TBI Classification Systems: Cross Walking TBI Definitions and Advancing CBI-M Injury-Level Modifiers

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Introduction

- Service members are at high risk for traumatic brain injury (TBI).
- Heterogeneity in TBI definitions across Department of Veterans Affairs/Department of War (VA/DoW), American Congress of Rehabilitation Medicine (ACRM), and Clinical, Biomarkers, Imaging, and Modifiers (CBI-M) frameworks limits comparability, prognostication, and care standardization.
- This fragmentation impedes progress toward multiple National Academies of Sciences, Engineering, and Medicine (NASEM) recommendations, including improving classification systems, advancing learning health systems, and strengthening study methodologies.
- We will describe a systematic crosswalk of TBI definitions and present initial findings from efforts to operationalize injury-level modifiers (e.g., mechanism of injury, secondary insults, comorbid injury) within the CBI-M framework.

Methods

- **Identify TBI ascertainment and characteristic elements** by system.
- **Systematic review** being conducted in accordance with a prospectively developed protocol registered in **PROSPERO** (protocol developed and uploaded prior to completion of the review).
- Review designed to evaluate **injury-level modifiers** within **CBI-M framework**, including injury mechanism (e.g., blast vs. non-blast) and acute injury characteristics.
- **Population:** Adults (≥18 years) with **mild traumatic brain injury (mTBI)**; studies involving moderate/severe TBI or pediatric populations were excluded.
- Included **peer-reviewed observational studies** (cohort, case-control, cross-sectional, and longitudinal); randomized trials, case reports, conference abstracts, and dissertations were excluded.
- Comprehensive literature search conducted in **MEDLINE, Embase, PsycINFO, CENTRAL, Web of Science, and Google Scholar**, with no date restrictions; reference list searching and expert consultation supplemented database searches.
- **Two independent reviewers** screened titles and abstracts, with a tie-breaker used for any disagreement.

Results

Comparison of TBI Ascertainment and Characterization Across Classification Frameworks

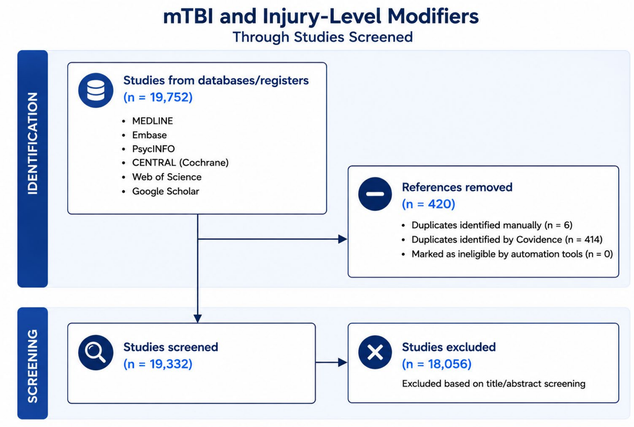
TBI ASCERTAINMENT ELEMENTS

ASCERTAINMENT ELEMENT	VA/DoD	ACRM	CBI-M FRAMEWORK
Injury Mechanism	• Traumatically induced structural injury and/or physiological disruption of brain function from an external force (e.g., head struck by object, head striking object, acceleration/deceleration without direct trauma, penetrating injury, blast/explosion, or other forces).	• Transfer of mechanical energy to the brain from external forces: (1) head struck by object; (2) head striking object/surface; (3) acceleration/deceleration without direct contact; and/or (4) forces from blast or explosion.	• Not articulated
Alteration of Mental Status or Consciousness (AOC)	• Confusion, disorientation, slowed thinking, alteration of consciousness/mental state immediately following the event.	• Reduced responsiveness, inappropriate responses, slowness to respond, agitation, inability to follow two-part commands, or disorientation to time/place/situation. Used to diagnose or suspect mild TBI depending on confounding factors.	• Not articulated
Loss of Consciousness (LOC)	• No protective actions taken on falling after impact or lying motionless and unresponsive immediately following the event.	• Same definition as VA/DoD. Used to diagnose or suspect mild TBI depending on confounding factors.	• Not articulated
Post-Traumatic Amnesia (PTA)	• Any loss of memory for events immediately before or after the injury.	• Complete or partial amnesia for events immediately following injury (or after regaining consciousness). If cannot be reliably assessed, retrograde amnesia can be used. Used to diagnose or suspect mild TBI depending on confounding factors.	• Not articulated
Acute Symptoms	• Not articulated	• At least two symptoms from: • Acute alteration in mental status • Physical symptoms • Cognitive symptoms • Emotional symptoms Used to diagnose or suspect mild TBI depending on confounding factors.	• Not articulated

TBI CHARACTERIZATION ELEMENTS

CHARACTERIZATION ELEMENT	VA/DoD	ACRM	CBI-M FRAMEWORK
Severity / Classification of TBI	• **Mild:** GCS 13–15 and mild range for LOC, AOC, PTA • **Moderate:** GCS 9–12 and moderate range • **Severe:** GCS <9 and severe range ("best score in first 24 hours)	• **Mild:** criteria met, GCS ≥13 after 30 min, LOC and PTA in mild range • **Greater than mild:** criteria met, GCS <13 after 30 min, LOC and PTA exceed mild range (diagnosed without "mild" qualifier)	• Assessment of Clinical, Biomarker, Imaging, and Modifier Pillars to facilitate prediction of outcomes.
Neuroimaging	• **Mild:** normal imaging • **Moderate:** normal or abnormal imaging • **Severe:** normal or abnormal imaging	• Not required, but qualifier may be used if completed: • Mild TBI with imaging evidence • Mild TBI without imaging evidence • Concussion (if imaging normal) **Greater than mild:** not articulated	• **Imaging Pillar:** Type and extent of brain injury; CT for acute phase (lesion size, location, vascular lesions, abnormalities); MRI more relevant for post-acute and chronic phases.
Biomarkers	• Not articulated	• Not articulated	• **Biomarker Pillar:** Informs triage, diagnosis, and treatment. Suggested cutoffs (acute <24 hr) with GCS 13–15 for very low risk of CT-detectable injury: GFAP 22–65 pg/mL; UCH-L1 327–400 pg/mL; S100B 0.105 µg/L.
Contextual / Confounding Factors	• Not articulated	• Not articulated	• **Modifier Pillar:** Includes injury factors, patient factors, and community/society factors to inform injury burden and factors affecting presentation and outcomes.

Note. VA/DoD = Department of Veterans Affairs/Defense; ACRM = American Congress of Rehabilitation Medicine Criteria for Mild TBI; CBI-M = Clinical, Biomarker, Imaging, and Modifier Framework; GCS = Glasgow Coma Scale; GFAP = glial fibrillary acidic protein; UCH-L1 = ubiquitin C-terminal hydrolase L1; S100B = S100 calcium-binding protein B.



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Conclusions and Next Steps

- The challenge is not simply identifying potential modifiers, but determining which are sufficiently defined, measurable, and prognostically informative to warrant inclusion in the CBI-M model.
- Next steps: To complete full-text screening and systematically map candidate modifiers to prespecified CBI-M injury-level domains.
- Subsequent work will address person- and community-level modifiers.

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