30 days to 1 year	> 1 year	Any or Unclear	Mild	Moderate/ Severe	Mixed (results not reported separately)
Xydakis, 2012[24]		ü	256			ü	ü						ü

[a] Patients admitted to US Army Institute of Surgical Research burn center
[b] Patients admitted to Polytrauma Rehabilitation System of Care with a disorder of consciousness (DOC)
[c] Initial assessment in Germany (n = 123 with TBI); followed 6-12 months post-injury at Washington University (US) (n = 82)
[d] Episodes (TBI hospitalizations with mechanism of injury data)
[e] Responded to self-administered mail questionnaire
? = unclear

Table 4. KQ3 Overview: Blast versus Non-blast TBI – Summary of Outcomes

Author, year	Data Source		Sample Size	Outcomes Reported											
	Registry/ Database	Clinical Cohort		Mortality	PTSD	Pain	Burn	Limb Loss	Vision Impairment	Hearing Impairment	Vestibular Dysfunction	Cognitive Function Loss	Quality of Life	Functional Status/ Employment	Other
Akin, 2011[15]		ü	18								↔				
Belanger, 2009[26]		ü	102		↔							↔			
Belanger, 2011[27]		ü	390		-										↔Post-concussive symptoms
Brahm, 2009[28]		ü	192						↔						
Clark, 2009[29]		ü	85		-	↔	↔	-	↔	↔		↔		↔	↔Depression - Any psychiatric diagnosis
Cockerham, 2013[30]		ü	53						↔						
Collen, 2012[31]		ü	116		↔										↔Depression - Anxiety **MIXED** Sleep disorders
Cooper, 2012[32]		ü	60		↔										↔Headache
DuBose, 2011[13]	ü		604	↔											
Fortier, 2014[33]		ü	56												↔TBI severity
French, 2014[25]		ü	579												↔Injury severity
Goodrich, 2013[34] Goodrich, 2014[35]		ü	100		-				↔						
Hoffer, 2009[36]		ü	127								↔ **VOR MIXED VSR**				
Kennedy, 2010[16]		ü	724		↔										
Kontos, 2013[22]	ü		2,813		-							-			
Lange, 2012[37]		ü	56									↔			↔Personality
Lew, 2011[14]	ü		12,521						–	-					
Lew, 2007[38]		ü	150							-					

Author, year	**Data Source**		**Sample Size**	**Outcomes Reported**											
	Registry/ Database	**Clinical Cohort**		**Mortality**	**PTSD**	**Pain**	**Burn**	**Limb Loss**	**Vision Impairment**	**Hearing Impairment**	**Vestibular Dysfunction**	**Cognitive Function Loss**	**Quality of Life**	**Functional Status/ Employment**	**Other**
Lippa, 2010[39]		ü	194		**MIXED**										↔Post-concussive symptoms
Luethcke, 2011[17] Blast is primary blast; non-blast includes secondary, tertiary, quaternary, and non-blast		ü	82		↔				↔	- Immediate ↔ Current	↔	↔			↔Global mental health ↔Insomnia ↔Immediate headache ¯Current headache
Mac Donald, 2014[18] Blast is blast plus other mechanism of head injury		ü	82[c]		↔					↔				↔	↔Neuro-behavioral & neuro-psychological assessments ↔Depression severity ↔Headache ¯Smell ↔Alcohol misuse
MacGregor, 2011[20]	ü		2,074												- HNF injuries ↔Extremity injuries - Spine/back injuries ¯mTBI - Moderate & severe TBI
Maguen, 2012[40]		ü	1,082 (968 for PTSD)		-										↔Depression ↔Alcohol misuse

Author, year	Data Source		Sample Size	Outcomes Reported											
	Registry/ Database	Clinical Cohort		Mortality	PTSD	Pain	Burn	Limb Loss	Vision Impairment	Hearing Impairment	Vestibular Dysfunction	Cognitive Function Loss	Quality of Life	Functional Status/ Employment	Other
Mendez, 2013[41] Mendez, 2013[42] Blast is primary blast only; non-blast is blunt injury		ü	24									**MIXED**	↔		↔Post-concussive symptoms **-** Psychopathy ↔Behavior
Mora, 2009[43] Blast is IED exposure with primary blast injury; non-blast is IED exposure without primary blast injury		ü	19[a]		↔		**?**								**?**Injury Severity Score
Nakase-Richardson, 2013[44]		ü	106[b]									**MIXED**		–	¯Recovery of consciousness (vs other trauma)
Oleksiak, 2012[45]		ü	189							↔					
Pogoda, 2012[46]	ü		9,998												↔Multi-sensory
Reid, 2014[47]		ü	573		**-**				**-**	**-**	**-**	**-**			**-** Post-concussive symptoms **-** Sleep ↔Depression
Sayer, 2008[48]		ü	188	↔	**-**	↔	**-**	↔	↔ **-** Injury	**-**	↔	↔		↔	↔Sleep ↔Depression
Schneiderman, 2008[23]		ü	275[e]												↔Post-concussive symptoms
Wilk, 2010[21]		ü	574		↔	↔				**MIXED**	↔	**MIXED**		↔	↔Depression **MIXED** Headache ↔Sleep ↔Alcohol misuse
Wojcik 2010[19]	ü		1,388[d]												**?**Severity of TBI
Xydakis, 2012[24]		ü	256												**?**Severity of TBI

VOR = vestibular-ocular reflex; VSR = vestibular-spinal reflex
[a] Patients admitted to US Army Institute of Surgical Research burn center
[b] Patients admitted to Polytrauma Rehabilitation System of Care with a disorder of consciousness (DOC)
[c] Episodes (TBI hospitalizations with mechanism of injury data)
[d] Initial assessment in Germany (n = 123 with TBI); followed 6-12 months post –injury at Washington University (US) (n = 82)
[e] Responded to self-administered mail questionnaire
[f] Significance of findings is across blast exposure groups: 0 blasts, 1 blast, 2 blasts, 3 blasts, 4-10 blasts
- Higher prevalence or more severe in blast TBI group; ‾ Higher prevalence or more severe in non-blast TBI group; **↔** Blast and non-blast groups similar; **?** P value not reported; **MIXED** Multiple tests with mixed results

Mortality (k = 2) (Appendix C, Table 4a)

< 30 days post-exposure

One study included service members receiving polytrauma/TBI inpatient rehabilitation at a VA polytrauma rehabilitation center (PRC).[48] Of 188 patients studied, 106 had a blast exposure and 82 did not; 97% had a TBI. Mortality was 3% in the blast group and 1% in the non-blast group. Mortality was similar between the groups (P = .63).

Other

A second study was based on data from the JTTR.[13] Time from exposure to evaluation was not specified. The 604 patients included in the study had an isolated TBI: 374 were associated with a blast exposure, 118 from gunshot, and 112 following blunt trauma. Mortality was 9% in the blast group, 7% in the gunshot group, and 10% in the blunt trauma group. Relative to the blunt trauma group, the odds ratios for mortality in the blast and gunshot groups, respectively, were 0.66 (95% CI 0.31, 1.41) and 0.60 (95% CI 0.19, 1.89), respectively.

Posttraumatic Stress Disorder (PTSD) (k = 16) (Appendix C, Table 4b)

< 30 days post-exposure

One study reported short-term results.[17] Eighty-two military and civilian contractors were evaluated within 72 hours of injury in an outpatient TBI clinic at a forward-deployed combat support hospital (CSH). The blast and comparator groups had similar Posttraumatic Stress Disorder Checklist (PCL) scores. The blast group included only those with primary blast exposure while the comparator group included secondary, tertiary, quaternary, and non-blast exposures.

30 to 365 days post-exposure

Seven studies evaluated patients 30 days to one year after exposure with 5 including only patients with mTBI[16,21,32,43,48] and 2 including any TBI severity.[18,34,35] Studies used variable definitions of non-blast injury (*eg,* some studies included secondary blast injuries as non-blast injuries) which could affect the prevalence and outcomes of estimates. Five studies reported the percentage of patients with a PTSD diagnosis. In 4 of the 5 studies, the blast and non-blast groups were similar.[16,18,21,43] One was a study of 724 patients screened and identified with mTBI at a military medical center.[16] Another was a small study (n = 19) of mTBI patients treated at a military burn center. Blast cases had experienced an improvised explosive device (IED) primary blast while non-blast cases had IED exposure without primary blast injury.[43] The third was a study of 82 patients, 52 with blast exposure. Blast cases in this study had experienced a blast explosion plus another mechanism of head injury.[18] The fourth study included 574 patients who reported concussion. The patients were further categorized as having experienced a loss of consciousness or a change in consciousness. Prevalence of PTSD was similar for blast and non-blast groups in both subgroups.[21] The study finding higher prevalence of PTSD in the blast TBI group was designed to assess vision outcomes but also reported PTSD prevalence in the 100 patients. The prevalence of PTSD was 62% in the blast group and 20% in the non-blast group ($P<.001$).[35]

Two studies reported PCL scores finding similar scores for blast and non-blast TBI groups.[16,32] One was a study of 60 patients referred to a TBI clinic at an Army medical center for neuropsychological testing[32] and the other was a study of 724 patients described above.[16] A third study with 188 patients (described in the Mortality outcomes section) reported the prevalence of PTSD symptoms was higher in the blast TBI group (42% vs 24%, P<.01).[48]

In another study, the blast TBI patients (n = 298) were evaluated less than 365 days after exposure and the non-blast TBI patients (n = 92) were evaluated more than 365 days after exposure.[27] PCL scores were significantly higher in the blast TBI group (42 vs 37, P = .047).

> 365 days post-exposure

Two studies reported PTSD findings at more than 365 days after exposure. Among 116 soldiers with combat-related TBI (85% mTBI) receiving care at an Army medical center, the percentage of patients with a comorbid diagnosis of PTSD was similar for the blast and non-blast groups.[31] A study of 339 patients referred for TBI screening in the VA system reported that PCL total scores were similar for the blast and non-blast groups but a higher percentage of patients with blast-related mTBI had a PCL score of 50 or higher (65% vs 45%, P<.05).[39]

Other

Five studies reported PTSD findings at any time post-exposure or did not specify the time.[22,26,29,40,47] One study of 128 active duty personnel and Veterans admitted to a PRC (80% with TBI) found a higher prevalence of PTSD in the blast group (45% vs 12%, P<.05).[29] A registry study of 2,813 US Army Special Operations Command (USASOC) personnel who completed Web-based evaluations in both deployed and non-deployed settings found significantly higher odds of clinical levels of PTSD symptoms in the blast mTBI group compared to the blunt mTBI group (OR 2.12 [95% CI 1.68, 2.66]).[22] A study of 968 Veterans reported a higher odds of a positive PTSD screen in Veterans with a blast-only head injury compared to TBI with no head injury (OR 4.7 [95% CI 2.9, 7.7]) or a blast plus other mechanism of injury compared to TBI with no head injury (OR 6.5 [95% CI 4.6, 9.3]).[40] A study of 102 VA patients reported similar PCL scores between blast and non-blast groups.[26]

A study of 573 male service members with combat-related mTBI evaluated one to 24 months post-injury reported a significant difference in PCL scores across self-reported blast exposure groups (0 blasts, 1 blast, 2 blasts, 3 blasts, or 4 to 10 blasts).[47] Subsequent analyses showed only that the PCL score for the group exposed to 4 to 10 blasts was significantly higher than the score for the group exposed to one blast. The study of USASOC personnel also reported that PTSD symptom scores increased significantly with an increased number of diagnosed blast-related mTBIs.[22] The odds ratio for clinical levels of PTSD symptoms associated with 3 or more blast-related mTBIs compared to one blast mTBI was 1.74 (95% CI 1.19, 2.54). The odds ratio for 3 or more blast-related mTBIs compared to 2 blast-related mTBIs was not significant (OR 1.32 [95% CI 0.82, 2.14]).

Pain (k = 3) (Appendix C, Table 4c)

30 to 365 days post-exposure

Impairment associated with pain was similar for blast and non-blast mTBI groups in a study of 188 Veterans.[48] The percentage of US soldiers reporting back pain or arm, leg, or joint pain was similar between blast and non-blast mTBI groups and subgroups experiencing either loss of or change in consciousness.[21] The percentage of soldiers with stomach pain was significantly higher for the non-blast mTBI group among those with a change in consciousness (15% vs 6%, P = .01) but not those with a loss of consciousness.

Other

A third study of 128 patients admitted to a PRC (80% with TBI) did not specify the time post-exposure. Pain intensity scores and the number of pain sites were similar for blast and non-blast TBI patients.[29]

Burns (k = 3) (Appendix C, Table 4d)

30 to 365 days post-exposure

The study of 188 Veterans assessed 30 days to one year post-exposure reported a higher percentage of patients with skin or soft tissue burn injury in the blast-related mTBI group compared to the non-blast group (13% vs 4%, P<.05).[48] The small study (n = 19) of mTBI patients treated at a military burn center reported the percentage of total body surface area (TBSA) burned. The mean TBSA for the blast cases (IED primary blast) was 8.1% compared to 17.0% for the non-blast cases (IED without primary blast injury).[43]

Other

The study of 128 patients admitted to a PRC (described above) reported a similar percentage of patients with a burn diagnosis in the blast and non-blast groups.[29]

Limb Loss (k = 2) (Appendix C, Table 4e)

30 to 365 days post-exposure

In the study of outcomes at 30 days to one year post-exposure (n = 188), the percentage of Veterans with an amputation was similar between blast and non-blast exposures (9% vs 6%) with 10 amputations in the blast group and 2 in the non-blast group.[48]

Other

The second study reported a significantly higher percentage of amputations in the blast group (16% vs 3%, P<.05).[29]

Vision Impairment (k = 8) (Appendix C, Table 4f)

< 30 days post-exposure

The study of patients assessed at a forward-deployed CSH reported blast and comparator groups experienced a similar incidence of vision loss symptoms both immediately after the injury and when assessed within 72 hours of the exposure.[17] Blast was defined as primary blast exposure in this study; the comparator group included other blast exposures and non-blast injuries.

30 to 365 days post-exposure

The study of 188 Veterans (described above) reported a significantly higher incidence of eye injuries in the blast-related mTBI group (47% vs 26%, P<.01) but the groups were similar in incidence of vision impairment (58% vs 46%, P not significant).[48] The study of 100 Veterans admitted to a PRC and undergoing eye examinations reported the blast and non-blast groups were similar in percentage with ocular injury, monocular vision, vision complaints, reading complaints, and poor visual acuity (in the worse eye). More patients in the blast group reported light sensitivity (67% vs 33%, P = .002).[34,35] Another study of 53 Veterans reported a similar incidence of dry eye disease between blast and non-blast TBI patients. Measures of tear production and tear osmolarity were also similar.[30]

Other

Four studies did not specify the time post-exposure or included any time post-injury. A study of polytrauma inpatients (n = 68) and outpatients (n = 124) reported similar vision outcomes (subjective visual complaint, ocular injury, legally blind status) between blast and non-blast groups for the outpatients while for the inpatients one of the outcomes, ocular injury, was significantly higher for the blast group (44% vs 9%, P = .04).[28] The study of 573 male service members evaluated at one to 24 months post-injury reported a significant difference across blast exposure groups for scores on the "vision problems, blurring, trouble seeing" component of the Neurobehavioral Symptom Inventory (NSI).[47] The highest score was observed in the group with 4 to 10 blast exposures. The study of 128 patients admitted to a PRC (described above) reported similar percentages with eye injury in the blast and non-blast groups.[29] A database study of 12,521 patients with deployment-related TBI reported a higher percentage of patients with visual impairment only in the non-blast group (16% vs 9%, P<.001).[14]

Hearing Impairment (k = 9) (Appendix C, Table 4g)

< 30 days post-exposure

The study of patients assessed at a forward-deployed CSH reported that a higher percentage of blast-exposed patients experienced hearing loss symptoms immediately after the injury (53% vs 17%, P = .001) but the groups were similar when assessed within 72 hours of the exposure.[17] The blast group included only primary blast-exposed patients.

30 to 365 days post-exposure

The study of 188 Veterans (described above) reported a higher percentage of patients in the blast group with otologic injury (46% vs 23%, P<.01), hearing loss (48% vs 33%, P<.05), and tinnitus (26% vs 12%, P<.05).[48] The study of soldiers with concussion reported a higher percentage reporting ringing in ears in the blast group among those who experienced loss of consciousness (34% vs 15%, P = .02) but not among those who experienced change in consciousness (22% vs 17%, P = .32).[21] In the study of 82 patients where blast was defined as blast plus another mechanism of head injury, the percentage of patients reporting hearing deficit was similar for the blast and non-blast groups.[18]

Other

Among the studies that did not specify a time post-exposure, the study of 128 patients admitted to a PRC found the percentage with "hearing problems" was similar for blast and non-blast groups.[29] The database study with 12,521 patients reported greater auditory impairment only in the blast group compared to the non-blast group (33% vs 23%, P<.001). The percentages of patients with dual sensory impairment were similar between groups (35% vs 30%).[14] An earlier, smaller study from this group (150 Veterans admitted for inpatient rehabilitation) found a greater percentage of patients in the blast group with hearing loss (62% vs 44%, P = .04) and tinnitus (38% vs 18%, P = .007).[38] The study of 573 male service members evaluated at one to 24 months post-injury reported a significant difference across blast exposure groups for scores on the "hearing difficulty" component of the NSI.[47] The highest score was observed in the group with 4 to 10 blast exposures. In a study of 198 Veterans with confirmed mTBI, "hearing difficulty" (from the NSI) was similar for blast and non-blast groups.[45]

Vestibular Dysfunction (k = 6) (Appendix C, Table 4h)

< 30 days post-exposure

The study that evaluated 82 patients at a forward-deployed CSH reported that blast (primary blast only) and comparator (other blast and non-blast exposure) groups were similar in balance and dizziness symptoms both immediately following the injury and at the time of assessment (72 hours or less post-exposure).[17]

30 to 365 days post-exposure

The studies evaluating 188 Veterans[48] or 574 soldiers with concussion[21] at 30 days to one year post-exposure reported blast and non-blast groups were similar in balance/equilibrium impairment[48] and dizziness or balance problems.[21] In the latter study, the groups were similar whether the patients had experienced loss of or change in consciousness.[21]

Other

Two studies did not report time since exposure and one included assessments at one to 24 months post-exposure. In one, a study of 18 Veterans referred to a VA Vestibular/Balance Laboratory for complaints of dizziness and/or imbalance, the mean Dizziness Handicap Inventory score for the blast-related mTBI group was in the "severe" range while the mean for the non-blast group was in the "moderate" range.[15] No statistical significance was reported. The percentage of patients with abnormal results for the Sensory Organization Test was similar between groups. Another study, conducted at a Naval medical center, included tests for vestibular-ocular reflex (VOR, n = 55) and vestibular-spinal reflex (VSR, n = 72).[36] Some "descriptive differences" were noted between blast and blunt force groups in the VOR study. In the VSR study, there was a trend toward better scores on the Sensory Organization Test in the blunt exposure group while significantly more patients in the blast exposure group had abnormal latency times on a Motor Control Test. The study of 573 male service members evaluated at one to 24 months post-injury reported a significant difference across blast exposure groups for scores on the "loss of balance" component of the NSI.[47] The highest score was observed in the group with 4 to 10 blast exposures.

