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Traumatic Brain Injury as a Chronic Condition: Epidemiological Evidence of Long-Term Sequelae

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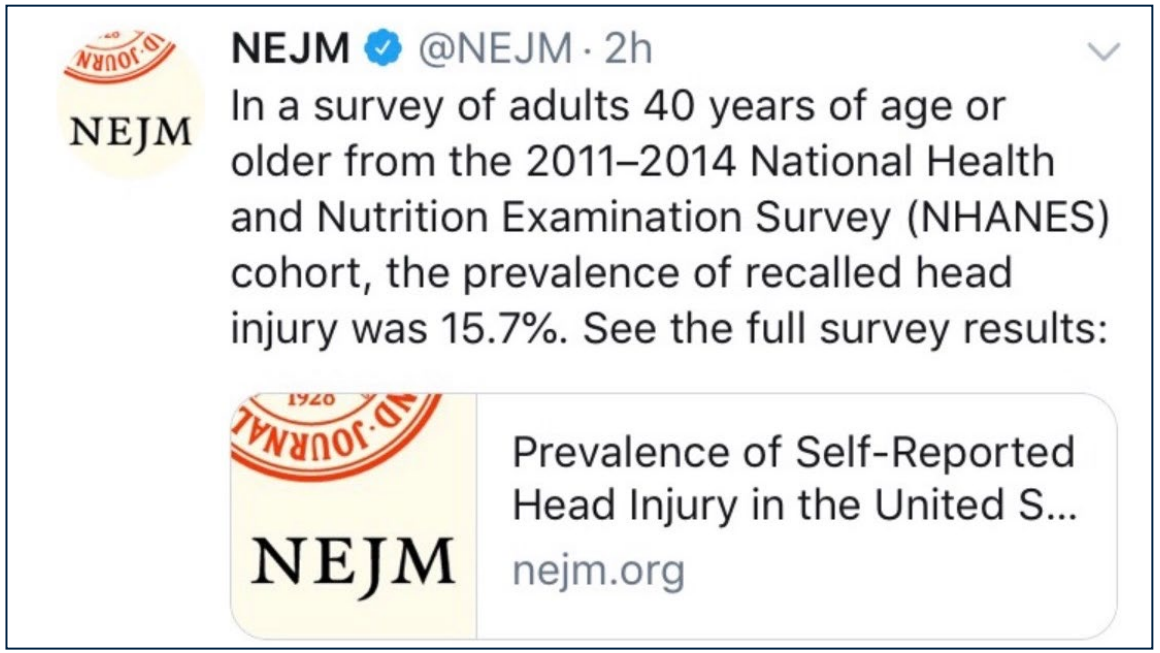
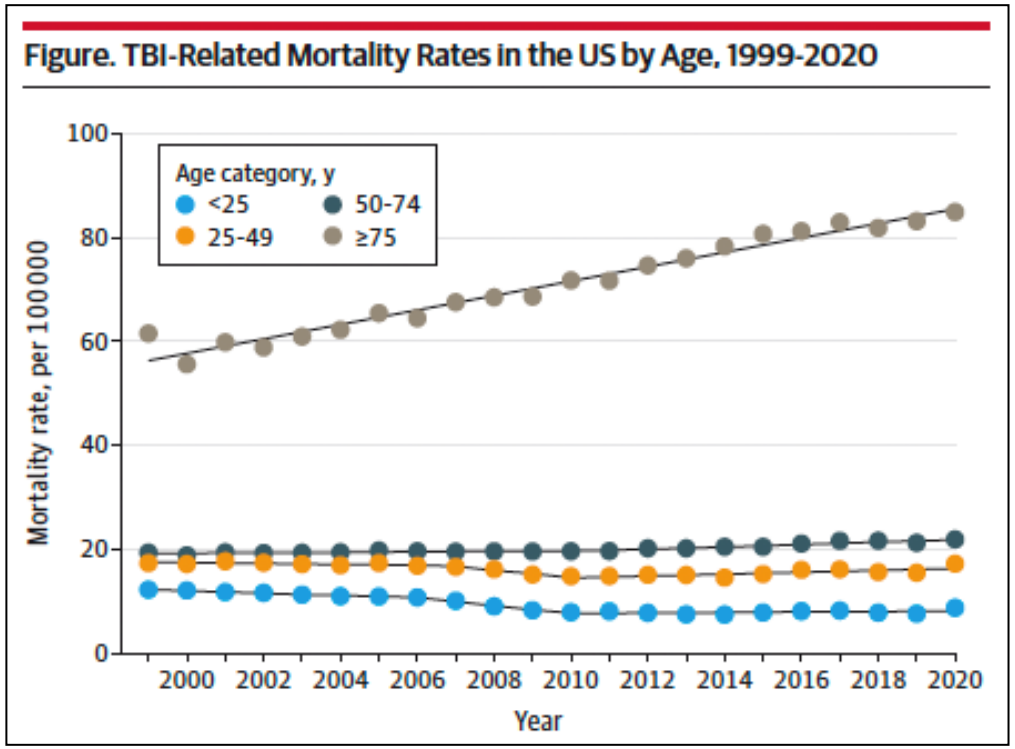
Epidemiology of TBI in the U.S.





