

OUTCOMES ASSOCIATED WITH BLAST VERSUS NON-BLAST RELATED TRAUMATIC BRAIN INJURY IN US MILITARY SERVICE MEMBERS AND VETERANS: A SYSTEMATIC REVIEW

**Journal of Head Trauma Rehabilitation, 2017 Apr 18.
[Epub ahead of print]**

Nancy Greer, PhD, Nina Sayer, PhD, Eva Koeller BA, Tina Velasquez, MS,
Timothy J. Wilt, MD, MPH

Center for Chronic Disease Outcomes Research
Minneapolis VA Health Care System

History

2016 VA Evidence-based Synthesis Program Report:

Greer N, Sayer N, Kramer M, Koeller E, Velasquez T, Wilt TJ. Prevalence and Epidemiology of Combat Blast Injuries from the Military Cohort 2001-2014. VA ESP Project #09-009; 2016.

Topic nominated for review by:

- **Ralph DePalma, MD; Special Operations Office, VA Office of Research and Development**

Additional stakeholders:

- **David Cifu, MD; Chair, VHA TBI Advisory Committee**
- **Stuart Hoffman, PhD; Scientific Program Manager for Brain Injury, VA Rehabilitation Research and Development Service**
- **Col. Todd Rasmussen, MD; Director, Combat Casualty Care Research Program, US Army Medical Research and Materiel Command**

Full report available at: <http://www.hsrd.research.va.gov/publications/esp/reports.cfm>

Disclosure

This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the Minneapolis VA Medical Center, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (eg, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

VA Evidence-based Synthesis Program (ESP) Overview

- Sponsored by VA Office of Research and Development and the Quality Enhancement Research Initiative (QUERI)
- Established to provide timely and accurate syntheses/reviews of healthcare topics identified by VA clinicians, managers, and policy-makers, as they work to improve the health and healthcare of Veterans.
- Reports conducted by internationally recognized VA clinician methodologists
- Builds on staff and expertise already in place at the Evidence-based Practice Centers (EPC) designated by AHRQ. Four of these EPCs are also ESP Centers
- Broad topic nomination process – *eg*, VACO, VISNs, field staff – facilitated by the ESP Coordinating Center (Portland) through an online process:

<http://www.hsrd.research.va.gov/publications/esp/TopicNominationForm.pdf>

Poll Question #1

What is your primary role in the VA?

- Student, trainee, or fellow
- Clinician
- Researcher
- Administrator, manager, or policy-maker
- Other

Outcomes Associated with Blast versus Non-Blast Related Traumatic Brain Injury in US Military Service Members and Veterans: A Systematic Review

Background

- Traumatic brain injury (TBI) - described as the “signature injury” of the wars in Iraq and Afghanistan (Operation Enduring Freedom [OEF], Operation Iraqi Freedom [OIF], and Operation New Dawn [OND])¹
- 2012-2015 Post-Deployment Health Assessment (>350,000 service members)²
 - >8,000 with positive TBI screen
 - >45% of those reported exposure to blast or explosion

¹Okie S. Traumatic brain injury in the war zone. *N Engl J Med.* 2005;352(20):2043-2047.

²Surveillance 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.

Background

- Department of Veterans Affairs¹
 - 36% reported TBI secondary to blast exposure
 - 44% reported TBI secondary to both blast and non-blast exposures
- National Post-Deployment Adjustment Study²
 - Web-based survey data from 1,102 Iraq and Afghanistan Veterans
 - 33% reported mechanism of injury was blast or explosion

¹Scholten JD, et al. Analysis of US Veterans Health Administration comprehensive evaluations for traumatic brain injury in Operation Enduring Freedom and Operation Iraqi Freedom Veterans. *Brain Inj.* 2012;26(10):1177-1184.

²Lindquist L, Elbogen EB. Traumatic brain injury in Iraq and Afghanistan Veterans: new results from a national random sample study. June 1, 2017.

http://www.hsrd.research.va.gov/for_researchers/cyber_seminars/archives/video_archive.cfm?SessionID=2326.