Cognitive Function Loss (k = 10) (Appendix C, Table 4i)

< 30 days post-exposure

The study from the forward-deployed CSH reported that blast (primary blast only) and comparator (other blast and non-blast exposures) groups had similar cognitive function scores when assessed at 72 hours or less post-exposure.[17]

30 to 365 days post-exposure

In a study of 60 service members referred to an Army medical center for neuropsychological testing, the cognitive functioning assessment yielded similar results for the blast and non-blast groups.[32] Another study of patients evaluated at an Army medical center following medical evacuation from the OEF/OIF combat theater found significant between-group (blast/non-blast) differences for 2 of 12 measures in a neurocognitive test battery with poorer performance by the non-blast group.[37] A study of 106 patients admitted to a polytrauma rehabilitation clinic with a disorder of consciousness found blast and non-blast groups had similar changes in cognitive scores from admission to discharge. The blast group improved by one point on an 8-point scale while the non-blast group with penetrating trauma improved by 2 points and the non-blast group with other trauma improved by 3 points. Similar results were observed for the cognitive component of the Functional Independence Measure (FIM).[44] The study of 188 Veterans receiving inpatient VA polytrauma/TBI inpatient rehabilitation services (described previously) reported that blast and non-blast groups were similar in the percent reporting cognitive impairment (88% vs 93%).[48] The study of 574 soldiers with concussions reported that similar percentages of the blast and non-blast groups that experienced loss of consciousness had memory problems (31% vs 30%, P = 1.0) or concentration problems (32% vs 34%, P = .85). In the blast and non-blast groups that experienced a change in consciousness, there was a higher percentage that experienced memory problems in the non-blast group (31% vs 18%, P = .01) while the percentage with concentration problems was similar (35% vs 24%, P = .05).[21]

> 365 days post-exposure

One study assessed cognitive function at more than 365 days post-exposure.[42] Three instruments were used and results were mixed. The blast group (defined for this study as primary blast force only) performed worse than the non-blast (blunt force) group on a serial addition test but the groups were similar on tests of "executive operations" and mental flexibility/decision-making.

Other

In 2 of the 4 studies reporting cognitive function outcomes but not specifying a time post-exposure, blast and non-blast groups had similar outcomes. One study enrolled 102 Veterans and reported similar scores on 4 neuropsychological tests.[26] The other enrolled 128 active duty personnel and Veterans and reported similar scores on a test of cognitive deficits associated with recovery from brain injury.[29] The third study, a database study of 2,813 USASOC personnel (described above), reported poorer performance in the blast mTBI group on tests of visual memory, visual processing speed, and reaction time. The groups were similar on the verbal memory test.[22] The fourth study, with 573 male service members evaluated at one to 24 months post-injury, reported a significant difference across blast exposure groups for scores on the cognitive element of the NSI.[47] The highest score was observed in the group with 4 to 10 blast exposures.

Quality of Life (k = 1) (Appendix C, Table 4j)

> 365 days post-exposure

One study reported quality of life based on responses to the Health-Related Quality of Life 36-item Short Form (SF-36).[42] Participants were 24 Veterans undergoing a Second Level TBI evaluation at a VA medical center and mean time from exposure was over 4 years. Blast-related injury was defined as injury due to primary blast force. SF-36 scores (Physical Composite, Mental Composite, and all sub-scales) were similar for the blast and non-blast (blunt) groups.

Functional Status/Employment (k = 5) (Appendix C, Table 4k)

30 to 365 days post-exposure

One study of 82 active duty US military evacuated from Iraq and Afghanistan and followed up in the US 6 to 12 months later found that blast and non-blast TBI groups were similar on a global outcome measure of disability.[18] The percentages of patients categorized as having moderate to severe disability were also similar (77% blast, 79% non-blast, P = .84). In this study, participants with a blast injury also had some other mechanism of head injury.

A study of 122 patients admitted to VA polytrauma care with a disorder of consciousness assessed functional independence at admission and discharge.[44] There was no change over time for the blast TBI group or for the non-blast TBI group that had experienced penetrating trauma. There was a significant change over time for the non-blast TBI group that had experienced "other trauma" relative to both the blast injury and penetrating trauma groups. In a similar population of 188 service members, 62% of the blast injury group and 65% of the non-blast injury group reported motor functioning impairment (P not significant).[48]

The study of 574 soldiers with concussion data reported on workdays missed.[21] The percentages reporting 2 or more missed workdays due to illness were similar in the blast and non-blast mTBI groups for the subgroups reporting loss of consciousness (21% vs 23%, P = .83) or change in consciousness (17% vs 10%, P = .11).

Other

One study that did not specify the time since exposure reported functional independence scores.[29] The scores for the blast and non-blast groups were similar.

Other Outcomes (Appendix C, Table 4l)

Depression (k = 7)

Seven studies reported on either depression diagnosis[21,29,31,40] or depression symptoms/severity.[18,47,48] All studies found blast and non-blast TBI groups to be similar. Three studies assessed outcomes 30 to 365 days post-exposure,[18,21,48] one at more than 365 days,[31] and 3 at unspecified or any time post-exposure.[29,40,47]

Insomnia (k = 5)

In 3 studies, blast and comparator groups had similar scores for insomnia severity (assessed less than 30 days post-exposure),[17] sleep impairment (assessed 30 to 365 days post-exposure),[48] and sleep problems (also at 30 to 365 days post-exposure).[21] A study of 573 male service members evaluated at one to 24 months post-injury reported a significant difference across blast exposure groups for scores on the “difficulty falling or staying asleep” component of the NSI with the highest score in the group with 4 to 10 blast exposures.[47] One study of 116 soldiers receiving care at an Army medical center and assessed more than 365 days post-exposure reported higher levels of insomnia in the blast injury group (63% vs 40%, P = .02) but fewer with a diagnosis of obstructive sleep apnea syndrome (26% vs 54%, P = .003) and lower mean scores on the Epworth Sleepiness Scale (9 vs 11, P = .04).[31]

Headache (k = 4)

Two studies, both assessing outcomes at 30 to 365 days post-exposure, reported that blast and non-blast TBI group were similar on measures of headache impact[32] or migraine disability.[18] Another study found similar percentages of patients in the blast (primary blast only) and non-blast groups with headache symptoms immediately post-injury (70% vs 81%, P = .25) but within 72 hours, there was a higher percentage with headache symptoms in the comparator (other blast and non-blast exposure) group (53% vs 83%, P = .003).[17] A fourth study reported a higher percentage of patients with headache in the blast with loss of consciousness group than the non-blast loss of consciousness group (40% vs 23%, P = .04) while the percentages of patients with headache in the blast and non-blast change in consciousness groups were similar (21% vs 18%, P = .57). Outcomes were assessed 30 to 365 days post-exposure.[21]

Severity of TBI (k = 4)

Four studies provided a measure of whether TBI severity differed between blast and non-blast exposures. A database study of 1,388 soldiers hospitalized with a TBI and a known associated mechanism of injury, found that 55% of explosion-related TBIs were Type 1 (most severe), 39% were Type 2, and 6% were Type 3 (least severe).[19] For non-blast TBIs the corresponding percentages were 43%, 50%, and 6%. Alternatively, 68% of the Type 1 (most severe) TBIs, 56% of the Type 2, and 63% of the Type 3 (least severe) were explosion-related. Statistical significance was not reported.

A study of polytrauma patients with combat-related closed head injuries (blunt or blast mechanism) requiring immediate evaluation at an Army medical center in the US reported that the percentages of patients with mTBI (68% of blast mechanism injuries, 58% of blunt mechanism injuries, P = .21), moderate TBI (28% vs 33%, P = .51), or severe TBI (5% vs 9%, P = .32) were similar for the blast mechanism and blunt mechanism groups.[24]

In a larger, database study (n = 2,074) of injured personnel who completed post-deployment health assessments within 365 days of injury, there were significant differences between the blast and non-blast groups.[20] Of 1,852 with mTBI, 98% had a blast injury and 2% had a non-blast injury. Of 90 with moderate TBI, 84% had a blast injury and 16% had a non-blast injury. Of 143 with severe TBI, 67% had a blast injury and 33% had a non-blast injury. Alternatively, of 1,987 with a blast injury, 92% had mTBI (vs 34% of the 87 with a non-blast injury), 4% had moderate TBI (vs 16% of the non-blast group), and 4% had severe TBI (vs 50% of the non-blast group).

In one study of 56 Veterans with military TBI assessed more than 365 days post-exposure, the percentages of patients in the blast and non-blast groups with Type 1 TBI (most severe), Type 2 TBI, or Type 3 TBI (least severe) were similar.[33]

Alcohol Misuse (k = 3)

Blast and non-blast groups were similar regarding alcohol misuse in 3 studies that reported this outcome. One was a study of 82 active duty US military evacuated from Iraq or Afghanistan with follow-up assessment 6 to 12 months later.[18] Blast-exposed service members had also experienced another mechanism of head injury. Another was a study of Veterans (n = 968 completing the alcohol misuse evaluation) that did not specify the time from blast exposure to assessment.[40] The third was the study of 574 with concussion (either loss of consciousness or change in consciousness) and outcomes assessed 30 to 365 days post-exposure.[21]

Post-concussive Symptoms (k = 5)

Five studies reported that blast and non-blast groups were similar on measures of post-concussive symptoms including a study of 339 Veterans with mTBI,[39] a study of 390 Veterans with mTBI,[27] a study of 24 Veterans that defined blast injury as primary blast only and non-blast as blunt force injury,[42] and a survey study with 275 reporting mTBI.[23] Two of the studies assessed outcomes more than 365 days post-exposure;[39,42] in the survey study, participants were more than 30 days post-exposure.[23] In the other study, the blast TBI patients (n = 298) were evaluated less than 365 days after exposure and the non-blast TBI patients (n = 92) were evaluated more than 365 days after exposure.[27] A fifth study, with 573 male service members evaluated at one to 24 months post-injury, reported a significant difference across blast exposure groups for scores on the NSI.[47] The highest score was observed in the group with 4 to 10 blast exposures and scores in that group were significantly different from the groups with no blast exposure or exposure to one or 2 blasts.

Injury Severity (k = 1)

A study of 579 male service members evaluated within 12 months of injury categorized severity of bodily injuries (excluding injury to the brain) as minor, moderate, serious, or severe/critical.[25] Severity of injury was not related to mechanism (blast versus non-blast) of injury.

Multisensory Impairment (k = 1)

A study of 9,998 Veterans (95% male) completing the VA comprehensive TBI evaluation (CTBIE) assessed multisensory impairment – the co-occurrence of self-reported auditory, visual, and vestibular impairment.[46] Relative to those with no reported etiology of injury, the odds ratios for predicting multisensory impairment were 1.00 (95% CI 0.80, 1.25) for those with one or more non-blast injuries and 1.03 (95% CI 0.84, 1.25) for those with one or more blast injuries.

KEY QUESTION #3A: What are the short-term (up to 30 days), mid-term (30 days to one year) and long-term (greater than one year) injury outcomes among US military personnel (2001-2014) who have sustained a blast-related TBI according to blast characteristics?

Few studies reported outcomes according to blast characteristics. One study of hearing outcomes in Veterans with confirmed mTBI reported findings for subgroups based on the type of blast injury (primary [n = 62] or secondary [n = 11]). Time since exposure was not reported. Hearing difficulty scores were similar for the 2 subgroups (2.1 for the primary blast group, 1.8 for the secondary blast group). A score of one represented mild and a score of 2 moderate hearing difficulty. The percentage of patients with a score of greater than one was also similar (94% primary, 100% secondary).[45]

Three studies defined blast injury as primary blast force only.[17,41-43] In one of these studies, mTBI patients were evaluated at a forward-deployed CSH within 72 hours of injury.[17] The comparator group included patients experiencing secondary, tertiary, and quaternary blast injuries along with injuries not involving blasts. The blast group was similar to the comparator group for most outcomes (PTSD symptoms, vision symptoms, hearing symptoms at the time of assessment, vestibular dysfunction symptoms, cognitive function, insomnia, global mental health, and headache immediately following injury). The blast group reported more or more-severe hearing symptoms and lesser headache symptoms at the time of assessment.

The second study reported outcomes for 24 Veterans assessed at a mean of 4 years post-exposure.[41,42] Of the 12 “blast-injury” (primary blast) subjects, 10 reported the blast was less than 10 feet from their location at the time of the blast, one reported less than 30 feet, and one reported less than 50 feet. The blast group was similar to the non-blast (blunt force) group on measures of quality of life, post-concussive symptoms, personality, and behavior. Scores on a measure of interpersonal behaviors associated with psychopathy were higher for the blast group. Results were mixed for cognitive outcomes with the blast group scoring poorer on one measure and blast and non-blast groups being similar on 2 measures.

The third study evaluated 19 mTBI patients treated at a military burn center 30 to 365 days post-exposure.[43] Six had primary blast injury associated with an IED and 13 had been wounded in an IED explosion but had not sustained a primary blast injury. The prevalence of PTSD was similar for the blast and non-blast groups. The mean injury severity score was lower in the blast group (7.8 vs 15.0) as was the measure of burn severity (TBSA, 8.1% vs 17.0%) but it was not reported if the differences were significant.

Summary of Findings for Key Question #3

In 34 studies of injury outcomes among military personnel sustaining a blast or non-blast TBI, we found blast and non-blast groups to be similar in terms of mortality, pain, vision loss, vestibular dysfunction, functional ability, depression, sleep disorders, alcohol misuse, and post-concussive symptoms. The results were consistent across studies despite the fact that these studies varied in sample size, location of assessment, time from exposure to assessment, and level of TBI severity.

There were less consistent findings for some outcomes. A diagnosis of PTSD or PTSD symptom severity was higher in the blast groups in 7 studies. An additional 8 studies found the blast and non-blast groups to be similar and one reported mixed results for different ways of reporting PTSD. Four studies reported greater hearing loss in the blast injury group while 3 other studies reported the blast and non-blast groups were similar. Two reported mixed results; one of these studies looked at immediate post-injury hearing loss and current hearing loss (with current defined as within 72 hours of injury) and reported greater hearing loss in the blast group early post-injury but no difference at the later assessment. Cognitive outcomes also were less consistent. Five studies reported that blast and non-blast groups were similar, 2 reported greater cognitive impairment in the blast group, and 3 reported mixed results across different measures or across subgroups within the study. For the headache outcome, 2 studies reported that the blast and non-blast groups were similar and 2 reported mixed results depending on time of assessment or state of consciousness following the exposure.

Other outcomes were rarely reported making conclusions difficult. Three studies reported burn and 2 reported limb loss. One study reported an increased percentage of patients with burn injuries in the blast group compared to the non-blast group while another reported the percentages with a burn diagnosis were similar in the 2 groups. The third reported that the total body surface area effected was similar in blast and non-blast TBI groups admitted to a burn center. One study reported an increased number of amputations in the blast group while the other reported that the groups were similar. Level of quality of life was reported in just one study with blast and non-blast groups similar.

There is little data on outcomes according to blast characteristics. One study reported similar hearing outcomes for groups who experienced either primary or secondary. Three studies that defined blast injury as due to primary blast force reported few differences between their blast injury group and comparator groups.

SUMMARY AND DISCUSSION

SUMMARY OF EVIDENCE BY KEY QUESTION

Key Questions 1 and 1a – Incidence

- The published literature provides limited information about the true incidence and prevalence of blast-related injuries experienced by US military personnel. Findings are likely influenced by assessment and reporting methods.
- The reported explosion injury incidence ranged from 4.5/1,000 deployed in 2005 to 1.7/1,000 deployed in 2009.
- During the Iraq troop surge (2007) explosion injury incidence was particularly high (83/1,000 deployed in a US Army Brigade Combat Team).
- Musculoskeletal explosion injury incidence (fractures, amputations, neurological injuries, joint dislocations, and soft tissue injuries) ranged from 3.5/1,000 deployed in 2005 to 1.3/1,000 deployed in 2009.
- Spinal injury incidence (fractures, dislocations, nerve root injuries, spinal cord injuries) ranged from 0.18/1,000 deployed in 2008 to 0.40/1,000 deployed in 2005.
- Thoracolumbar burst fracture incidence was low (0.45 to 2.1 per 10,000 soldier years between 2008 and 2010) but higher in Afghanistan than Iraq and increased over the study period.
- No study reported incidence by blast characteristics.

Key Question 2 and 2a – Prevalence

- Nearly three-quarters of all combat injuries over the period from 2005 to 2009 (31 per 10,000 deployed) were due to explosions.
- A high proportion of musculoskeletal injuries (82%; 23 per 10,000 deployed) and spinal injuries (75%; 3 per 10,000 deployed) between 2005 and 2009 were due to explosions. Of the musculoskeletal injuries, 80% of axial skeletal and extremity fractures, 94% of amputations, and 85% of soft tissue injuries were explosion-related. Another study reported explosion-related amputations in 4 per 10,000 troop-years (Iraq) and 9 per 10,000 troop-years (Afghanistan) over the period from 2001 to 2011.
- No study reported prevalence by blast characteristics.

Key Question 3

- The published literature provides limited information on outcomes associated with blast versus non-blast TBI experienced by US military personnel. Definitions of blast/non-blast injury, assessment of outcomes, and reporting methods vary and often are based on small selected groups.

- Blast and non-blast TBI groups had similar rates of pain, vision loss, vestibular dysfunction, functional ability, depression, sleep disorders, alcohol misuse, and post-concussive symptoms.

- Comparative outcomes in individuals with blast versus non-blast TBI were inconsistent across studies with regard to PTSD diagnosis or symptom severity, hearing loss, cognitive function, and headache in blast and non-blast TBI groups.

- Mortality, burn injuries, limb loss, and quality of life were infrequently reported in studies comparing blast versus non-blast TBI.

- Results were consistent across studies that varied by location of assessment (combat zone, medical facility), time from exposure to assessment (< 30 days, 30 days to one year, or > one year), and level of TBI severity, although the most studies were small, clinical cohort studies, with mTBI patients evaluated at a DoD or VA medical facility.

- There is little data on outcomes among those with TBI according to blast characteristics.

DISCUSSION

Numerous studies have reported combat casualties but do not provide a denominator to allow for determination of true incidence or prevalence in the deployed population at risk.[49] For example, Ivey et al reported that 2,049 of 23,797 wounded US military personnel documented in the JTTR from January 2003 to May 2011 sustained thoracic injuries, a "prevalence" of 8.6%.[50] They further note that an explosive device was the source of injury for 62% of the thoracic injuries. However, these data do not allow a true determination of prevalence of thoracic injuries associated with explosive devices among deployed service members. Our literature search identified studies like the Ivey et al study for deaths (Eastridge 2012) and other types of injuries including spinal column, craniomaxillofacial, colorectal, ocular, otologic, and extremity.[51-56]

Similarly, we identified a recent systematic review and meta-analysis reporting the "prevalence" and characteristics of battle casualties in Iraq and Afghanistan.[57] The review included 8 studies spanning 2001 to 2013. Four of the studies are included in our review; the remaining 4 studies would not have been eligible for our review because they were either single facility or short-term studies, not published in English, and/or not predominantly US soldiers. Different studies addressed the casualty classifications (died of wounds, killed in action [KIA], wounded in action, and returned to duty) differently (*eg,* one study included only KIA; 2 other studies excluded KIA) but the results of all 8 studies were combined. Of 19,671 battle casualties, 14,056 (72%) were caused by blasts but, again, no denominator of deployed service members was provided.