CDC WONDER

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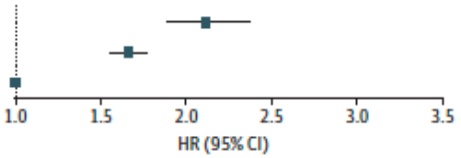
TBI is Associated with Significant Mortality and Morbidity

- TBI was associated with 2 times the risk of mortality over a median of 28 years

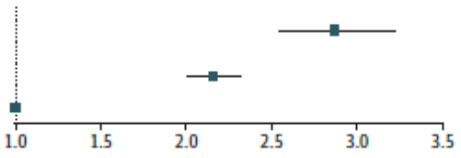
A All-cause mortality risk by head injury vs no head injury

No. of head injuries	No. of participants	Person-years	HR (95% CI)
≥2	330	4003	2.11 (1.89-2.37)
1	1275	29475	1.66 (1.56-1.77)
0	5801	289 204	1 [Reference]



B All-cause mortality by head injury severity vs no head injury

Severity	No. of participants	Person-years	HR (95% CI)
Moderate, severe, or penetrating	299	2847	2.87 (2.55-3.22)
Mild	1031	14881	2.16 (2.01-2.31)
No injury	5801	296 114	1 [Reference]



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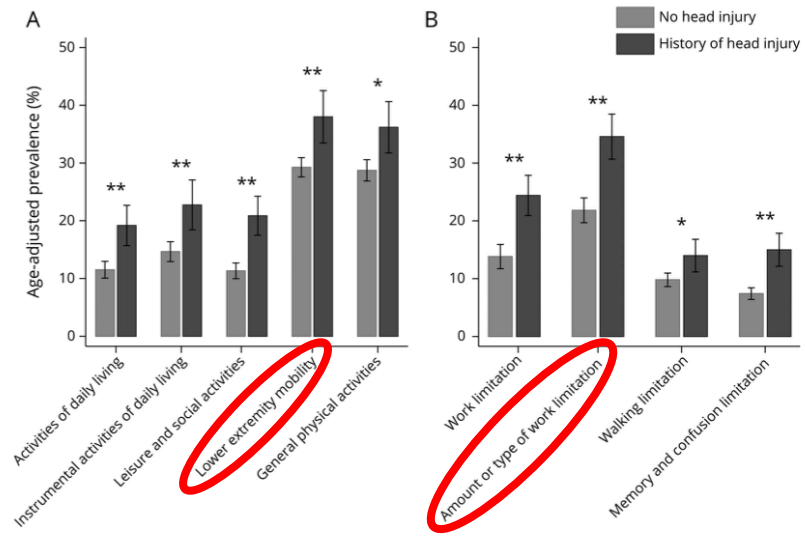
- Individuals with TBI had higher prevalence of disability compared to individuals without TBI (47% versus 39%)