Background

- Blast injuries often categorized as primary, secondary, tertiary, quaternary, or quinary¹
 - Factors: type of explosive, distance from explosion, body orientation relative to explosion, frequency of exposure
 - Polytraumatic (ie, associated with injuries to multiple body parts and organ systems)
- TBI associated with psychiatric comorbidity, postconcussive symptoms, and somatic sequelae even in absence of blast-exposure²
- Understanding outcomes associated with blast and non-blast TBI could assist in identifying areas of focus for rehabilitation services for service members and Veterans

¹https://blastinjuryresearch.amedd.army.mil/index.cfm/blast_injury_101

²Sayer NA. Traumatic brain injury and its neuropsychiatric sequelae in war Veterans. Annual Rev Med. 2012;63:405-419.

Poll Question #2

What is your level of familiarity/experience with systematic reviews?

- High (lead author, methodologist)
- Moderate (participated on research team, systematic review coursework)
- Low (have read systematic reviews)
- None

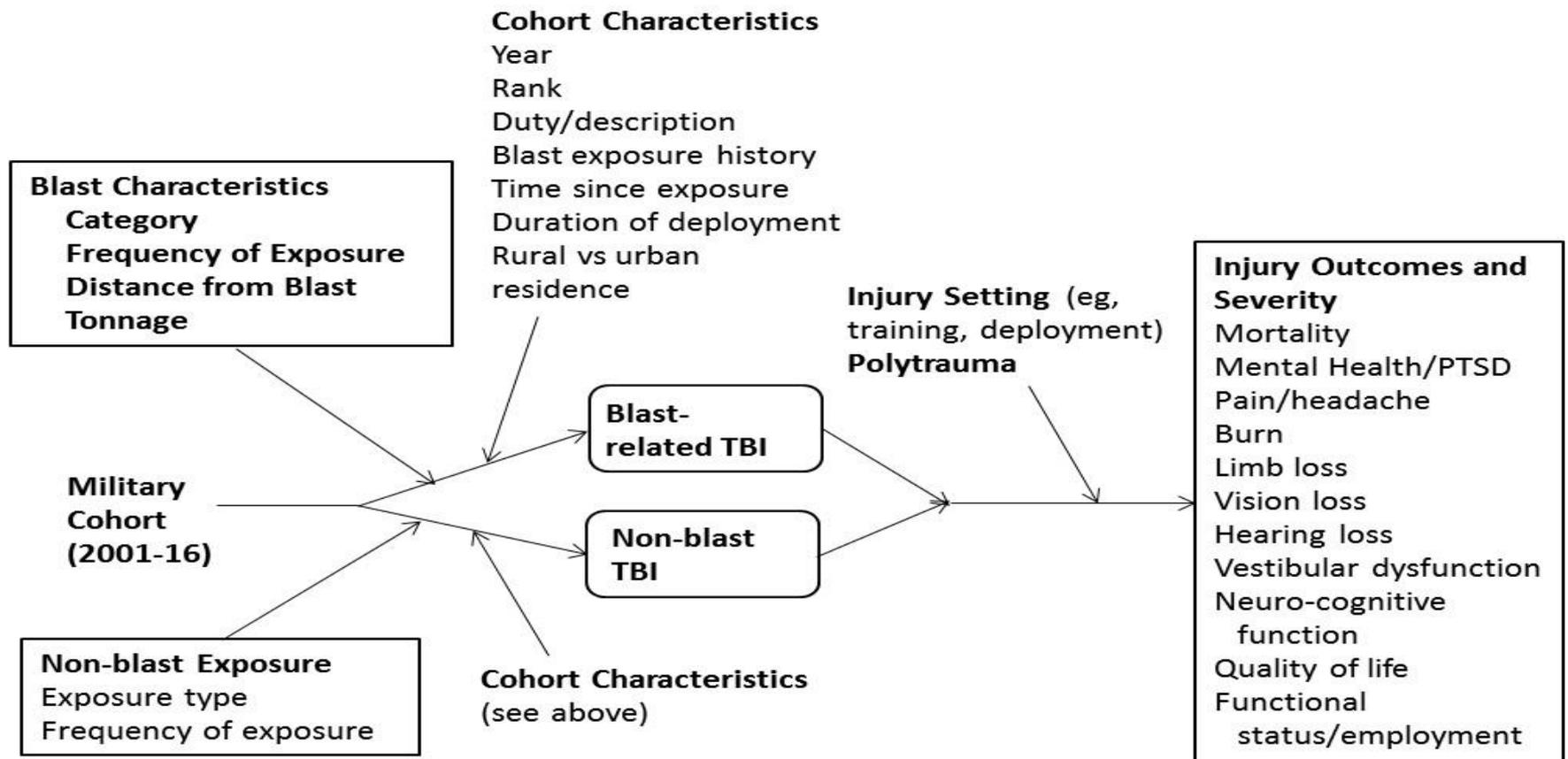
Systematic Review – Key Questions

1) What are the clinical and functional outcomes among US military personnel (2001-2016) who have sustained a blast-related TBI versus a non-blast TBI or a combined blast/non-blast TBI?

- Mortality, mental health, pain/headache, burn, limb loss, vision loss, hearing loss, vestibular dysfunction, neuro-cognitive function, quality of life, functional status/employment

2) What are the clinical and functional outcomes among US military personnel (2001-2016) who have sustained a blast-related TBI *according to blast characteristics*?

Analytic Framework



PICOTS

- Population: Military cohort 2001-2016
- Intervention: Blast-related TBI
- Comparator: Non-blast or combined blast/non-blast TBI
- Outcomes: Injury outcomes for blast vs non-blast or combined TBI and injury outcomes by blast characteristics for blast-related TBI
- 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)

