Mass General Brigham
Brigham Research Institute

Long-term risks of cardiovascular diseases after Traumatic brain injury

3/11/2025

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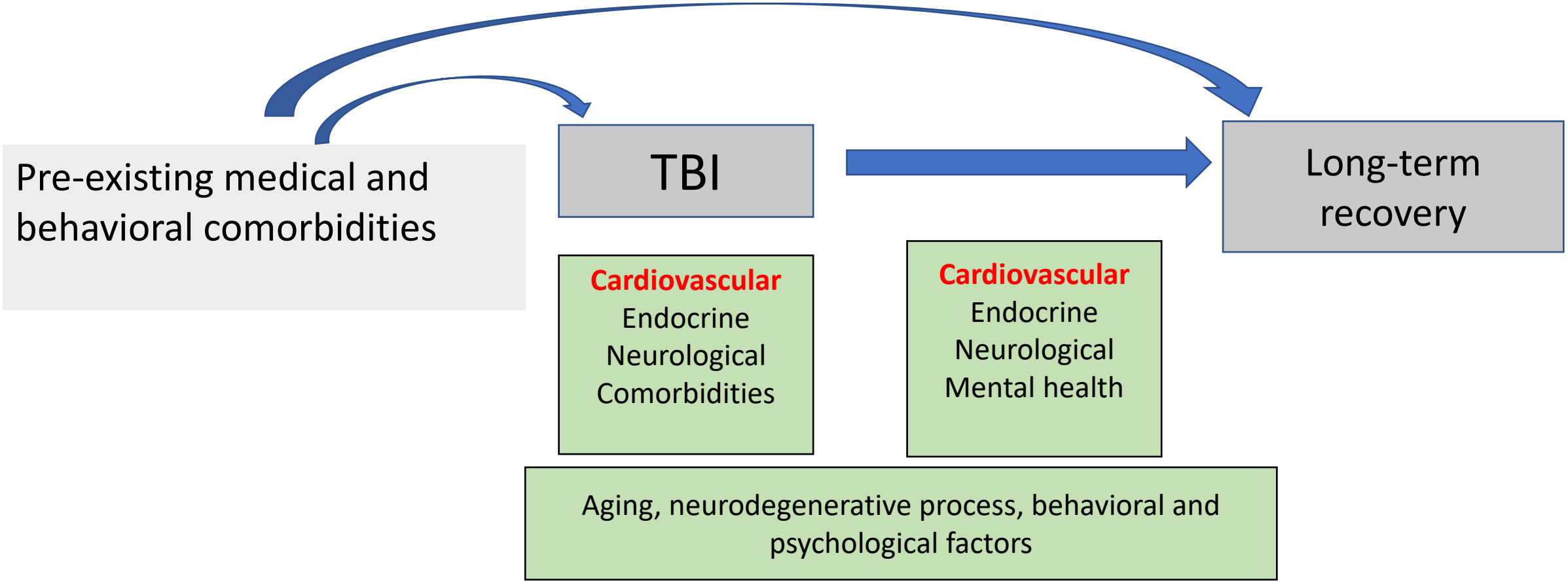
Poor long-term outcomes may represent direct sequelae of TBI, pre-TBI comorbidities, or a combination of these factors



Original Investigation

September 6, 2022

Association Between Traumatic Brain Injury and Subsequent Cardiovascular Disease Among Post-9/11-Era Veterans

Ian J. Stewart, MD[1,2]; Megan E. Amuan, MPH[3,4]; Chen-Pin Wang, PhD[5]; Eamonn Kennedy, PhD[3,4]; Kimbra Kenney, MD[6,7]; J. Kent Werner, MD, PhD[7]; Kathleen F. Carlson, PhD[8]; David F. Tate, PhD[3,9]; Terri K. Pogoda, PhD[10]; Clara E. Dismuke-Greer, PhD[11]; W. Shea Wright, MD[3,9]; Elisabeth A. Wilde, PhD[3,9]; Mary Jo Pugh, PhD[3,4]

Circulation

Association Between Concussion Burden During Professional American-Style Football and Postcareer Hypertension

Rachel Grashow, Can Ozan Tan, Saef Izzy, Herman A. Taylor Jr, Marc G. Weisskopf, Meagan M. Wasfy, Alicia J. Whittington, Frank Speizer, Ross Zafonte and Aaron L. Baggish

Originally published 7 Feb 2023 | https://doi.org/10.1161/CIRCULATIONAHA.122.063767 | Circulation. 2023;147:1112–1114

Other version(s) of this article

CONCUSSION | JANUARY 05 2021

Long-Term Influence of Concussion on Cardio-Autonomic Function in Adolescent Hockey Players

Allyssa K. Memmini, MS, ATC ; Michael F. La Fountaine, EdD, ATC, FACSM; Steven P. Broglio, PhD, ATC, FACSM; Robert D. Moore, PhD, ATC

J Athl Train (2021) 56 (2): 141–147.

ELSEVIER

World Neurosurgery

Volume 122, February 2019, Pages e740-e753

Original Article

Traumatic Brain Injury Increases the Risk of Major Adverse Cardiovascular and Cerebrovascular Events: A 13-Year, Population-Based Study

Tee-Tau Eric Nyam [1], Chung-Han Ho [2 3], Chung-Ching Chio [1], Sher-Wei Lim [4], Jhi-Joung Wang [2], Ching-Hung Chang [1], Jinn-Rung Kuo [1 2 5], Che-Chuan Wang [1 6]

CONCUSSION | SEPTEMBER 20 2021

Concussion History and Heart Rate Variability During Bouts of Acute Stress

Adam Harrison, PhD, MSc ; Abbi Lane-Cordova, PhD; Michael F. La Fountaine, EdD, ATC; Robert Davis Moore, PhD

J Athl Train (2022) 57 (8): 741–747.