Figure 2 Age-Adjusted Prevalence (95% confidence interval) of Disability by History of Head Injury With Loss of Consciousness



(A) Physical functioning domains. (B) Functional limitations domains. *$p < 0.01$ comparing no head injury to history of head injury. **$p < 0.001$ comparing no head injury to history of head injury.

nhanes

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Long-term Sequelae of TBI

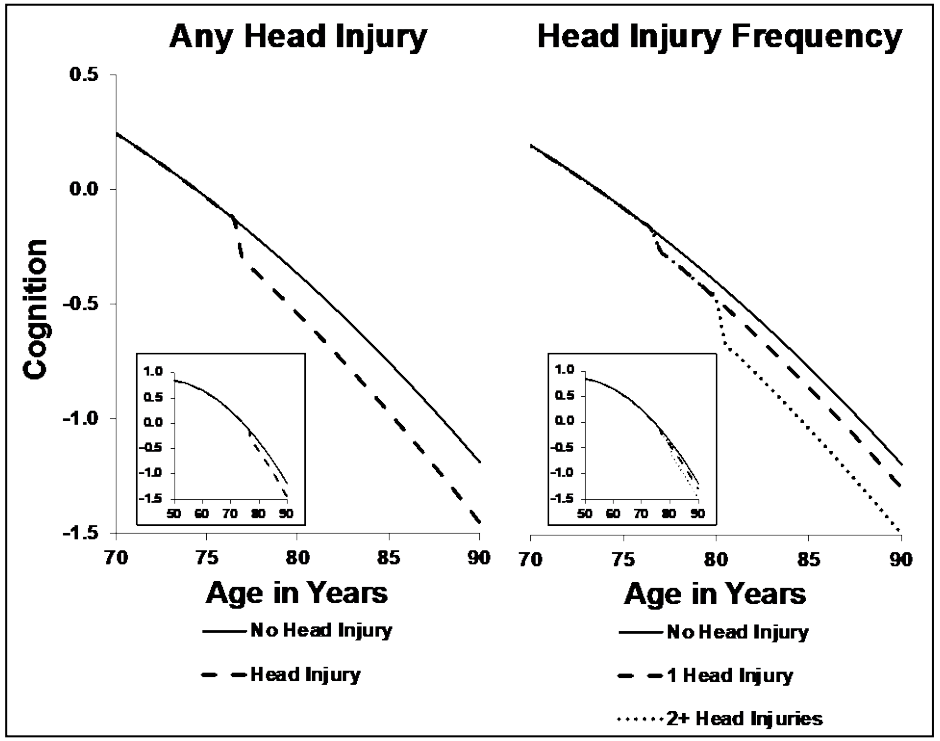
- Cognitive Decline and Dementia
- Epilepsy
- Stroke
- Falls, Frailty

- How do we study long-term outcomes after TBI when very few studies designed to study TBI from the time of injury have long-term follow-up (i.e., 30+ years)?
  - Leverage data from ongoing, deeply phenotyped epidemiologic studies such as the Atherosclerosis Risk in Communities (ARIC) Study (and others)

