

# **The Assessment and Treatment of Individuals with History of Traumatic Brain Injury and Post-traumatic Stress Disorder**

**A Systematic Review of the Evidence**

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# Acknowledgements

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# Overview

- VA Evidence-based Synthesis Program (ESP)
- Current Report
  - Background
  - Key questions
  - Methods
  - Results
  - Conclusions
  - Recommendations for future research
- Q & A

# VA Evidence-based Synthesis Program (ESP)

- Sponsored by VA Office of R&D and HSR&D
- Syntheses of health care topics for VA leaders
- Inform clinical policy, CPGs, future research, performance measures, and drug formulary decisions
- Topics identified by HSR&D Field Based Science Advisory or similar advisory groups and by program officials in VA Central Office
  - Topics may also be nominated using form on ESP web site:

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

- Conducted by 1 of 4 centers with systematic review expertise (Portland, West LA, Durham, Minneapolis)

# VA Evidence-based Synthesis Program (ESP)

- Planning and Oversight Committee
  - HSR&D, Patient Care Services, OQP, & VISN Clinical & Quality Management Officers
  - Identifies priority issues & ensures quality
- Technical Advisory Panel (TAP)
  - Recruited for each topic to provide content expertise
  - Develop, review, refine, and approve topic and key questions
  - Review data/draft report
- External Peer Reviewers
  - Review and comment on draft report
- Final reports posted on VA HSR&D website:  
<http://www.hsrd.research.va.gov/publications/esp/>

# Current Report

The Assessment and Treatment of Individuals with History of  
Traumatic Brain Injury and Post-traumatic Stress Disorder: A  
Systematic Review of the Evidence  
(August, 2009)

Full-length report available on ESP web site:

[http://www.hsrd.research.va.gov/publications/esp/TBI-PTSD-  
2009.pdf](http://www.hsrd.research.va.gov/publications/esp/TBI-PTSD-2009.pdf)



# Background

- Traumatic Brain Injury (TBI): Trauma to the head resulting in alteration or loss of consciousness or post-traumatic amnesia (CDC, 1999)
  - Falls, motor vehicle crashes, blasts
- Blunt force TBI differentiated by level of severity: mild, moderate, severe
- Up to 23% of soldiers/veterans reported to have experienced a TBI (mostly mild TBI) (Terrio et al., 2009)
- While most with mild TBI will fully recover, a minority will suffer ongoing post-concussive somatic, cognitive, and/or behavioral symptoms
  - Persistent post-concussive symptoms may be mistaken for symptoms of chronic stress or other mental health disorders

# Background

- Post-traumatic Stress Disorder (PTSD): Anxiety disorder characterized by re-experiencing, avoidance, and hyperarousal symptoms following exposure to a traumatic event (APA, 2000)
- Prevalence estimated from 1.4% - 31% of OIF soldiers (Sundin et al., 2009)
- VA treated >100,000 OEF/OIF veterans for PTSD from 2002-2008 (Kang, 2009)
- There are efficacious treatments for PTSD
- Many symptoms of PTSD can also occur among those with a history of mild TBI (i.e., anxiety, insomnia and fatigue, problems thinking or remembering, irritability, anger, or aggression)

# Background

- Overlap between TBI and PTSD has been studied (and debated) for many years
  - Memory of traumatic event presumed necessary for PTSD but often absent in more severe cases of TBI
- Continued evidence of comorbid TBI and PTSD across study populations and TBI severity levels
  - Same exposures/events
  - TBI increase susceptibility to PTSD?
  - PTSD increase risk of TBI?
- Clinicians in DoD, VA, and private sector treating patients with both conditions
  - Veterans of OEF/OIF
  - Mild TBI

# Uncertainties

- Prevalence of comorbid (mild) TBI and PTSD unknown
- Unknown whether diagnostic/screening instruments for assessing history and symptoms of mild TBI and PTSD are accurate if patient has both conditions
  - Screening for mild TBI history based on recall of event, which may be affected by current PTSD symptoms
- Unknown whether evidence-based treatments for symptomatic mild TBI and PTSD alone are effective when the conditions co-occur
  - Pharmacologic agents used to treat symptoms of PTSD may exacerbate TBI-related cognitive symptoms
  - Cognitive limitations, problems with emotion regulation or impulse control, or pain associated with mild TBI may decrease effectiveness of PTSD treatments

# VA Consensus Conference

- In 2009, expert clinicians and researchers were convened to develop practice recommendations for treatment of veterans with comorbid mild TBI, PTSD, and pain
- Additionally, a systematic review of evidence was commissioned through the VA ESP to help provide background for this conference

# 3 Key Questions

KQ1) What is the **prevalence** of comorbid TBI and PTSD?

