Military-Related Traumatic Brain Injury Increases Long-Term Vulnerability to Psychotic Spectrum Disorders

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IDEAS
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Disclaimer

The views expressed in this article are those of the authors and do not necessarily reflect the position or policy of the Department of Veterans Affairs, Department of War, or the United States government.

Learning Objectives

Longitudinal Trends

Analyze the dose-dependent relationship between TBI severity and incident psychosis over 10 years.

Military Profile

Evaluate how unique combat injury profiles diverge from civilian data regarding psychiatric sequelae.

Clinical Action

Describe targeted recommendations for VA/DoD clinical monitoring and early intervention.

TBI is a Signature Injury of Post-9/11 Conflicts[1]

Traumatic Brain Injury (TBI) is the signature injury of post-9/11 conflicts, affecting over **528,000 personnel**.

- 82% are mild TBIs (concussions).
- 36% of mild events occur during combat.
- accumulation of exposures (blast, burns, trauma) increases neurological impact compared to civilians.

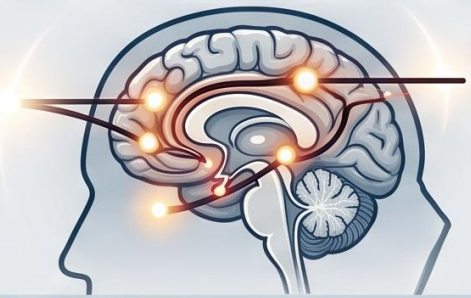
Although TBI is often associated with acute sequelae (e.g., headache, dizziness),[2-3] symptoms can persist and result in, as well as exacerbate, chronic health conditions[4-6]

THE POST-TBI PROGRESSION CASCADE:
From Injury to Psychossis Risk

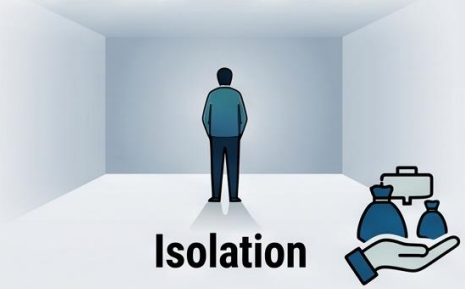
1. NEUROTRAUMA EXPOSURE
Primary Brain Injury Events

2. ACUTE SEQUELAE
Headaches
Dizziness
Anxiety
Sadness

3. NEUROBIOLOGICAL & STRESS PATHWAYS

NEUROBIOLOGICAL DISRUPTION

Frontotemporal Limbic Network & Limbic Network

CHRONIC PSYCHOSOCIAL STRESS

Loss of Employment

Isolation

4. CHRONIC PSYCHOSOCIAL DECLINE PSYCHOTIC SPECTRUM DISORDERS
ELEVATED RISK: 2x to 5x VS. GENERAL POPULATION

ADVANCING TBI RESEARCH: THE METHODOLOGICAL ADVANCEMENT [7]

ANCHORING THE THESIS: THE LIMBIC-CENC STUDY ADVANCEMENT

PRIOR EXTANT LITERATURE: KEY LIMITATIONS

CROSS-SECTIONAL

Cross-sectional designs with **short timelines**

Days | weeks | Days | Weeks

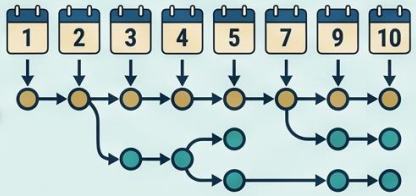
Civilian-focused cohorts that **lack** the **dynamics of combat exposure**

Aggregated TBI data that failed to isolate **severity levels**

THE LIMBIC-CENC STUDY: CORE ADVANCEMENTS

STUDY DESIGN & TIMELINE

METHODOLOGICAL ADVANCEMENT



10-year longitudinal tracking using **massive, linked DHA/VHA records.**

COHORT & CONTEXT

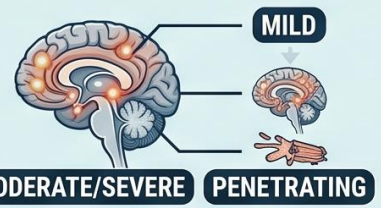
COHORT ADVANCEMENT

1.2M+
VETERANS

Focused on a massive national cohort of over 1.2M Post-9/11 Veterans.