The Relationship between Military Combat and Cardiovascular Risk: A Systematic Review and Meta-Analysis

Christopher J. Boos ,[1,2,3,4] Norman De Villiers,[1,2,3] Daniel Dyball,[1,2] Alison McConnell,[3] and Alexander N. Bennett[1,5]

Show more

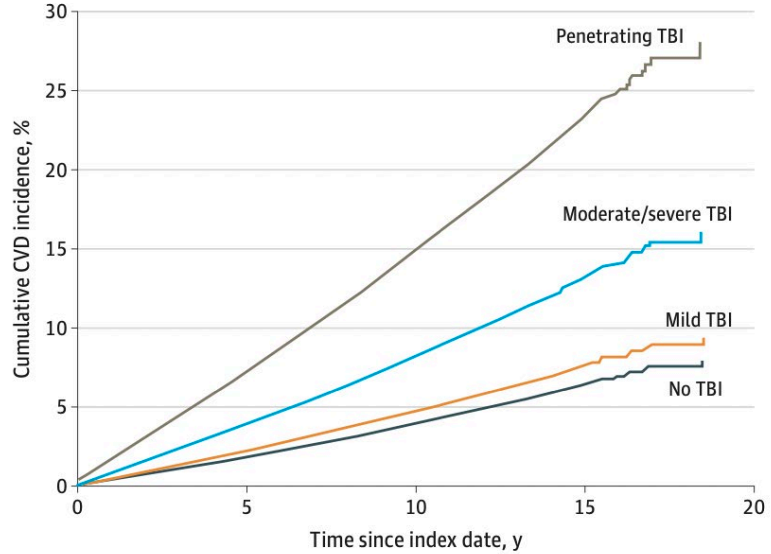
JAMA Neurology | Original Investigation

Association Between Traumatic Brain Injury and Subsequent Cardiovascular Disease Among Post-9/11–Era Veterans

Ian J. Stewart, MD; Megan E. Amuan, MPH; Chen-Pin Wang, PhD; Eamonn Kennedy, PhD; Kimbra Kenney, MD; J. Kent Werner, MD, PhD; Kathleen F. Carlson, PhD; David F. Tate, PhD; Terri K. Pogoda, PhD; Clara E. Dismuke-Greer, PhD; W. Shea Wright, MD; Elisabeth A. Wilde, PhD; Mary Jo Pugh, PhD

- ✓ Retrospective cohort study
- ✓ October 1, 1999, to September 30, 2016
- ✓ Administrative data from the US Department of Veterans Affairs and the Department of Defense from the Long-term Impact of Military-Relevant Brain Injury Consortium–Chronic Effects of Neurotrauma Consortium
- ✓ Studied 1 559 928 veterans (301 169 veterans with h/o TBI and 258 759 without h/o TBI)
- ✓ Composite end point of CVD: coronary artery disease, stroke, peripheral artery disease, and cardiovascular death.

Figure 2. Cumulative Incidence Functions for the Composite Outcome Stratified by Traumatic Brain Injury (TBI) Severity



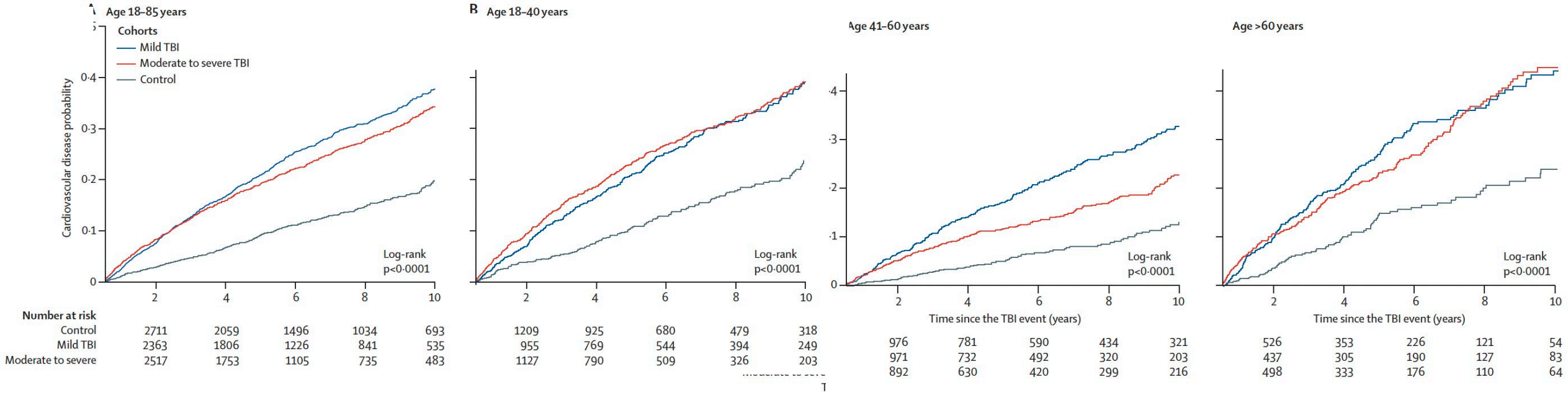
No. at risk				
No TBI	1 258 759	774 768	203 489	6084
Mild TBI	251 177	183 077	57 516	3737
Moderate/severe TBI	40 978	23 794	8919	1088
Penetrating TBI	9014	4326	1539	182

Long-term risk of cardiovascular disease after traumatic brain injury: screening and prevention

