

Military Risk Factors for Cognitive Aging and Dementia

Kristine Yaffe, MD

Scola Endowed Chair & Vice Chair

Professor of Psychiatry, Neurology & Epidemiology

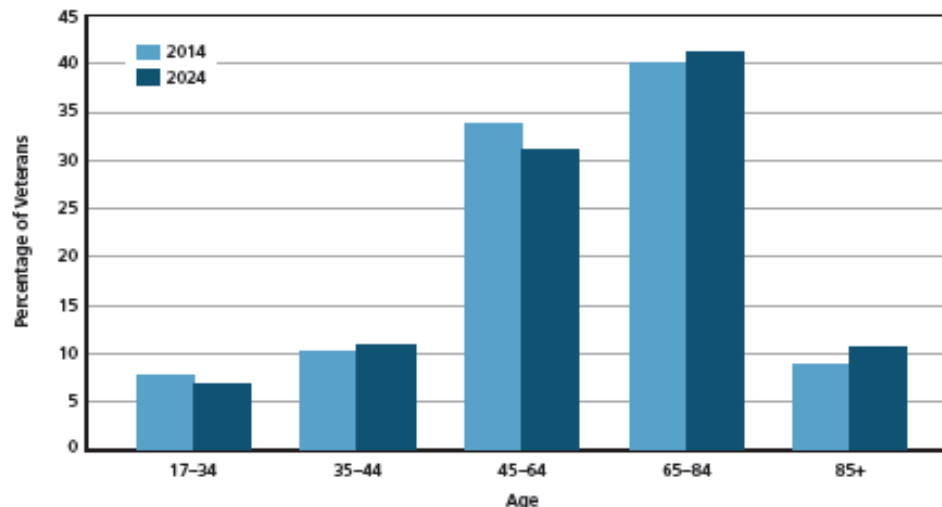
University of California, San Francisco

Chief of NeuroPsychiatry & Director, Memory Clinic, San Francisco VA Medical Center

Veterans at Risk for Cognitive Aging & Dementia

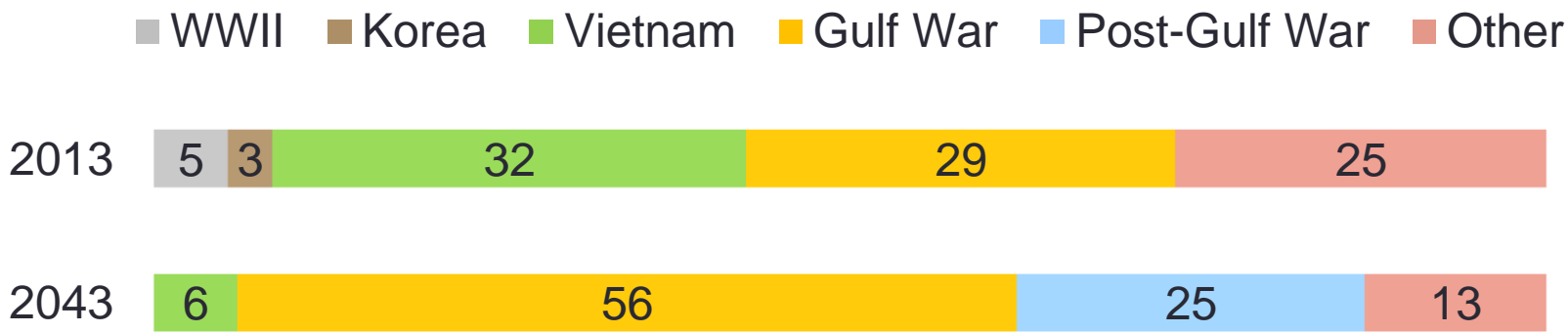
- Almost 50% of veterans are older than 65 years of age
- Veterans face a unique set of military risk factors for dementia including PTSD and TBI
- In addition, veterans are at risk due to a similar set of risk factors as older adults in the general population
- But the burden of these risk factors may be even greater in veterans

Age of Veterans, 2014 and 2024 (Projected)



Rand Health, 2015.

Projected Changes in Veterans by Era of Service

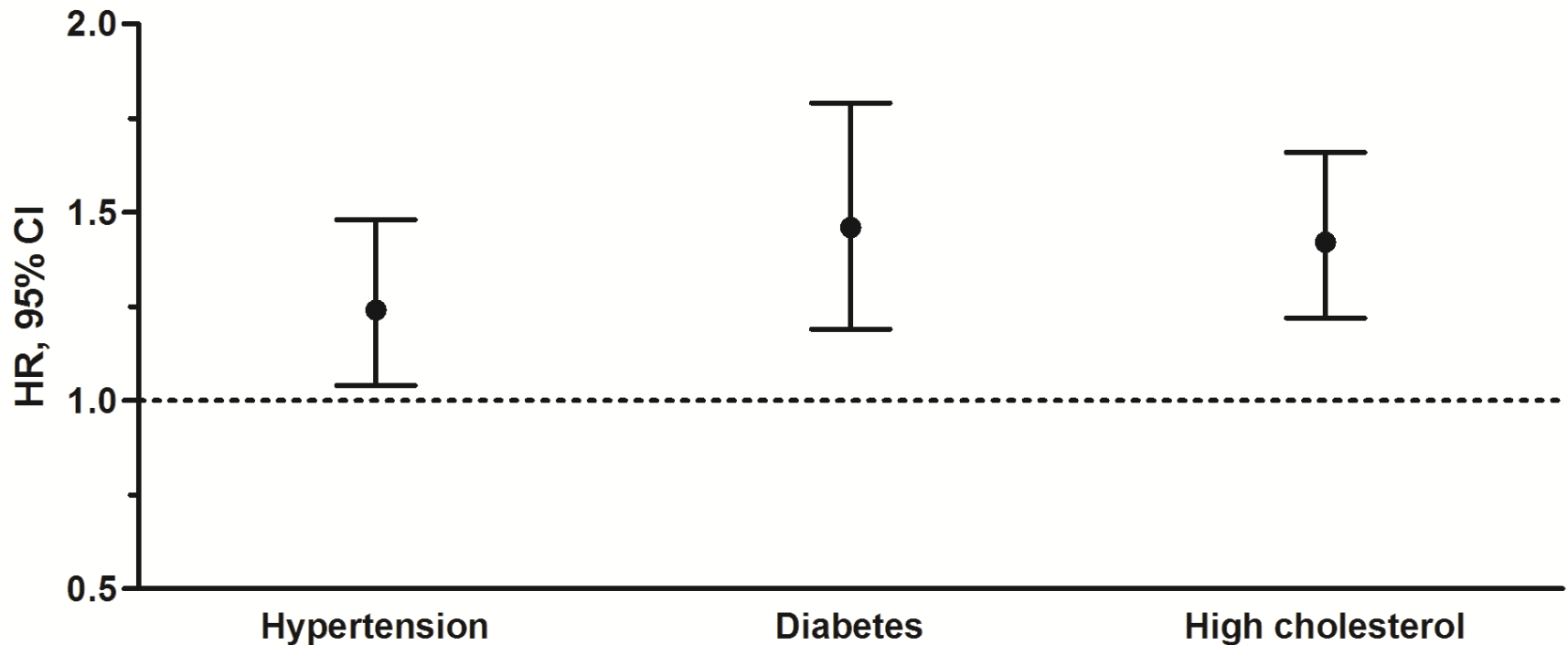


In the next few decades, Gulf War veterans will comprise more than half of the veteran population