- Does reported prevalence vary by study population, injury etiology, TBI severity (mild versus moderate/severe), or methods of case ascertainment?

KQ2) What is the relative accuracy of **diagnostic** tests used for:

- Assessing mild TBI when mild TBI is comorbid with PTSD?
- Assessing PTSD when PTSD is comorbid with mild TBI?

KQ3) Are there psychosocial or pharmacological therapies used for **treatment** of mild TBI and PTSD simultaneously?

- Are therapies for treatment of mild TBI effective when mild TBI is comorbid with PTSD? Is there evidence of harms?
- Are therapies for treatment of PTSD effective when PTSD is comorbid with mild TBI? Is there evidence of harms?

# Methods

- **Key questions, scope, and work plan developed and refined with TAP**
- **Operational definitions:**
  - TBI**
    - confusion, disorientation, or loss of consciousness due to force or blow to head
    - studies must have included participants with reported hx of TBI, regardless of current symptoms
  - PTSD**
    - development of symptoms characterized as PTSD by DSM-III or IV
    - studies must have included participants with DSM diagnoses of, or positive screens for, PTSD as determined through clinical diagnosis, semi-structured interviews, or scores exceeding specified cut-off indicating probable PTSD on self-report inventories

# Methods

- **Literature Search**

- 2 respective searches of PubMed, PsycInfo, REHABDATA, and Cochrane Review databases
  - TBI (e.g., “coma,” “head injuries, closed”)
  - PTSD (e.g., “post-traumatic stress”)
- Results then merged
- Limited to English-language articles presenting primary data on adult human subjects and published from January, 1980 to June, 2009
- Reference lists were searched for additional references
- Expert recommendations were solicited



# Methods

- **Inclusion/Exclusion Criteria**

- All study designs except case report were included
- Studies must have assessed participants for a “probable” history of TBI or diagnosed TBI history, regardless of current symptoms
- Studies must have assessed participants for DSM-III or IV diagnoses of PTSD determined through clinical diagnoses or interviews, or “probable” PTSD based on indicated cut-off scores using self-report inventories or screening measures
- Studies were excluded if they did not meet the above criteria, or if they did not present data in a manner that addressed key questions

# Methods

- **Data Extraction**

- Titles and abstracts reviewed by investigator to select studies that may address key questions
- Full text review conducted to determine whether study met inclusion criteria
- For included studies, data were abstracted onto standardized article abstraction forms

**TBI/PTSD Review  
Article Abstraction Form**

Author (first): \_\_\_\_\_

Journal: \_\_\_\_\_

Year Publication: \_\_\_\_\_

Country: \_\_\_\_\_ (where study performed)

Reviewer: \_\_\_\_\_

**VERIFICATION/SELECTION OF STUDY ELIGIBILITY**

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

**DESIGN (circle)**

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

**KEY QUESTION(S) (circle)**

KQ1: Epidemiology  
 KQ2: Assessment  
 KQ3: Treatment  
 Background

**NOTES:**

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

**PARTICIPANTS**

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

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

# Methods

- **Outcomes of Interest**

- KQ1: Frequency of TBI + PTSD, according to:
  - # of injuries/severity (mild vs. moderate/severe)
  - Etiology (e.g., military vs. civilian)
  - Method and timing of assessment
  - Patient demographics (e.g., gender, race, age, education)
- KQ2: Sensitivity, specificity, and disease/Txt reclassification
- KQ3: Improvement in symptoms, loss of dx, functional status, pain, QOL, harms
- Assess study quality and external validity