TBI SEVERITY & PRECISION

DIAGNOSTIC PRECISION ADVANCEMENT



Hierarchical stratification tracking: tracking: **Mild, Moderate/Severe,** and **Penetrating injuries.**

THE THESIS ANCHOR: DEFINITIVE ADVANCEMENT

Overcoming these critical limitations allows the **LIMBIC-CENC study to establish a **definitive, dose-dependent link between military-specific TBI severity** and **subsequent psychotic spectrum disorder risk**, making it a major advancement in the field.**

LIMBIC Phenotype Study

DHA & VHA **Phenotype Study** Records

CONSOLIDATED PARTICIPANT FLOWCHART: COHORT WINNOWING PROCESS

1 BASE TARGET POPULATION

START:
***N* = 2,530,847**
(Initial Merged DHA/VHA Dataset)

EXCLUSIONS:
Insufficient Timeline Data (e.g.,
Short healthcare windows, timeline mismatch)

RESULTING POOL:
~ 2.04 Million

2 AGE & MORTALITY CLEANING

EXCLUSIONS: Age <17 at index date, deaths prior to index timeline, index misalignment with service dates

RESULTING POOL:
~1.88 Million

3 DIAGNOSTIC DATA REFINEMENT

EXCLUSIONS: Psychosis scrubbing (pre-existing/unverified outpatient instance), TBI verification (screening with no follow-up, self-reports lacking clinical support)

RESULTING POOL:
~1.25 Million

4 FINAL ANALYTICAL COHORT

EXCLUSIONS: Administrative non-DoD registry anomalies, TBI severity unclassified (*n* = 17,697)