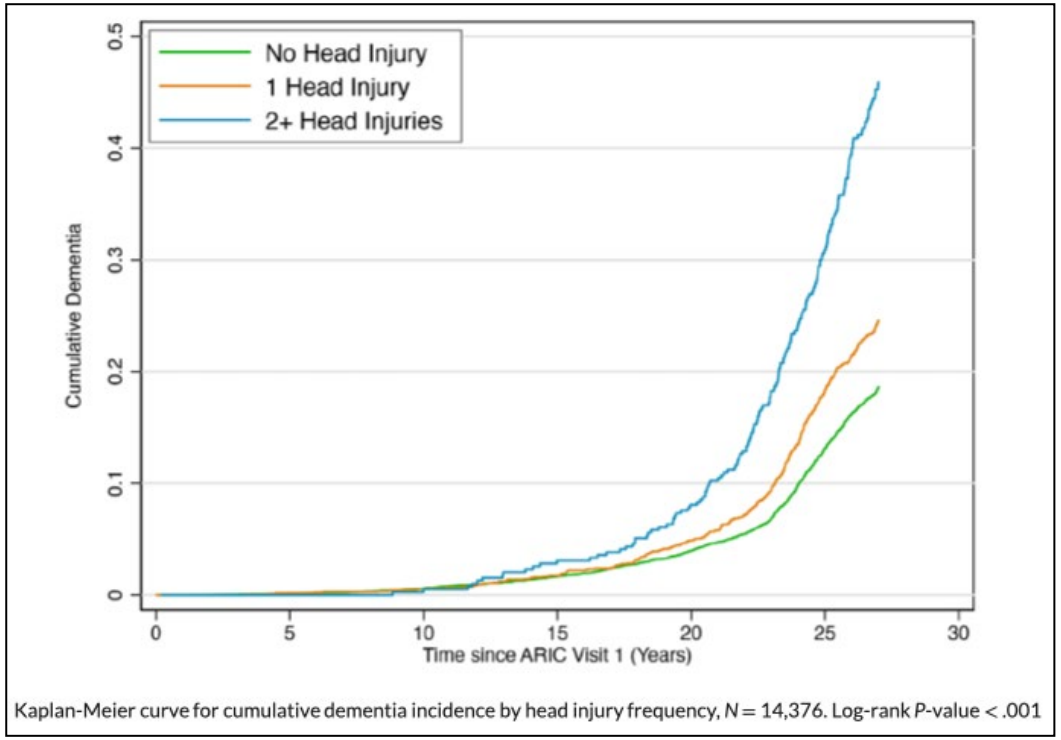
- The study of long-term outcomes after TBI has methodological challenges that must be addressed:
  - Repeated measures
  - Attrition and missing data

Long-term Sequelae of TBI – Cognitive Decline and Dementia

- Over 30-years, the difference in cognitive decline between individuals with versus without TBI is equivalent to individuals with TBI being 7.4 years older at baseline



- TBI was associated with 1.4 times the risk of dementia over a median of 25 years



Kaplan-Meier curve for cumulative dementia incidence by head injury frequency, $N = 14,376$. Log-rank P-value < .001