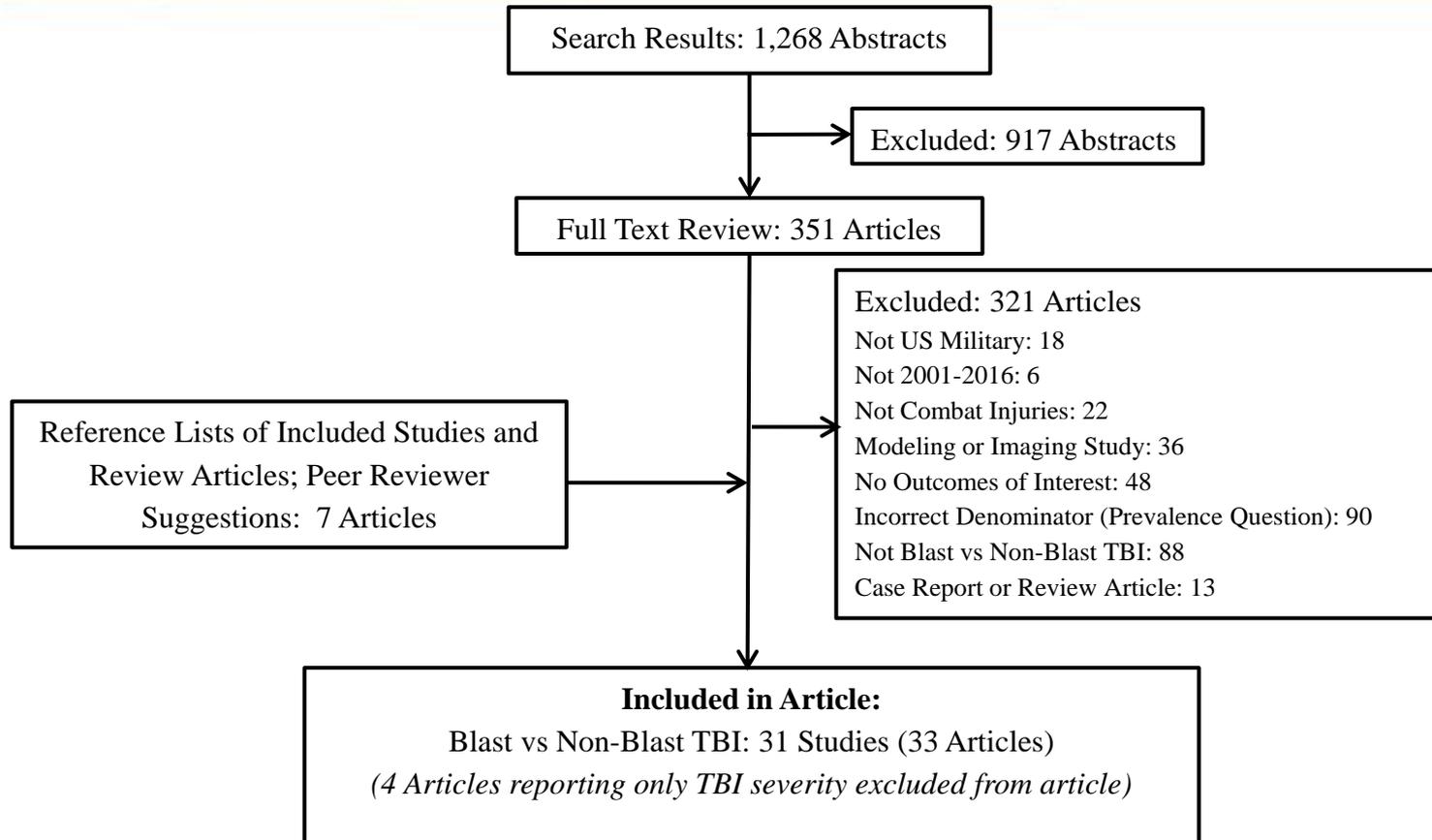
Methods

- Literature Search
 - MEDLINE (Ovid): January 2001 – June 2016, English language publications
 - Consultation with medical librarian
 - Additional articles from reference lists of systematic reviews and other reports, from references suggested by the topic stakeholders and technical expert panel members for ESP report
- Study Selection
 - Full text of potentially relevant studies reviewed in duplicate
 - Excluded:
 - Case reports
 - Studies not including US military personnel from OEF, OIF, or OND
 - Studies not involving combat injuries
 - Studies that did not report outcomes of interest for both blast and non-blast TBI groups

Methods

- **Data Abstraction and Risk of Bias**
 - Study characteristics (data source, inclusion/exclusion criteria, cohort characteristics) and outcomes for blast-related TBI and nonblast-related TBI groups abstracted by one researcher and verified by another
 - Reviewed articles for selection, performance, detection, attrition, and reporting bias
 - Overall risk of bias for each article rated high, moderate, or low
- **Data Synthesis**
 - Calculated effect sizes for scale scores and odds ratios for categorical data from individual studies if reported data allowed
 - Limited to outcomes reported by at least 5 studies
 - No pooled analyses – inappropriate due to heterogeneity of the study populations and outcome measures