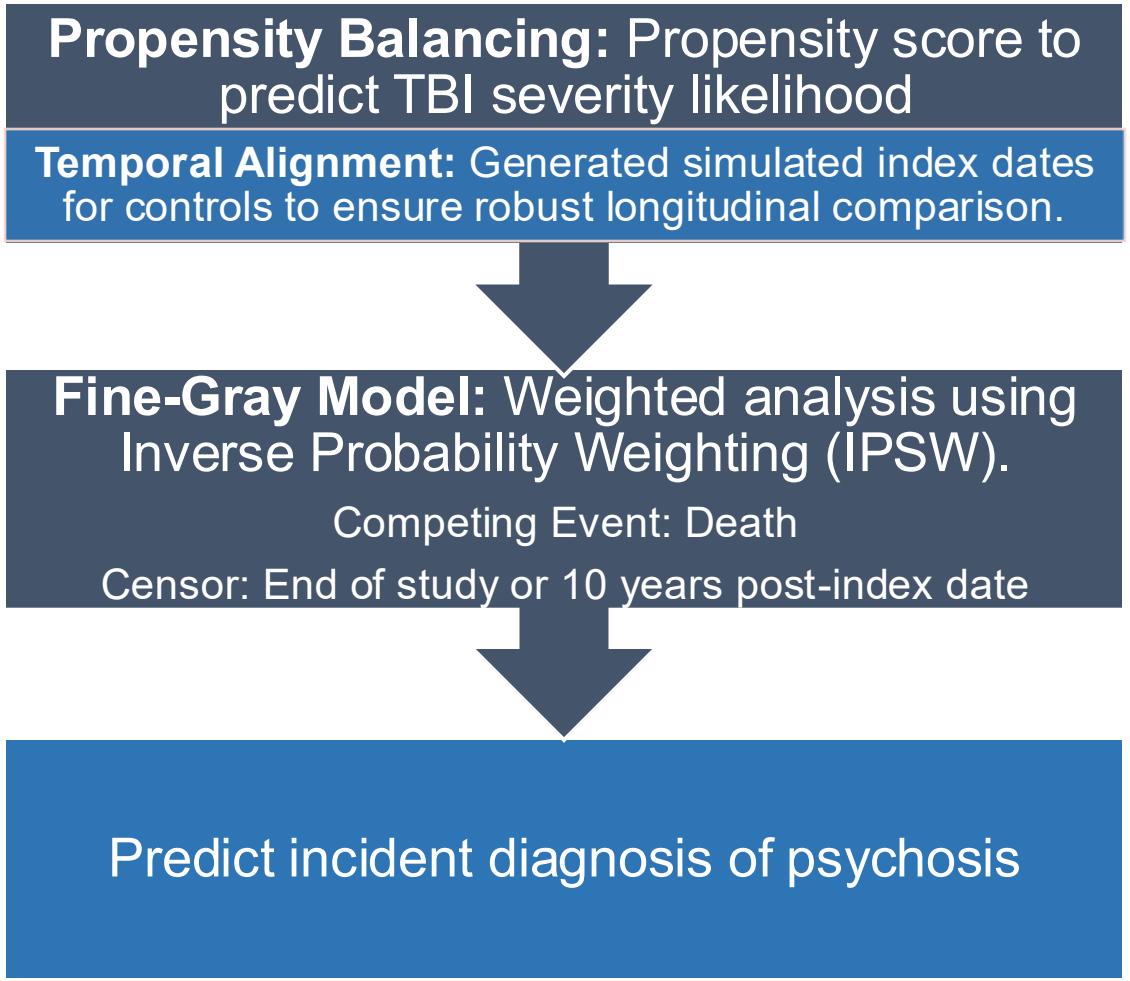
FINAL STUDY POPULATION: *N* = 1,233,763
Clean, Post-9/11 Service Members and Veterans

TBI Definition

TBI Severity	Clinical Criteria/Definition	Cohort Count n (%)
No TBI	No clinical evidence of brain injury in MHS/VHA records	932,242 (76%)
Mild TBI	Loss of consciousness 0-30 minutes	236,470 (19%)
Moderate/Severe TBI	Loss of consciousness >30 minutes	48,948 (4%)
Penetrating TBI	Open head injury or skull penetration	16,093 (1%)

Defined using information from the DoD Trauma Registry, MHS diagnosis codes, VHA diagnosis codes, self-reported head injury characteristics in VA Comprehensive TBI Evaluation[7-8]