The Importance of Modifiable Risk Factors for Cognitive Aging and Dementia

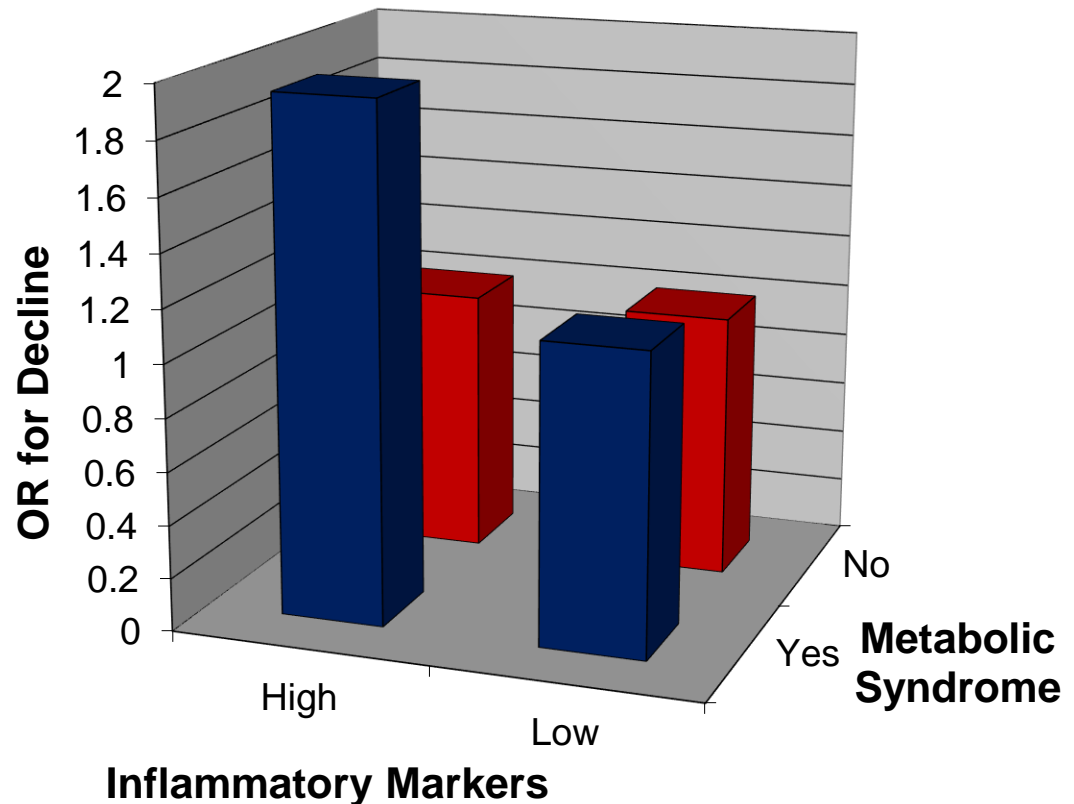
- Identification of modifiable risk factors can help
 - Understand the biological mechanisms associated with cognitive impairment & dementia development
 - Identify those at highest risk of developing dementia
 - Improve prevention and treatment options
- Need to understand the role of both non-military and military risk factors for aging veterans

Midlife Cardiovascular Risk Factors Increase Risk of Dementia



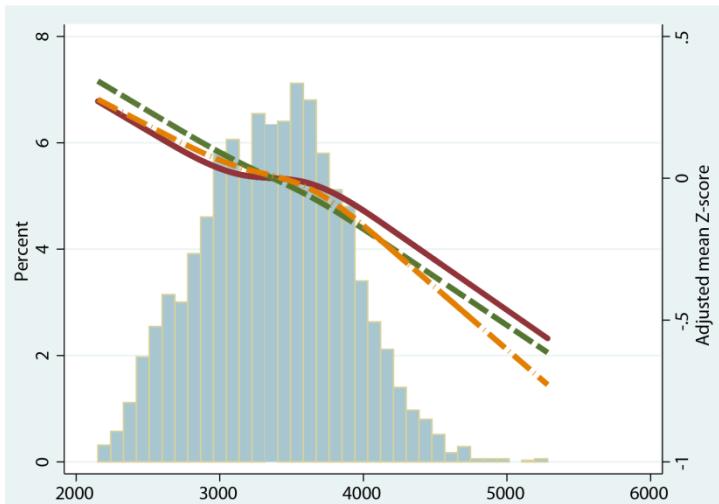
Multiple Cardiovascular Risk Factors Together Increase Risk of Dementia

- Metabolic syndrome:
 - ↑ blood pressure
 - ↑ cholesterol
 - ↑ triglycerides
 - ↑ blood sugar
 - ↑ body weight
- Together may be greater than individual components
- Role of inflammation
- Offer strategies to modify risk factors as a group

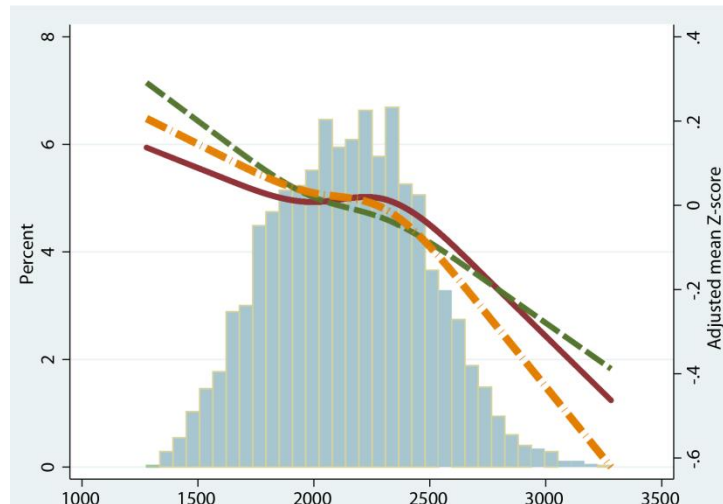


P for interaction = 0.04

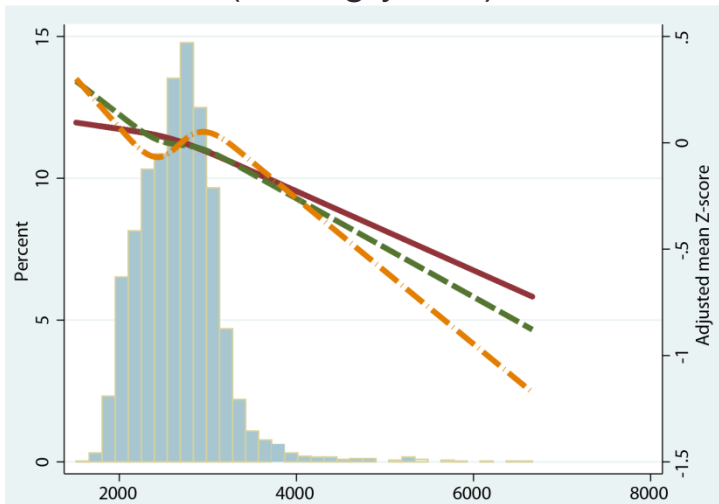
Cardiovascular Risk Factors in Early-Mid Adulthood & Cognition at Midlife



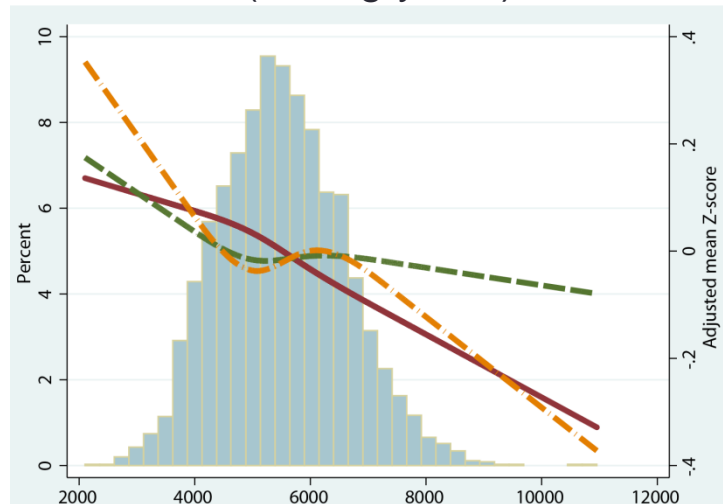
Systolic Blood Pressure AUC (mmHg-years)



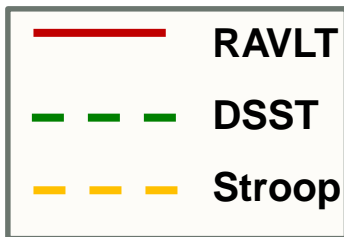
Diastolic Blood Pressure AUC (mmHg-years)



Fasting Blood Glucose AUC (mg/dl-years)



Total Cholesterol AUC (mg/dL-years)



Yaffe et al,
Circulation, 2014.