Lancet Neurol 2023; 22: 959–70

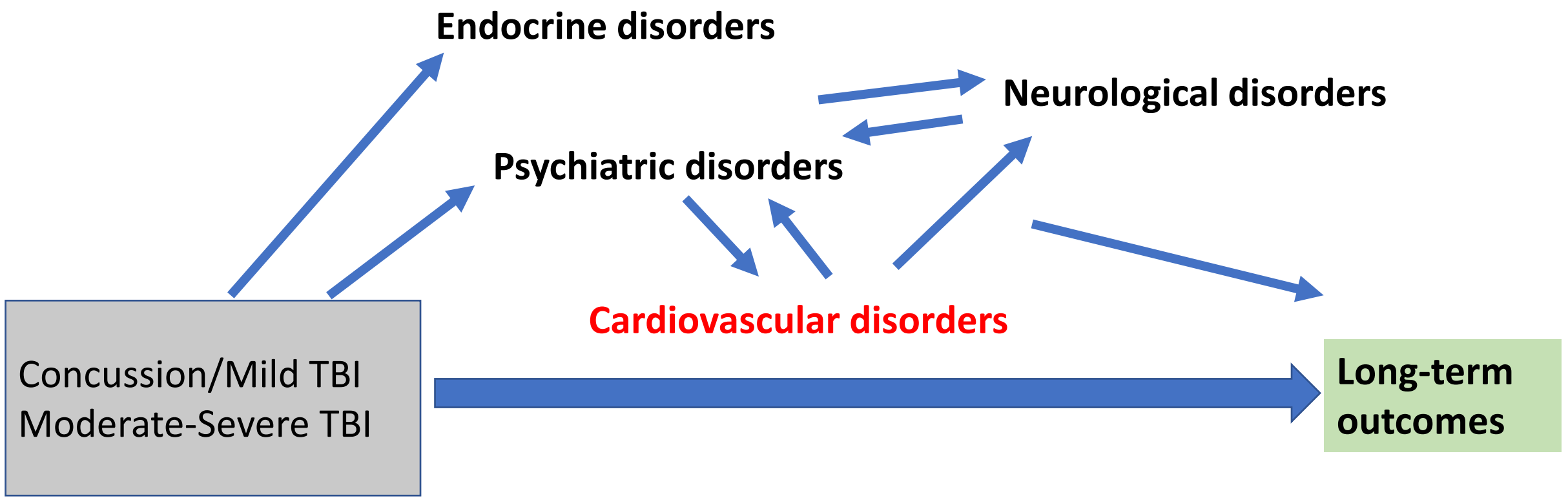
See **Comment** page 878

Saef Izzy, Rachel Grashow, Farid Radmanesh, Patrick Chen, Herman Taylor, Rita Formisano, Fiona Wilson, Meagan Wasfy, Aaron Baggish, Ross Zafonte



Traumatic brain injury: a chronic disease that affects more than the brain

The directionality of these post TBI patterns is still needs to be further investigated



Long-term risk of cardiovascular disease after traumatic brain injury: screening and prevention