# Methods

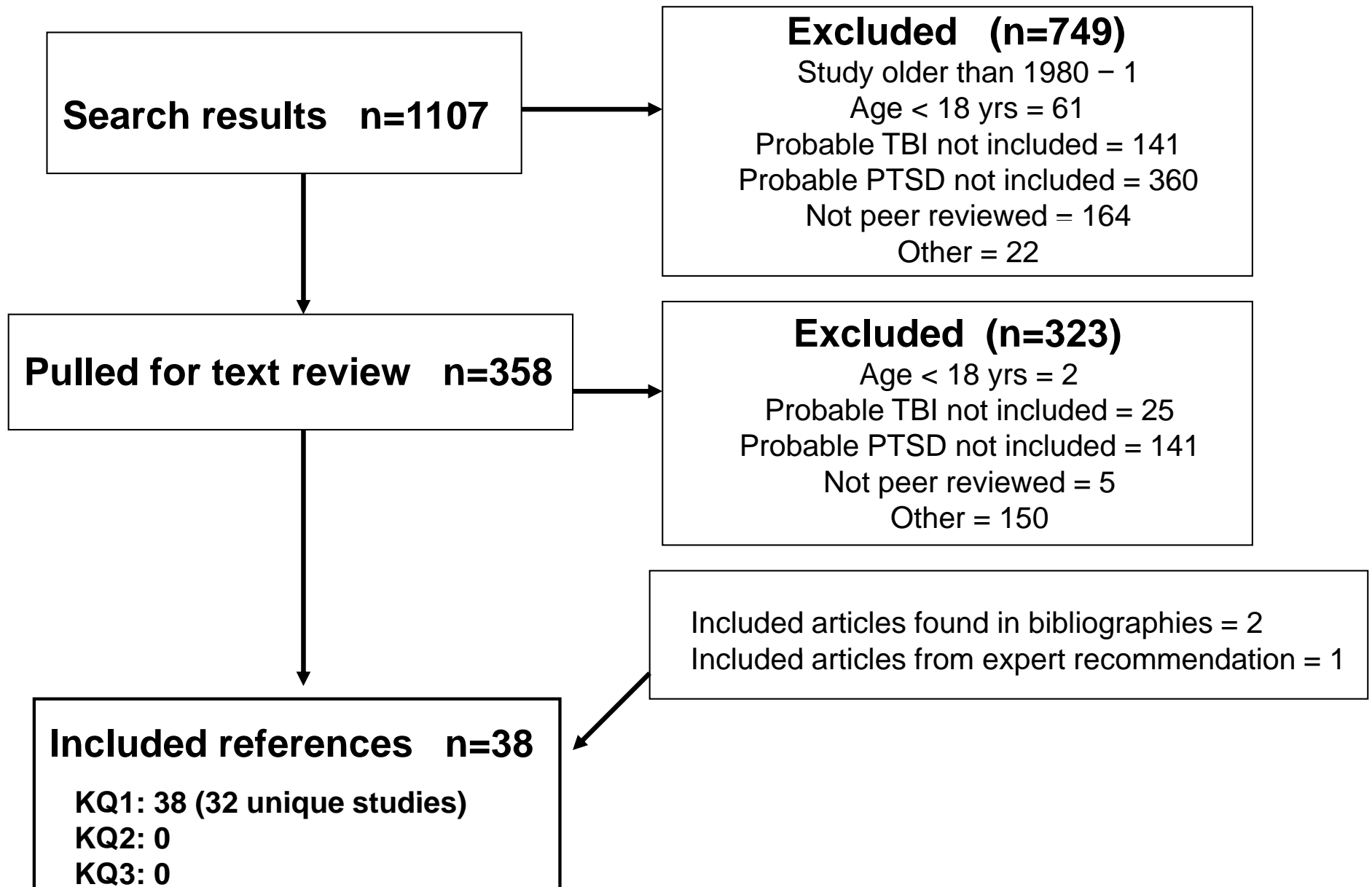
- **Data Synthesis**

- Critically analyzed studies, comparing methods and results, and drew conclusions based on qualitative synthesis of findings
  - Heterogeneity across studies precluded pooled analysis or formal quality ratings
  - Emphasis on studies with greatest applicability to mild TBI/PTSD among OEF/OIF veterans

# Results

- Combined reference library contained 1,107 citations
- 32 unique studies, described in 38 references, met inclusion criteria

# Study flow diagram



# Description of Studies

- All 32 studies reported data on frequency of TBI/PTSD
  - 24 reported on mild TBI/PTSD
- Involved 10-2,525 participants (majority <200)
- Most were cohort or cross-sectional studies
- Considerable variation in study design
  - Participant characteristics
  - Trauma etiology
  - Methods and timing of participant enrollment
  - Methods and timing of TBI and PTSD assessment
- 10 studies involved US military personnel and veterans
  - 3 largest studies involved individuals who served in OEF/OIF (Hoge et al., 2008; Schneiderman et al., 2008; RAND, 2008)