Methodological Framework



Results

Cohort Demographics

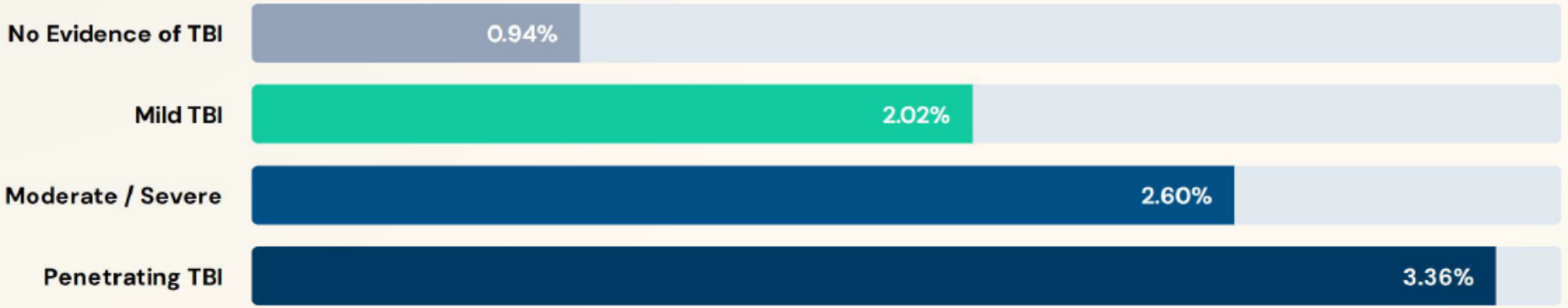
82%
Male Population

37%
Aged 25–34 Years

61%
White, Non-Hispanic

Results

Unadjusted Psychosis Incidence



Dose-Dependent Trend ($p < .0001$): Increasing injury severity directly correlates with higher incident psychosis rates.

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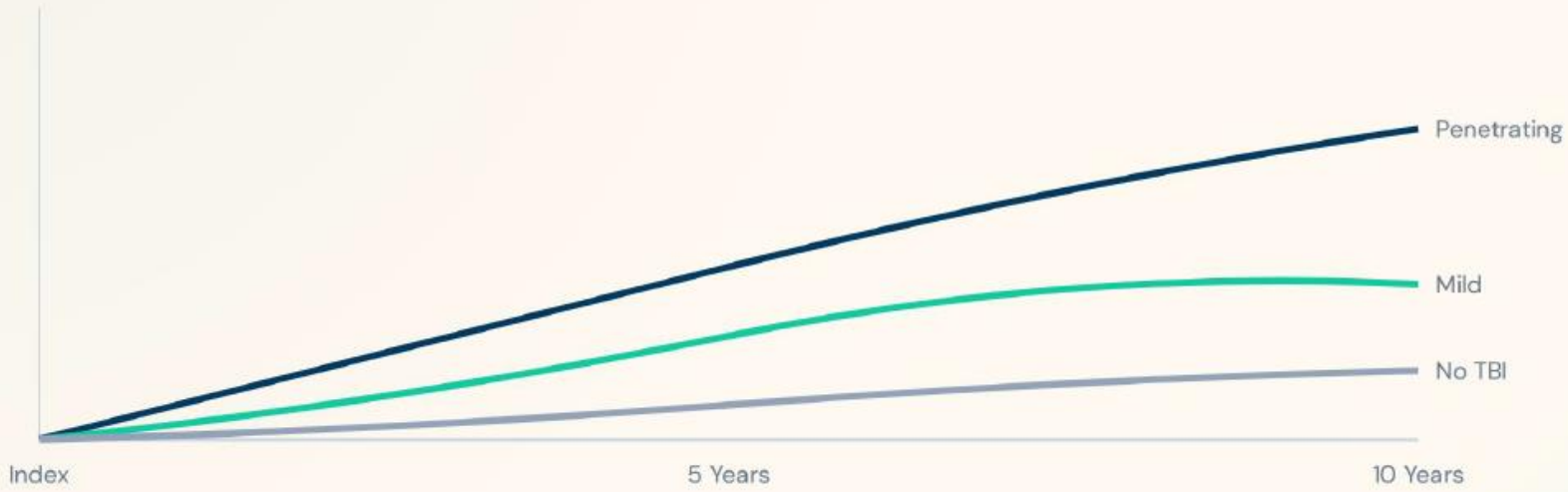
Results: Longitudinal Trends