The DoDTR (formerly the JTTR) is recognized as the best available source of data for the study of US military combat injuries, but it is not without limitations.[7] The DoDTR provides data on all combat casualty cases initially entering the Joint Theater Trauma System at Level III medical facilities (combat zone). Information is added to the DoDTR as the service member moves to an out-of-theater facility and ultimately to a facility in the United States (if required for their care). Disadvantages of the DoDTR include variations in the reliability of the data entered by non-researchers involved in the delivery of care, absence of data on service members killed in action or returned to duty (*ie,* not medically evacuated), and absence of data on US troops treated at

North Atlantic Treaty Organization Facilities prior to late 2008.[7,50] Furthermore, in 2007, the system for classifying mechanism of injury used in the JTTR was changed and injuries are now classified as primarily blunt or penetrating. As a result, blast injury is now less frequently reported.[50]

Few studies of blast incidence or blast-related TBI outcomes report any of the important characteristics of a blast injury: how far the individual was from the blast, whether they experienced a blast wave, whether there was loss of consciousness or altered consciousness, whether there was amnesia (and length of time), and whether there was additional trauma.[58] There have been attempts to document this information, however. Data from 367,555 service members who completed a Post-Deployment Health Assessment (PDHA) that included questions about possible TBI events experienced during deployments from 2012 to 2015 showed that 45.7% with a positive TBI screen experienced a blast or explosion.[59] Among those who reported the distance from the blast, the majority were less than 25 meters away. Over 30% reported receiving more than one concussive event during the deployment. Among those with a positive TBI screen, 11.5% reported 3 or more events.

We found no reports of blast injuries associated with different combat roles. One combat role considered to place soldiers at higher risk of injury due to repeated low-level primary blast exposure is that of breacher. Breachers place explosives on structures where access is needed and then stand at a “safe” distance away during the explosion. A study of US Marines enrolled in a 2-week Breacher Training Course focused on auditory and vestibular effects.[60] Clinically significant hearing loss was noted while the vestibular effects were “unremarkable.” A similar study enrolling US Marine instructors measured effects on vision.[61] The analysis included 9 breacher instructors (estimated to be exposed to 500 to 600 “low-level” blasts each year of a 2-to-3-year assignment) and a control group of 4 breacher engineers (not exposed to blasts) with repeat testing of both groups over a 2-year period. Vision test results for the blast-exposed group were within or slightly lower (worse) than normal ranges and symptom scores did not differ between blast-exposed and control. A study of 21 participants in a 2-week New Zealand military breacher training course where blast exposures occurred one to 20 times per day on 5 of the training days observed changes in neurocognitive performance and self-reported symptom scores warranting further investigation.[62] A report of neuropsychological and neurocognitive outcomes following a Canadian Explosives Forced Entry course (10 days of lectures and training on use of explosives to gain entry into building walls, doors, and windows) for police (4 instructors and 10 students) found no significant changes from baseline to the end of the course.[63]

LIMITATIONS

The limitations of this review relate to little published information on blast injuries and variations in reporting across studies. There is no information on incidence and prevalence of blast injuries by blast mechanism (*eg*, primary, secondary, tertiary, quaternary, quinary) and limited reporting in studies comparing blast and non-blast TBI. For determination of incidence and prevalence, there are also limited published data on numbers of soldiers deployed that accurately take into account factors such as true deployment length, combat intensity, and type of unit.[7] Clear and consistent definitions for injuries (*eg*, casualties, battle injuries, wounded in action, *etc*) and consistent standards for what to include in numerators and denominators when calculating incidence is necessary for accurate interpretation of combat trauma data.[64]

In the TBI studies, diagnoses and outcomes assessment were done at different time points following the blast and using different instruments, making comparisons across studies difficult. Reporting of symptoms may change over time and persistent or late-occurring symptoms may or may not be related to an earlier TBI.[4] For example, a recent study of 119,353 active duty US service members who began their first deployment in 2011 and were followed for approximately 4 years reported 11,498 first-time TBI diagnoses in the cohort including 2,525 prior to deployment, 3,086 during deployment, and 5,897 after deployment.[65] Cause of injury data were not complete and were not fully reported. In addition, authors used varying definitions of blast/non-blast injury. It was unclear whether the increased rate of TBI diagnoses post-deployment was a result of late diagnoses of TBI that occurred during deployment, delayed diagnoses during a more complete evaluation of severe injuries obtained during deployment, or increased post-deployment injury, possibly due to increased risk-taking behaviors.

Furthermore, confounding factors in studies of blast-exposed soldiers make it difficult to isolate the effects of the blast.[63] In studies comparing individuals with blast and non-blast TBI, outcomes such as headache, sleep disturbance, memory difficulties, and depression may be attributed to factors other than blast exposure (*eg,* deployment status, chronic pain and other physical injuries, substance use disorders).[4]

APPLICABILITY OF FINDINGS TO THE VA POPULATION

Our review was limited to studies of combat injuries associated with OEF, OIF, and OND. The findings are highly applicable to military personnel and organizations that provide direct acute or chronic health care services including rehabilitation as well as employment to those either currently serving or of recent Veteran status. Additionally, an understanding of the incidence, prevalence, outcomes, and causal factors of blast and non-blast injuries may be used to help reduce these injuries in future combat operations.

However, many studies reported findings from individuals presenting to medical facilities and undergoing treatment for a specific combat injury. Patient and injury characteristics and subsequent health outcomes from these selected patients may differ in unknown ways from the broader group of individuals who had combat injuries. We also have little information on very long-term effects (*eg,* cognitive function decline over decades).

The Analysis of VA Health Care Utilization among Operation Enduring Freedom (OEF), Operation Iraqi Freedom (OIF), and Operation New Dawn (OND) Veterans (released June 2015) reports that 1,906,754 OEF/OIF/OND Veterans have become eligible for VA health care since fiscal year 2002 (beginning October 1, 2001) and approximately 2.7 million troops (as of December 31, 2014) have served or are serving in the 2 theaters of operation since the beginning of the conflicts in Iraq and Afghanistan (http://www.publichealth.va.gov/docs/epidemiology/healthcare-utilization-report-fy2015-qtr1.pdf Accessed 10 August 2015). In 2007, the VA began a program of TBI screening and comprehensive. OEF/OIF/OND Veterans who present for care at a VA facility undergo a screen for TBI.[66] One of the screening questions addresses exposure to physical trauma. Veterans who screen positive for TBI undergo a comprehensive evaluation. An analysis of data from October 2007 to June 2010 found that 55% (30,267/55,070) of those evaluated for TBI after a positive screen were diagnosed with TBI. Of those, 36% had blast exposure and 44% had both blast and non-blast exposures.[67]

RESEARCH GAPS/FUTURE RESEARCH

In the Institute of Medicine's "Gulf War and Health, Volume 9: Long-term Effects of Blast Exposures," recommendations for future work highlighted the need to fill the gaps in the evidence base pertaining to the health effects of blast exposure and the need for greater emphasis on identifying and treating the complex injury patterns that often follow blast exposure. Collaborative efforts between the VA, DoD, and others were encouraged including the development of more complete registries with detailed information about the blast environment, information about both blast-injured and blast-exposed service members, and measurement of long-term health outcomes.[68]

Accurately recording in a standardized fashion every injury to every individual who experiences a blast (including type of blast [*eg*, primary, secondary, *etc*], distance from the blast, *etc*), and then following those individuals to assess long-term outcomes, would be ideal insofar as possible within the combat environment. However, for those who have been determined to have received blast-related injuries, additional information on the circumstances surrounding the injury should include: type of blast, distance from the blast, history of blast exposure, injury severity, assigned and actual duties, and military member's physical and psychosocial characteristics. Additional information gathered would be useful to evaluate methods to reduce combat-related blast injuries. Comparisons versus deployed controls may facilitate our understanding of the mechanisms and severity of blast-related injuries and the long-term health and social consequences of those injuries. This includes not only the treatments and health outcomes specific to the blast injury but also the long-term psychosocial, employment, and economic impact of blast injuries and the role and capacity needs for health care systems and the work force as these individuals reintegrate into the civilian society. Existing databases may already contain some of this information and future analyses should incorporate blast data where possible.

CONCLUSIONS

- The published literature provides limited information about the true incidence and prevalence of blast-related injuries experienced by US military personnel and the outcomes associated with blast versus non-blast TBI. We found no reports of incidence and prevalence of blast injuries associated with different combat roles.

- Few studies of incidence of blast-related injuries or outcomes associated with blast versus non-blast TBI report important characteristics of a blast injury: type of blast, how far the individual was from the blast, whether they experienced a blast wave, whether there was loss of consciousness or altered consciousness, whether there was amnesia (and length of time), and whether there was additional trauma.

- Only 6 studies, 3 of which were derived from the same data set, provide information about the incidence and prevalence of blast-related injuries in the deployed population at risk.

- Pain, vision loss, vestibular dysfunction, functional status, depression, sleep disturbance, alcohol misuse, and post-concussive symptoms were similar in groups of patients with blast and non-blast TBI. Findings were less consistent for PTSD, hearing loss, cognitive function, and headache. Few studies reported mortality, burn outcomes, limb loss, or quality of life.

- Reporting studies were often small and involved highly selected patients and thus may not be fully representative of all individuals with blast or non-blast TBI. There are little data on very long-term outcomes that may be particularly relevant to assessment of cognitive function and quality of life.

- Blast and blast injuries (including TBI) are often defined differently. Therefore, the incidence, prevalence, and patient outcomes may vary across studies in part due to differences in how blast injury is categorized.

- To more adequately address questions about consequences of blast exposure, future research efforts should focus on comprehensive and consistent documentation at the time of and following blast exposure and more complete analyses of databases that may have already captured blast exposure information.

REFERENCES

1. Centers for Disease Control and Prevention (CDC). Explosion and Blast Injuries: A Primer for Clinicians. Available at: http://www.cdc.gov/masstrauma/preparedness/primer.pdf. Accessed August 24, 2015.
2. Department of Defense (DoD) Blast Injury Research Program. Defining Blast Injuries (DoDD 6026.21E). Available at: https://blastinjuryresearch.amedd.army.mil/index.cfm?f = application.introduction#blastInjury. Accessed August 24, 2015.
3. Cernak I, Noble-Haeusslein LJ. Traumatic brain injury: an overview of pathobiology with emphasis on military populations. *J Cereb Blood Flow Metab.* 2010;30(2):255-266.
4. Howe LL. Giving context to post-deployment post-concussive-like symptoms: blast-related potential mild traumatic brain injury and comorbidities. *Clin Neuropsychol.* 2009;23(8):1315-1337.
5. Wolf W, Beharta VS, B onnett CJ, Pons PT, Cantrill SV. Blast injuries. *Lancet.* 2009;374:405-415.
6. Belmont PJ, Jr., Goodman GP, Zacchilli M, Posner M, Evans C, Owens BD. Incidence and epidemiology of combat injuries sustained during "the surge" portion of Operation Iraqi Freedom by a U.S. Army Brigade Combat Team. *J Trauma.* 2010;68:204-210.
7. Belmont PJ, Jr., McCriskin BJ, Hsiao MS, Burks R, Nelson KJ, Schoenfeld AJ. The nature and incidence of musculoskeletal combat wounds in Iraq and Afghanistan (2005-2009). *J Orthop Trauma.* 2013;27(5):e107-113.
8. Belmont PJ, Jr., McCriskin BJ, Sieg RN, Burks R, Schoenfeld AJ. Combat wounds in Iraq and Afghanistan from 2005 to 2009. *J Trauma Acute Care Surg.* 2012;73(1):3-12.
9. Schoenfeld AJ, Laughlin MD, McCriskin BJ, Bader JO, Waterman BR, Belmont PJ, Jr. Spinal injuries in United States military personnel deployed to Iraq and Afghanistan. *Spine.* 2013;38:1770-1778.
10. Freedman BA, Serrano JA, Belmont PJ, Jr., et al. The combat burst fracture study--results of a cohort analysis of the most prevalent combat specific mechanism of major thoracolumbar spinal injury. *Arch Orthop Trauma Surg.* 2014;134(10):1353-1359.
11. Goldberg MS. Updated death and injury rates of U.S. military personnel during the conflicts in Iraq and Afghanistan. Congressional Budget Office Working Paper 2014-08. Washington, DC: 2014.
12. National Institute of Mental Health. What is Prevalence? http://www.nimh.nih.gov/health/statistics/prevalence/index.shtml. Accessed September 10, 2015.
13. DuBose JJ, Barmparas G, Inaba K, et al. Isolated severe traumatic brain injuries sustained during combat operations: demographics, mortality outcomes, and lessons to be learned from contrasts to civilian counterparts. *J Trauma.* 2011;70(1):11-16.
14. Lew HL, Pogoda TK, Baker E, et al. Prevalence of dual sensory impairment and its association with traumatic brain injury and blast exposure in OEF/OIF veterans. *J Head Trauma Rehabil.* 2011;26(6):489-496.

15. Akin FW, Murnane OD. Head injury and blast exposure: vestibular consequences. *Otolaryngol. Clin. North Am.* 2011;44(2):323-334.

16. Kennedy JE, Leal FO, Lewis JD, Cullen MA, Amador RR. Posttraumatic stress symptoms in OIF/OEF service members with blast-related and non-blast-related mild TBI. *NeuroRehabilitation.* 2010;26(3):223-231.

17. Luethcke CA, Bryan CJ, Morrow CE, Isler WC. Comparison of concussive symptoms, cognitive performance, and psychological symptoms between acute blast-versus nonblast-induced mild traumatic brain injury. *J Int Neuropsychol Soc.* 2011;17(1):36-45.

18. Mac Donald CL, Johnson AM, Wierzechowski L, et al. Prospectively assessed clinical outcomes in concussive blast vs nonblast traumatic brain injury among evacuated US military personnel. *JAMA Neurology.* 2014;71(8):994-1002.

19. Wojcik BE, Stein CR, Bagg K, Humphrey RJ, Orosco J. Traumatic brain injury hospitalizations of U.S. Army soldiers deployed to Afghanistan and Iraq. *Am J Prev Med.* 2010;38(S1):S108-S116.

20. MacGregor AJ, Dougherty AL, Galarneau MR. Injury-specific correlates of combat-related traumatic brain injury in Operation Iraqi Freedom. *J Head Trauma Rehabil.* 2011;26(4):312-318.

21. Wilk JE, Thomas JL, McGurk DM, Riviere LA, Castro CA, Hoge CW. Mild traumatic brain injury (concussion) during combat: lack of association of blast mechanism with persistent postconcussive symptoms. *J Head Trauma Rehabil.* 2010;25(1):9-14.

22. Kontos AP, Kotwal RS, Elbin RJ, et al. Residual effects of combat-related mild traumatic brain injury. *J Neurotrauma.* 2013;30(8):680-686.

23. Schneiderman AI, Braver ER, Kang HK. Understanding sequelae of injury mechanisms and mild traumatic brain injury incurred during the conflicts in Iraq and Afghanistan: persistent postconcussive symptoms and posttraumatic stress disorder. *Am J Epidemiol.* 2008;167(12):1446-1452.

24. Xydakis MS, Ling GS, Mulligan LP, Olsen CH, Dorlac WC. Epidemiologic aspects of traumatic brain injury in acute combat casualties at a major military medical center: a cohort study. *Ann Neurol.* 2012;72(5):673-681.

25. French LM, Lange RT, Marshall K, et al. Influence of the severity and location of bodily injuries on post-concussive and combat stress symptom reporting after military-related concurrent mild traumatic brain injuries and polytrauma. *J Neurotrauma.* 2014;31(19):1607-1616.

26. Belanger HG, Kretzmer T, Yoash-Gantz R, Pickett T, Tupler L. Cognitive sequelae of blast-related versus other mechanisms of brain trauma. *J Int Neuropsyhchol Soc.* 2009;15:1-8.

27. Belanger HG, Proctor-Weber Z, Kretzmer T, Kim M, French LM, Vanderploeg RD. Symptom complaints following reports of blast versus non-blast mild TBI: does mechanism of injury matter? *Clin Neuropsychol.* 2011;25(5):702-715.

28. Brahm KD, Wilgenburg HM, Kirby J, Ingalla S, Chang CY, Goodrich GL. Visual impairment and dysfunction in combat-injured servicemembers with traumatic brain injury. *Optom Vis Sci.* 2009;86(7):817-825.

29. Clark ME, Walker RL, Gironda RJ, Scholten JD. Comparison of pain and emotional symptoms in soldiers with polytrauma: unique aspects of blast exposure. *Pain Med.* 2009;10:447-455.

30. Cockerham GC, Lemke S, Glynn-Milley C, Zumhagen L, Cockerham KP. Visual performance and the ocular surface in traumatic brain injury. *Ocul Surf.* 2013;11(1):25-34.

31. Collen J, Orr N, Lettieri CJ, Carter K, Holley AB. Sleep disturbances among soldiers with combat-related traumatic brain injury. *Chest.* 2012;142(3):622-630.

32. Cooper DB, Chau PM, Armistead-Jehle P, Vanderploeg RD, Bowles AO. Relationship between mechanism of injury and neurocognitive functioning in OEF/OIF service members with mild traumatic brain injuries. *Mil Med.* 2012;177(10):1157-1160.

33. Fortier CB, Amick MM, Grande L, et al. The Boston Assessment of Traumatic Brain Injury-Lifetime (BAT-L) semistructured interview: evidence of research utility and validity. *J Head Trauma Rehabil.* 2014;29(1):89-98.

34. Goodrich GL, Flyg HM, Kirby JE, Chang CY, Martinsen GL. Mechanisms of TBI and visual consequences in military and veteran populations. *Optom Vis Sci.* 2013;90(2):105-112.

35. Goodrich GL, Martinsen GL, Flyg HM, Kirby J, Garvert SW, Tyler CW. Visual function, traumatic brain injury, and posttraumatic stress disorder. *J Rehabil Res Dev.* 2014;51:547-558.

36. Hoffer ME, Donaldson C, Gottshall KR, Balaban C, Balough BJ. Blunt and blast head trauma: different entities. *Int Tinnitus J.* 2009;15(2):115-118.

37. Lange RT, Pancholi S, Brickell TA, et al. Neuropsychological outcome from blast versus non-blast: mild traumatic brain injury in U.S. military service members. *J Int Neuropsychol Soc.* 2012;18(3):595-605.

38. Lew HL, Jerger JF, Guillory SB, Henry JA. Auditory dysfunction in traumatic brain injury. *J Rehabil Res Dev.* 2007;44(7):921-928.

39. Lippa SM, Pastorek NJ, Benge JF, Thornton GM. Postconcussive symptoms after blast and nonblast-related mild traumatic brain injuries in Afghanistan and Iraq war veterans. *J Int Neuropsychol Soc.* 2010;16(5):856-866.

40. Maguen S, Madden E, Lau KM, Seal K. The impact of head injury mechanism on mental health symptoms in veterans: do number and type of exposures matter? *J Trauma Stress.* 2012;25(1):3-9.

41. Mendez MF, Owens EM, Jimenez EE, Peppers D, Licht EA. Changes in personality after mild traumatic brain injury from primary blast vs. blunt forces. *Brain Injury.* 2013;27(1):10-18.

42. Mendez MF, Owens EM, Reza Berenji G, Peppers DC, Liang LJ, Licht EA. Mild traumatic brain injury from primary blast vs. blunt forces: post-concussion consequences and functional neuroimaging. *NeuroRehabilitation.* 2013;32(2):397-407.

43. Mora AG, Ritenour AE, Wade CE, Holcomb JB, Blackbourne LH, Gaylord KM. Posttraumatic stress disorder in combat casualties with burns sustaining primary blast and concussive injuries. *J Trauma.* 2009;66(4 Suppl):S178-185.