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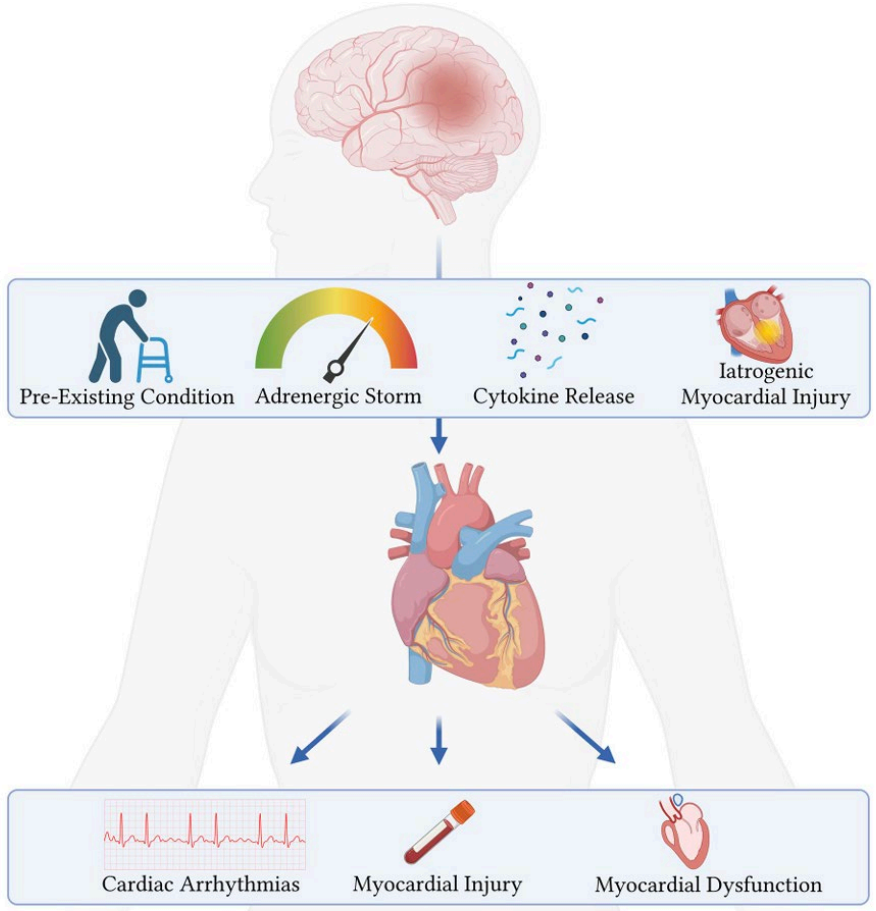
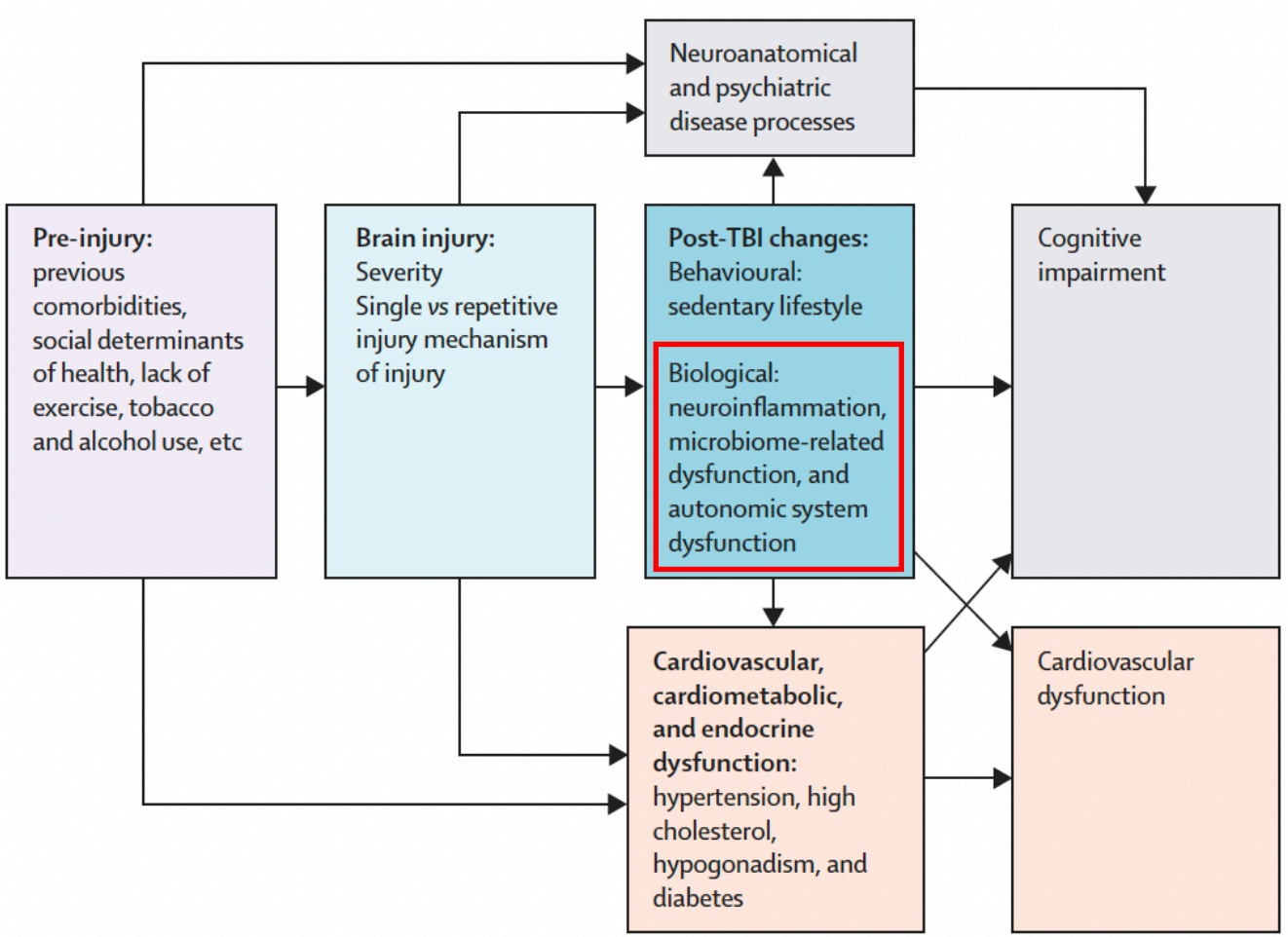
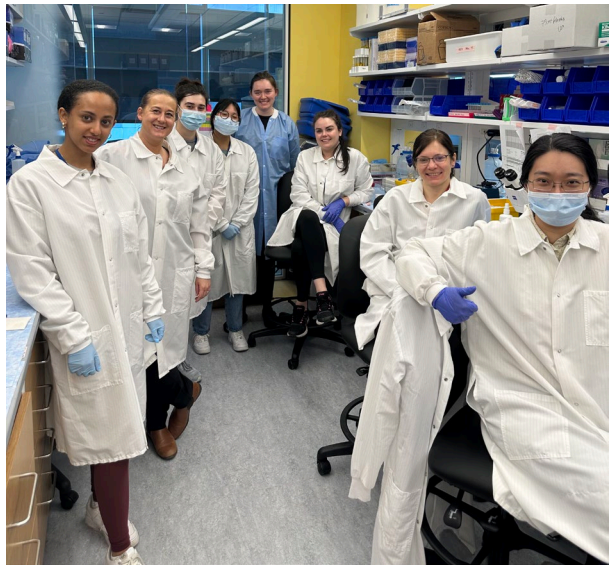