Long-Term Risk Trajectories



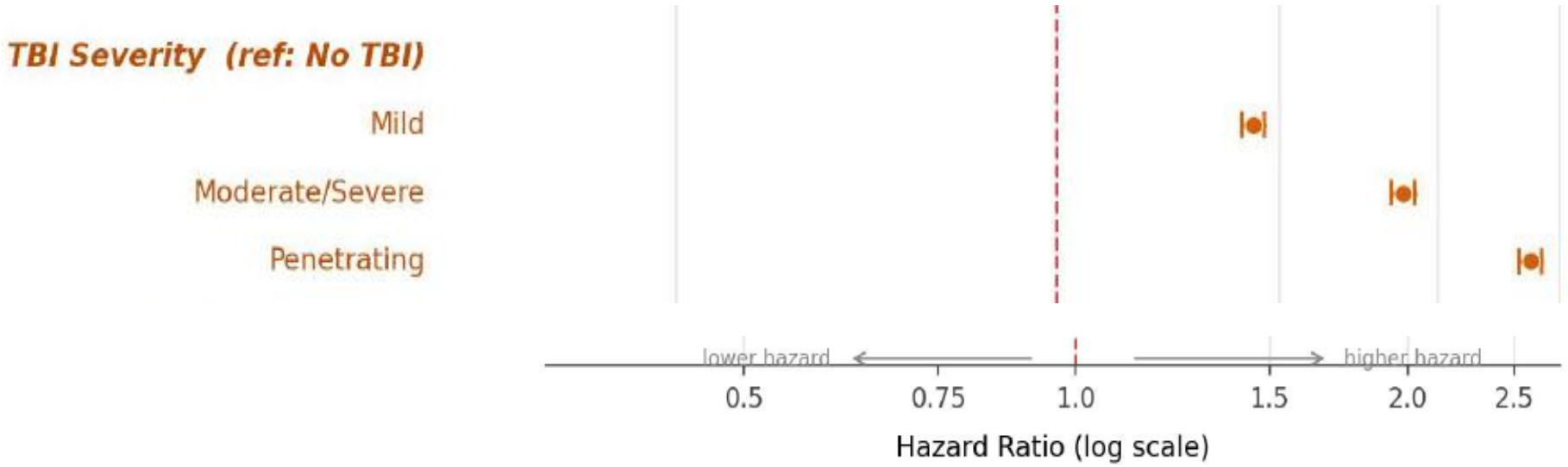
Fine-Gray Model Results (Weighted): Adjusted HR for Mild = 1.43, Moderate/Severe = 1.88, Penetrating = 2.37.