44. Nakase-Richardson R, McNamee S, Howe LL, et al. Descriptive characteristics and rehabilitation outcomes in active duty military personnel and veterans with disorders of consciousness with combat- and noncombat-related brain injury. *Arch Phys Med Rehabil.* 2013;94(10):1861-1869.
45. Oleksiak M, Smith BM, St Andre JR, Caughlan CM, Steiner M. Audiological issues and hearing loss among Veterans with mild traumatic brain injury. *J Rehabil Res Dev.* 2012;49(7):995-1004.
46. Pogoda TK, Hendricks AM, Iverson KM, et al. Multisensory impairment reported by veterans with and without mild traumatic brain injury history. *J Rehabil Res Dev.* 2012;49(7):971-984.
47. Reid MW, Miller KJ, Lange RT, et al. A multisite study of the relationships between blast exposures and symptom reporting in a post-deployment active duty military population with mild traumatic brain injury. *J Neurotrauma.* Dec 1 2014;31(23):1899-1906.
48. Sayer NA, Chiros CE, Sigford B, et al. Characteristics and rehabilitation outcomes among patients with blast and other injuries sustained during the Global War on Terror. *Arch Phys Med Rehabil.* 2008;89(1):163-170.
49. Heltemes KJ, Dougherty AL, MacGregor AJ, Galarneau MR. Inpatient hospitalizations of U.S. military personnel medically evacuated from Iraq and Afghanistan with combat-related traumatic brain injury. *Mil Med.* Feb 2011;176(2):132-135.
50. Ivey KM, White CE, Wallum TE, al. e. Thoracic injuries in US combat casualties: a 10-year review of Operation Enduring Freedom and Iraqi Freedom. *J Trauma Acute Care Surg.* 2012;73:S514-S519.
51. Chan RK, Siller-Jackson A, Verrett AJ, Wu J, Hale RG. Ten years of war: a characterization of craniomaxillofacial injuries incurred during operations Enduring Freedom and Iraqi Freedom. *J Trauma Acute Care Surg.* 2012;73(6 Suppl 5):S453-458.
52. Blair JA, Patzkowski JC, Schoenfeld AJ, al. e. Spinal column injuries among Americans in the Global War on Terrorism. *J Bone Joint Surg Am.* 2012;94:e136(131-139).
53. Thach AB, Johnson AJ, Carroll RB, al. e. Severe eye injuries in the war in Iraq, 2003-2005. *Ophthalmology.* 2008;115:377-382.
54. Glasgow S, Steele SR, Duncan JE, Rasmussen TE. Epidemiology of modern battlefield colorectal trauma: a review of 977 coalition casualties. *J Trauma Acute Care Surg.* 2012;73:S503-S508.
55. Shah A, Syala M, Capra G, Fox D, Hoffer M. Otologic assessment of blast and non-blast injujry in returning Middle East-deployed service members. *Laryngoscope.* 2014;124:272-277.
56. Fleming M, Waterman S, Dunne J, D'Alleyrand J-C, Andersen RC. Dismounted complex blast injuries; patterns of injuries and resource utilization associated with the multiple extremity amputee. *J Surg Orthop Adv.* 2012;21:32-37.
57. Hoencamp R, Vermetten E, Tan EC, Putter H, Leenen LP, Hamming JF. Systematic review of the prevalence and characteristics of battle casualties from NATO coalition forces in Iraq and Afghanistan. *Injury.* 2014;45(7):1028-1034.

58. Elder GA, Cristian A. Blast-related mild traumatic brain injury: mechanisms of injury and impact on clinical care. *Mt Sinai J Med.* 2009;76(111-118).

59. Surveillance snapshot: Responses to the traumatic brain injury (TBI) screening questions on the 2012 version of the post-deployment health assessment (DD Form 2796). *MSMR.* 2015;22(2):12-13.

60. St. Onge P, McIlwain DS, Hill ME, Walilko TJ, Bardolf LB. Marine Corps breacher training study: auditory and vestibular findings. *US Army Med Dep J.* 2011:97-107.

61. Capo-Aponte JE, Jurek GM, Walsh DV, Temme LA, Ahroon WA, Riggs DW. Effects of repetitive low-level blast exposure on visual system and ocular structures. *J Rehabil Res Dev.* 2015;52(3):273-290.

62. Tate CM, Wang KKW, Eonta S, et al. Serum brain biomarker level, neurocognitive performance, and self-reported symptoms changes in soldiers repeatedly exposed to low-level blast: a breacher pilot study. *J Neurotrauma.* 2013;30:1620-1630.

63. Baker AJ, Topolovec-Vranic J, Michalak A, et al. Controlled blast exposure during forced explosive entry training and mild traumatic brain injury. *J Trauma.* 2011;71:S472-S477.

64. Holcomb JB, Stansbury LG, Champion HR, Wade C, Bellamy RF. Understanding combat casualty care statistics. *J Trauma.* 2006;60(2):397-401.

65. Regasa LE, Thomas DM, Gill RS, Marion DW, Ivins BJ. Military Deployment May Increase the Risk for Traumatic Brain Injury Following Deployment. *J Head Trauma Rehabil.* 2016;31(1):E28-35.

66. DePalma RG. Combat TBI: History, Epidemiology, and Injury Modes. In: Kobeissy FH, ed. *Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects*. Boca Raton (FL): CRC Press/Taylor & Francis; 2015.

67. Scholten JD, Sayer NA, Vanderploeg RD, Bidelspach DE, Cifu DX. Analysis of US Veterans Health Administration comprehensive evaluations for traumatic brain injury in Operation Enduring Freedom and Operation Iraqi Freedom Veterans. *Brain Inj.* 2012;26(10):1177-1184.

68. Institute of Medicine. Gulf War and Health, Volume 9: Long-term Effects of Blast Exposures. Washington, DC: The National Academies Press; 2014.

APPENDIX A. SEARCH STRATEGIES

KEY QUESTIONS 1 AND 2

1. (operation enduring freedom or operation iraqi freedom or operation new dawn).mp.
2. (OEF or OIF or OND).mp.
3. exp Afghan Campaign 2001-/
4. exp Iraq War, 2003-2011/
5. 1 or 2 or 3 or 4
6. (blast$ and injur$).mp.
7. blast$.mp.
8. ep.fs.
9. incidence.mp.
10. prevalence.mp.
11. 8 or 9 or 10
12. 6 or 7
13. 5 and 11 and 12
14. military personnel.mp. or exp Military Personnel/
15. 5 or 14
16. blast injuries.mp. or exp Blast Injuries/
17. 6 or 7 or 16
18. 11 and 15 and 17
19. limit 18 to (english language and yr = "2001 -Current")

KEY QUESTION 3

1. brain injury.mp. or exp Brain Injuries/
2. exp Wounds, Nonpenetrating/
3. exp Wounds, Penetrating/
4. (blast or (non-blast or nonblast)).mp.
5. (traumatic brain injur$ or tbi).mp.
6. brain.mp.
7. exp Afghan Campaign 2001-/
8. exp Iraq War, 2003-2011/
9. (operation enduring freedom or operation iraqi freedom or operation new dawn).mp.
10. (OEF or OIF or OND).mp.
11. 7 or 8 or 9 or 10
12. 2 or 3 or 4
13. 1 or 5 or 6
14. 11 and 12 and 13
15. (military or combat or deploy$).mp.
16. 12 and 13 and 15
17. 14 or 16
18. limit 17 to (english language and yr = "2001 -Current")
19. military personnel.mp. or exp Military Personnel/
20. (military or veteran$ or soldier$).mp.
21. 15 or 19 or 20
22. 12 and 13 and 21
23. 16 or 22
24. limit 23 to (english language and yr = "2001 -Current")

APPENDIX B. PEER REVIEWER COMMENTS AND RESPONSES

	Reviewer Comment	Response
Are the objectives, scope, and methods for this review clearly described?	Yes	
	Yes	
	Yes	
	Yes	
	Yes	
	No - The questions were too broad. In light of the lack of detail in reporting, we should have picked one or two types of injury common to blast. In addition, failure to answer the first two questions indicates a problem with the process of reporting.	We sought input from Operational Partners and Technical Expert Panels to guide the report development.
Is there any indication of bias in our synthesis of the evidence?	No	
	No	
	No	
	No	
	No	
	No	
Are there any <u>published</u> or <u>unpublished</u> studies that we may have overlooked?	No	
	Yes - Consider including the following article for DoD TBI incidence/denominator sample data: Regasa, et.al. (2015, JHTR ahead of pub) "Military Deployment May Increase the Risk for TBI Following Deployment". Posted under Reviewer attachments for your consideration.	We have included this article in the Discussion section. Although it includes a large sample, it is not truly an incidence report given that some service members were excluded. Furthermore, there was inadequate data for the authors to comment on causes of injury.
	Yes - Noted within the comments but there are unpublished, classified studies that we do not mention and it appears that no attempts were made to obtain data from JTAPIC.	Classified studies would be out of scope. We looked at the military injury database sites for posted reports.
	Yes - Not sure if these were reviewed, but there is limited mention of VA data related to the TBI screening and evaluation process. There are questions specific to blast in both the screen and evaluation template. Studies with this data may not have been strong enough to include, but it would appear to be an area for possible expanded use in the future.	We have added information about the VA TBI screening and evaluation process including the findings of Scholten et al.(2012). We did not find other reports of findings related to the VA protocol. We have noted in the Future Research section that additional analyses of existing databases are needed.

	Yes - The data from VA re incidence/prevalence for key questions 1 and 2: Scholten JD,Sayer NA et al: Analysis of US Veterans Health Administration for Traumatic Brain Injury...Brain Injury ISSN: 0269 = 9052; DePalma RG Combat TBI: History, Epidemiology, and Injury Modes. DePalma RG.In:Kobeissy FH, editor: Brain Neurotrauma: Molecular, Neuropsychological, and Rehabilitation Aspects. Boca Raton (FL): CRC Press/Taylor & Francis; 2015. Chapter 2. Frontiers in Neuroengineering	We have reviewed the suggested references and have included them in the Applicability section. We have noted that most studies do not include a denominator that allows determination of true incidence or prevalence.
	Yes - MSMR was not cited, a major resource of traumatic injuries due to blast. VA TBI Screen and Comprehensive Eval publications were not cited.	We searched the contents of MSMR for relevant publications and have added the Surveillance Snapshot from the February 2015 edition. Other reports either did not distinguish blast-related injuries (combining gun and explosive events), included all service members (not limited to OEF/OIF/OND), or did not provide an appropriate denominator.
Additional suggestions or comments can be provided below. If applicable, please indicate the page and line numbers from the draft report.	Thank you for an excellent and very focused review. It is unfortunate that after so many years of research, we continue to find there is little known about a variety of TBI-related issues. The root cause of many of our lingering questions stems from our shortcomings in diagnostic accuracy, among other limitations of existing data. We have a growing expertise treating symptoms associated with TBI, but without objective diagnostic criteria and without adequately controlled, comparative studies the best outcomes may elude us. In addition to the DoDTR and MTR (which likely contain the best blast data), data from the Armed Forces Health Surveillance Center (AFHSC) may be the most comprehensive for (first) TBI incident reporting (see 2015 article attached). Editing comments: 1) Page 34 - Cognitive Function / Other, review of Clark 2009 was not easy to read/follow. The sentence seems broken. 2) Page 40 - vestibular EFFECTS (not affects)	We have added information about limitations of the existing data in the Discussion section. We have cited the Regassa 2015 reference. As noted above, we have checked military injury database sites for posted reports. Editing: 1) we have revised this sentence 2) we have made the suggested change

	p. 7, line 22 - citation to Cernak or Okie related to definition of injury would be best here p. 11, line 15 - are we certain that there is no study related to amputation due to blast injury -is this included in extremity injury. I think amputation is considered differently than musculoskeletal injury p. 14, line 33 - I would refer to this as musculoskeletal injury and again would clarify if this is extremity trauma vs. orthopedic injury (fracture/soft tissue) p. 14, line 53 - I believe there are citations related to burn related to explosion 1: Escolas SM, Archuleta DJ, Orman JA, Chung KK, Renz EM. Postdischarge Cause-of-Death Analysis of Combat-Related Burn Patients. J Burn Care Res. 2015 Dec 1. [Epub ahead of print] PubMed PMID: 26629656. 2: Barillo DJ, Pozza M, Margaret-Brandt M. A literature review of the military uses of silver-nylon dressings with emphasis on wartime operations. Burns. 2014 Dec;40 Suppl 1:S24-9. doi: 10.1016/j.burns.2014.09.017. Review. PubMed PMID: 25418434. 3: Valerio IL, Sabino J, Mundinger GS, Kumar A. From battleside to stateside: the reconstructive journey of our wounded warriors. Ann Plast Surg. 2014 May;72 Suppl 1:S38-45. doi: 10.1097/SAP.0000000000000168. PubMed PMID: 24740023. 4: Jeevaratnam JA, Pandya AN. One year of burns at a role 3 Medical Treatment Facility in Afghanistan. J R Army Med Corps. 2014 Mar;160(1):22-6. doi: 10.1136/jramc-2013-000100. Epub 2013 Jun 7. PubMed PMID: 24109100. 5: Feldt BA, Salinas NL, Rasmussen TE, Brennan J. The joint facial and invasive neck trauma (J-FAINT) project, Iraq and Afghanistan 2003-2011. Otolaryngol Head Neck Surg. 2013 Mar;148(3):403-8. doi: 10.1177/0194599812472874. Epub 2013 Jan 11. PubMed PMID: 23314163. 6: Chan RK, Siller-Jackson A, Verrett AJ, Wu J, Hale RG. Ten years of war: a characterization of craniomaxillofacial injuries incurred during operations Enduring Freedom and Iraqi Freedom. J Trauma Acute Care Surg. 2012 Dec;73(6 Suppl 5):S453-8. doi: 10.1097/TA.0b013e3182754868. PubMed PMID: 23192069. 7: Mora AG, Ritenour AE, Wade CE, Holcomb JB, Blackbourne LH, Gaylord KM. Posttraumatic stress disorder in combat casualties with burns sustaining primary blast and concussive injuries. J Trauma. 2009 Apr;66(4 Suppl):S178-85. doi: 10.1097/TA.0b013e31819ce2d6. PubMed PMID: 19359963. 8: Gaylord KM, Cooper DB, Mercado JM, Kennedy JE, Yoder LH, Holcomb JB. Incidence of posttraumatic stress disorder and mild	p7/22. We have added the Cernak reference to the full report (we did not include references in the Executive Summary). p11/15. The report of musculoskeletal injuries included amputations. We have noted this in the Executive Summary and full report and have added data to the Appendix tables. p14/33. We have made this change and clarified the type of injury. p14/53. We have reviewed each of the suggested references. Two were already included (Chan, Mora) although Chan has now been removed because the denominator was not number deployed. We added a burn outcome reported by Mora to the outcomes for KQ3. None of the other references provided outcomes pertaining to the key questions. p17/26. We have added the Cernak reference. p26/14. The study this comment refers to has been deleted because it did not provide a suitable denominator. p26/23. The study this comment refers to has also been deleted because it did not provide a suitable denominator. p28/30. The inconsistency and spacing issues noted have been eliminated with the switch to superscript reference citations in the final version of the report. p35/8. We have made this correction. p45/35. We have made this change and clarified the type of injury included. p46/6. We have made this change. p46/50. We included only published data. As noted above, we looked at the military injury database sites for posted reports. p47//21. We have added “published” to this sentence. p47/55. We have revised this sentence.

	traumatic brain injury in burned service members: preliminary report. J Trauma. 2008 Feb;64(2 Suppl):S200-5; discussion S205-6. doi: 10.1097/TA.0b013e318160ba42. PubMed PMID: 18376167. p. 17, line 26 - again would reference Okie or Cernak p. 26, line 14 - Did they include deployed population at time as the denominator? Should that be reported for consistency p. 26, line 23 - suggest overall number be reported p. 28, line 30 - this happens multiple times in the document, after this point, the period and the parentheses seem misaligned and are done inconsistently - some with period before, some after; other formatting problems with spacing should also be checked, noted this throughout the document. p. 35, line 8 - s missing from patients p. 45, line 35 - usually referred to as musculoskeletal injury and unclear if this includes SCI p. 46, line 6 - change contraction don't to do not p. 46, line 50 - was any attempt made to request data or technical reports from JTAPIC or DVBIC for unpublished data? http://jtapic.amedd.army.mil/getStarted.php p. 47, line 21 - I think the caveat here is related to what is available in the published literature. There are unpublished data on the classified side that we know exist but to which we do not have access. p. 47, line 55 - this sentence is awkward and I cannot rewrite because I cannot understand what is meant by it.	
	Applicability of Report page9 lines 9-18 references the 1,906 754 OEF/OIF/OND veterans becoming eligible for VA Care. It is known that ~55% reported for VA care. All those screened for TBI; the numbers reporting, screened and completing TBI evaluation are also known. Currently these approach 80-90,000; with additional arriving with DOD diagnosed TBI 125-126,000(Bidelspach/Cifu). This is a partial denominator which needs to be taken into consideration, recognizing that we cannot extrapolate to those not reporting and seen.	There were many reports of "proportional" outcomes – the fraction of an exposed group (*ie,* those injured in combat)(Holcomb 2006) but we have defined incidence based on number deployed and included only studies that report incidence or prevalence for the deployed population. We have included information about the VA TBI evaluation program in the Applicability section of the report.

APPENDIX C. EVIDENCE TABLES

Table 1. Study Characteristics – Key Questions 1 and 2

Author, Year Funding Source	Data Source: Registry/ Database	Data Source: Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics
Belmont, 2010[6] Funding Source: No external funding received	✓ Joint Theater Trauma Registry Electronic medical records 4,122 deployed during study period		2007 Iraq (surge) US Army Brigade Combat Team (BCT) ICD-9 Codes 800-960	Branch of service: 100% Army Rank: E1-E4 (junior enlisted): 50% E5-E9 (senior enlisted): 40% O1-O3/WO1-WO5 (junior officers and warrant officers): 8% O4-O6 (senior officers): 1% Duty/description: NR Blast exposure history: NR Time since exposure: N/A Duration of deployment: 15 months Rural vs urban residence: NR Gender (% male): 92 Mean age (years): 27
Belmont, 2012[8] Funding Source: None reported	✓ Joint Theater Trauma Registry 1,992,232 deployed during study period		2005-2009 Iraq and Afghanistan ICD-9 Codes 800-960 Did not include killed in action (KIA)	**Combat Casualty Cohort** Branch of service: 78% Army, 2% Navy, 1% Air Force, 19% Marines Rank: E1-E4 (junior-enlisted): 59% E5-E9 (senior-enlisted): 34% O1-O3 (junior officers) and all warrant officers: 6% O4-O10 (senior officers): 1% Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural vs urban residence: NR Gender (% male): 99 Mean age (years): 26
Belmont, 2013[7] Funding Source: None received (Additional analysis of cohort described in Belmont 2012)	✓ Joint Theater Trauma Registry 1,992,232 deployed during study period		2005-2009 Iraq and Afghanistan Musculoskeletal combat casualty: wound to upper or lower extremities, spine, or pelvis	**Musculoskeletal Combat Casualty Cohort** Branch of service: 78% Army, 2% Navy, 1% Airforce, 19% Marines Rank: 59% Junior Enlisted, 34% Senior Enlisted, 6% Junior Officer, 1% Senior Officer, <1% unknown Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural vs urban residence: NR Gender (% male): 99 Mean age (years): 26

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics
	Registry/ Database	Clinical Cohort		
Schoenfeld, 2013[9] Funding Source: None received (Additional analysis of cohort described in Belmont 2012)	✓ Department of Defense Trauma Registry[a] 1,992,236 person-years of exposure during study period		2005-2009 Iraq and Afghanistan Spinal injury identified from manual search of records from 7,877 casualties; included spine fractures, spinal dislocations, disk displacements, nerve root injuries, and spinal cord injuries (Additional analysis of data reported in Belmont 2012)	**Spinal Injury Cohort** Branch of service: 81% Army, 2% Navy, 1% Airforce, 16% Marines Rank: 57% Junior Enlisted, 36% Senior Enlisted, 7% Officers, 1% unknown Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural vs urban residence: NR Gender (% male): 99 Mean age (years): 27
Freedman, 2014[10] Funding Source: None reported	✓ Joint Theater Trauma Registry Landstuhl Regional Medical Center (spinal surgery and radiology reports)		2007-2010 (test cohort 2009-2010, historical controls 2007-2008 and 2008-2009) Iraq and Afghanistan Thoracolumbar *combat* burst fracture defined as improvised explosive device attack against an armored vehicle	**Combat Casualty Cohort** Branch of service: Army > Marines > Air Force Rank: 59% from lowest four enlisted ranks Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural vs urban residence: NR Gender (% male): 97 Mean age (years): 30
Goldberg, 2014[11] Funding Source: Congressional Budget Office	✓ Department of Defense tabular reports		OEF, OIF, OND from beginning of conflicts to April 4, 2011 Major amputation defined as loss of limb at or proximal to wrist or ankle	**Amputation Cohort** n = 1,186 service members with at least 1 major amputation (809 in Iraq, 377 in Afghanistan) Branch of service: NR Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural vs urban residence: NR Gender (% male): NR Mean age (years): NR