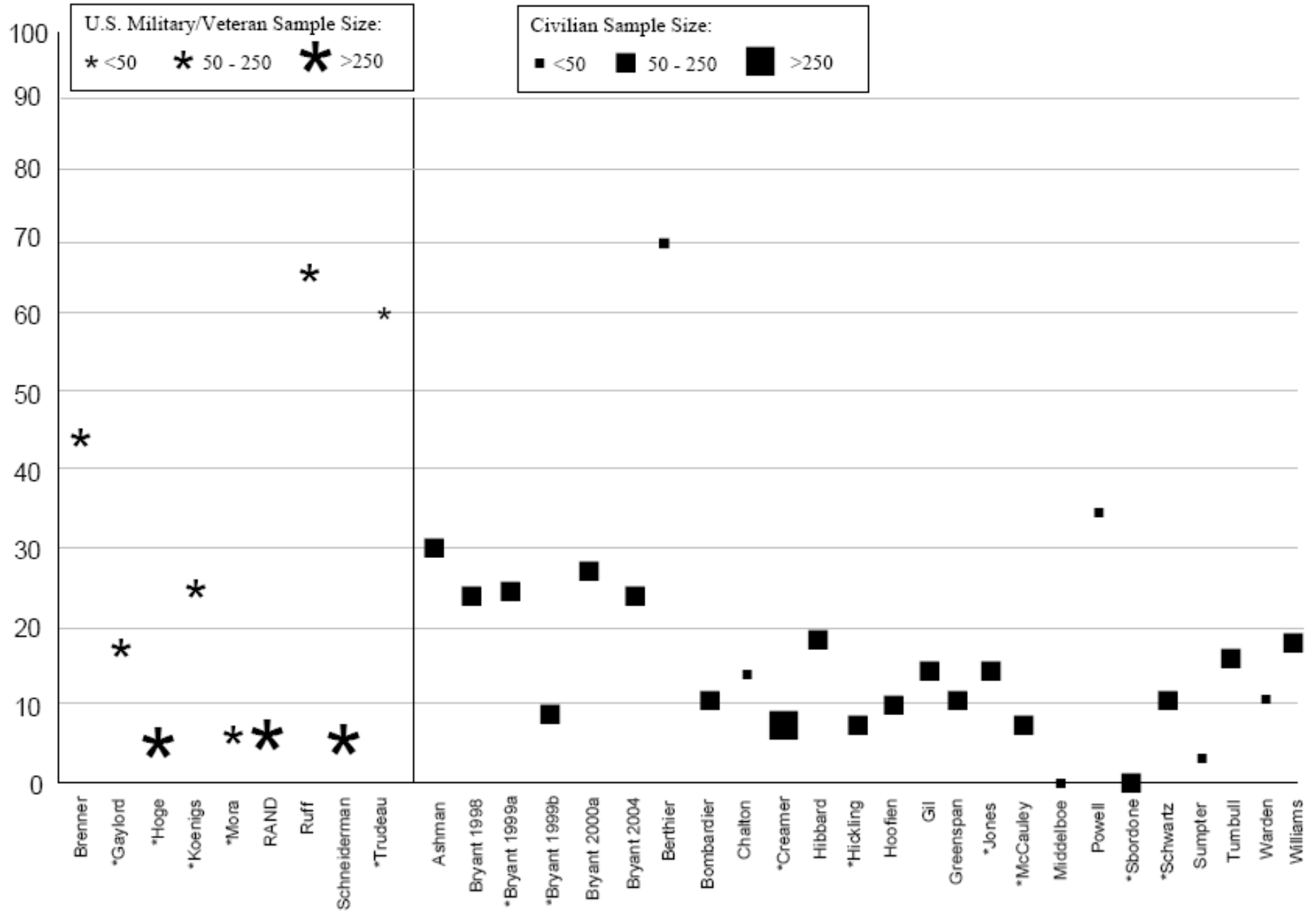
# KQ1: Prevalence

- Frequency of TBI/PTSD ranged from 0% to 70%
  - Majority (n=23) reported frequencies <20%
  - Few reporting frequencies >50% were small and/or had especially non-representative study samples
- 3 large studies involving U.S. military/veterans reported frequencies between 5 and 7%
- 2 largest studies involving non-military participants reported frequencies of 8%