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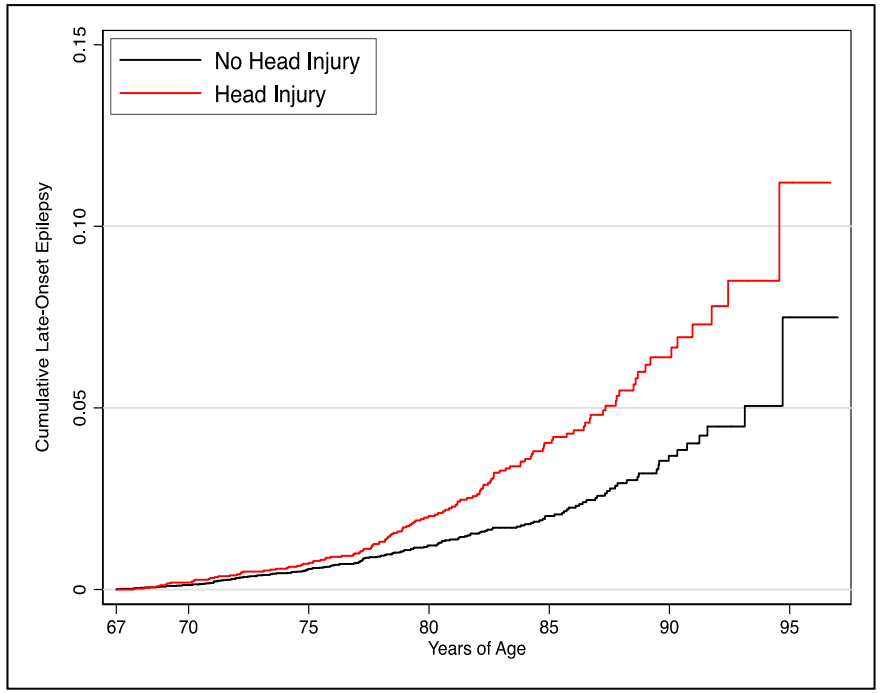
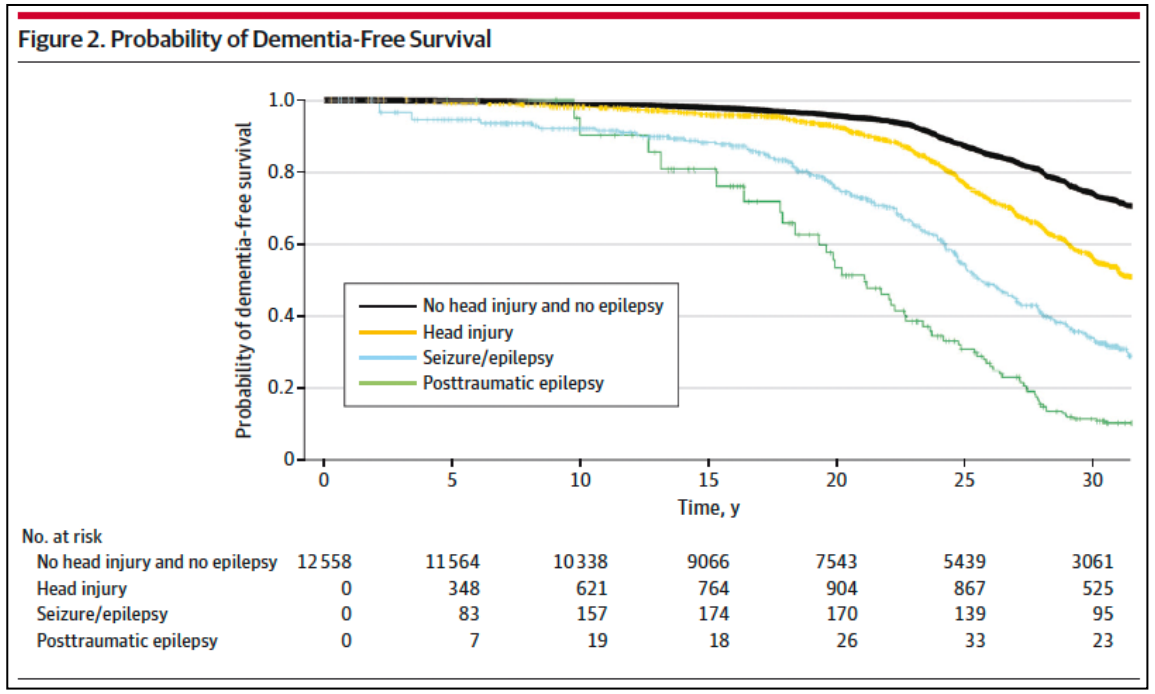
- **Schneider ALC**, Pike JR, Elser H, Coresh J, Mosley TH, Diaz-Arrastia R, Gottesman RF. Traumatic brain injury and cognitive change over 30 years among community-dwelling older adults. *Alzheimer's and Dementia*. 2024 Sep;20(9):6232-6242.

Long-term Sequelae of TBI – Epilepsy and Dementia

- Among 8,878 participants, TBI was associated with 1.9 times the risk of epilepsy over a median of 11 years



- Over a median of 25-years of follow-up of 12,558 individuals, post-traumatic epilepsy was associated with greater dementia risk than TBI or epilepsy alone