[a] Joint Theater Trauma Registry renamed Department of Defense Trauma Registry in 2012

Table 2. Incidence and Prevalence Outcomes

Author, Year	Blast Injury Incidence	Other Incidence Findings	Blast Injury Prevalence	Other Prevalence Findings
Belmont, 2010[6]	2007: 8% (341 explosion casualties/4,122 deployed or 83 explosion casualties/1,000 deployed)[a] KIA: 0.6% (25/4,122) DOW: 0.05% (2/4,122) MEDEVAC: 1.6% (68/4,122) RTD: 6.0% (246/4,122)	Blast Characteristics: NR Injury Site (number of body regions injured by explosion/total number of body regions injured): Head/Neck: 49.3% Thorax: 2.9% Abdomen: 4.4% Extremity: 31.2% Injury Outcome: 97.8% of concussions were explosion related		
Belmont, 2012[8]	WIA-DOW 2005: 0.45% (1,476 explosion casualties/ 331,593 deployed or 4.5/1,000) 2006: 0.35% (1,347/383,896 or 3.5/1,000) 2007: 0.40% (1,549/390,943 or 4.0/1,000) 2008: 0.17% (736/438,220 or 1.7/1,000) 2009: 0.17% (754/447,580 or 1.7/1,000)	Blast Characteristics: NR Injury Site: NR Injury Outcome: NR	5 years (2005-2009) WIA-DOW: 0.29% (5,862 explosion casualties/ 1,992,232 deployed) 74.4% (5,862/7,877) WIA-DOW casualties were explosion related	Blast Characteristics: NR Injury Site: NR Injury Outcome: NR

Author, Year	Blast Injury Incidence	Other Incidence Findings	Blast Injury Prevalence	Other Prevalence Findings
Belmont, 2013[7] (Additional analysis of cohort described in Belmont 2012)	WIA-DOW 2005: 0.35% (1,177 explosion-related musculoskeletal casualties/331,593 deployed or 3.5/1,000) 2006: 0.27% (1,048/383,896 or 2.7/1,000) 2007: 0.31% (1,205/390,943 or 3.1/1,000) 2008: 0.13% (563/438,220 or 1.3/1000) 2009: 0.13% (570/447,580 or 1.3/1,000)	Blast Characteristics: NR Injury Site NR Injury Outcome: NR	Musculoskeletal Injury (2005-2009) WIA-DOW: 0.23% (4,563 explosion-related musculoskeletal casualties/1,992,232 deployed) 82% (14,158/17,177) of musculoskeletal wounds were explosion related	Blast Characteristics: NR Blast-related Injury Site: Axial skeleton fracture 0.42/1,000 deployed per year (841/1,142 fractures [74%]) Upper extremity fracture 0.96/1,000 deployed per year (1,917/2,470 fractures [78%]) Lower extremity fracture 1.32/1,000 deployed per year (2,662/3,182 fractures [84%]) Amputation 0.49/1,000 deployed per year (976/1,039 amputations [94%]) Neurological injury 0.30/1,000 deployed per year (596/927 injuries [64%]; includes 45/96 spinal cord injuries [47%]) Joint dislocation 0.15/1,000 deployed per year (304/361 dislocations [84%]) Soft tissue injury 3.42/1,000 deployed per year (6,862/8,056 injuries [85%]) Injury Outcome: NR
Schoenfeld, 2013[9] (Additional analysis of cohort described in Belmont 2012)	Spinal Injury 2005: 0.04% (134 explosion-related spinal injuries/331,593 deployed or 0.40/1,000) 2006: 0.04% (144/383,900 or 0.38/1,000) 2007: 0.04% (152/390,943 or 0.38/1,000) 2008: 0.02% (78/438,220 or 0.18/1,000) 2009: 0.03% (137/447,580 or 0.31/1,000)	Blast Characteristics: NR Injury Site: NR Injury Outcome: NR	Spinal Injury (2005-2009) 0.03% (650 with explosion-related spinal injuries/1,992,236 deployed) or 3.3/10,000 75% (650/872) of individuals with spinal injuries had explosion-related injuries	Blast Characteristics: NR Injury Site: NR Injury Outcome: NR

Author, Year	Blast Injury Incidence	Other Incidence Findings	Blast Injury Prevalence	Other Prevalence Findings
Freedman, 2014[10]	Thoracolumbar burst fracture incidence per 10,000 soldier-years 2007-2008: 0.45 (9 events [4 IED related]) 2008-2009: 0.60 (11 events [6 IED related]) 2009-2010: 2.08 (38 events [32 IED related])[b]	Blast Characteristics: NR Injury Site: NR Injury Outcome: NR	Thoracolumbar burst fractures per 10,000 soldier-years (2007-2010) Combat mechanism of injury (IED): 2.02 (38 events) Other mechanisms of injury: 1.06 (20 events)	Blast Characteristics: NR Blast Injury Site: All thoracolumbar Injury Outcome: NR
Goldberg, 2015[11]			Major IED-related amputations (2001-April 2011): OIF, OND (Iraq): 38.3/100,000 troop years OEF (Afghanistan): 87.8/100,000 troop years.	Blast Characteristics: NR Injury Site: NR Injury Outcome: NR

[a] Some soldiers had >1 casualty but exact number of soldiers with explosion and non-explosion casualties not reported
[b] In the 2009-2010 cohort, there were 38 events among Service Members; 28 of those events were IED-related; 4 events were in non-US Service Members
DOW = died of wounds; WIA = wounded in action; KIA = killed in action; MEDEVAC = medically evacuated; RTD = returned to duty; IED = improvised explosive device; NR = not reported

Table 3. Study Characteristics – Key Question 3

Author, Year Funding Source	Data Source: Registry/ Database	Data Source: Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Akin, 2011[15] Funding Source: VA		✓	Inclusion: Consecutive Veterans with history of blast and/or mTBI; referred to VAMC Vestibular/Balance Laboratory for complaints of dizziness and/or imbalance	N = 18 with mTBI (n = 9 blast, n = 9 non-blast) Age (years): 37 (total sample); range 23-76; 25 (81%) Veterans from Iraq/Afghanistan wars Gender: NR Cohort or service year(s): NR Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR	Vestibular and balance assessment a. Horizontal semicircular canal function (rotary chair videonystagmography) b. Otolith function (cVEMPs and SVV tests during unilateral centrifugation) c. Tests for BPPV (Dix-Hallpike, roll test) d. Central vestibular function (ocular motor and fixation tests) d. Postural stability (SOT) e. Self-perceived handicap (Dizziness Handicap Inventory)
Belanger, 2009[26] Funding Source: resources and use of facilities at 4 VA Medical Centers and the Mid-Atlantic MIRECC		✓	Inclusion: Consecutively assessed individuals from Tampa VAMC and selected research volunteers from 3 VAMCs in the Mid-Atlantic MIRECC Exclusion: Suspected of poor effort and malingering based on clinical presentation and/or failed certain measured of symptom validity; other known neurological disorders (apart from TBI), brain injury due to gunshot	N = 102 (n = 61 blast, n = 41 non-blast) Age (years) at evaluation: -Blast: 29 -Non-blast: 28 (P>.59) Gender (% male): 96 Cohort or service years(s): NR (Iraq and Afghanistan) Rank: NR Duty/description: active duty: 67% Blast exposure history: NR Time since exposure: 443 days (blast); 954 days (non-blast); P>.13 Duration of deployment: NR Rural or urban residence: NR	Trail Making Test Digit Symbol-Coding subset of Wechsler Adult Intelligence Scale-3rd edition (WAIS-III) Brief Visuospatial Memory Test-Revised (BVMT-R) California Verbal Learning Test-II (CVLT-II) Post-traumatic stress disorder checklist (PCL) (self-report)

Author, Year Funding Source	Data Source: Registry/ Database	Data Source: Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Belanger, 2011[27] Funding Source: VHA, DVBIC		✓	Inclusion: Patient from Tampa or Bay Pines VAMC or WRAMC; reported history of mTBI based on diagnostic interview and available records; TBI diagnosis based on DoD criteria (external force acting on individual resulting in alteration or loss of consciousness); mild TBI was loss of consciousness < 30 minutes and post-traumatic amnesia < 24 hours; completed measures used in study; consented to participate	N = 390 (n = 298 blast, n = 92 non-blast) Tampa VAMC: 40; Bay Pines VAMC: 25; WRAMC: 325 Age (years): -Blast: 28 -Non-blast: 30 (P = .08) Gender (% male): 94% Cohort years: NR Rank: NR Duty/description: 87% active duty Time since exposure (mean): -Blast: 11.9 months -Non-blast: 25.9 months (P = .002) Duration of deployment: NR Rural or urban residence: NR	PTSD Checklist (PCL); self-report; 17 items (rated 1-5 with 1 = not at all and 5 = extremely) Neurobehavioral Symptom Inventory (NSI); self-report; post-concussion symptoms; 22 items (rated 0-4 with 0 = none and 4 = very severe)
Brahm, 2009[28] Funding Source: VA Quality and Enhancement Research Initiative (QUERI) grant		✓	Inclusion: Consecutive polytrauma inpatients (PRC) or outpatients (PNS); combat-injured PRC: 84% with moderate to severe TBI, polytrauma; typically acute or sub-acute stage of rehabilitation PNS: mTBI, postacute	<u>Inpatients</u> N = 68 (n = 57 blast, n = 11 non-blast) Age (years): -Blast: 28.6 -Non-blast: 28.8 Gender (% male): 96% overall Cohort years: 2004-2006 <u>Outpatients</u> N = 124 (n = 112 blast, n = 12 non-blast) Age (years): -Blast: 29.7 -Non-blast: 37.9 (P<.025) Gender (% male): 96 overall Cohort years: 2006-2007 <u>Both Groups:</u> Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural vs urban residence. NR	Visual impairment: loss of visual acuity (Feinbloom chart or other tests used for verbally non-responsive patients) or visual field (Goldmann visual fields if patient capable) Ocular injuries Subjective visual complaint

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Clark, 2009[29] Funding Source: Department of Veterans Affairs Rehabilitation Research and Development grant		✓	Inclusion: Consecutively admitted to TPRC; active duty and Veterans; patient's medical records had self-reported admission pain scores Exclusion: Severe brain injuries and associated significant communications deficits TBI: 83% of blast group, 79% of non-blast group; more penetrating TBI in blast group, more closed TBI in non-blast group	N = 128 (n = 51 combat blast; n = 34 combat non-blast)* Age (years): -Blast: 28 -Non-blast: 27 Gender (% male) -Blast: 96 -Non-blast: 94 Cohort years: 2003-2006 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR *NOTE: n = 43 non-combat not included in analysis	Functional Independence Measure (FIM) – 18 items a) ability for independent function in daily activities b) cognitive function -Rancho Los Amigos Scale (Rancho) – behavioral characteristics and cognitive deficits associated with recovery from brain injury -Pain Numeric Rating Scale (NRS) – pain intensity in those capable of self-report; extracted if Rancho ≥ VI -Number of pain sites -Number of psychiatric diagnoses
Cockerham, 2013[30] Funding Source: Veterans Administration Merit Review Award		✓	Inclusion: Diagnosis of TBI; ability to undergo clinical examination and psychometric testing Exclusion: Eyes with open-globe injury; using topical ocular medications	N = 53 (n = 44 blast, n = 9 non-blast) Age (years): 26 Gender (% male): 100 Cohort years: NR Rank: NR Duty/description: 100% Veterans Blast exposure history: Time since exposure (median): 6 months (range 1-60) Duration of deployment: NR Rural or urban residence: NR	Ocular Surface Disease Index (OSDI) – interview by research team member to assess dry eye disease (DED) symptoms; 12 items scored 0 (none of the time) to 4 (all of the time); higher scores = greater disability
Collen, 2012[31] Funding Source: No funding received		✓	Inclusion: Consecutive soldiers with combat-related TBI (85% mTBI, 9% moderate, 6% severe); receiving care at WRAMC; age ≥ 18y; sustained non-penetrating TBI Exclusion: sleep disorders diagnosed prior to injury	N = 116 (n = 82 blast, n = 34 blunt) Age (years): -Blast: 30 -Non-blast: 35 (P = .01) Gender (% male): 97 Cohort years: 2005-2010 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: 16 months Duration of deployment: NR Rural vs urban residence. NR	Epworth Sleepiness Scale (ESS): subjective assessment of daytime somnolence Polysomnography: to detect insomnia and obstructive sleep apnea syndrome (OSAS); completed in 79% of patients

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Cooper, 2012[32] Funding Source: None reported		✓	Inclusion: Consecutive admissions of OEF/OIF service members referred to TBI clinic at BAMC for neuropsychological testing Jan 2008-Jan 2010; at least 18 years old; fluent English; sustained injury while on active duty military service Exclusion: no mTBI; major body burns and/or traumatic amputations affecting administration of neurocognitive measures; fell below empirically derived cut scores for suboptimal effort o psychometric testing; missing variables on key measures of interest	N = 60 (n = 32 blast, n = 28 non-blast) Age (years): -Blast: 29.5 -Non-blast: 29.4 (P = .97) Gender (%male): -Blast: 100 -Non-blast: 79% (P = .006) Cohort years: 2008-2010 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: -Blast: 192 days -Non-blast: 149 days Duration of deployment: NR Rural or urban residence: NR	Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) – cognitive functioning Headache Impact Test (HIT-6) – headache severity and impact on daily function Post-Traumatic Checklist-Military version (PCL-M) – self-rated
DuBose, 2011[13] Funding Source: None reported	✓ Joint Theater Trauma Registry		Inclusion: 18 to 55 years old; sustained isolated TBI	N = 604 (n = 374 blast, n = 118 gunshot, n = 112 blunt) Age (years): -Blast: 25.5 -Gunshot: 25.1 -Blunt: 27.1 (P = .04) Gender (% male): -Blast: 98.4 -Gunshot: 100 -Blunt: 94.6 (P = .01) Cohort years: 2003-2007 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR	Mortality

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Fortier, 2014[33] Funding Source: Translational Research Center for TBI and Stress Disorders, a VA Rehabilitation Research and Development (RR&D) Traumatic Brain Injury Center of Excellence		✓	Inclusion: Consecutive deployed Veterans of OEF/OIF; enrolled in VA RR&D-supported TBI Center of Excellence Exclusion: History of seizures; prior serious medical illness; current active suicidal and/or homicidal ideation, intent, or plan; bipolar disorder, schizophrenia, or other psychotic disorder; cognitive disorder not due to TBI NOTE: total sample of 131 enrolled (56 with military TBI)	N = 56 (n = 26 blast, n = 30 non-blast) Age (years): 34 (total sample) Gender (% male): 86 (total sample) Cohort years: NR Rank: NR Duty/description: NR Blast exposure history (for 101/131 with blast exposure within 100 meters: mean blasts/person = 14, median = 2 Time since exposure (mean): 31 months (range 1-99) since last deployment (total sample) Duration of deployment (mean): 13 months (range 3-38) (total sample) Rural vs urban residence. NR	Boston Assessment of Traumatic Brain Injury-Lifetime (BAT-L): questionnaire for preliminary screen administered as a self-report questionnaire; captures number of exposures to blasts within 100 meters and number of TBIs due to blast, TBIs and their severity, and neurobehavioral symptoms (occurrence, timing of onset, and duration)
French, 2014[25] Funding Source: No funding received		✓	Inclusion: US male Service members who sustained closed mTBI and were evaluated at WRAMC or SAMMC after injuries sustained during OEF/OIF (typically with other injuries); deployed ≤3 times; completed NSI, PCL-C, and Abbreviated Injury Scale (AIS); divided into 4 groups based on injury severity based in Injury Severity Score (ISS) Exclusion: no additional criteria reported	N = 579 (n = 73 minor injury, 278 moderate, 148 serious, 80 severe/critical); 82% injured as a result of blast exposure Age (years): 27 Gender (% male): 100 Cohort years: NR Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure (mean): 12 months or less (mean 73 days) Duration of deployment (mean): NR Rural vs urban residence. NR	-Neurobehavioral Symptom Inventory (NSI): 22 items, presence/severity of each symptom rated 0 (none) to 4 (very severe); total 0 (no symptoms) to 88 (all symptoms at very severe level); 3 cluster scores (somatic/sensory, cognitive, affective) -PCL-C: 17 items; self-reported PTSD symptoms; range 17 (not at all) to 85 (all symptoms at extreme level); 3 cluster scores (re-experiencing, avoidance, hyper-arousal) -ISS: based on AIS for 3 most severely injured body region (brain excluded for this study)

Author, Year Funding Source	**Data Source**		**Inclusion/Exclusion Criteria**	**Cohort Characteristics**	**Measures**
	Registry/ Database	**Clinical Cohort**			
Goodrich, 2013 Goodrich, 2014[34,35] Funding Source: Veterans Affairs Quality Enhancement Research Initiative (QUERI) grant		✓	Inclusion: Admitted to VA PRC; documented eye exams with optometry; history of TBI Exclusion: None reported NOTES: a. many of the 50 non-blast TBIs occurred in non-combat settings b. mTBI: -Blast: 53% (26/49) -Non-blast: 2% (1/49) (P = .0001) c. 16 in blast group had *documented* secondary or tertiary trauma (non-primary injuries *may not* have been documented in remaining patients)	N = 100 (n = 50 blast, n = 50 non-blast) Age (years): -Blast: 29 -Non-blast: 29 Gender (% male) -Blast: 94% -Non-blast: 96% Cohort years: NR Rank: NR Duty/description: NR Blast exposure history: -32% (16/50) of blast group had documented secondary or tertiary trauma -32% (16/50) had >1 exposure Time since exposure (mean): -Blast: 1 year (range 0.03-4.79) -Non-blast: 0.32 years (range 0.02-3.13) Duration of deployment: NR Rural or urban residence: NR	Subjective and objective ocular and vision data from eye examinations nearest in date to injury date Self-reported vision complaints Visual acuity Reading ability Ocular injuries
Hoffer, 2009[36] Funding Source: None reported		✓	Inclusion: war-injured with diagnosis of or significant risk factors for mTBI; presented over 9 month period	**VOR study:** N = 55 (n = 21 blast, n = 34 blunt) Age (years): 26 Gender (% male): 100 **VSR study:** N = 72 (n = 39 blast, n = 32 blunt) Age (years): 24 Gender (% male): 96 **Both studies:** Cohort years: NR Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR	**VOR study:** Gain, phase and symmetry of sinusoidal harmonic acceleration testing (rotational chair) **VSR study:** a. Sensory organization test (SOT) b. Motor control test (latency times)