# KQ1: Prevalence

- No consistent patterns in frequency of PTSD over time in longitudinal studies of participants with TBI history
- No consistent patterns when comparing different trauma etiologies
  - 32% to 66% of military related TBI also had PTSD
  - 14% to 56% of non-military TBI also had PTSD
- No clear patterns in frequency of TBI/PTSD based on methods of case identification
  - 3% to 70% in studies utilizing structured interviews to assess PTSD
  - 5% to 60% in studies using self-report instruments to assess PTSD

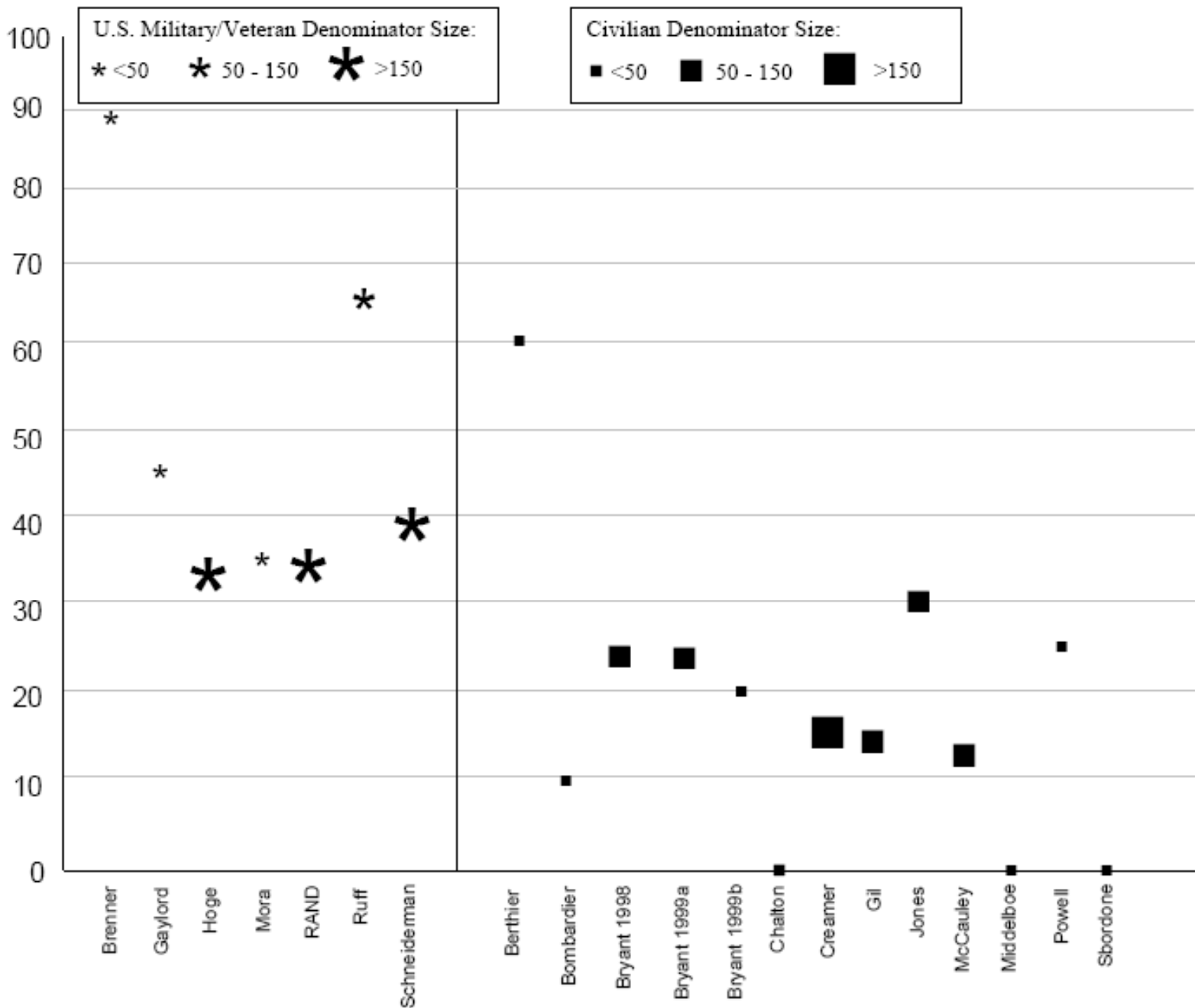
# Frequency of TBI/PTSD Across Studies



# KQ1: Prevalence (mild TBI/PTSD)

- Analyses restricted to studies exclusive to individuals with history of mild TBI or those that stratified results by TBI severity
- Frequency of PTSD in individuals with mild TBI history ranged from 0 to 89%
  - Majority (n=12) reported values between 10% and 40%
- The 3 largest studies involving US OEF/OIF military personnel/veterans reported 33% to 39% of individuals with probable mild TBI also had probable PTSD
- The 5 largest civilian studies reported 12% to 27% of individuals with mild TBI also had PTSD