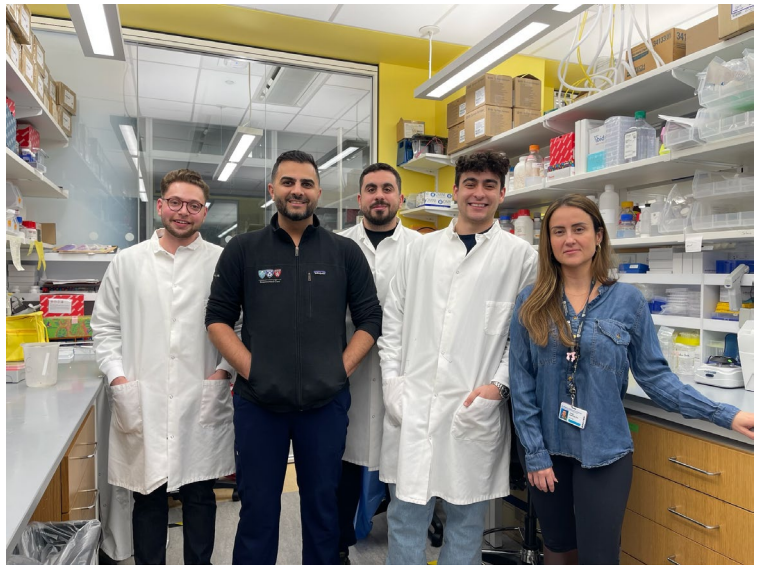


Coppalini et al, Neurocritical Care, 2024

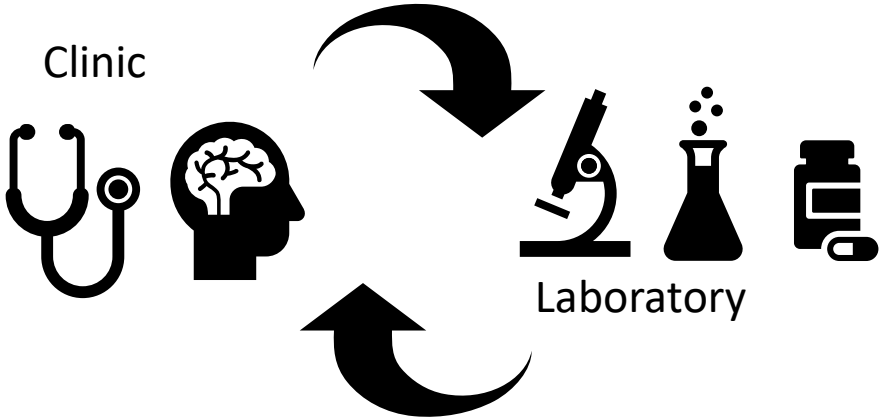
Need for proactive screening program and updated guidelines to effectively detect and treat post TBI comorbidities

Path forward for therapeutics in TBI and neurodegenerative diseases





Breaking down silos



Collaborators

Tufts University

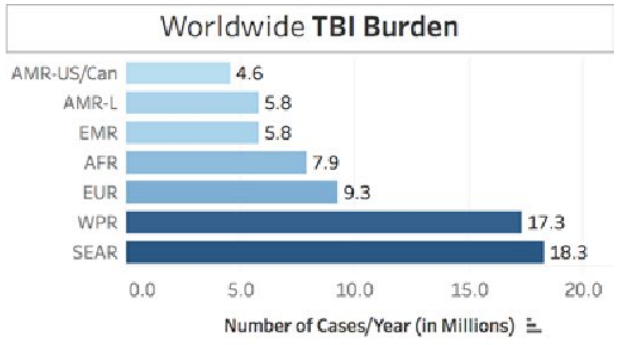
Penn University of Pennsylvania

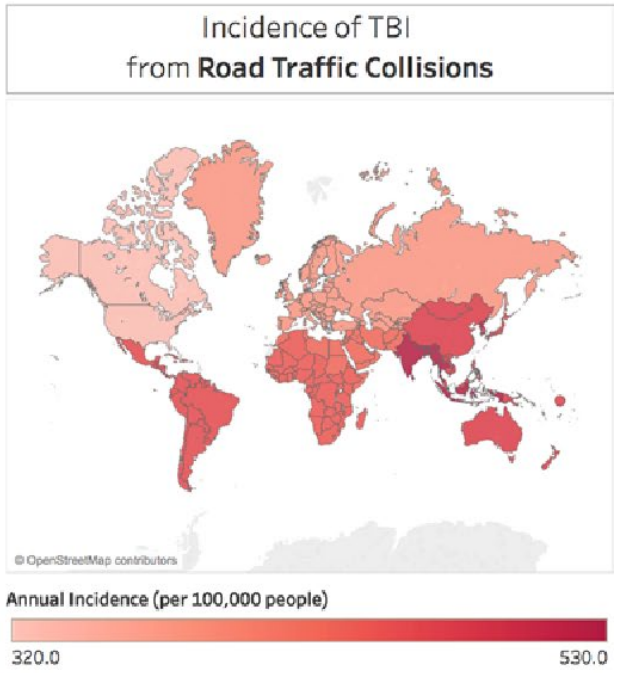
Yale

Funding
NINDS
Department of Defense
Army Research Office

Other slides – if needed during panel discussion

TBI is chronic disease with global impact





Five-year outcomes of persons with TBI*

*Data are US population estimates based on the TBIMS National Database. Data refer to people 16 years of age and older who received inpatient rehabilitation services for a primary diagnosis of TBI.

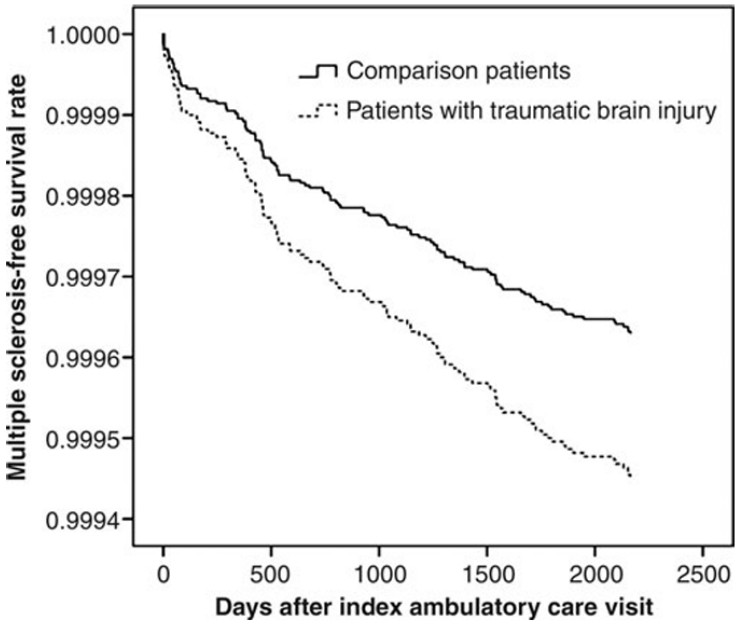
No therapies exist to mitigate long-term outcomes