 - No formal rating of strength of evidence for outcomes

Results – Literature Flow



Results – Characteristics of 31 Included Studies

Data Source			Sample Size Blast/ Non blast	Risk of Bias	Time Since Injury				TBI Severity		
Registry/ Database	Survey	Clinical Sample			< 30 days	30 days to 1 year	> 1 year	Any or Unclear	Mild	Moderate/ Severe	Mixed (results not reported separately)
5	2	24	25,020 (6-10,431) 2,090 (9-2,090)	2 Low 23 Moderate 6 High	3 ^a	12	4	13	20 ^b	4	11

^a1 study reported outcomes at <30 days and 30 days to 1 year post exposure

^b2 studies included mild and moderate/severe TBI with results reported separately; 1 included all severity levels reporting some results separately

NOTE: Assessment of Blast Exposure

Medical record or database entries: 16 studies; Self-report: 7 studies; Unclear: 8 studies

Results – Question 1

Outcome	Increased in Blast TBI Group	No Difference – Blast vs Nonblast TBI	Notes
PTSD Symptoms	◆ ◆ ◆ ◆ ^a	◆ ◆ ◆ ◆ ◆	^a increased if 4+ blasts, otherwise no difference or lower in blast group (1 study)
PTSD Diagnosis	◆	◆ ◆ ◆	
Headache	◆ ^b	◆ ◆ ◆ ^c	^b increased if loss of consciousness ^c immediate post-injury
Vision Impairment	◆	◆ ◆ ◆ ◆ ◆	+1 study with lower impairment in blast group; one study reported increased <i>injury</i> in blast group and one reported no difference