# Frequency of PTSD in Subjects with Mild TBI



# KQ2: Diagnostic Accuracy

- No studies examining methods of PTSD assessment in individuals with mild TBI or methods of mild TBI assessment in individuals with PTSD

# KQ2: Diagnostic Accuracy

## Secondary Studies

- Sumpter & McMillan (2005) compared relative accuracy of 4 PTSD assessment tools in 34 individuals with severe TBI
  - Post-traumatic Diagnostic Scale (n=20; 59%)
  - Impact of Events Scale (n=15; 44%)
  - CAPS, criteria B-F, without clinical judgment (n=6; 18%)
  - CAPS, criteria B-F, with clinical judgment (n=1; 3%)
- Sumpter & McMillan (2006) interviewed participants to help identify reasons for false positives
  - “Curiosity about event” vs. “re-experiencing”
  - Upsetting thoughts re “effects of TBI” vs. “event itself”

# KQ3: Treatment

- No studies were identified that examined the effectiveness of therapies for treatment of symptomatic mild TBI or PTSD in individuals with both



# KQ3: Treatment

## Secondary Studies

- Bryant et al. (2003) conducted a small (n=24), good-quality RCT examined effectiveness of 5 weekly CBT sessions on individuals with mild TBI and Acute Stress Disorder (~80% of individuals with ASD have been found to develop PTSD)
  - Patients receiving CBT developed PTSD at lower rate than patients who received supportive counseling
    - Time 1 (immediately after treatment): 8% vs. 58%
    - Time 2 (6 months after treatment): 17% vs. 58%
- Two case reports (1 involving OEF/OIF veteran) that described use of CBT to treat symptoms of PTSD in individuals with mild TBI (Batten & Pollack, 2008; McGrath, 1997)
  - Reported decrease in symptoms of anxiety and depression but significant residual symptoms remained

# Limitations

- Search only through June 2009
- Potential publication bias
- Few population-based studies
  - Poor external validity
- Study populations, timing and diagnostic criteria used to classify TBI and PTSD varied widely
- Key variables frequently not reported
- Study outcomes often not stratified by key variables

# Conclusions

- Reported frequencies of TBI/PTSD varied widely
  - Observed heterogeneity likely due to variations in study parameters
  - Most studies were not designed to answer question of TBI/PTSD prevalence
- Results of 3 large cross-sectional studies in OEF/OIF veterans strikingly consistent
  - Probable mild TBI/PTSD “population” prevalence of 5-7%
  - Probable PTSD in 33-39% of individuals with probable history of mild TBI
- However...
  - Cross-sectional in nature
  - Case identification based on self-report screening instruments
  - Response rates ranged from 34% to 59%

# Conclusions

- Even without understanding population prevalence, data seem to indicate PTSD is a substantial problem among those with a TBI history
  - Most studies reported probable or diagnosed PTSD in 10% to 40% of study participants with probable or diagnosed TBI history
  - 33% - 39% of respondents in 3 large US military/veteran studies
- More research needed to help inform provision and coordination of rehabilitation and mental health services!
  - Epidemiologic studies to understand population prevalence
  - Studies of diagnostic accuracy
  - Studies evaluating efficacy and effectiveness vs. harms of therapies

# Future Research Needs

- Large, prospective epidemiologic studies
  - Recruit and retain the most representative samples possible
  - Utilize standard definitions and measures
  - Collect and report outcomes by potentially relevant patient characteristics, etiology and severity of injury, and time since trauma
- Diagnostic accuracy studies needed that utilize established gold standard methods
  - Efforts will benefit by adhering to Standards for Reporting Diagnostic Accuracy (STARD) statement
- High quality (i.e., randomized and controlled) studies needed to evaluate clinical services
  - Start with empirically supported treatments
  - Also explore facets of clinical effectiveness

# THANK YOU!

## For more information:

Full Report:

<http://www.hsrd.research.va.gov/publications/esp/TBI-PTSD-2009.pdf>

Tailored manuscript presenting results currently in press at  
*Journal of Head Trauma Rehabilitation*

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