Dewan m et al, J Neurosurgery, 2019. CDC. gov, traumatic brain injury, 2022

Traumatic brain injury and risk of neurodegenerative diseases

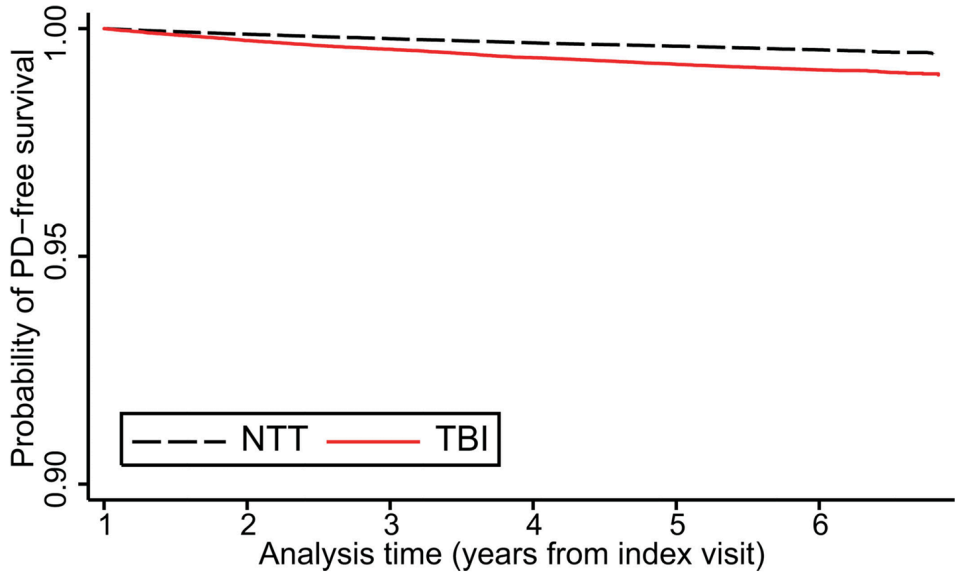
Increased Risk of Multiple Sclerosis after Traumatic Brain Injury: A Nationwide Population-Based Study

Jiunn-Horng Kang[1–3] and Herng-Ching Lin[4]



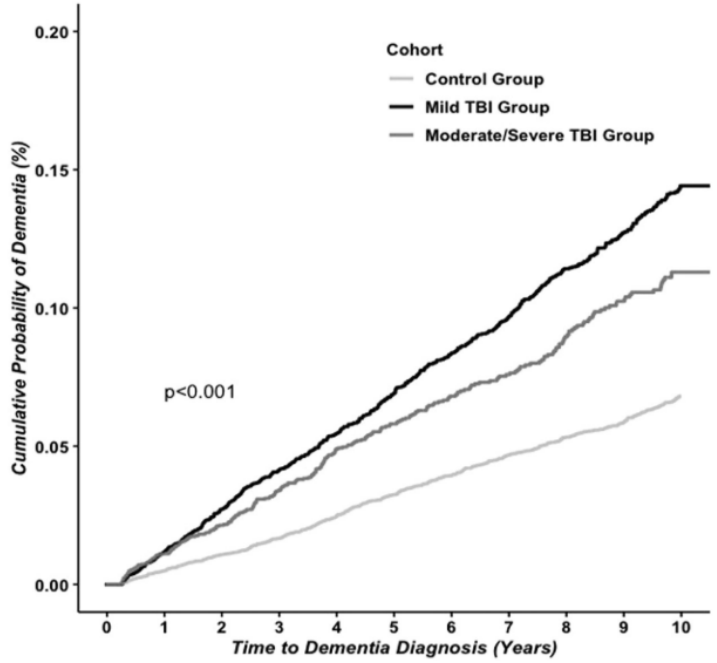
Traumatic brain injury in later life increases risk for Parkinson's disease

Raquel C. Gardner, MD[1,2], James F. Burke, MD[3], Jasmine Nettiksimmons, PhD[2,4], Sam Goldman, MD, MPH[1,2], Caroline M. Tanner, MD[1,2], and Kristine Yaffe, MD[1,2,4,5]



The Impact of Age and Severity on Dementia After Traumatic Brain Injury: A Comparison Study

Stopa, Brittany M MPH; Tahir, Zabreen MD; Mezzalira, Elisabetta RN, MS; Boaro, Alessandro MD; Khawaja, Ayaz MD; Grashow, Rachel PhD, MS; Zafonte, Ross D DO; Smith, Timothy R MD, PhD, MPH; Gormley, William B MD, MPH, MBA; Izzy, Saef MD Author Information



- **Mechanisms leading to increased risk of neurodegenerative diseases after TBI are still poorly understood**
- **No therapies exist to mitigate long-term cognitive consequences after TBI**