◆ = 1 study

Results – Question 1

Outcome	Increased in Blast TBI Group	No Difference – Blast vs Nonblast TBI	Comments
Hearing Loss	◆ ◆ ◆ ◆ ◆ ^a ◆ ^b	◆ ◆ ◆	^a increased if loss of consciousness ^b immediate post-injury
Depression		◆ ◆ ◆ ◆ ◆ ◆ ◆	
Insomnia/ Sleep Disorders	◆ ^c	◆ ◆ ◆	+1 study with mixed results ^c increased if 4+ blasts, otherwise no difference or lower in blast group
Alcohol Misuse		◆ ◆ ◆	

◆ = 1 study

Results – Question 1

Outcome	Increased in Blast TBI Group	No Difference – Blast vs Nonblast TBI	Comments
Vestibular Dysfunction	◆	◆ ◆ ◆	
Neurocognitive Function	◆ ^a	◆ ◆ ◆ ◆ ◆ ◆ ◆ ◆	+ 5 studies with mixed results (different elements) ^a increased if no loss of consciousness
Functional Status		◆ ◆ ◆ ◆	+ 1 study with mixed results (different non-blast trauma types)

Few reports of mortality, burn injuries, limb loss and other musculoskeletal injuries, or quality of life

◆ = 1 study

Results – Question 2

- Primary vs Secondary Blast (Oleksiak 2012)
 - Similar hearing difficulty scores for primary (mean 2.1) and secondary (mean 1.8) blast injury groups
 - % with more than “mild” hearing loss similar for primary (94%) and secondary (100%) blast injury groups
- Primary vs All Other Blast + Nonblast
 - Similar PTSD symptoms, vision symptoms, hearing symptoms, vestibular dysfunction symptoms, cognitive function, insomnia, and headache (Luethcke 2011)
 - Similar quality of life and post-concussive symptoms; mixed results for different cognitive measures (Mendez 2013, 2 studies)
 - Similar prevalence of PTSD; lower injury severity score and burn injury severity in primary blast group (Mora 2009)

Summary of Findings

- Similar rates of vision loss, vestibular dysfunction, functional ability, depression, sleep disorders, and alcohol misuse
- Inconsistent results for PTSD diagnosis or symptom severity, headache, hearing loss, and neuro-cognitive function
- Little data on mortality, burn injuries, limb loss, and quality of life
- 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)
 - level of TBI severity
- Little data on outcomes according to blast characteristics

Summary of Findings - Limitations

- Limited information in published literature on outcomes associated with blast versus non-blast TBI among US military personnel
- Definitions of blast/non-blast injury, assessment of outcomes (timing of assessment relative to exposure, scales used), and reporting methods vary
- Few studies report 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)
 - whether there was additional trauma
- Few studies report long-term outcomes
- Most studies - small, clinical cohort studies, mTBI patients, evaluated at a DoD or VA medical facility

Conclusions

- Prevalence of *most* clinical and functional outcomes reviewed did not differ between blast and nonblast-related TBI groups
- With inconsistent results for some outcomes and limited reporting of others – findings may change with future research
- Future studies of blast-related injuries should attempt to capture information about history of blast exposure, blast type, distance from the blast, injury type, and injury severity

Resources

Recent Cyberseminars:

<https://www.hsrd.research.va.gov/cyberseminars/default.cfm>

Characterizing Traumatic Brain Injury in Iraq and Afghanistan War Era Veterans

Eric Elbogen, Lisa Lindquist

https://www.hsrd.research.va.gov/for_researchers/cyber_seminars/archives/video_archive.cfm?SessionID=2326

Brain Injury and Psychological Health Following Combat Deployment: Implications for Long Term Outcome

Christine MacDonald

https://www.hsrd.research.va.gov/for_researchers/cyber_seminars/archives/video_archive.cfm?SessionID=2321

Questions?

If you have further questions, please feel free to contact:

Nancy Greer, PhD

nancy.greer@va.gov

Full-length report available on ESP website:

<http://www.hsrd.research.va.gov/publications/esp/reports.cfm>