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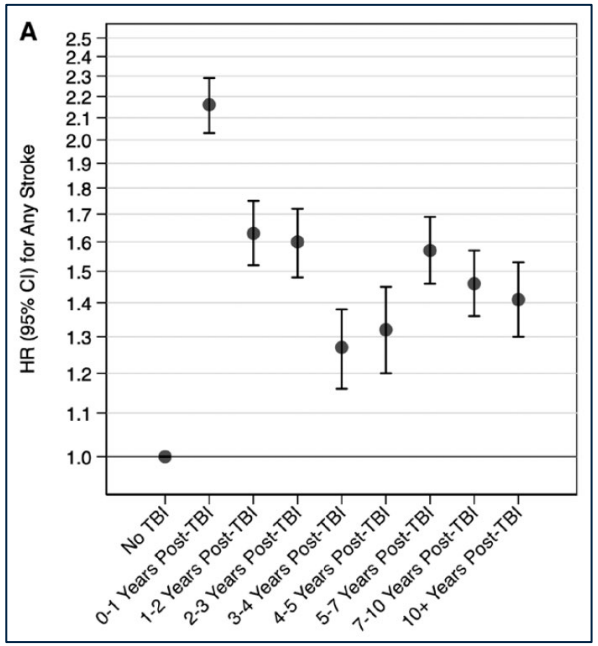
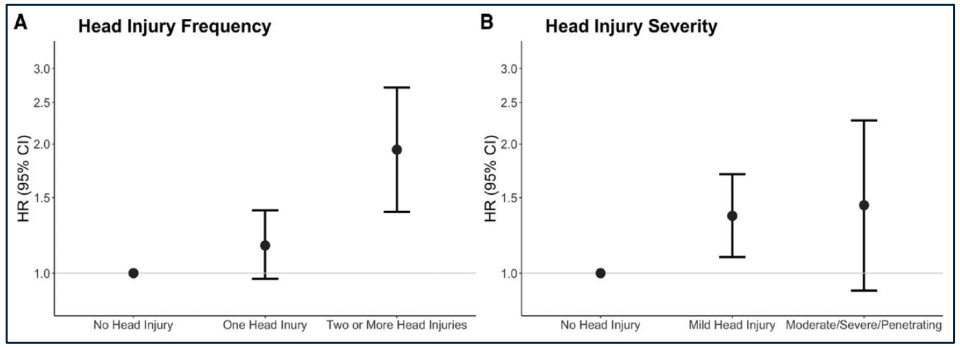
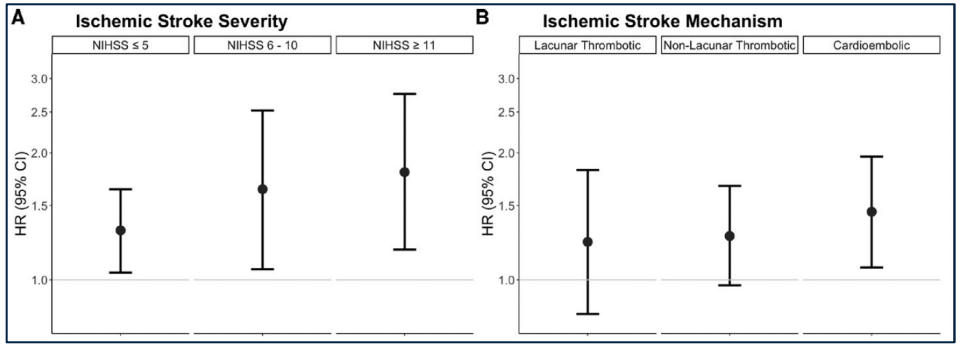
Long-term Sequelae of TBI – Stroke

- 306,796 Veterans with TBI matched 1:1 to 306,796 Veterans without TBI
- TBI associated with 1.7 times the risk of incident (ischemic or hemorrhagic) stroke over a median of 5 years



- TBI associated with 1.3 times the risk of ischemic stroke among 12,813 community-dwelling participants followed for a median of 27 years