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Kennedy, 2010[16] Funding Source: US Army Medical Research and Materiel Command		✓	Inclusion: outpatients at SAMMC; screened and identified with mTBI due to blast or other mechanism while deployed; consented to allow information to be used for research Exclusion: incomplete data on Posttraumatic Stress Disorder Checklist-Civilian version (PCL-C); more severe TBI; no clear date of injury NOTE: Blast group included significantly more Army soldiers (described as "more likely to engage in activities involving high risk of exposure to explosive munitions")	N = 724 (n = 586 blast, n = 138 non-blast) Age (years): -Blast: 27.4 -Non-blast: 30.0 (P = .001) Gender (% male) -Blast: 98 -Non-blast: 92 (P = .001) Cohort years: 2005-2009 Rank: -Blast: 95% enlisted, 5% officer -Non-blast: 92% enlisted, 8% officer (P = .16 for blast vs non-blast) Duty/description: NR (See NOTE) Blast exposure history: NR Time since exposure (mean): 31 weeks (range 2 days to 5.4 years); P = .43 (blast vs non-blast) Duration of deployment: NR Rural or urban residence: NR	PCL-C: 17- items measuring severity of PTSD symptoms; PTSD = score>50

Author, Year Funding Source	Data Source Registry/ Database	Data Source Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Kontos, 2013[22] Funding Source: US Special Operations Command Biomedical Initiatives Steering Committee	✓		Inclusion: US Army Special Operations Command (USASOC) personnel completing web-based standardized baseline evaluations for mTBI symptoms, PTSD symptoms, and neurocognitive performance; at least 1 diagnosis of mTBI; deployed and non-deployed settings Exclusion: history of diagnosed moderate to severe TBI, brain surgery, major psychiatric disorder or neurologic disorder; neurocognitive assessment deemed invalid	N = 2,813 (n = 861 blast, n = 1,700 blunt, n = 252 blast-blunt combination) Age (years): 29.5 Gender (% male): 96 Cohort years: 2009-2011 Rank: NR Duty/description: NR* Blast exposure history: 1,113 with blast or combination (764 [69%] 1 blast, 181 [16%] 2 blasts, 168 [15%] ≥3 blasts) Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR *USASOC includes “Special Forces, Army Rangers, and other unconventional units involved in high-risk training, multifaceted global operations, and challenging combat missions”	Immediate Post-Concussion Assessment Cognitive Test (ImPACT) – military version: neurocognitive performance; 4 composite scores Post-Concussion Symptom Scale (PCSS): 22 self-reported symptoms rated from 0 (none) to 6 (severe) PTSD Check List (PCL):17 items, how much each item bothered them for past month; 0 (not at all) to 5 (extremely)

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Lange, 2012[37] Funding Source: No financial support received for completion of manuscript		✓	Inclusion: sustained deployment related closed mTBI and evaluated at WRAMC following medical evacuation from OEF/OIF combat theater; completed core neuropsychological test battery; adequate effort on Word Memory Test; valid clinical profile on Personality Assessment Inventory; able to classify severity of injury as mild; assessed by TBI Service within 14 months of injury; male NOTES: a. most patients evacuated for limb loss or systemic injuries b. selected from sample of 662 evaluated at WRAMC	N = 56 (n = 35 blast plus, n = 21 non-blast) Age (years): -Blast: 32.7 -Non-blast: 31.4 (P = .58) Gender (% male): 100 Cohort years: 2002-2009 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure (mean): -Blast: 4.5 months -Non-blast: 4.3 months (P = .83) Duration of deployment (mean): NR Rural or urban residence: NR	Personality Assessment Inventory (PAI): T-score ≥ 60 = mild or higher, ≥ 70 = moderate or higher Neurocognitive measures: a. Trail Making Test (TMT) b. California Verbal Learning Test 2nd ed (CVLT-II) c. Conner's Continuous Performance Test-2nd ed (CPT-II) d. Subsets from Wechsler Adult Intelligence Scale-3rd ed e. Wechsler Test of Adult Reading f. Word Memory Test (WMT)
Lew, 2011[14] Funding Source: VA Office of Research and Development, Health Services Research and Development Service	✓ DoD Defense Management Data Center		Inclusion: medical records with information on demographics and results of comprehensive TBI evaluations performed in Veterans Health Administration Exclusion: test cases; duplicate TBI evaluations; cases involving inconsistent responses regarding blast exposure; reported sustaining TBI at time other than deployment	N = 12,521 deployment related TBI (n = 10,431 blast, n = 2,090 non-blast) (85% mTBI) Age (years): 31.3 Gender (% male): 93.9 Cohort years: 2007-2009 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure (mean): NR Duration of deployment (mean): NR (median number of deployments = 1.0 [range 1-19]; median years of service = 4.0 [range 0-36]) Rural or urban residence: NR	Neurobehavioral Symptom Inventory (NSI-22): 22 items, self-report extent to which cognitive, affective, somatic, or sensory symptoms have impacted them in past 30 days

Author, Year Funding Source	Data Source: Registry/ Database	Data Source: Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Lew, 2007[38] Funding Source: Unfunded at time of manuscript publication		✓	Inclusion: new admissions to inpatient rehabilitation unit of a VAMC; TBI Exclusion: none reported NOTE: blast vs non-blast analysis only includes patients admitted 2003-2006 (no blast-related TBI in patients earlier)	N = 150 (n = 42 blast, n = 108 non-blast) Age (years): 31.6 Gender (% male): 93 Cohort years: 2003-2006 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure (mean): NR Duration of deployment (mean): NR Rural or urban residence: NR	Hearing loss Tinnitus
Lippa, 2010[39] Funding Source: Supported in part by a Department of VA Center of Excellence Grant		✓	Inclusion: Referred for TBI screening by nationwide VA process (*ie,* Veteran endorses each item): 1) Injury during deployment 2) Injury resulted in any of the following: dazed, confused, memory problems, losing consciousness, head injury, *etc*) 3) Symptoms begin or get worse afterward 4) Presented with symptoms in the past week Only patients with both *possible history of TBI* and *current symptoms* referred for evaluation Exclusion: Did not report altered mental status or LOC post injury, altered mental status for > 24 hr post-injury or LOC for > 30 mins; incomplete data	N = 339 with mTBI (n = 138 blast, n = 56 non-blast) 2 VAMCs Age (years): -Blast: 30 -Non-blast: 33 (P = .02) Gender (% male): -Blast: 99% -Non-blast: 89% Cohort years: NR Rank: NR Duty/description: NR Time since exposure: -Blast: 35 months -Non-blast: 42 months Duration of deployment: NR Rural or urban residence: NR	PSTD Checklist (PCL): self-report, 17 items (rated 1-5 with 1 = not at all and 5 = extremely) Neurobehavioral Symptom Inventory (NSI): self-report; 22 items (rated 0-4 with 0 = none and 4 = very severe) Injury Questionnaire: date(s), mechanism(s) (*ie,* fall, motor vehicle, bullet, blast or a combination), and number of deployment related injuries

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
Luethcke, 2011[17] Funding Source: No sources of financial support		✓	Inclusion: Military and civilian contractors referred to outpatient TBI Clinic at a forward-deployed combat support hospital (CSH) in Iraq (OIF); assessed within 72 hr of injury; meeting the DoD and VA criteria for mild TBI Exclusion: none reported NOTE: Blast injury defined as primary blast injury (blast wave); "non-blast" injury included secondary, tertiary, or quaternary blast injuries plus injuries not involving blasts	N = 82 (n = 40 blast, n = 42 non-blast) Age (years) -Blast: 27.1 -Non-blast: 26.6 (P = .73) Gender (% male) -Blast: 98% -Non-blast: 91% (P = .18) Cohort years: NR Rank (P = .07) Junior enlisted (E1-E4): -Blast: 63% -Non-blast: 61% Duty/description (P = .20) Active duty: -Blast: 53% -Non-blast: 74% Blast exposure history: NR Time since exposure: -Blast: 1.5 days -Non-blast: 1.6 days Duration of deployment (mean): 4.8 months Rural or urban residence: NR	Concussive Symptoms: Self-report and clinical interview Automated Neuropsychological Assessment Metrics (ANAM): 6 cognitive domains reported in 2 dimensions (speed, accuracy) PTSD Checklist – Military (PCL-M): 17 items, self-report Behavioral Health Measure (BHM): 20 items, self-report Insomnia Severity Index (ISI): 7 items

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
Mac Donald, 2014[18] Funding Source: Congressionally Directed Medical Research program		✓	Inclusion: Active duty US military evacuated from Iraq or Afghanistan to Landstuhl Regional Medical Center (Germany); met DoD criteria for TBI Exclusion: none reported Followed 6-12 months after injury at Washington University in St. Louis NOTE: blast plus impact TBI group had blast exposure plus another mechanism of head injury (*eg,* fall, motor vehicle crash, strike by blunt object); non-blast TBI group experienced falls, motor vehicle crashes, blunt object strikes without blast exposure	N = 178 with follow-up data including n = 53 blast plus impact TBI, n = 29 non-blast TBI* Age (years): -Blast: 25 (median) -Non-blast: 27 (median) Gender (% male): -Blast: 95 -Non-blast: 91 Cohort years: NR Rank: Enlisted: -Blast: 97% -Non-blast: 95% Duty/description: Active duty: -Blast: 76% -Non-blast: 73% Blast exposure history: NR Time since exposure (for initial evaluation): -Blast: 11.5 days -Non-blast: 13.8 days Duration of deployment: NR Rural or urban residence: NR *data for n = 96 without TBI not included in this review	Glasgow Outcome Scale-Extended: monthly telephone or e-mail for 6-12 months In-person 1. Standard neurological exam a. Structured interview (Neurobehavioral Rating Scale-Revised) b. 2 headache interviews capturing recent frequency and intensity (Migraine Disability Assessment [MIDAS] & Headache Impact Test 6) c. Neurological Outcomes scale for Traumatic Brain Injury (NOS-TBI) 2. Neuropsychological test battery - 9 standard quantitative tests 3. Psychiatric evaluation a. Clinician-Administered PTSD scale for DSM-IV (CAPS) b. Montgomery-Asberg Depression Rating Scale c. Combat Exposures Scale (CES) d. Michigan Alcoholism Screening Test

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
MacGregor, 2011[20] Funding Source: US Navy Medicine Bureau of Medicine and Surgery	✓ EMED		Inclusion: Sustained TBI in OIF; identified from EMED with query for all personnel injured during OIF (3/2004 to 4/2008) who completed Post-Deployment Health Assessment (PDHA) and Post-Deployment Health Re-Assessment (PDHRA); both surveys completed within 1 year of injury date	N = 2074 (n = 1987 blast, n = 87 non-blast) Age (years): 22 Gender (% male): 99.5% Enlisted: 96% (49% E1-E2, 40% E4-E6) Cohort years: 2004-2008 Rank: - Enlisted: 96% Duty/description: Infantry 58% Blast exposure history: NR Time since exposure: <1 year Duration of deployment: NR Rural or urban residence: NR	Abbreviated Injury Scale (AIS): TBI severity (mild = 1 or 2, moderate = 3, severe = 4, 5, or 6) Concomitant injuries
Maguen, 2012[40] Funding Source: Supported by Department of Defense Psychological Health and Traumatic Brain Injury Research Program and VA Health Sciences Research and Development Career Development Award		✓	Inclusion: OEF/OIF Veterans who received a TBI screen at a VA from April 1, 2007 through Jan 8, 2010; either reported no head injury or both a head injury mechanism and TBI-related symptoms Exclusion: Previously screened elsewhere and data not available; previous TBI diagnosis; refused screening; reported head injury with unknown mechanism or no TBI symptoms; incomplete screen	N = 1,082 (968 for PTSD analysis) N = 152 with 1 mechanism of injury (n = 103 blast) N = 310 with 2+ mechanisms of injury (n = 287 blast + other) Age (years): 29.5 Gender (% male): 95% Cohort years: 2007-2010 Rank: Enlisted: 96% Duty/description: Active duty: 70% Blast exposure history: NR Time since exposure: NR Duration of deployment: NR (42% with multiple deployments) Rural or urban residence: NR	Primary Care PTSD Screen (PC-PTSD): 4 item self-report screening instrument Patient Health Questionnaire-2 (PHQ-2): 2 item self-report screening instrument; responses on 4 point scale (0-3); score ≥ 3 is positive screen for depression Alcohol Use Disorders Identification Test Consumption (AUDIT-C): 3 item self-report screening instrument; total score from 0 to 12; ≥4 for men or ≥3 for women is positive screen for hazardous or harmful consumption

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
Mendez, 2013[42] Mendez, 2013[41] Funding Source: Veterans Affairs Administration		✓	Inclusion: Recent US Veterans of Iraq or Afghanistan wars; presented at VAMC for Second Level TBI evaluation; community dwelling outpatients; reported deployment-related mTBI and met DoD/VA criteria for mTBI; history of primary blast or primary blunt force mTBI; patient reported persistent symptoms they attributed to mTBI; medically and psychiatrically stable; availability of significant other informant willing to participate in study Exclusion: Mixed TBI; blunt controls with blast exposure/effects; PTSD, depression, or other mental illness; intervening head injuries, focal neurological deficits, visual impairments sufficient to impair reading, or abnormalities on prior, clinically-obtained brain imaging (magnetic resonance imaging (MRI) or computerized tomography (CT)) **NOTE: blast is primary blast force only**	N = 24 (n = 12 blast, n = 12 blunt) Age (years): -Blast: 31 -Blunt: 31 Gender (% male): NR Cohort years: NR Rank: NR Duty/description: NR Blast exposure history: 33% (4/12) reported multiple "pure" blast exposures related to combat duties Time since exposure: -Blast: 52 months -Blunt: 49 months Duration of deployment: NR Rural or urban residence: NR NOTE: of 12 blast injury subjects, 10 reported distances of < 10 feet from blast exposure, 1 reported < 30 feet, 1 reported < 50 feet	**Mendez 2013[42]:** -Neurobehavioral Symptom Inventory (NSI) self-report of difficulties on 22 symptoms; 5 point scale (4 = very severe) -Rivermead Post-Concussion Symptom Questionnaire (RPQ): 16 symptoms, self-rate degree to which symptoms are more of a problem compared with premorbid levels; scale of 0 (no change) to 4 (most severe symptoms) -Health Related Quality of Life 36-item Short Form for Veterans (SF36-V): self -administered; 8 subscales and 2 summary scores (physical, mental) -Paced Auditory Serial Addition Test (PASAT): cognitive; single digits presented at 3 second intervals; patient adds new digit to one immediately prior -Iowa Gambling Test (IGT): mental flexibility and decision-making ability; calculated by advantageous minus disadvantageous card selections -Frontal Assessment Battery (FAB): six executive operations; items rated 0-3; lower scores indicate greater impairment **Mendez 2013[41]:** -Interpersonal Measure of Psychopathy (IM-P): interpersonal behaviors associated with psychopathy -Big Five Inventory (BFI): 5-factor model of personality -Interpersonal Adjectives Scale (IAS): primary dimensions of

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
					interpersonal transaction -Frontal Systems Behavior Scale (FrSBe): dimension of apathy and disinhibition and executive dysfunction
Mora, 2009[43] Funding Source: None reported		✓[a]	Inclusion: OEF/OIF combat casualties injured in explosions and treated at USAISR Burn Center March 2003 to March 2006; PLC-M assessment at least 30 days post-injury NOTE: Blast is IED with primary blast injury; non-blast is IED without primary blast injury	N = 19 with mTBI (n = 6 blast, n = 13 non-blast) Age (years): -Blast: 28 -Non-blast: 29 Gender (%male): -Blast: 83% -Non-blast: 86% Cohort years: 2003-2006 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: -Blast 117 days -Non-blast: 233 days Duration of deployment: NR Rural or urban residence: NR	PCL-M: 17 item self-report; PTSD indicated by score of 44 and above

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
Nakase-Richardson, 2013[44] Funding Source: Veterans Affairs Health Services Research and Development/ Rehabilitation Research and Development Center of Excellence for Maximizing Rehabilitation Outcomes		✓	Inclusion: Consecutive admissions to Polytrauma Rehabilitation System of Care (Jan 2004 to Oct 2009) with a disorder of consciousness (DOC) Exclusion: none reported	N = 122 (29 blast, 10 penetrating, 67 other trauma, 16 non-trauma*) Age (years, median): -Blast: 25 -Non-blast: 25 Gender (% male): -Blast: 100 -Non-blast: 95 Cohort years: 2004-2009 Rank: NR Duty/description – Active duty: -Blast: 97 -Non-blast: 80 Blast exposure history: NR Time since exposure(median): -Blast: 67 days -Non-blast: 46 days (P = .04) Duration of deployment: NR Rural or urban residence: NR *Non-trauma patients not included in non-blast group	-Rancho Levels of Cognitive Functioning Scale (LCFS): 8 level index; awareness, behavioral competence and environmental interaction; higher levels = greater cognitive functioning -Functional Independence Measure (FIM): 18 items; functional independence in self-care and cognition; higher scores = greater level of independence; cognitive and motor subscales -Return to consciousness: assessed with Coma Recovery Scale-Revised (CRS-R) or evidence of interactive communication, functional object use during self-care tasks, or Rancho LCFS score ≥4
Oleksiak, 2012[45] Funding Source: VA Office of Research and Development, Health Services Research and Development grant		✓	Inclusion: Confirmed diagnosis of mTBI Exclusion: moderate/severe TBI, prior history of ear disease or hearing loss, non-VA care for hearing loss	N = 189 (n = 154 blast or mixed, n = 35 non-blast) Age (years): 27.9 Gender (% male): 92% Cohort years: 2007-2009 Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR	Comprehensive 2nd level TBI evaluation Neurobehavioral Symptom Inventory (NSI): 22 symptoms including hearing difficulty

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
Pogoda, 2012[46] Funding Source: VA Office of Research and Development, Health Services Research and Development Service	✓ Defense Management Data Center		Inclusion: Veterans completing VA CTBIE Oct 2007 to June 2009; did not report brain injury pre-deployment or since returning from deployment; met criteria for mTBI history (self-report); VA clinician-confirmed deployment related mTBI history Exclusion: none reported	N = 9,998 (n = 8,038 blast, n = 1,960 non-blast/etiology NR) Age(years): 31* Gender (% male): 95% Cohort years: 2007-2009 Rank: -Junior Enlisted 52% -Mid-level Enlisted 39% -Senior Enlisted/Officer 9% Duty/description: NR Blast exposure history: NR Time since exposure: NR Duration of deployment: NR Rural or urban residence: NR *demographic information not reported for blast vs non-blast mTBI	Diagnostic codes for depression and PTSD (2007- 2009) Comprehensive Traumatic Brain Injury Evaluation (CTBIE): performed by VA clinician Neurobehavioral Symptom Inventory (NSI -22): patient self-report checklist administered during CTBIE; rate extent to which each symptom has affected them in past 30 days from 0 (none) to 4 (very severe)
Reid, 2014[47] Funding Source: None reported		✓	Inclusion: service members evaluated at 1 of 6 Military Medical Centers (all in US); CHI only; valid and complete PCL-C and NSI; injury sustained in OEF/OIF; tested 1-24 months post-injury; mTBI associated with most recent blast exposure; male Exclusion: missing data regarding number of previous blast exposures; exposure to >10 blasts **NOTE: unknown whether prior blast exposures resulted in undocumented mTBI**	N = 573 (n = 505 blast, n = 68 non-blast) Age (years): 27 Gender (% male); 100% Cohort years: NR Rank: -E1-4: 59% -E5+: 41% Duty/description: NR Blast exposure history: 1 blast: n = 123 2 blasts: n = 178 3 blasts: n = 106 4-10 blasts: n = 98 Time since exposure: 1-24 months Duration of deployment: NR; Rural or urban residence: NR	Neurobehavioral Symptom Inventory (NSI -22): presence/severity of each symptom within past 2 weeks; 0 = none, 4 = very severe; total score and subscales (cognitive, affective, sensory, somatic) Posttraumatic Checklist – Civilian version (PCL-C): self-rated, 17 items (clusters for re-experiencing, avoidance, hyperarousal); how much bothered by symptom in past month; 1 = not at all, 5 = extremely; scores range from 17 to 85