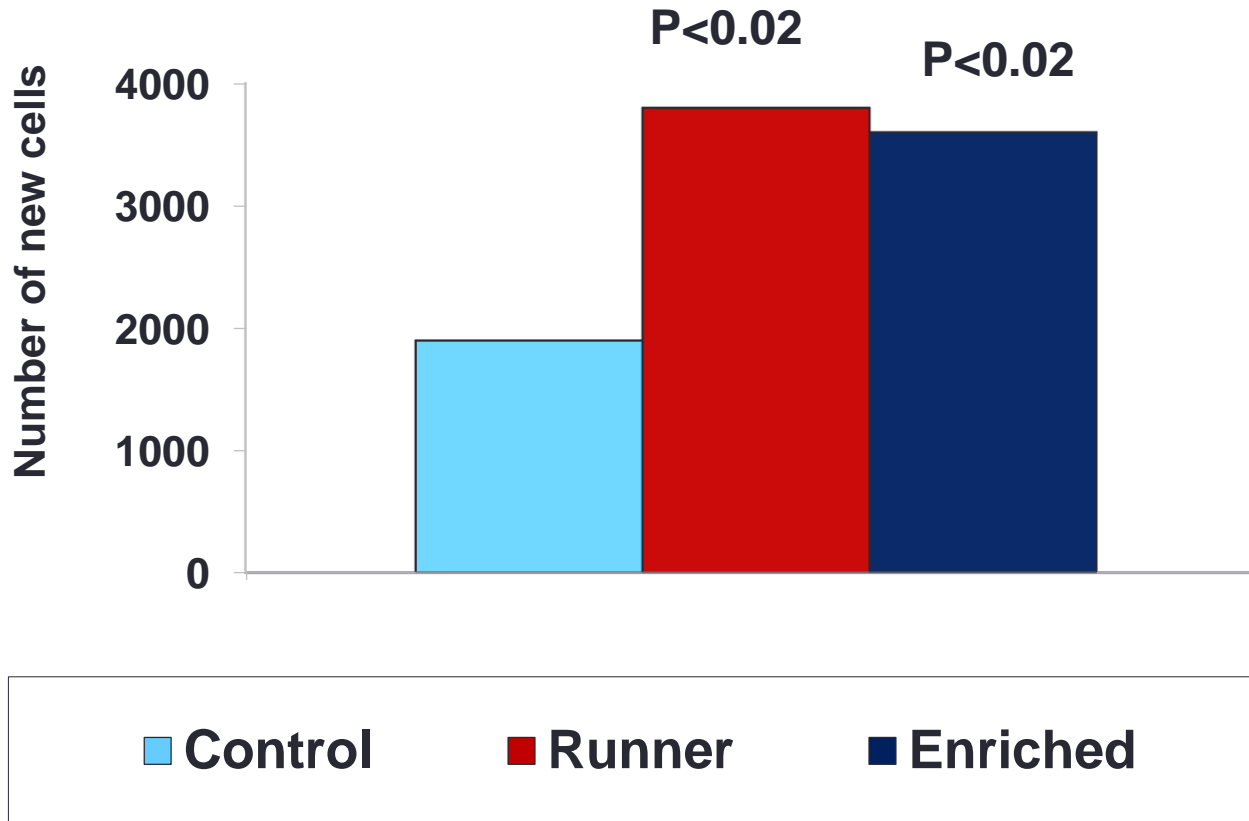
Burden of Cardiovascular Risk Factors in Veterans

Survey of Veteran Enrollees in VHA ≥ 65 years old

Hypertension	63.8%
Diabetes	27.1%
Myocardial infarction	26.8%
Stroke	15.0%

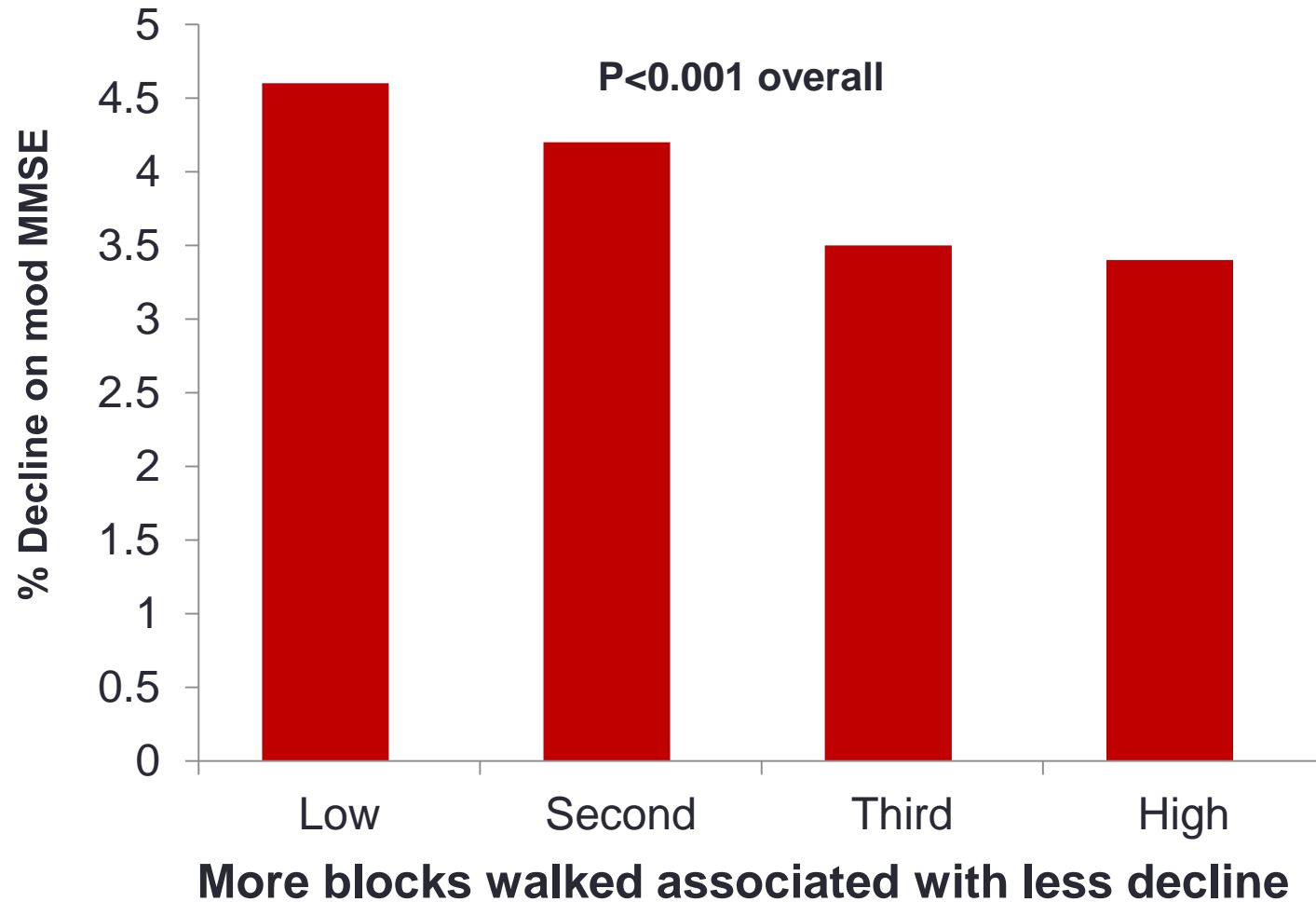
Among VA patients ≥ 65 years old, an estimated 29.1% have diabetes, hyperlipidemia, and hypertension.

Mouse Model of Physical & Cognitive Activity: Use it or Lose it?