Results of Fine-Gray Model

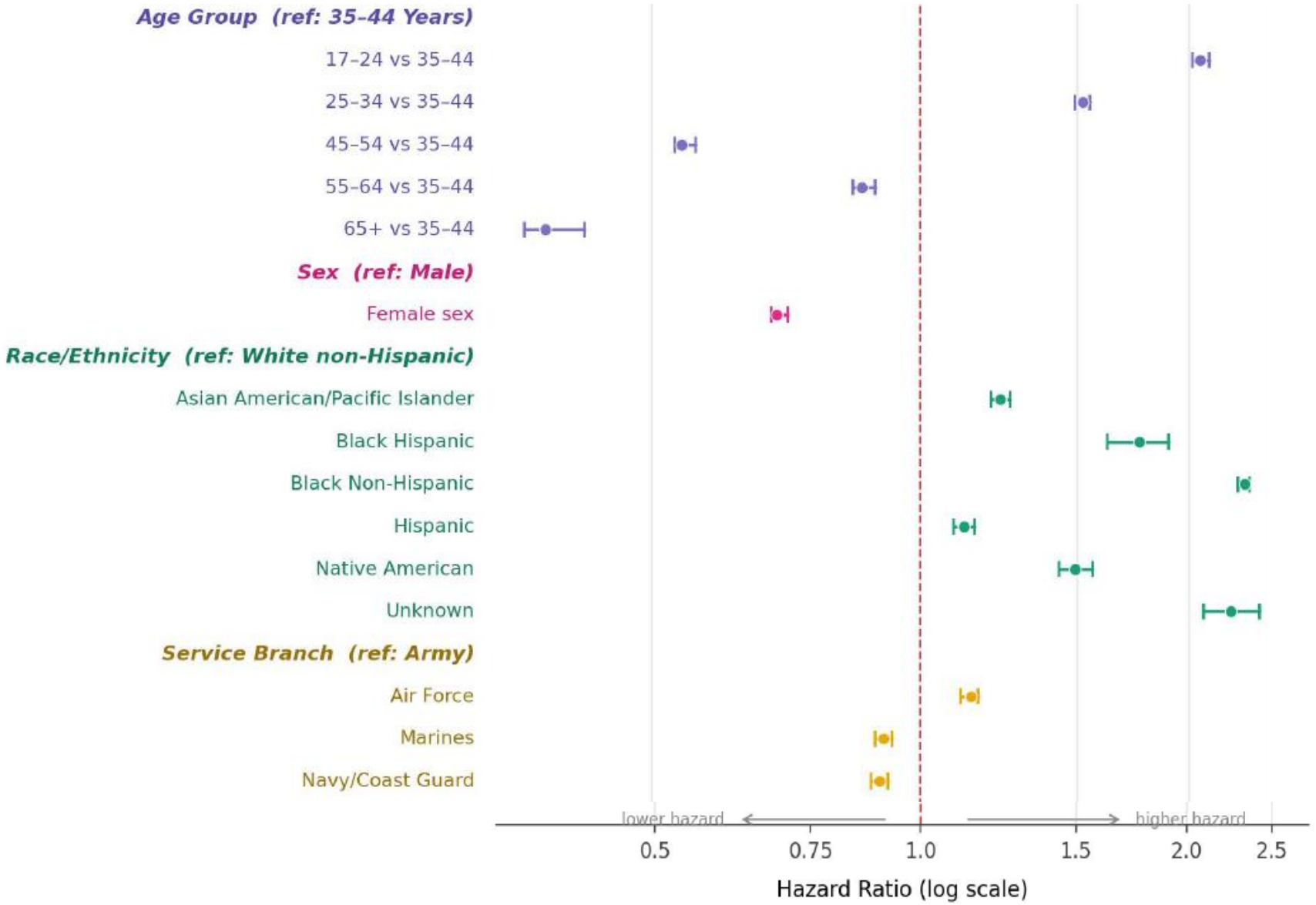
Adjusted hazard ratios

- Controlling for sociodemographic and military characteristics
- Health covariates identified before index date