Author, Year Funding Source	Data Source		Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
	Registry/ Database	Clinical Cohort			
Sayer, 2008[48] Funding Source: VA Health Service Research and Development grant		✓	Inclusion: all service members injuries in OEF/OIF and receiving inpatient VA rehabilitation services at a polytrauma rehabilitation center (PRC) Exclusion: none reported	N = 188 (n = 106 blast, n = 82 non-blast); 97% with TBI Age (years): 28 Gender (% male): 97% Cohort years: 2001-2006 Rank: NR Duty/description: 74% active duty, 26% Reserves/National Guard Blast exposure history: 6 with injuries secondary to >1 blast Time since exposure: 87 days Duration of deployment: NR Rural or urban residence: NR	Mortality from VA administrative database Impairments in body structures and organs from medical records; classified using World Health Organization *International Classification of Functioning, Disability and Health* Psychiatric symptoms from medical records: PTSD, anxiety disorders other than PTSD, depression, psychosis Functional Independence Measure (FIM): 13 motor items, 5 cognitive items
Schneiderman, 2008[23] Funding Source: Department of Veterans Affairs, War-Related Illness and Injury Study Center		✓	Inclusion: responded to self-administered mail questionnaire (addresses/info obtained from National Change of Address databased and the US Department of Defense); OEF/OIF Veterans who left combat theaters by 9/30/2004; living in northern Virginia, Maryland, Washington DC or eastern West Virginia; active duty personnel separated from the military and National Guard/Reserve members were eligible Exclusion: none reported	N = 2,235 surveys returned (34% response) N = 275 with mTBI (n = 70 blast, n = 205 non-blast) Age (years): NR Gender (% male): 86% Cohort years: OEF/OIF before 9/30/2004 Rank: NR Duty/description: 27% active duty Blast exposure history: NR Time since exposure: “left combat theaters at least 5 months earlier” Duration of deployment: NR Rural or urban residence: NR	3-item Brief Traumatic Brain Injury Screen for diagnosis of mTBI PCS 3+: self-attribution of ≥3 current neuropsychiatric symptoms to possible head injury or concussion

Author, Year Funding Source	Data Source Registry/ Database	 Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Wilk, 2010[21] Funding Source: None reported		✓	Inclusion: US soldiers from one National Guard and 2 Active Duty infantry brigades; surveyed in 2006 and 2007 (3-6 months after return from combat deployment to Iraq); consented and completed some portion of the questionnaire (N = 4,383) Exclusion: none reported	N = 574 with concussion data (15% of 3,952 who completed concussion questions) Age (years): 67% <30 years Gender (% male): 98 Cohort years: Rank: Junior Enlisted 53% Duty/description: "soldiers in this study saw high levels of combat" Blast exposure history: NR Time since exposure: NR (surveyed 3-6 months post-deployment) Duration of deployment: 1 year Rural or urban residence: NR	Concussion (mTBI): self-report of "dazed, confused, or seeing stars," "not remembering the injury," or "losing consciousness" as a result of injury during deployment Patient Health Questionnaire 15-item scale (PHQ-15): how much individual has been bothered by each symptom in past 4 weeks (0 = not, 2 = bothered a lot); high severity is score ≥15 Posttraumatic Stress Disorder Checklist 17-item (PCL-17): PTSD defined by presence of intrusion, avoidance, and hyperarousal symptoms with total score ≥50 PHQ depression module (PHQ-9): depression defined as ≥5 DSM-IV symptoms and functional impairment at very difficult or extremely difficult level Two-Item Conjoint Screen for Alcohol (modified): alcohol misuse defined by positive answer on either item

Author, Year Funding Source	Data Source: Registry/ Database	Data Source: Clinical Cohort	Inclusion/Exclusion Criteria	Cohort Characteristics	Measures
Wojcik, 2010[19] Funding Source: None reported	✓ Defense Manpower Data Center; Standard Inpatient Data Record (Army); Defense Casualty Information Processing System (Army); Joint Theater Trauma Registry		Inclusion: hospitalized in Army facility in-theater, Europe, or US; TBI Exclusion: none reported	N = 2,448 episodes of hospitalization with TBI (n = 1,388 episodes with mechanism of injury data: 871 blast, 517 non-blast) Age (years): mean NR (66% of all TBI hospitalizations in 20-29 year range) Gender (% male): 97.5% (all TBI hospitalizations) Cohort years: 2001-2007 Rank: 93% enlisted, 7% officers (all TBI hospitalizations) Duty/description: 76% active duty; also 66% combat, 16% combat service, 13% combat service support, 5% unknown Blast exposure history: NR Time since exposure: <30 days Duration of deployment: NR Rural or urban residence: NR	TBI severity (based on ICD-9-CM codes and Barell Matrix classification): -Type 1 [most severe] -Type 2 -Type 3 [least severe])
Xydakis, 2012[24] Funding Source: None reported		✓	Inclusion: consecutive polytrauma inpatients; transported to WRAMC following injury during combat operations requiring immediate stateside evaluation; closed head injury (CHI) from blunt or blast mechanism Exclusion: none reported	N = 365 blast CHI, 198 with TBI N = 102 non-blast CHI, 58 with TBI Age (years): 24 (blast group only) Gender (% male): 99 (blast group only) Cohort years: NR Rank: NR Duty/description: NR Blast exposure history: NR Time since exposure: 8 days (median, blast group only) Duration of deployment: NR Rural or urban residence: NR	TBI evaluation

BAMC = Brooke Army Medical Center; DoD = Department of Defense; DVBIC = Defense and Veterans Brain Injury Center; EMED = Expeditionary Medical Encounter Database; SAMMC = San Antonio Military Medical Center; TPRC = Tampa Polytrauma Rehabilitation Center; VAMC = VA Medical Center; VHA = Veterans Health Administration; WRAMC = Walter Reed Army Medical Center; MIRECC = Mental Illness Research, Education, and Clinical Center; PRC = Polytrauma Rehabilitation Center (inpatients); PNS = Polytrauma Network Site (outpatients); USAISR = US Army Institute of Surgical Research; mTBI = mild traumatic brain injury; LOC = loss of consciousness; NBR = non-blast-related; BR = blast-related; BPPV = benign paroxysmal positional vertigo; cVEMP = cervical vestibular evoked myogenic potential; SVV = subjective visual vertical; SOT = sensory organization test; PCL-C = PTSD Checklist – Civilian version PCL-M = PTSD Checklist – Military version; NSI = Neurobehavioral Symptom Inventory; CHI = closed head injury; VOR = vestibular-ocular reflex; VSR = vestibular-spinal reflex

[a] Patients treated at US Army Institute of Surgical Research (USAISR) Burn Center; medical records obtained from Joint Theater Trauma Registry

Table 4a. Mortality Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
DuBose, 2011[13]							Blunt: 9.8% (11/112) Blast (explosion): 8.6% (32/374); OR 0.66 (0.31, 1.41) Gunshot: 6.8% (8/118); OR 0.60 (0.19, 1.89)	
Sayer, 2008[48]							3% (3/106)	1% (1/82); P = .63

Table 4b. PTSD Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Belanger, 2009[26]							**PCL:** 41.1 (18.0)	**PCL:** 32.9 (17.2); P<.07
Belanger, 2011[27]			**PCL:** 41.5 (17.4)			**PCL:** 37.3 (17.6); P = .047		
Clark, 2009[29]							**PTSD diagnosis:** 45.1%	**PTSD diagnosis:** 11.8%; P<.05
Collen, 2012[31]					**PTSD (comorbid diagnosis)** 60.5%	**PTSD** 48.6%; P = .24		
Cooper, 2012[32]			**PCL-M:** 37.88 (16.42)	**PCL-M:** 36.29 (14.72); P = .696				
Goodrich, 2014[35]			**PTSD diagnosis:** 62% (31/50)	**PTSD diagnosis:** 20% (10/50); P<.001				

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Kennedy, 2010[16]			**PCL-C total:** 44.3 (17.6) **PCL-C > 50:** 38.2% **Re-experiencing**: 13.3 (5.9) **Avoidance:** 15.8 (7.4) **Hyper-Arousal:** 15.2 (5.6)	**PCL-C total:** 42.7 (16.9); P = .20 **PCL-C > 50:** 33.3%; P = .29 **Re-experiencing:** 12.0 (5.7); P = .02 **Avoidance**: 15.6 (7.0); P = .83 **Hyper-Arousal**: 14.5 (5.7); P = .20				
Kontos, 2013[22]							**PTSD symptoms, Mean (SD):** 22.6 (8.8) **OR - clinical levels of PTSD symptoms (blast vs blunt):** 2.12 (1.68, 2.66); P = .001 **Blast history dose-response[a]**: a. Symptom scores increased significantly with increased number of diagnosed blast mTBIs b. OR for clinical levels of PTSD symptoms significant for 3+ blasts vs 1 blast but not 2 vs 1 or 3+ vs 2	**PTSD symptoms:** 20.3 (7.1); P<.01

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Lippa, 2010[39]					**PCL total Mean (SD):** 54. 5 (15.0) **PCL total ≥ 50** 89/138 (64.5%)	**PCL total:** 49.8 (15.1); P = .054 **PCL total ≥ 50** 25/56 (44.6%); P<.05		
Luethcke, 2011[17] Blast is primary blast Non-blast includes secondary, tertiary, quaternary, and non-blast	**PCL-M Mean (SD)** 27.8 (8.9)	**PCL-M Mean (SD)** 26.7 (13.2); P = .33						
Mac Donald, 2014[18] Blast is blast plus other mechanism of head injury Non-blast is other mechanism of head injury only			**PTSD** 22/53 (42%)	**PTSD** 14/29 (48%); P = .56 **PTSD Severity** P = .90				

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Maguen, 2012[40] (n = 968 for PTSD analysis)							**PTSD positive screen** Blast only head injury: 55/90 (61%) OR 4.7 (2.9, 7.7)* Blast plus other mechanism of head injury : 185/266 (70%) OR 6.5 (4.6, 9.3)*	**PTSD positive screen** 1 Non-blast head injury: 25/43 (58%) OR 4.6 (2.4, 8.8)* 2+ Non-blast head injuries: 9/19 (47%) OR 3.4 (1.3, 8.6)* *Reference for all ORs is TBI with no head injury (129/550; 24%)
Mora, 2009[43] Blast is IED exposure with primary blast injury Non-blast is IED exposure without primary blast injury			**PTSD Prevalence:** 67% (4/6)	**PTSD Prevalence:** 21% (3/13); P = .13 (calculated)				
Reid, 2014[47]							**PCL-C** **Mean (SD)**; P = .016 across groups Non-blast: 42.9 (18.2) 1 blast: 34.9 (17.1) 2 blasts: 41.5 (16.5) 3 blasts: 45.8 (17.5) 4-10 blasts: 46.5 (17.5)	
Sayer, 2008[48]			**PTSD Symptoms:** 42% (45/106)	**PTSD Symptoms:** 24% (20/82); P<.01				

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Wilk, 2010[21]			**PTSD Diagnosis** LOC: 72/161 (45%) CIC: 79/263 (30%)	**PTSD Diagnosis** LOC: 15/39 (39%); P = .59 CIC: 32/110 (29%); P = .90				

CIC = concussion with change in consciousness; LOC = concussion with loss of consciousness; NSI = Neurobehavioral Symptom Inventory; PCL = Post-traumatic Stress Disorder Checklist; PCL-M = PCL Military version; PCL-C = PCL Civilian version
[a] Analysis includes blast-only mTBI and combination blast-blunt mTB

Table 4c. Pain Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (< 30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Clark, 2009[29]							**Pain intensity (NRS):** 5.4 (2.3) **Number of pain sites:** 2.4 (1.3)	**Pain intensity:** 4.4 (2.8); P = NS **Number of pain sites:** 2.0 (1.5); P = NS
Sayer, 2008[48]			**Impairment:** 83% (88/106)	**Impairment:** 80% (65/82); P = NS				
Wilk, 2010[21]			**Stomach pain** LOC: 13/156 (8.3%) CIC: 14/254 (5.5%) **Back pain** LOC: 71/157 (45.2%) CIC: 84/257 (32.7%) **Arm, leg or joint pain** LOC: 78/156 (50.0%) CIC: 105/256 (41.0%)	**Stomach pain** LOC: 4/40 (10.0%); P = .76 CIC: 16/107 (15.0%); P = .01 **Back pain** LOC: 14/40 (35.0%); P = .29 CIC: 36/108 (33.3); P = .90 **Arm, leg or joint pain** LOC: 17/40 (42.5); P = .48 CIC: 54/107 (50.5); P = .11				

CIC = concussion with change in consciousness; LOC = concussion with loss of consciousness; NRS = Pain Numeric Rating Scale (0 = no pain, 10 = worst pain)

Table 4d. Burn Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Clark, 2009[29]							**Burn diagnosis:** 9.9%	**Burn diagnosis:** 2.1%; P = NS
Mora, 2009[43] Blast is IED exposure with primary blast injury Non-blast is IED exposure without primary blast injury			**TBSA** 8.1% (6.9%)	17.0% (10.6%); P = NR				
Sayer, 2008[48]			**Skin or soft tissue burn injury:** 13% (14/106)	**Skin or soft tissue burn injury:** 4% (3/62); P<.05				

TBSA = total body surface area

Table 4e. Limb Loss Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (< 30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Clark, 2009[29]							**Amputation:** 16.0%	**Amputation:** 2.9%; P<.05
Sayer, 2008[48]			**Amputation:** 9% (10/106)	**Amputation:** 2% (2/82) P<.10 (NS)				

Table 4f. Vision Loss Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Brahm, 2009[28] NOTE: Inpatients had moderate/severe TBI; outpatients had mTBI							*Inpatients* **Subjective visual complaint:** 77% (41/53) **Ocular injury:** 44% (25/57) **Legally blind:** 9% (5/54) *Outpatients* **Subjective visual complaint:** 76% (85/112) **Ocular injury:** 7% (8/112) **Legally blind:** 2% (2/112)	*Inpatients* **Subjective visual complaint:** 63% (5/8); P = .39 **Ocular injury:** 9% (1/11); P = .04 **Legally blind:** 33% (3/9); P = .08 *Outpatients* **Subjective visual complaint:** 75% (9/12); P = 1.0 **Ocular injury:** 17% (2/12); P = .25 **Legally blind:** (0/12); P = 1.0
Clark, 2009[29]							**Eye injury:** 37.5%	**Eye injury:** 23.5%; P = NS
Cockerham, 2013[30] (NOTE: Analyses of blast/non-blast were considered exploratory due to small size of non-blast sample; OSDI and dry eye disease measures were reported to be similar for blast and non-blast TBI)			**OSDI:** mean (SD): 21 (25) n = 44 **Tear production < 4mm:** 17 /44 (39%) **Tear osmolarity: >314:** 13/24 (54%) **Ocular surface staining:** 35/44 (80%)	**OSDI:** 16 (13) n = 9 **Tear production < 4mm:** 2/9 (22%) **Tear osmolarity >314:** 6/9 (67%) **Ocular surface staining:** 7/9 (78%)				

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Goodrich, 2013[34]			**Ocular injury:** 31% (15/49) **Monocular vision:** 12% (6/50) **Vision complaints**: 66% (33/50) **Light sensitivity:** 67% (31/46) **Reading complaints:** 56% (27/48) **Visual acuity poor (worse eye):** 28% (15/50)	**Ocular Injury:** 29% (14/49); P = 1.0 **Monocular vision:** 2% (1/5); P = .112 **Vision complaints:** 69% (34/49); P = NS **Light sensitivity**: 33% (13/40); P = .002 **Reading complaints:** 47% (20/43); P = NS **Visual acuity poor (worse eye):** 18% (9/50); P = .34				
Lew, 2011[14]							**Visual impairment only:** 8.8% (918/10431) (blast exposure was significant predictor of visual impairment with more with non-blast TBI reporting severe impairment P≤.001)	**Visual impairment only:** 15.7% (328/2090); P<.001 (calculated)

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Luethcke, 2011[17] Blast is primary blast Non-blast includes secondary, tertiary, quaternary, and non-blast	**Symptoms** Immediate 7/40 (18%) Current 5/40 (13%)	**Symptoms** Immediate 12/42 (29%); P = .24 Current 4/42 (10%); P = .67						
Reid, 2014[47]							**NSI Vision Problems** **Mean (SD);** P<.001 across groups adjusted for demographics and loss of consciousness Non-blast: 0.83 (1.02) 1 blast: 0.58 (0.84) 2 blasts: 0.97 (1.12) 3 blasts: 1.14 (1.17) 4-10 blasts: 1.20 (1.21)	
Sayer, 2008[48]			**Eye injury:** 47% (50/206) **Vision impairment** 58% (61/106)	**Eye injury:** 26% (21/82); P<.01 **Vision impairment:** 46% (38/82); P = NS				

OSDI = Ocular Surface Disease Index; SD = standard deviation

Table 4g. Hearing Loss Outcomes by Time Post-exposure – Key Question 3

Author, Year	**Short-term (< 30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Clark, 2009[29]							**Hearing problems** 35.3%	**Hearing problems** 32.4%; P = NS

Author, Year	Short-term (< 30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Lew, 2011[14]							**Auditory impairment only:** 33.1% (3453/10431) (blast exposure was significant predictor of auditory impairment; P≤.001) **Dual sensory impairment:** 35.4% (3692/10431)	**Auditory impairment only:** 22.7% (474/2090); P<.001 (calculated) **Dual sensory impairment:** 30.3% (622/2090); P<.001 (calculated)
Lew, 2007[38]							**Hearing loss:** 62% (26/42) **Tinnitus:** 38% (16/42)	**Hearing loss:** 44% (48/108); P = .04 **Tinnitus:** 18% (19/108); P = .007
Luethcke, 2011[17] Blast is primary blast Non-blast includes secondary, tertiary, quaternary, and non-blast	**Symptoms** Immediate 21/40 (53%) Current 9/40 (23%)	**Symptoms** Immediate 7/42 (17%); P = .001 Current 4/42 (10%); P = .11						
Mac Donald, 2014[18] Blast is blast plus other mechanism of head injury Non-blast is other mechanism of head injury only			**Hearing deficit** 10/53 (19%)	**Hearing deficit** 4/29 (14%); P = NS				

Author, Year	Short-term (< 30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Oleksiak, 2012[45]							**NSI-Hearing Difficulty score** Blast: 1.99 (0.98) Mixed: 1.83 (1.04)[a] Primary Blast: 2.09 (0.98) Secondary Blast: 1.81 (0.87); P = NS between blast types **% with score >1**[b] Blast: 93% Mixed: 88% Primary blast: 94% Secondary blast: 100%	**NSI-Hearing Difficulty score** Fall: 1.92 (1.15) Vehicle: 1.50 (1.08); P = NS across groups **% with score >1** Fall: 84% Vehicle: 80%
Reid, 2014[47]							**NSI Hearing Difficulty Mean (SD)**; P<.001 across groups adjusted for demographics and loss of consciousness Non-blast: 1.10 (0.99) 1 blast: 1.48 (1.16) 2 blasts: 1.34 (1.19) 3 blasts: 1.53 (1.17) 4-10 blasts: 1.84 (1.08)	

Author, Year	Short-term (< 30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Sayer, 2008[48]			**Otologic injury:** 46% (49/106) **Hearing loss:** 48% (51/106) **Tinnitus:** 26% (28/106)	**Otologic injury:** 23% (19/82); P<.01 **Hearing loss:** 33% (27/82); P<.05 **Tinnitus:** 12% (10/82); P<.05				
Wilk, 2010[21]			**Ringing in Ears** LOC 53/154 (34.4%) CIC 57/257 (22.2%)	**Ringing in Ears** LOC 6/40 (15%); P = .02 CIC 18/106 (17.0%); P = .32				