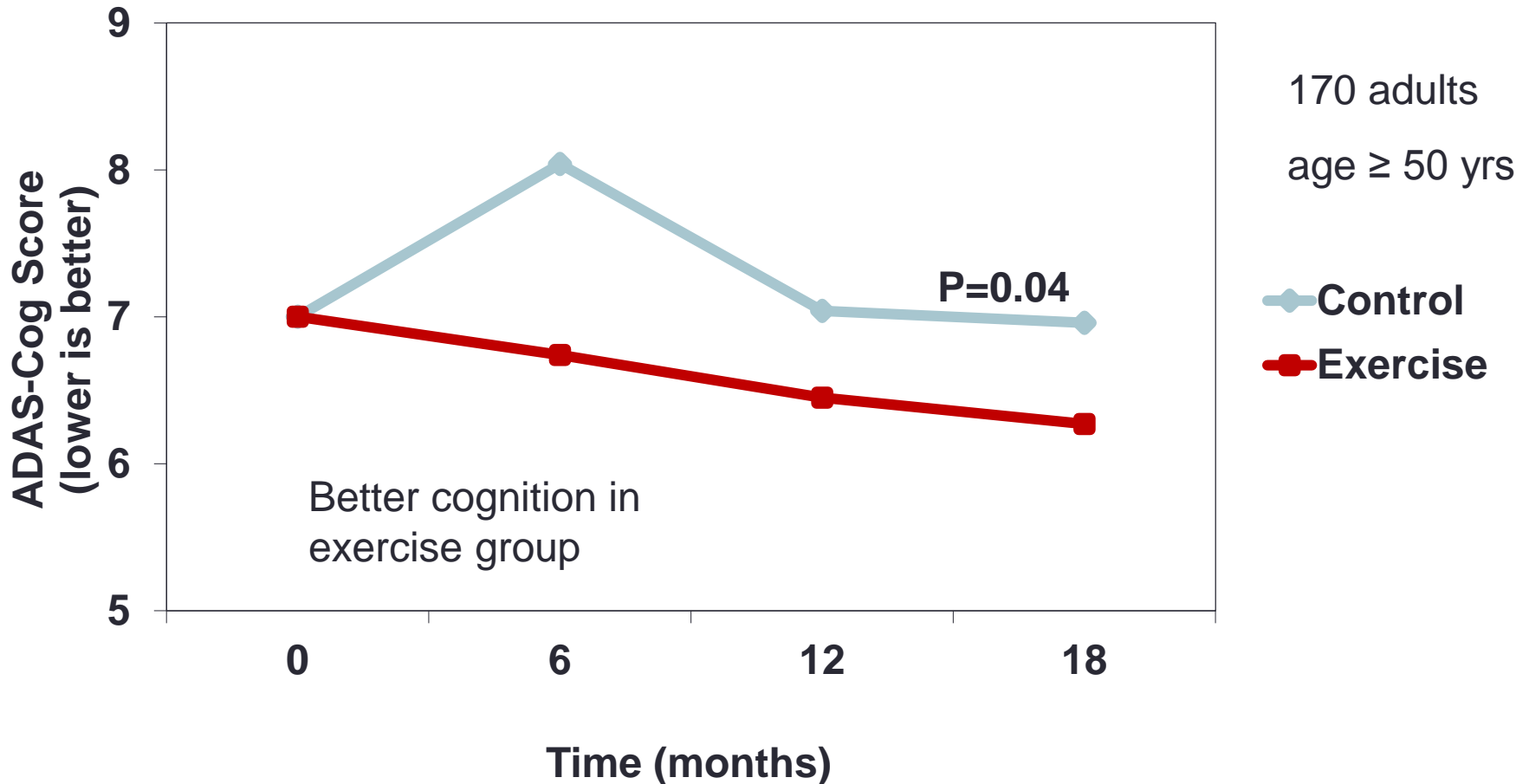


Physical activity &
mental activity increase
new brain cell
development in
mice

Walking and Rate of Cognitive Decline



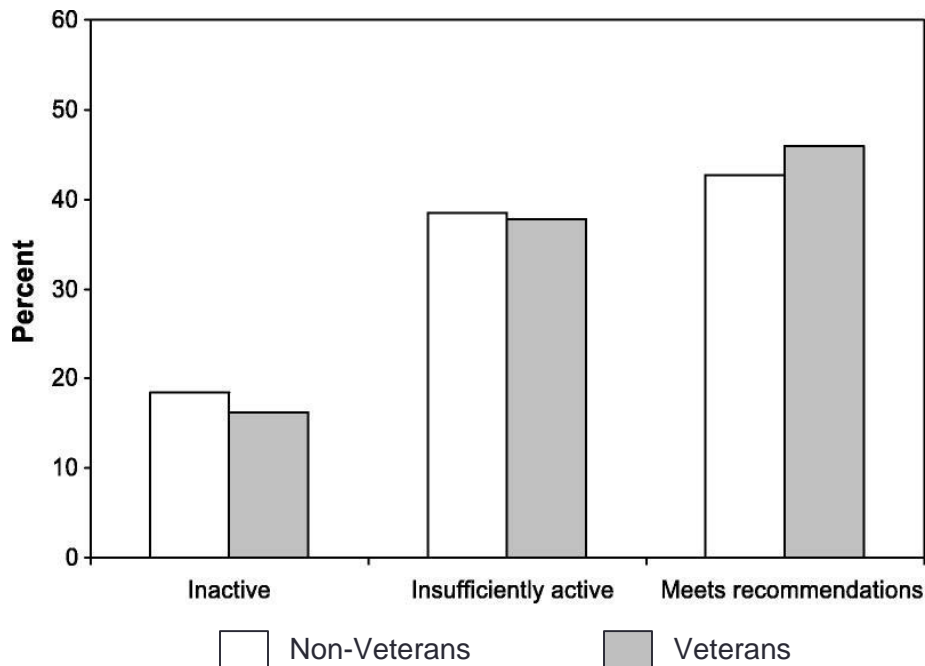
Exercise Improves Cognitive Function in Older Adults with Memory Complaints



Physical Activity in Veterans

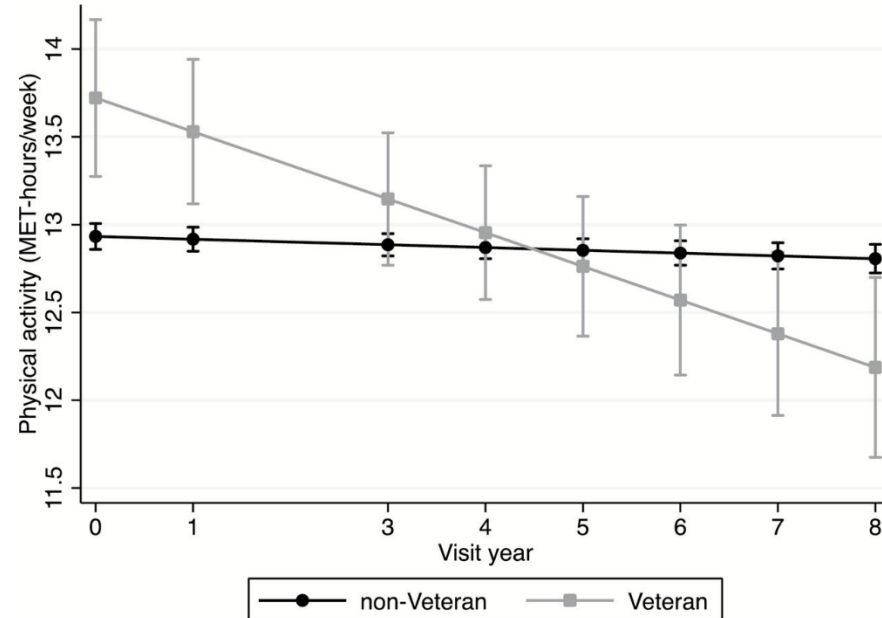
Active duty members report high levels of physical activity, but veterans do not maintain those levels.

Physical activity in veterans vs non-veterans, Behavioral Risk Factor Surveillance System



Littman et al, *Med Sci Sports Exerc*, 2009.