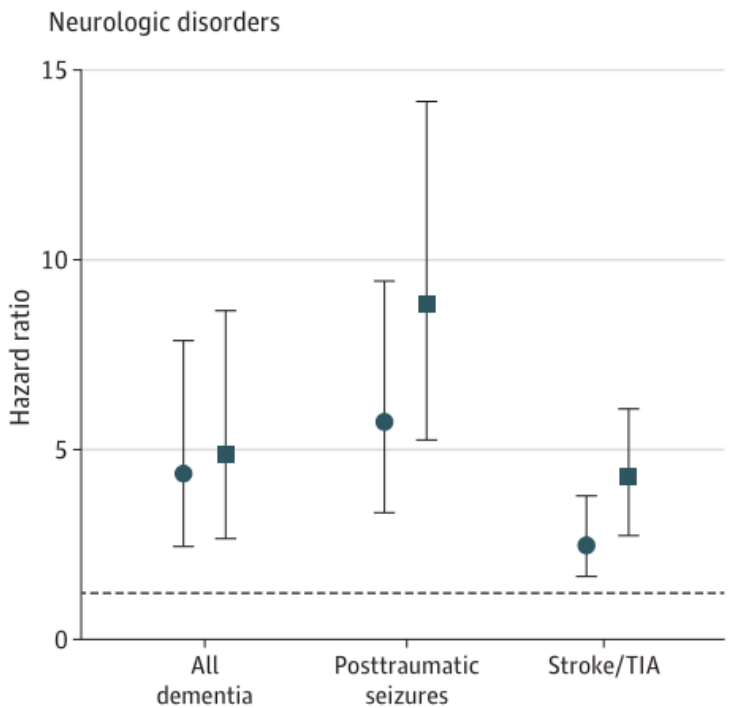
Original Investigation | Neurology

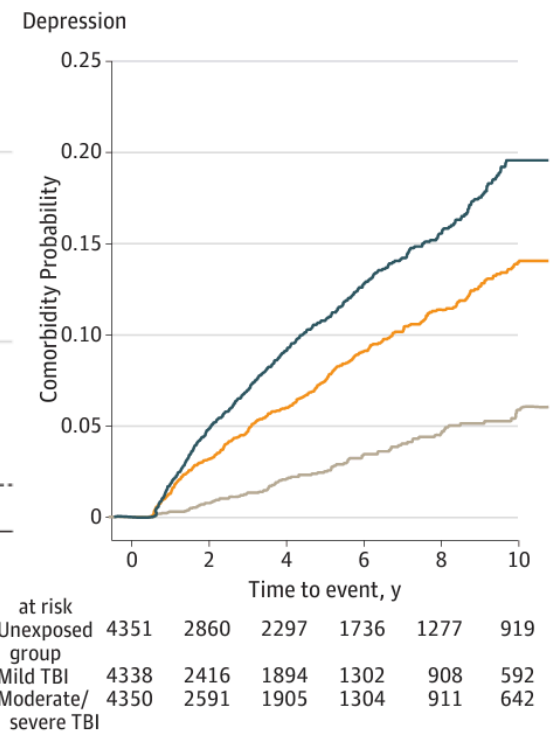
April 28, 2022

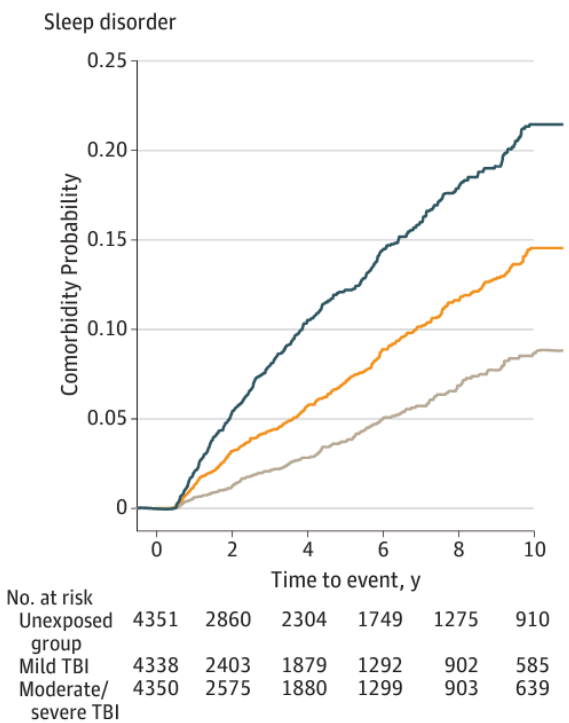
Association of Traumatic Brain Injury With the Risk of Developing Chronic Cardiovascular, Endocrine, Neurological, and Psychiatric Disorders

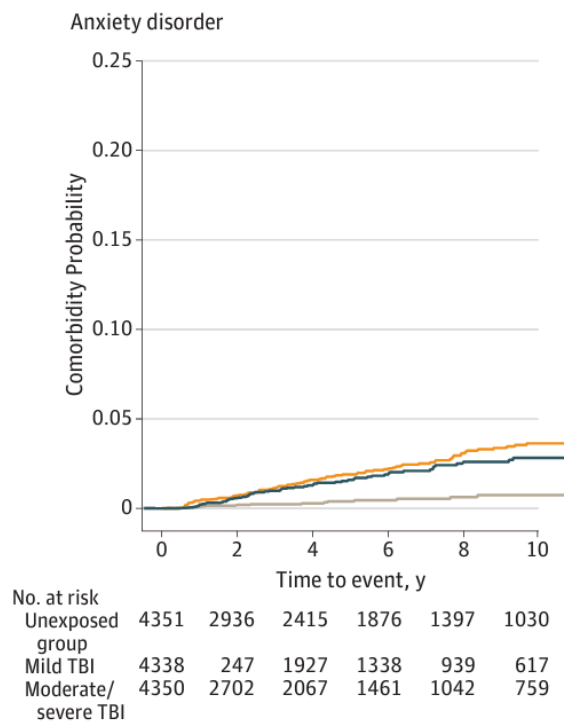
Saef Izzy, MD[1,2]; Patrick M. Chen, MD[1,2]; Zabreen Tahir, MD[1]; et al