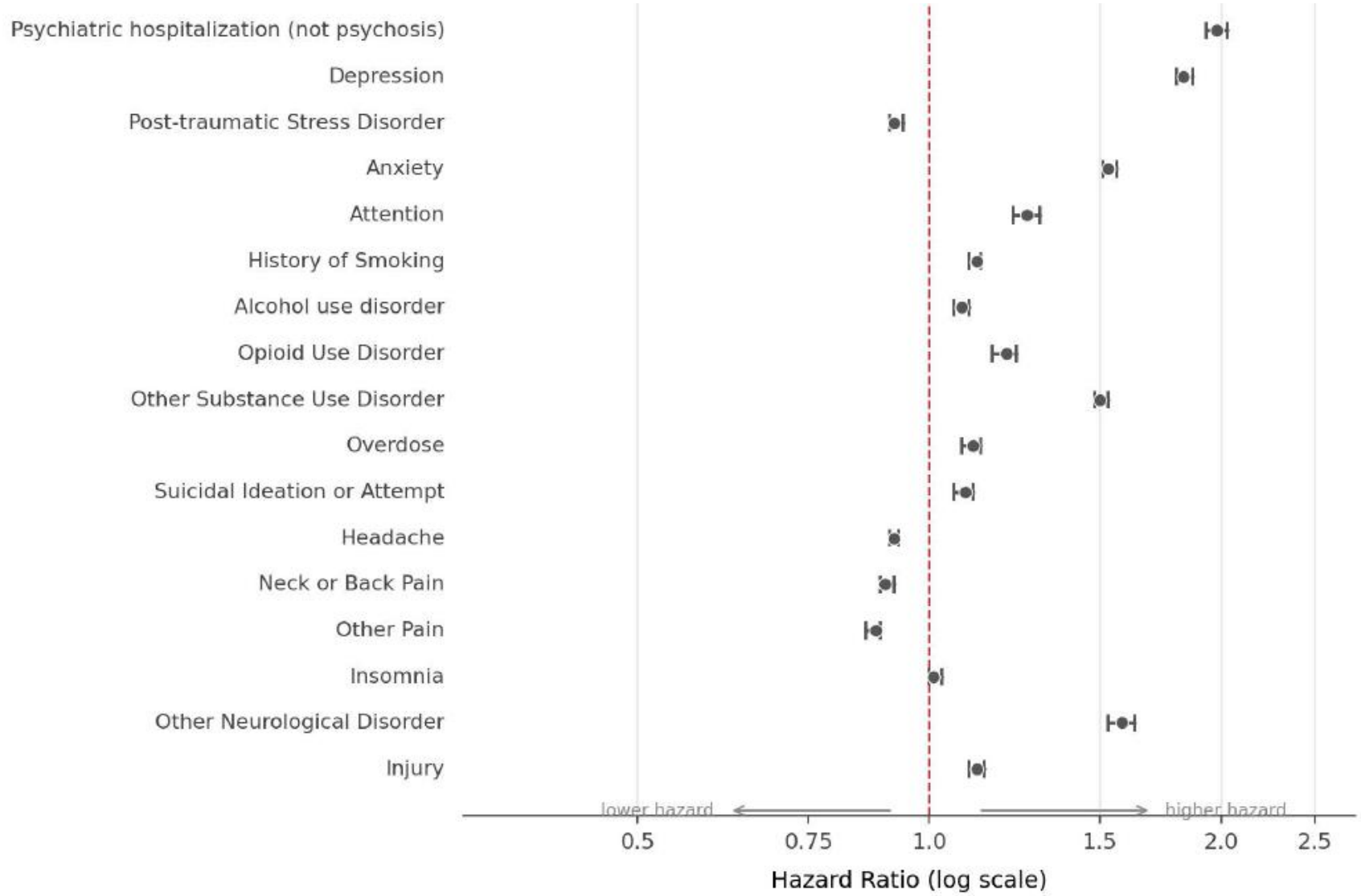
TBI Severity



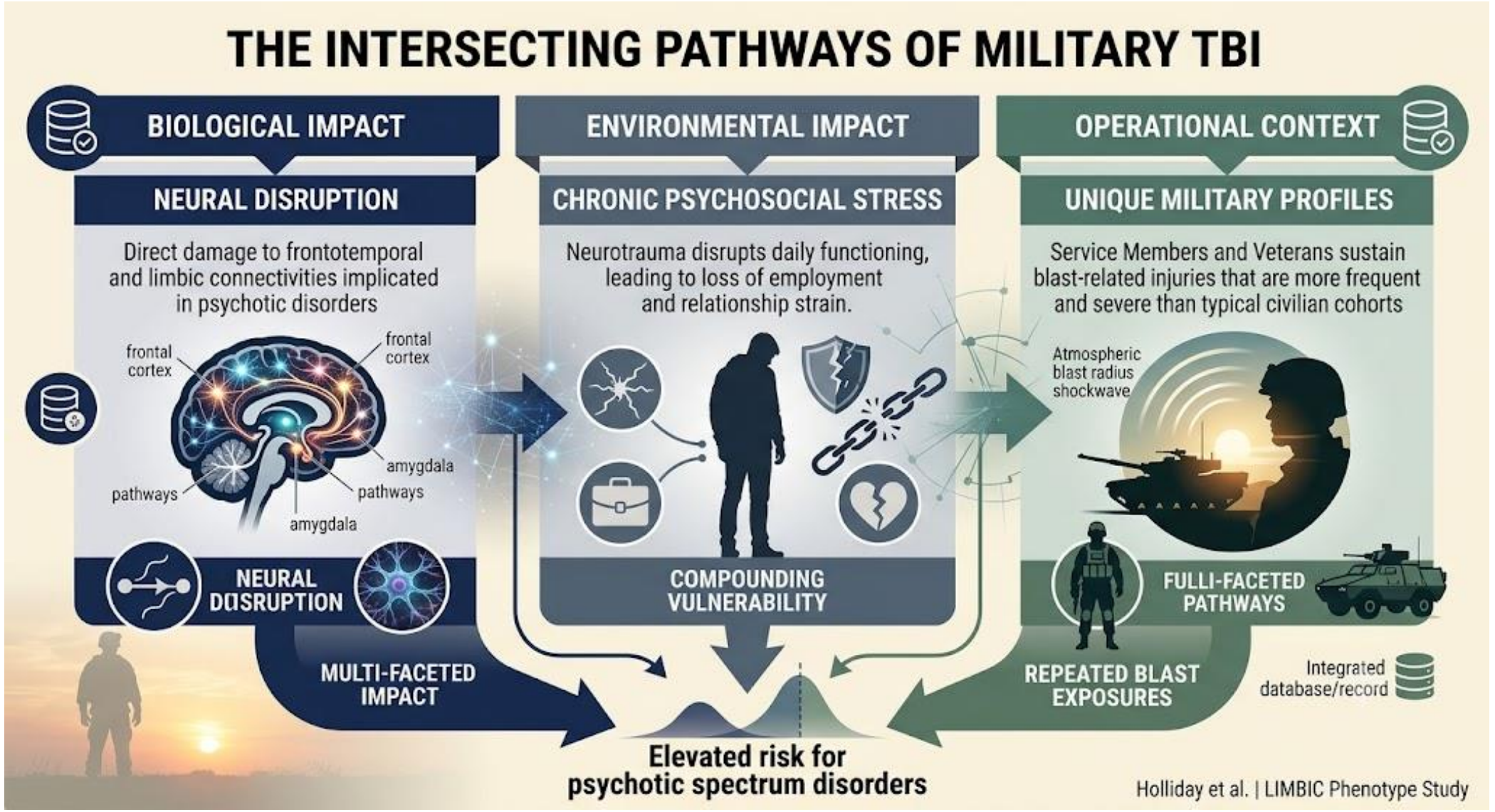
Sociodemographic Characteristics



Health Covariates Before Index Date



Discussion


THE INTERSECTING PATHWAYS OF MILITARY TBI
BIOLOGICAL IMPACT
NEURAL DISRUPTION
Direct damage to frontotemporal and limbic connectivities implicated in psychotic disorders
frontal cortex
frontal cortex
amygdala
pathways
pathways
amygdala
NEURAL DISRUPTION
MULTI-FACETED IMPACT
ENVIRONMENTAL IMPACT
CHRONIC PSYCHOSOCIAL STRESS
Neurotrauma disrupts daily functioning, leading to loss of employment and relationship strain.
COMPOUNDING VULNERABILITY
OPERATIONAL CONTEXT
UNIQUE MILITARY PROFILES
Service Members and Veterans sustain blast-related injuries that are more frequent and severe than typical civilian cohorts
Atmospheric blast radius shockwave
FULLI-FACETED PATHWAYS
REPEATED BLAST EXPOSURES
Integrated database/record
Elevated risk for psychotic spectrum disorders
Holliday et al. | LIMBIC Phenotype Study

Clinical Recommendations

Extended Monitoring: Longitudinal screening for all TBI severities as risk persists long after injury

Early identification: Appropriate treatment may mitigate adverse outcomes

Early treatment for TBI-related sequelae (headache, PTSD) may mitigate chronic psychosocial decline and secondary psychosis risk; however, further research remains needed

Prediction Models need to be validated to guide VA/DoW monitoring

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Questions?

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