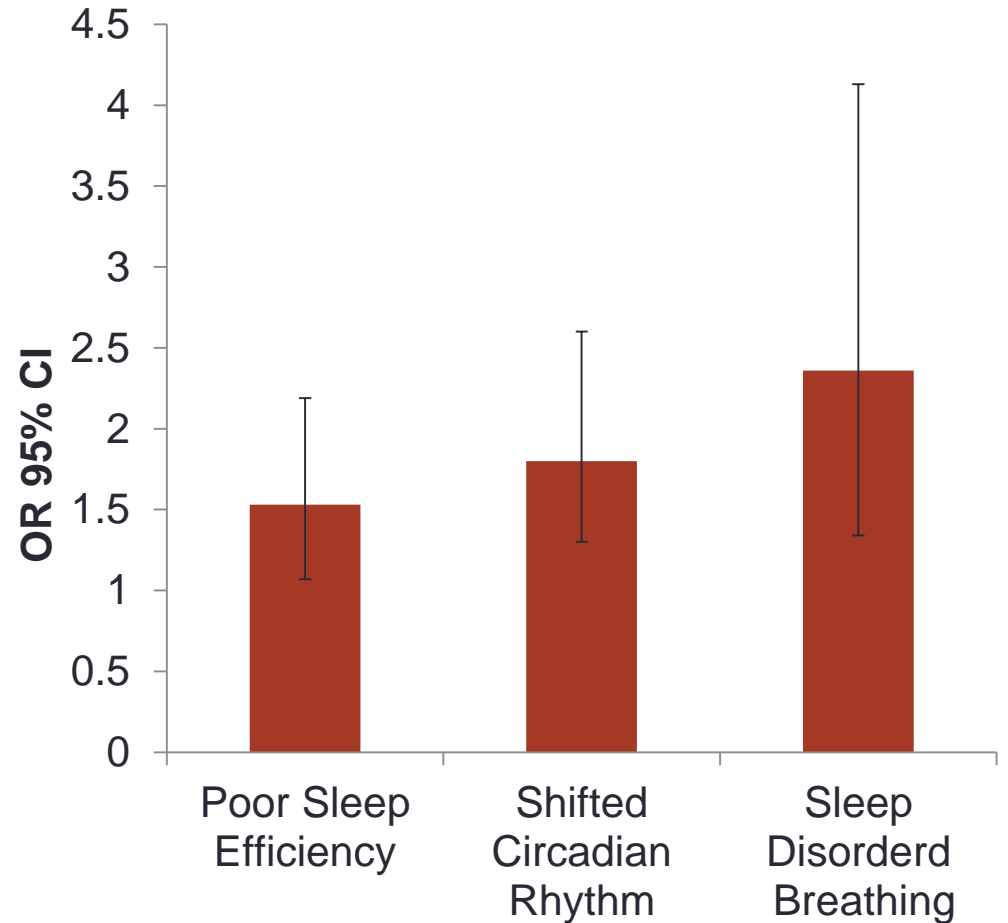
Physical activity trajectories in older women veterans vs older women non-veterans, Women's Health Initiative



Washington et al, *Gerontologist*, 2015.

Sleep and Dementia Risk

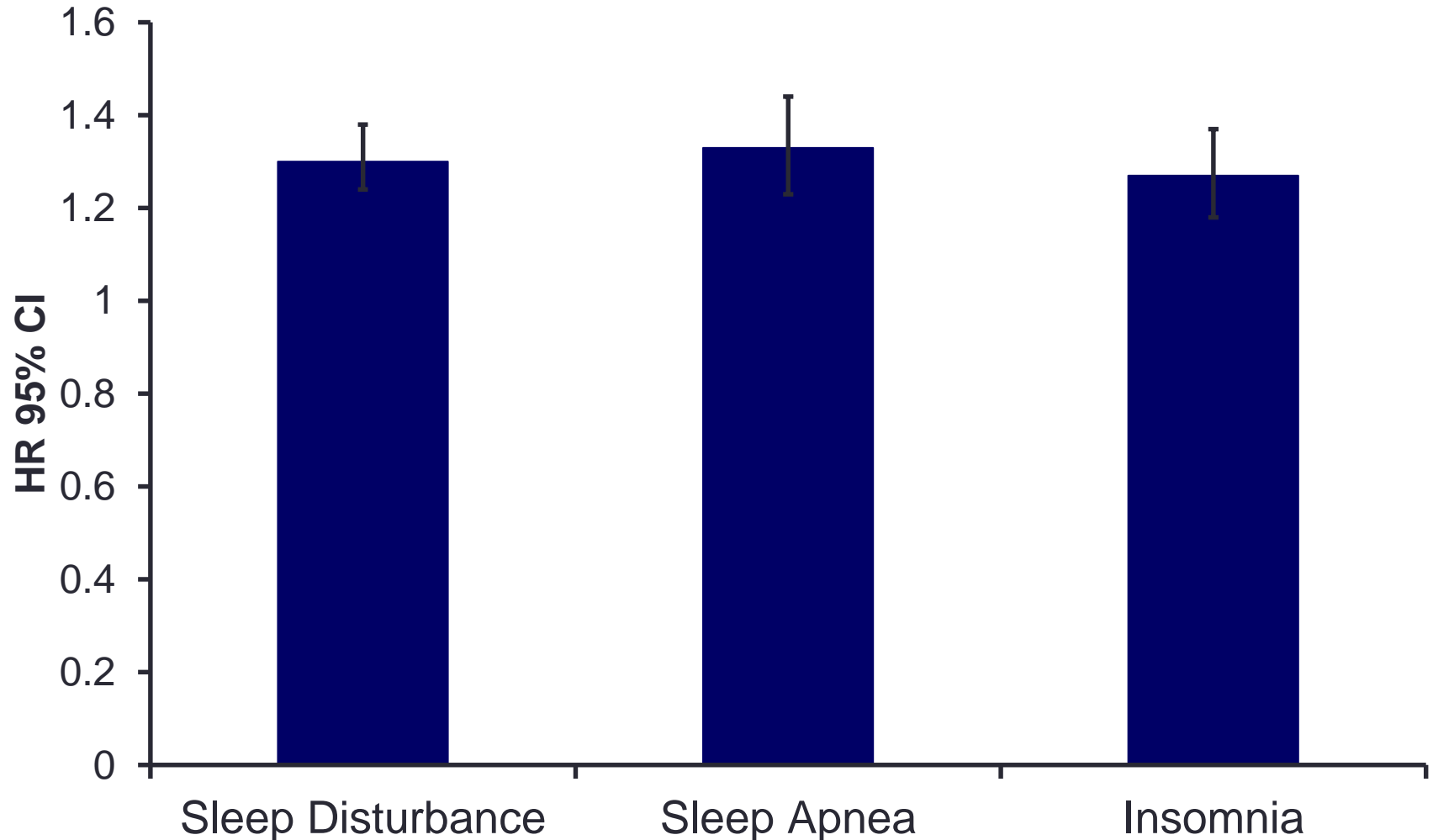
Emerging evidence that sleep disturbances and poor sleep quality increase risk of developing dementia



Sleep in Veterans

- Greater than 20% of veterans report insufficient sleep and almost 35% report sleeping <7hrs/night
- Recent study of VHA users suggest diagnoses of sleep disorders are increasing
- Sleep apnea and insomnia were the most common diagnoses of sleep disorders
- Sleep disorders often comorbid with PTSD and TBI