» Author Affiliations | Article Information





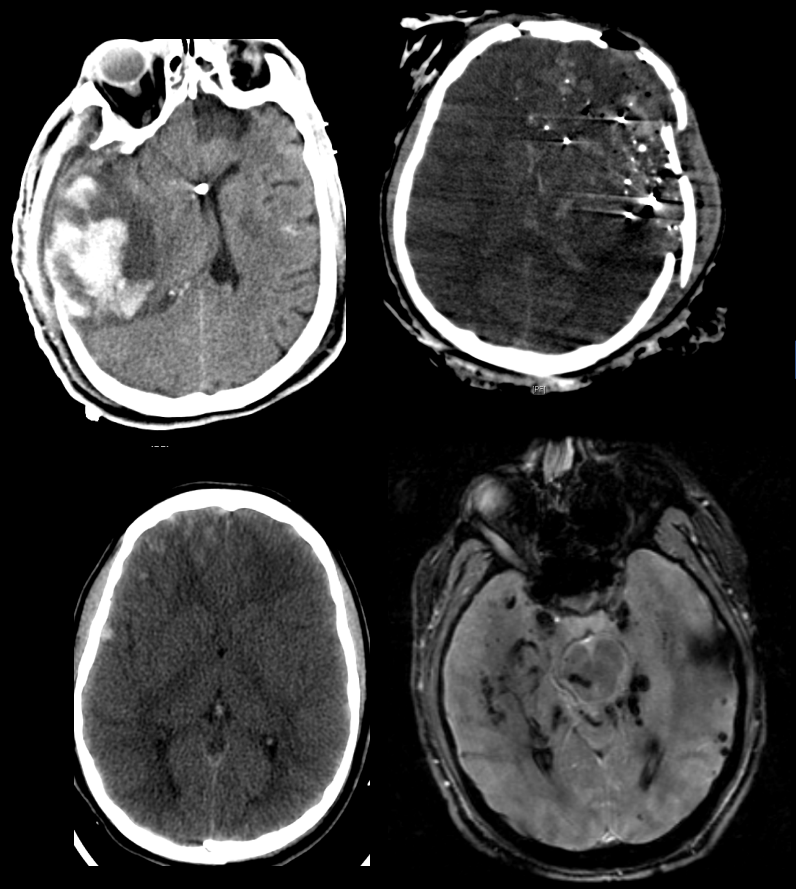




Primary vs secondary brain injury

Primary injury

Skull laceration
Skull fracture
Concussion
Contusion
Intracerebral hemorrhage
Diffuse axonal injury



Secondary injury

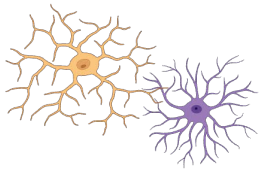
Hypoxia
Hypotension
Free radicles
Neuroinflammation
Hypothermia
Intracranial pressure

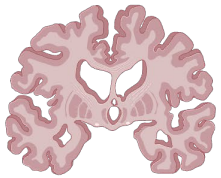
Izzy* Jassam et al, Neuron, 2017
Brain trauma foundation, 2017

ARCND brain injury vision

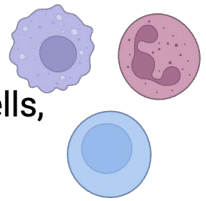
Traumatic brain injury → Progression of Disease → **Neurodegenerative diseases**

CNS resident immune cells
Macrophages, Astrocytes



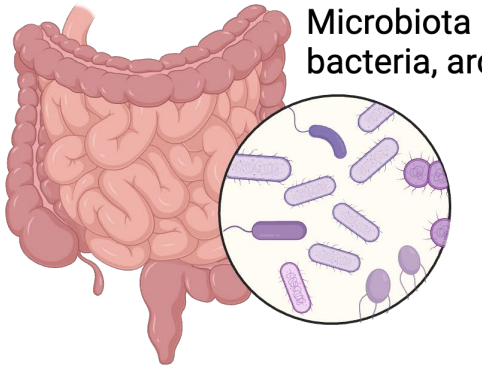


Immunity (peripheral)
T-cells,NK cells, Dendritic cells,
Mast cells

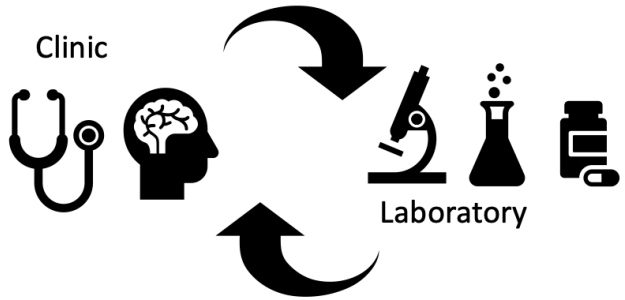


Microbiota
bacteria, archaea, fungi

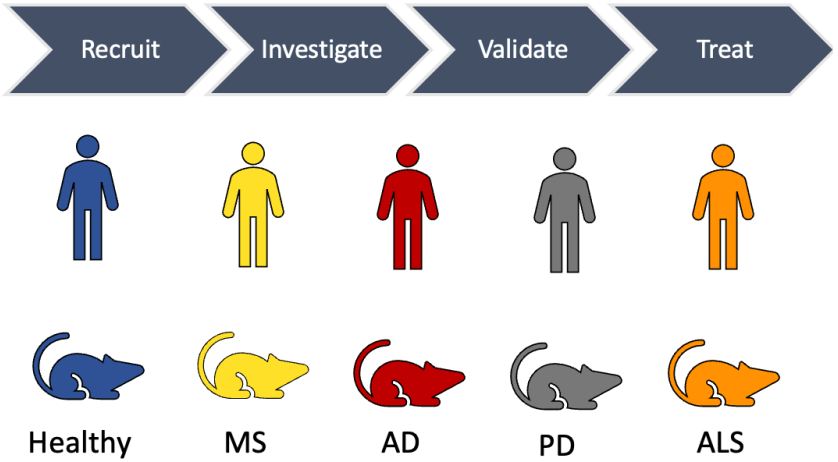
Gut dysbiosis



Breaking down silos



Pipeline for Discovery



Ultimate Goals

- Understanding pathogenesis of TBI and progression of neurodegeneration
- Developing novel immune based therapeutics and diagnostic tests to improve disease & treatment management