CIC = concussion with change in consciousness; LOC = concussion with loss of consciousness; NSI = Neurobehavioral Symptom Inventory (0 = no hearing loss, 4 = very severe hearing loss)

[a] Mixed = any combination of accident types

[b] Score > 1 is mild or more severe hearing loss

Table 4h. Vestibular Dysfunction Outcomes by Time Post-exposure – Key Question 3

Author, Year	**Short-term (< 30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Akin, 2011[15]							**DHI:** 58.9 (mean) (score of > 54 = severe) **SOT** -abnormal: 8/9 (89%) -normal: 1/9 (11%)	**DHI:** 41.8 (mean) (scores of 36 to 52 = moderate) **SOT** -abnormal: 5/9 (56%); P = .29 (calculated) -normal: 2/9 (22%) -did not complete: 2/9 (22%)
Hoffer, 2009[36]							**VOR study:** Descriptive differences between blunt and blast for phase and symmetry; no difference in gain function **VSR study:** **Sensory organization test (SOT):** Trend toward significantly better scores for blunt exposure groups, particularly if migraine-associated dizziness diagnosis **Motor Control Test (MCT):** Significantly more patients in blast groups had abnormal latency times	

Author, Year	**Short-term (< 30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Luethcke, 2011[17] Blast is primary blast Non-blast includes secondary, tertiary, quaternary, and non-blast	**Balance Symptoms**: Immediate 10/40 (25%) Current 3/40 (8%) **Dizziness Symptoms** Immediate 22/40 (55%) Current 7/40 (18%)	**Balance Symptoms**: Immediate 19/42 (45%); P = .06 Current symptoms: 5/41 (12%); P = .50 **Dizziness Symptoms** Immediate 28/42 (67%); P = .28 Current 9/42 (21%); P = .65						
Reid, 2014[47]							**NSI Loss of Balance Mean (SD)**; P<.001 across groups adjusted for demographics and loss of consciousness Non-blast: 0.98 (1.07) 1 blast: 0.72 (0.86) 2 blasts: 0.87 (0.95) 3 blasts: 1.18 (1.08) 4-10 blasts: 1.28 (0.91)	
Sayer, 2008[48]			**Balance/ equilibrium impairment:** 68% (72/106)					

Author, Year	**Short-term (< 30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Wilk, 2010[21]			**Dizziness** LOC: 15/155 (9.7%) CIC: 16/258 (6.2%) **Balance Problems** LOC: 14/155 (9.0%) CIC: 17/258 (6.6%)	**Dizziness** LOC: 5/40 (12.5%); P = .57 CIC: 7/107 (6.5%); P = 1.0 **Balance Problems** LOC: 6/40 (15.0%); P = .26 CIC: 6/106 (5.7%); P = .82				

CIC = concussion with change in consciousness; LOC = concussion with loss of consciousness; DHI = Dizziness Handicap Inventory (higher score = greater perceived handicap due to dizziness); SOT = Sensory Organization Test (composite equilibrium); VOR = vestibular-ocular reflex; VSR = vestibular-spinal reflex

Table 4i. Cognitive Function Outcomes by Time Post-exposure – Key Question 3

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Belanger, 2009[26]							**Trail Making Test** **WAIS-III** **BVMT-R[a]** **CLVT-II** No between-subjects effect for TBI etiology	
Clark, 2009[29]							**Rancho Score** 6.3 (1.4)	**Rancho Score** 6.0 (1.0); P = NS
Cooper, 2012[32]			**RBANS – total:** 94.88 (12.92)	98.62 (9.33); P = .211 (Groups also similar on all RBANS subscales)				
Kontos, 2013[22]							**Verbal memory:** 90.2 (7.9) **Visual memory:** 70.3 (13.0) **Visual processing speed:** 27.5 (4.3) **Reaction time:** 1.2 (0.2) **Blast history dose-response:** slower reaction time if 3+ blast mTBIs vs no mTBI; P<.05 **All scores: mean (SD)**	**Verbal memory:** 90.9 (7.7); P = NS **Visual memory:** 72.6 (13.2); P = .001 **Visual processing speed**: 28.3 (4. 5); P<.01 **Reaction time:** 1.1 (0.2); P = .001

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Lange, 2012[37]			**Neurocognitive Tests:** Between group differences (P<.05) for 2 of 12 measures with non-blast group performing worse; similar results with adjustment for months tested post-injury					
Luethcke, 2011[17] Blast is primary blast Non-blast includes secondary, tertiary, quaternary, and non-blast	**ANAM - Cognitive** Across 6 cognitive domains, speed (P = .74) and accuracy (P = .65) scores did not differ by injury type (blast/non-blast)							
Mendez, 2013[42] Blast is primary blast only Non-blast is blunt injury					Mean (SD) **PASAT** 28.9 (11.1) **FAB** 16.5 (1.4) **IGT** -7.0 (13.6)	**PASAT** 44.0 (4.5); P<.001 **FAB** 16.7 (2.2); P = NS **IGT** 2.2 (17.4); P = NS		
Nakase-Richardson, 2013[44]			**Rancho LCFS (median)** admission: 3 discharge: 4 **FIM-cognitive (median)** admission: 5 discharge: 7	**Rancho LCFS (median)** admission: 2 discharge: 4 (penetrating trauma), 5 (other trauma); P = NS **FIM-cognitive (median)** admission: 5 discharge: 5 (penetrating), 12 (other); P = NR				

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Reid, 2014[47]							**NSI Cognitive Mean (SD) unadjusted**; P<.001 across groups (unadjusted); P = .003 across groups adjusted for demographics and PCL-C) Non-blast: 8.3 (5.0) 1 blast: 6.5 (5.0) 2 blasts: 7.3 (5.2) 3 blasts: 9.0 (5.3) 4-10 blasts: 9.6 (5.2)	
Sayer, 2008[48]			**Cognition impairment:** 88% (93/106)	**Cognition impairment:** 93% (76/82); P = NS				
Wilk, 2010[21]			**Memory Problems** LOC: 48/154 (31.2%) CIC: 45/257 (17.5%) **Concentration Problems** LOC: 49/155 (31.6%) CIC: 62/255 (24.3%)	**Memory Problems** LOC: 12/40 (30%); P = 1.0 CIC: 33/107 (30.8%); P = .01 **Concentration Problems** LOC: 13/38 (34.2%); P = .85 CIC: 37/106 (34.9%); P = .05				

WAIS-III = Digit Symbol-Coding subset of Wechsler Adult Intelligence Scale-3rd edition; BVMT-R = Brief Visuospatial Memory Test-Revised; CVLT-II = California Verbal Learning Test-II; RBANS = Repeatable Battery for the Assessment of Neuropsychological Status; Rancho = Rancho Los Amigos Scale; ANAM = Automated Neuropsychological Assessment Metrics; PSAT = Paced Auditory Serial Addition Test; FAB = frontal Assessment Battery; IGT = Iowa Gambling Task; Rancho LCFS = Rancho Levels of Cognitive Functioning Scale; FIM = Functional Independence Measure; CIC = concussion with change in consciousness; LOC = concussion with loss of consciousness

[a] Etiology X severity interaction for BVMT-R with highest scores (best performance) for blast-injured mild TBI and lowest scores (worst performance for blast-injured moderate/severe TBI (means for non-blast mTBI and moderate/severe TBI were between means for blast mTBI and moderate/severe TBI)

Table 4j. Quality of Life Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Mendez, 2013[42] Blast is primary blast only Non-blast is blunt injury					**SF36-V*** Physical Composite 45.3 (9.4) Mental Composite 35.5 (13.2) *P = NS for all sub-scales	Physical 44.1 (12.3); P = NS Mental 37.3 (10.7); P = NS		

SF36-V = Health Related Quality of Life 36-item Short Form for Veterans

Table 4k. Functional Status/Employment Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Clark, 2009[29]							**FIM** 81.0 (31.8)	**FIM** 80.1 (30.4); P = NS
Mac Donald, 2014[18] Blast is blast plus other mechanism of head injury Non-blast is other mechanism of head injury only			**Global outcome (GOS-E)** P = .82 Moderate to severe disability (GOS-E ≤6): -Blast plus impact TBI: 41/53 (77%) -Non blast TBI 23/29 (79%); P = .84					

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Nakase-Richardsion, 2013[44]			**FIM-motor (median)** admission: 13 discharge:13	**FIM-motor (median)** admission: 13 discharge:13 (penetrating trauma), 28 (other trauma) P = .02 for other trauma vs blast/ penetrating				
Sayer, 2008[48]			**Motor functioning impairment:** 62% (66/106)	**Motor functioning impairment:** 65% (53/82); P = NS				
Wilk, 2010[21]			**≥ 2 missed workdays due to illness** LOC: 32/156 (20.5%) CIC: 44/260 (16.9%)	**≥ 2 missed workdays due to illness** LOC: 9/40 (22.5%); P = .83 CIC: 11/108 (10.2%); P = .11				

FIM = Functional Independence Measure (higher scores = greater independence); GOS-E = Glasgow Outcome Scale-Extended; CIC = concussion with change in consciousness; LOC = concussion with loss of consciousness

Table 4l. Other Outcomes by Time Post-exposure – Key Question 3

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Belanger, 2011[27]					**NSI** no significant effect for mechanism of injury (P = .36)			
Clark, 2009[29]							**Depression diagnosis** 25.5% **Any psychiatric diagnosis** 86.3%	**Depression diagnosis** 14.7%; P = NS **Any psychiatric diagnosis** 52.9%; P<.05
Collen, 2012[31]					**Sleep** Insomnia: 63% OSAS: 25.9% ESS: 8.8 (4.6) **Depression (comorbid diagnosis)** 87.7% **Anxiety (comorbid diagnosis)** 50.6%	**Sleep** Insomnia: 40%; P = .02 OSAS: 54.3%; P = .003 ESS: 11.3 (5.7); P = .04 **Depression** 80%; P = .29 **Anxiety** 20%; P = .002		
Cooper, 2012[32]			**HIT-6:** 56.03 (9.54)	54.32 (9.44); P = .489				
Fortier, 2014[33]					**mTBI Grade[a]** I: 14/26 (54%) II: 11/26 (42%) III: 1/26 (4%)	**mTBI Grade** I: 16/30 (53%) II: 12/30 (40%) III: 2/30 (7%); P = NS (calculated)		

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
French, 2014[25]			**Injury Severity (of 474 with blast mTBI)** Minor: 12% Moderate: 46% Serious: 27% Severe/critical: 15%	**(of 105 with non-blast mTBI)** Minor: 13% Moderate: 56% Serious: 21% Severe/critical: 10%; P = .202				
Lange, 2012[37]			**Personality Assessment Inventory (14 items including depression, anxiety, alcohol problems):** No significant between-group differences (P<.05); similar results with adjustment for months tested post-injury					
Lippa, 2010[39]					**Post-concussive symptoms** (cognitive, affective, sensory, somatic, and headache) were similar (blast vs non-blast)			
Luethcke, 2011[17] Blast is primary blast Non-blast includes secondary, tertiary, quaternary, and non-blast	**Global Mental Health Mean (SD)** 3.5 (0.4) **Insomnia Severity Index Mean (SD)** 7.7 (6.0) **Headache Symptoms** Immediate: 28/40 (70%) Current 21/40 (53%)	**Global Mental Health Mean (SD)** 3.4 (0.6); P = .87 **Insomnia Severity Index Mean (SD)** 8.2 (6.6); P = .87 **Headache Symptoms** Immediate: 34/42 (81%); P = .25 Current symptoms: 35/42 (83%); P = .003						

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Mac Donald, 2014[18] Blast is blast plus other mechanism of head injury Non-blast is other mechanism of head injury only			**Smell (Deficit)** 9/53 (17%) **Headache (MIDAS):** Blast and non-blast TBI groups similar (P = .48) **Neuropsychological testing:** Blast and non-blast TBI groups similar (P = NS) **Neuro-behavioral assessment:** Blast and non-blast TBI groups similar (P = NS) **Alcohol Misuse:** Blast and non-blast TBI groups similar (P = NR) **Depression Severity:** Blast and non-blast TBI groups similar (P = .38)	**Smell (Deficit)** 15/29 (52%); P = .0009				

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
MacGregor, 2011[20]			**TBI Blast-related** Mild: 1822/1852 (98%) Moderate: 76/90 (84%) Severe: 89/132 (67%) **Concomitant Injuries** Other HNF 1204/1987 (61%) Any extremity 611/1987 (31%) Spine/Back Injury 237/1987 (12%)	**TBI Non-blast** Mild: 30/1852 (2%) Moderate: 14/90 (16%) Severe: 43/132 (33%); P<.001 **Concomitant Injuries** Other HNF 41/87 (47%); P = .01 Any extremity 22/87 (25%); P = .28 Spine/Back 2/87 (3%); P = .006				

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Maguen, 2012[40] (n = 974 for depression analysis; n = 968 for alcohol analysis)							**Depression Positive Screen** Blast only head injury: 24/86 (28%) OR 2.2 (1.3, 3.8)* Blast plus other mechanism of head injury: 119/267 (45%) OR 4.4 (3.0, 6.4)* **Alcohol Misuse Positive Screen** Blast injury only 48/89 (54%) OR 1.5 (0.9, 2.5)* Blast plus other mechanism of head injury 143/262 (55%) OR1.6 (1.1, 2.2)*	**Depression Positive Screen** 1 non-blast head injury: 15/42 (36%); P = .42 (calculated) OR 3.2 (1.6, 6.3)* 2 + non-blast head injury: 5/22 (23%) OR 1.66 (0.6, 4.7)* **Alcohol Misuse Positive Screen** 1 non-blast head injury 19/43 (44%); P = .35 (calculated) OR 1.2 (0.6, 2.2)* 2+non-blast head injury 13/21 (62%) OR 2.4 (1.0, 6.0)* *Reference is TBI with no head injury

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Mendez, 2013[42] Blast is primary blast only Non-blast is blunt injury					Mean (SD) **RPQ-Total** 38.0 (8.8) **NSI** 42.1 (17.8) **IM-P** 23.2 (2.3)	**RPQ Total** 41.6 (9.2); P = NS **NSI** 46.2 (10.7); P = NS **IM-P** 21.3 (0.7); P<.001 **BFI, FrSBe, IAS** P = NS for all items		
Mora, 2009[43] Blast is IED exposure with primary blast injury Non-blast is IED exposure without primary blast injury			**ISS:** 7.8 (9.3)	**ISS:** 15.0 (11.6)				
Nakase-Richardson, 2013[44]			**Emergence from LOC** 60%	**Emergence from LOC** 56% (penetrating trauma) 76% (other trauma) P = .03 for other trauma vs blast/ penetrating				

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Pogoda, 2012[46]							**Multisensory Impairment** Reference: no mTBI etiology reported Non-blast only: OR 1.00 (0.80, 1.25); P = .99 Blast only: OR 1.03 (0.84, 1.25); P = .81 >1 Non-blast and >1 blast: OR 1.61 (1.30, 2.00); P<.001	
Reid, 2014[47]							**NSI (total)** **Mean (SD) unadjusted**; P<.001 across groups (unadjusted); P = .001 across groups adjusted for demographics and PCL-C) Non-blast: 29.3 (17.9) 1 blast: 24.1 (16.6) 2 blasts: 27.6 (17.2) 3 blasts: 32.9 (17.7) 4-10 blasts: 35.0 (17.8) **NSI Difficulty Falling or Staying Asleep** **Mean (SD)**; P<.001 across groups adjusted for demographics and loss of consciousness Non-blast: 2.37 (1.19) 1 blast: 1.82 (1.30) 2 blasts: 2.21 (1.32) 3 blasts: 2.34 (1.28) 4-10 blasts: 2.55 (1.28) **NSI Feeling Depressed or Sad** **Mean (SD)** P = .087cross groups adjusted for demographics and loss of consciousness Non-blast: 1.14 (1.33) 1 blast: 0.88 (1.11) 2 blasts: 1.01 (1.11) 3 blasts: 1.21 (1.24) 4-10 blasts: 1.17 (1.22)	

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Sayer, 2008[48]			**Sleep impairment:** 60% (64/106) **Depressive symptoms:** 37% (39/106)	**Sleep impairment:** 57% (47/82); P = NS **Depressive symptoms:** 38% (29/82); P = NS				
Schneiderman, 2008[23]							**PCS 3+** Prevalence ratio (PR) = 1.19 (CI not reported) Blast exposure vs non-blast (defined as no high-energy injury mechanism) NOTE: PR 1.02 (95% CI 0.69, 1.52) for any high-energy injury mechanism vs none; high-energy includes blast, bullet, shrapnel, motor vehicle crash, fall, air/water transport	

Author, Year	Short-term (<30 days)		Mid-term (30 days to 1 year)		Long-term (> 1 year)		Not Specified	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Wilk, 2010[21]			**Major Depression** LOC: 33/156 (21.2%) CIC: 26/255 (10.2%) **Sleep Problems** LOC: 95/154 (61.7%) CIC: 126/251 (50.2%) **Alcohol Misuse** LOC: 60/154 (39.0%) CIC: 72/255 (28.2%) **Headache** LOC: 63/157 (40.1%) CIC: 53/258 (20.5%)	**Major Depression** LOC: 6/38 (15.8%); P = .65 CIC: 17/106 (16%); P = .15 **Sleep Problems** LOC: 22/38 (57.9%); P = .71 CIC: 53/106 (50%); P = 1.0 **Alcohol Misuse** LOC: 16/38 (42.1%); P = .72 CIC: 40/107 (37.4%); P = .11 **Headache** LOC: 9/40 (22.5); P = .04 CIC: 19/108 (17.6); P = .57				
Wojcik, 2010[19]	***TBI Severity[a] (Hospitalization episodes)*** **Type 1 TBI:** 55% (501/911)**Type 2 TBI:** 39% (353/911) **Type 3 TBI:** 6% (57/911)	***TBI Severity[b] (Hospitalization episodes)*** **Type 1 TBI:** 43% (239/550)**Type 2 TBI:** 50% (277/550) **Type 3 TBI:** 6% (34/550) All: P = NR						

Author, Year	**Short-term (<30 days)**		**Mid-term (30 days to 1 year)**		**Long-term (> 1 year)**		**Not Specified**	
	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI	Blast TBI	Non-blast TBI
Xydakis, 2012[24]	***TBI Severity*** **Mild:** 68% (134/198) **Moderate:** 28% (55/198) **Severe:** 5% (9/198)	***TBI Severity*** **Mild:** 58% (34/58) **Moderate:** 33% (19/58) **Severe:** 9% (5/58) All: P = NR						

BFI = Big Five Inventory; FrSBe = Frontal Systems Behavior Scale; IAS = Interpersonal Adjectives Scale; IM-P = Interpersonal Measure of Psychopathy; MIDAS = Migraine Disability Assessment; NSI = Neurobehavioral Symptom Inventory; RPQ = Rivermead Post-Concussion Symptom Questionnaire; LOC = loss of consciousness; CIC = concussion with change in consciousness; PCS 3+ = post concussive symptoms (≥3 persistent); NSI = Neurobehavioral Symptom Inventory (post-concussion symptoms); HIT-6 = Headache Impact Test; ESS = Epworth Sleepiness Scale; OSAS = obstructive sleep apnea syndrome; LOC = loss of consciousness; AMS = alteration of mental state; PTA = posttraumatic amnesia

[a] Grade I = no LOC, 0-15 min of AMS, 0-15 min PTA; Grade II = LOC < 5 min, AMS >15 min to < 24 hours, PTA >15 min to < 24 hours; Grade II = LOC >5 and < 30 min, AMS > 24 hours, PTA > 24 hours

[b]Type 1 TBI = most severe; Type 3 TBI = least severe (Barell Injury Matrix)