Sleep Disturbances and Increased Risk of Dementia in Veterans





DoD Numbers for Traumatic Brain Injury Worldwide - Incidence by Severity

No. of cases

30,000

25,000

20,000

15,000

10,000

5,000

0

'00 '01 '02 '03 '04 '05 '06 '07 '08 '09 '10 '11 '12 '13 '14

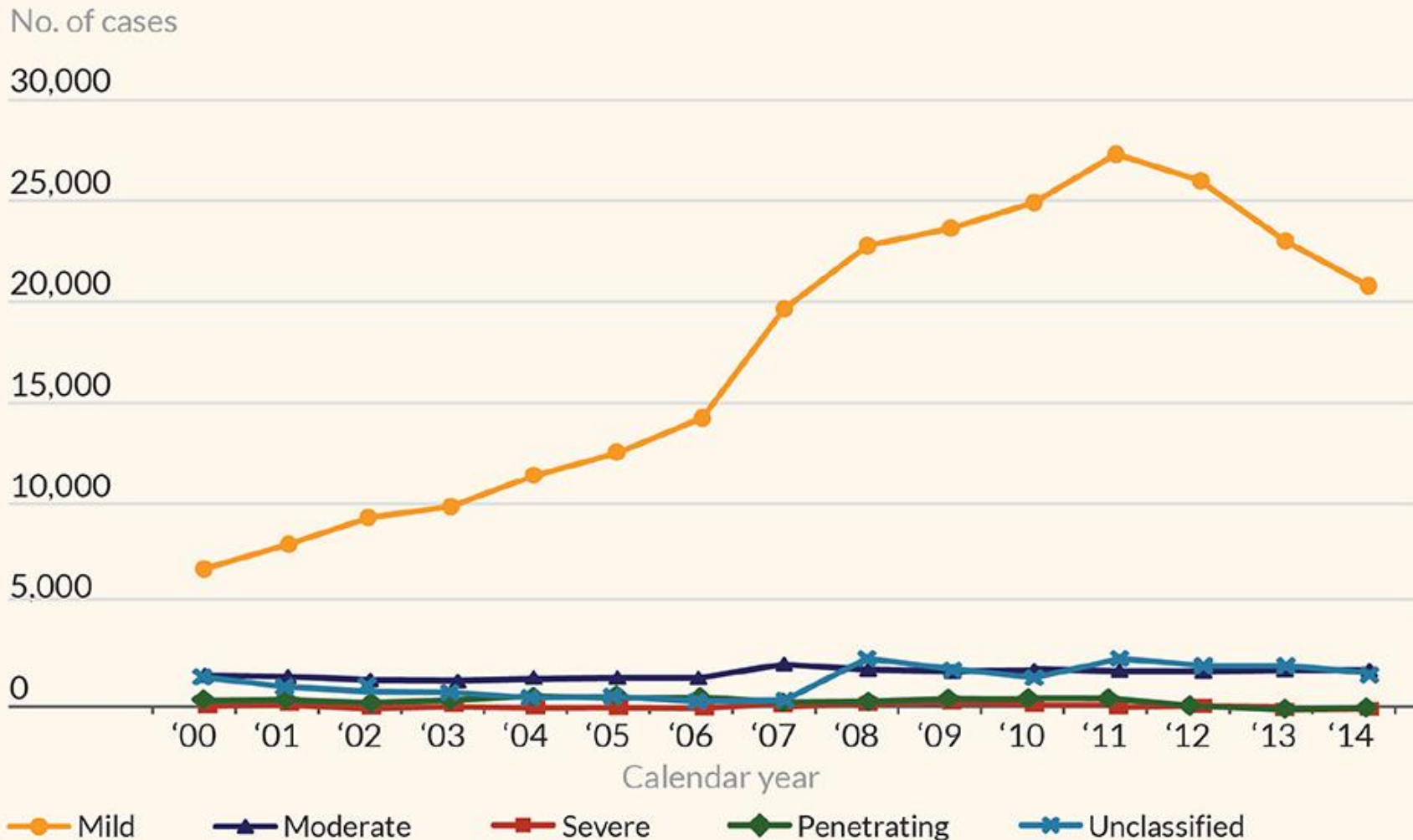
Calendar year

● Mild ▲ Moderate ■ Severe ◆ Penetrating ✕ Unclassified

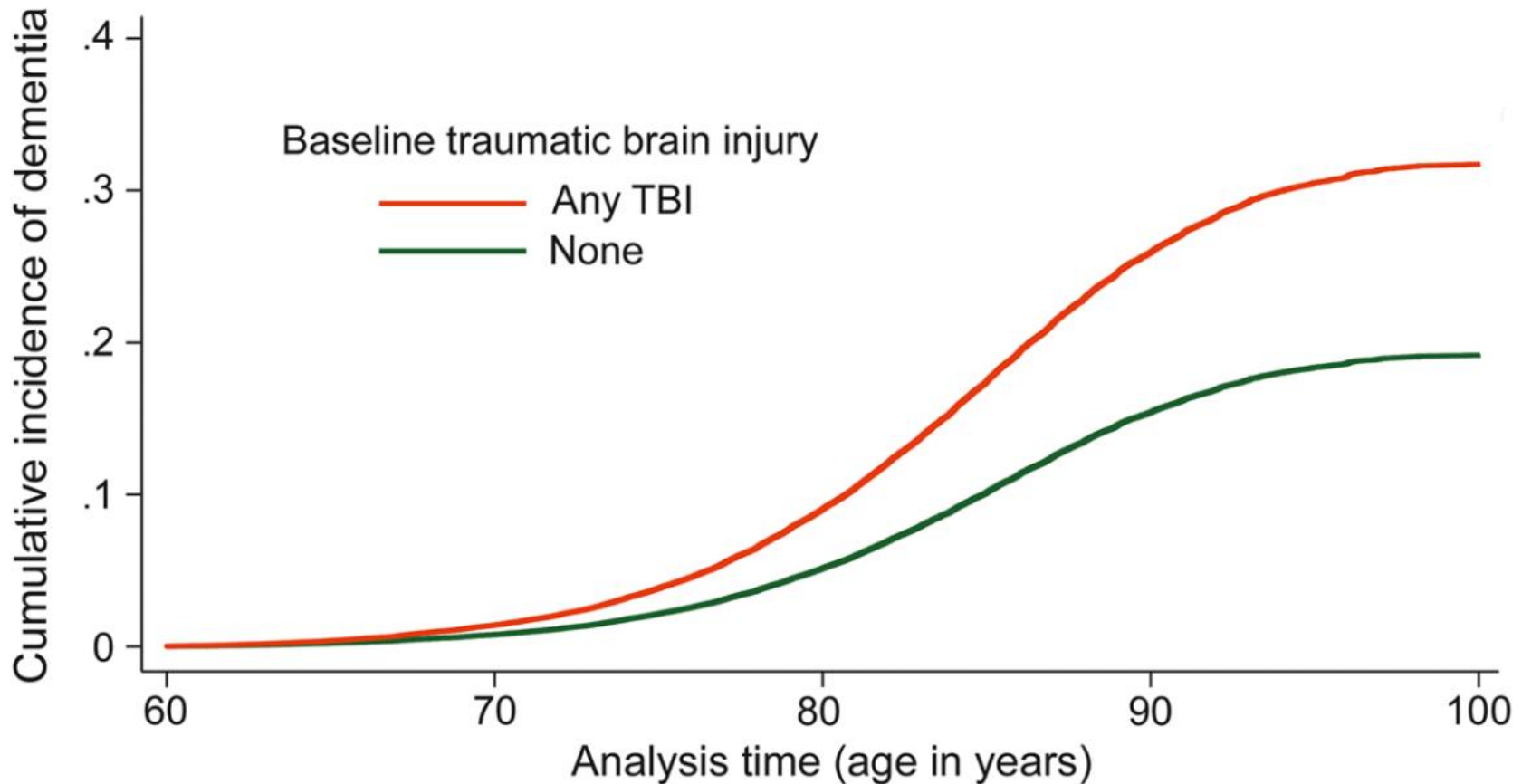
Source: Defense Medical Surveillance System (DMSS), Theater Medical Data Store (TMDS) provided by the Armed Forces Health Surveillance Center (AFHSC)

Prepared by the Defense and Veterans Brain Injury Center (DVBIC)