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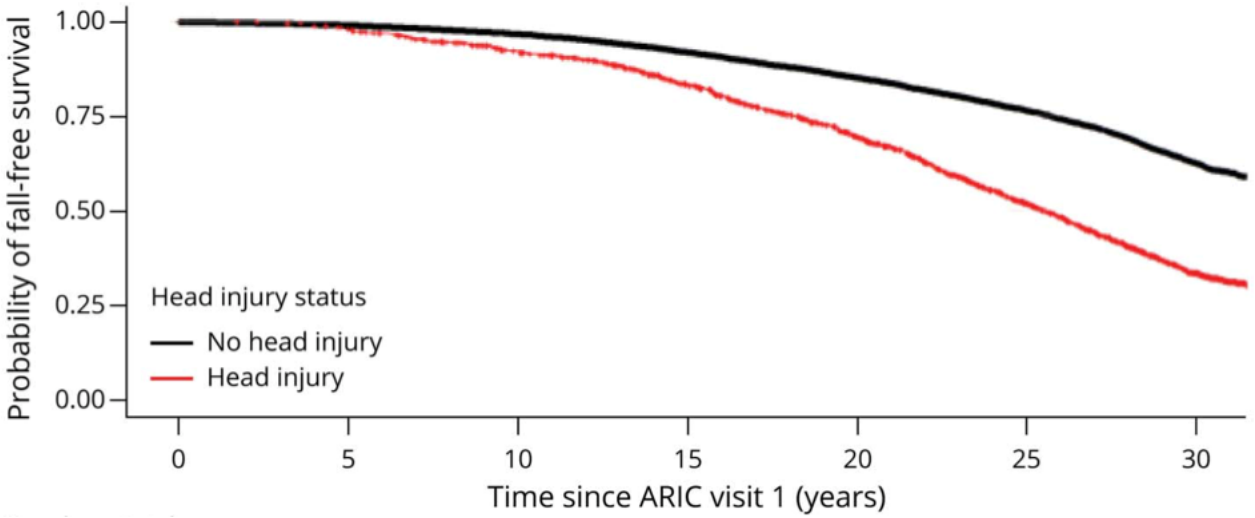
- Elser H, Pappalardo LW, Gottesman RF, Coresh J, Diaz-Arrastia R, Mosley TH, Kasner SE, Koton S, **Schneider ALC**. Head Injury and Risk of Incident Ischemic Stroke in Community-Dwelling Adults. *Stroke*. 2024 Jun;55(6):1562-1571.

Long-term Sequelae of TBI – Falls and Frailty

- Among 13,081 participants followed a median of 23 years, individuals with TBI had 1.7 times the risk of a subsequent injurious fall requiring hospitalization, after accounting for the competing risk of mortality



- Individuals with TBI were more likely to be pre-frail or frail at baseline
- Individuals with TBI were also more likely to develop incident pre-frailty or frailty over a median of 5 years

	Odds ratio (95% CI)
Baseline	
Robust	1 (Ref.)
Pre-frail	1.19 (1.04, 1.35)
Frail	1.40 (1.08, 1.80)
Longitudinal	
Robust	1 (Ref.)
Pre-frail	1.32 (1.04, 1.67)
Frail	1.92 (1.05, 3.51)

ARIC

- Hunzinger KJ, Law CA, Elser H, Walter AE, Windham BG, Palta P, Juraschek SP, Hicks CW, Gottesman RF, **Schneider ALC**. Associations Between Head Injury and Subsequent Risk of Falls: Results From the Atherosclerosis Risk in Communities (ARIC) Study. *Neurology*. 2023 Nov 27;101(22):e2234-e2242.
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Research Gaps and Recommendations for Research Priorities

- Epidemiological research provides strong evidence supporting TBI as a chronic condition, but most research to date has focused on TBI as an independent risk factor for outcomes

- Recommendation: Consider how pre- and post-injury comorbid factors across the life course may influence associations of TBI with long-term outcomes to identify high-risk population subgroups
  - Medical comorbidities
  - Social and environmental determinants of health
  - Targeting modifiable comorbidities is an attractive avenue to improve overall health after TBI

- Recommendation: Prioritize leveraging existing longitudinal datasets to gain new insights (with appropriate consideration of methodological challenges)
  - Cost-effective