2000 -2014, as of May 15, 2015



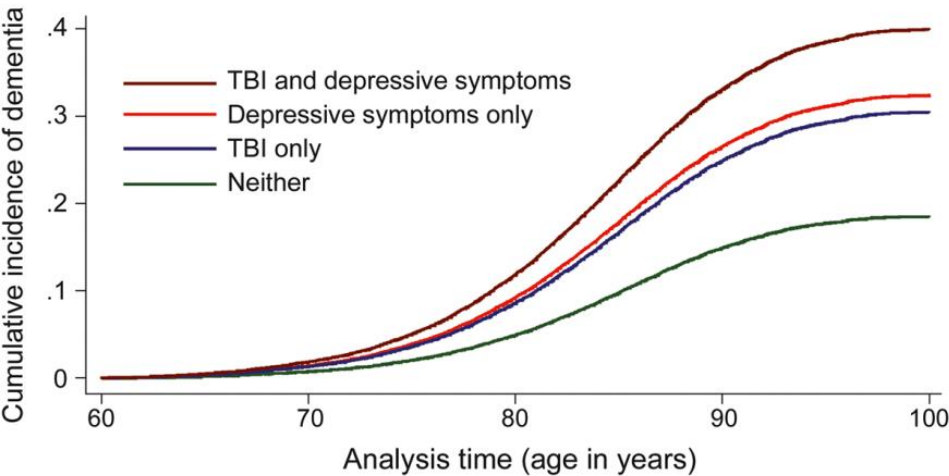
Traumatic Brain Injury: 60% Increased Risk of Dementia with TBI



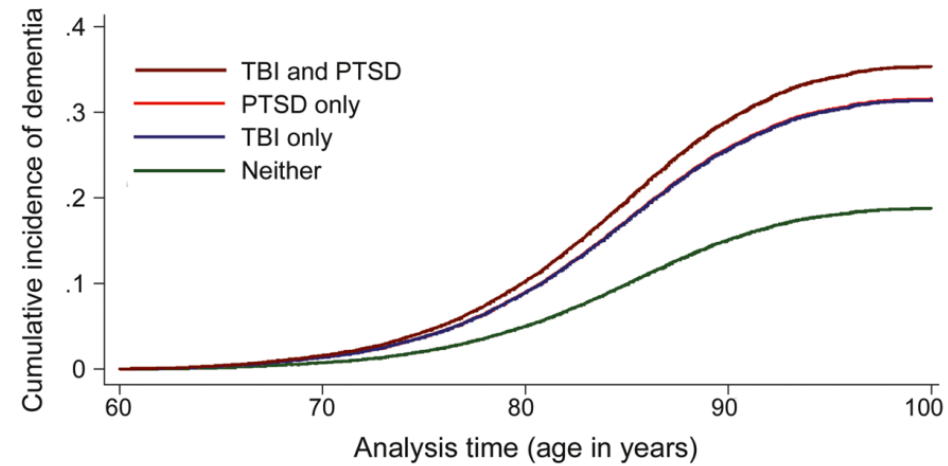
Adjusted HR:1.57; 95% CI (1.35–1.83)

Comorbidities Have an Additive Effect with TBI on Dementia Risk

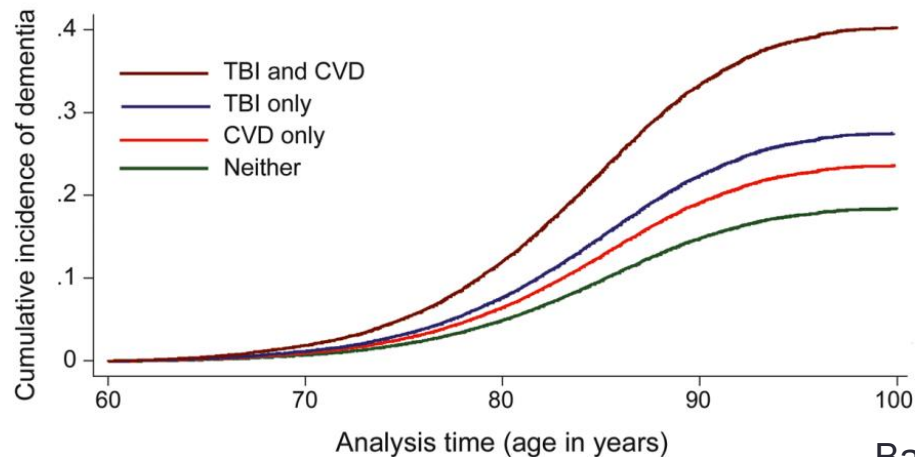
Depression



PTSD



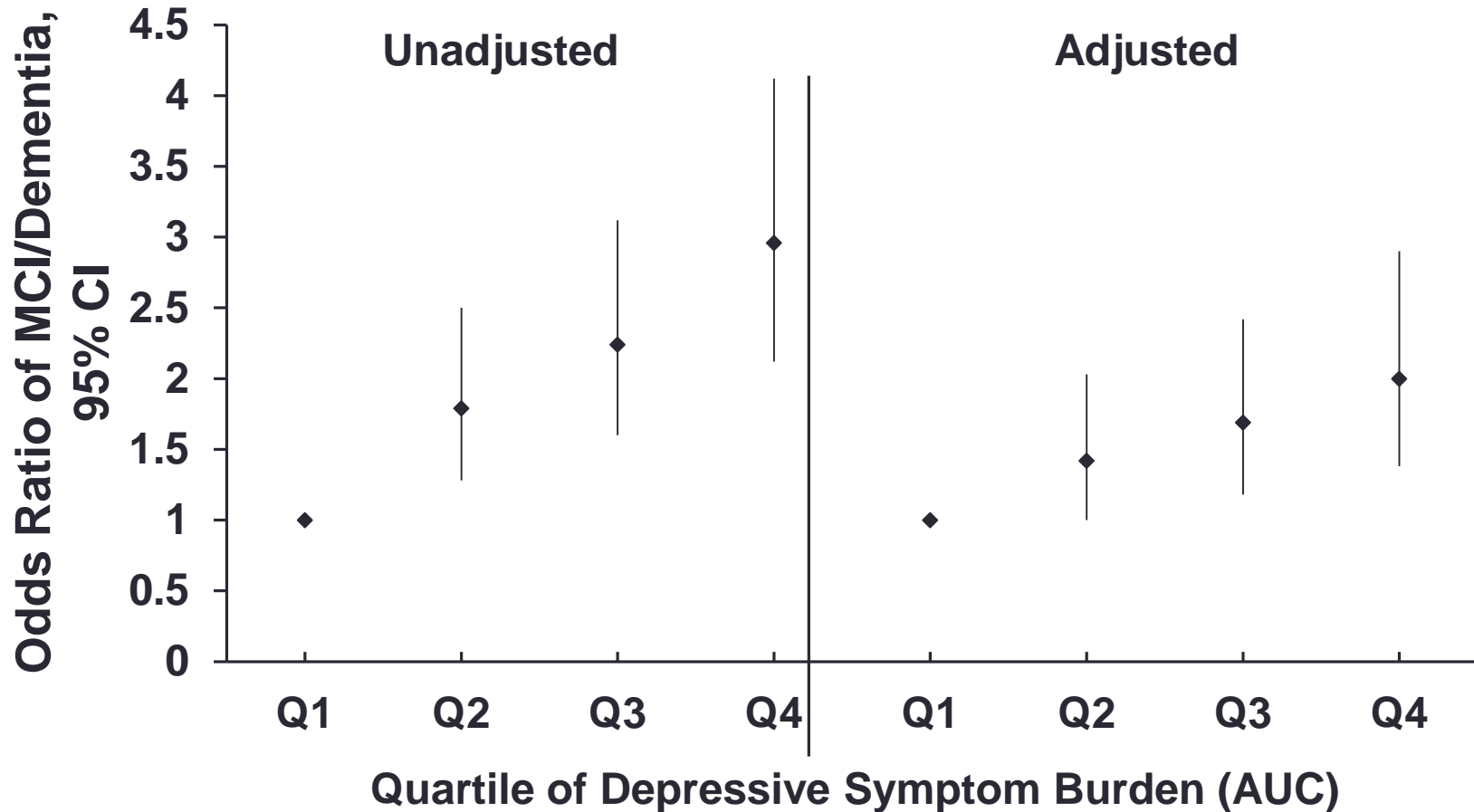
Cardiovascular Disease



Psychiatric Risk Factors & Dementia Risk

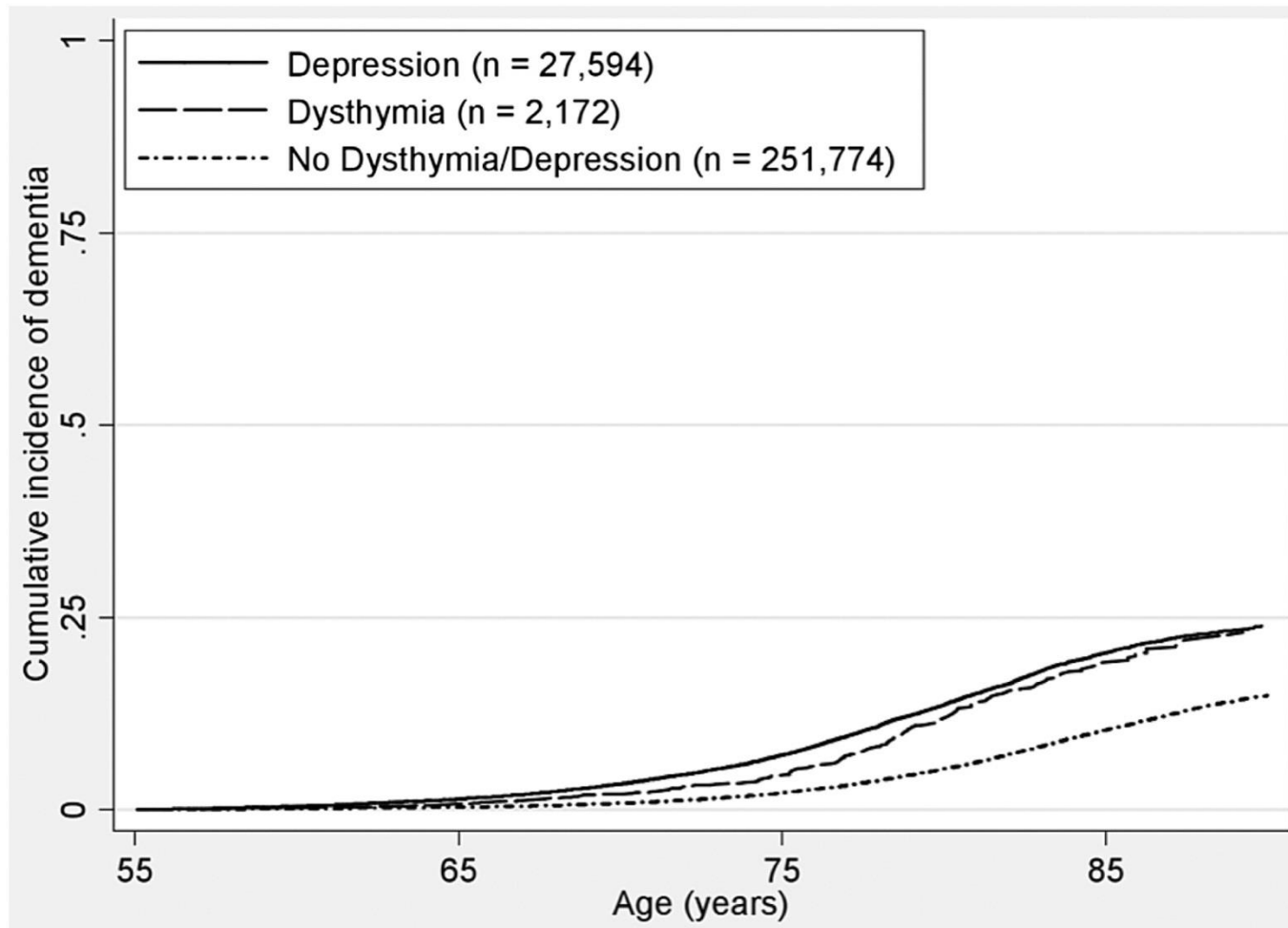
- More and more data on depression and PTSD as risk factors for dementia
- High burden of psychiatric diagnoses among veterans
- Odds of depression in Gulf War veterans is 2 times higher compared to non-deployed military personnel
- Odds of PTSD in Gulf War veterans is 3 times higher compared to non-deployed veterans

Greater Depressive Symptom Burden Over Time Increases Risk of MCI/Dementia



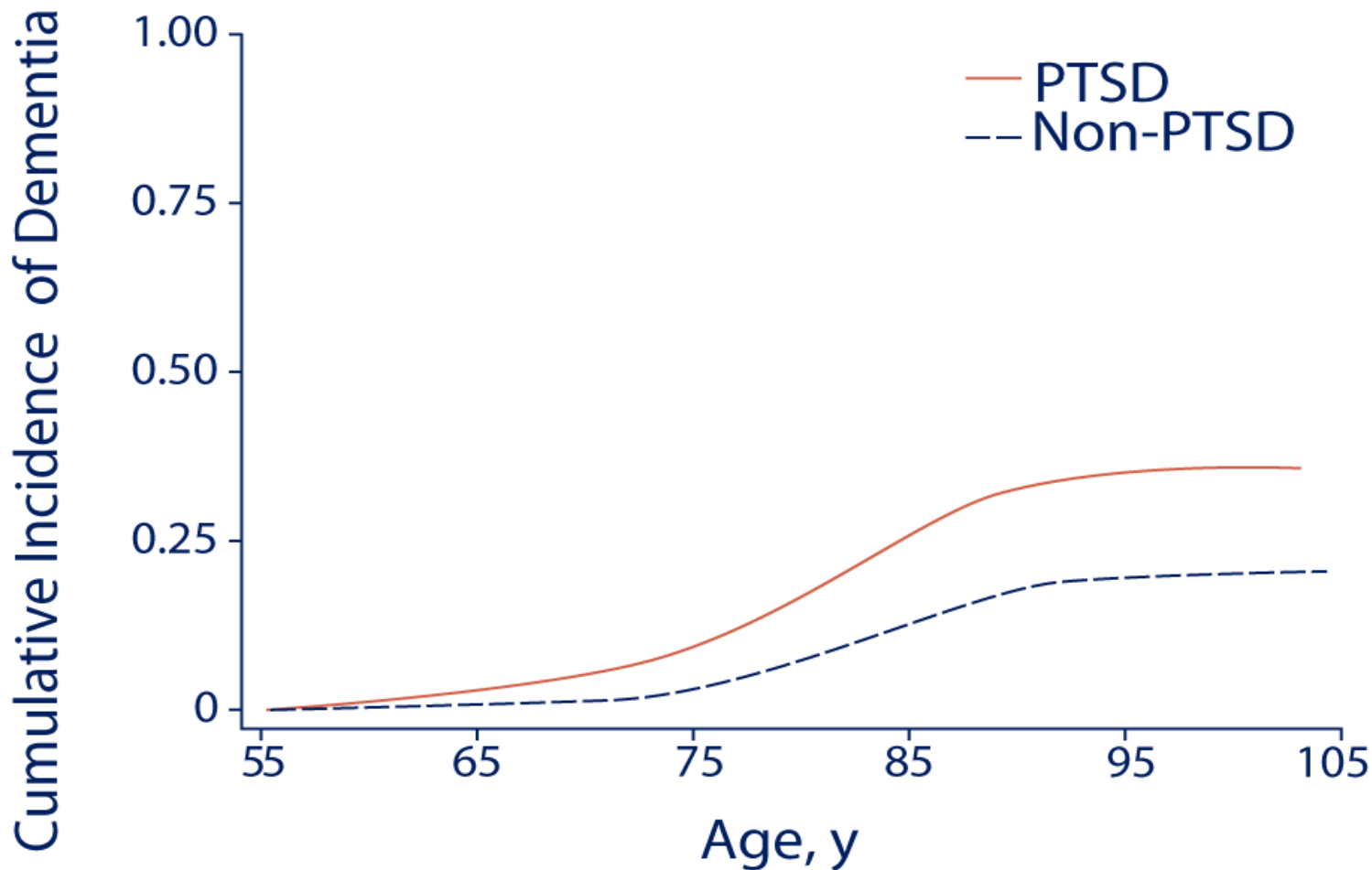
* Adjusted for socio-demographics, health behaviors, co-morbidities, and use of anti-depressants

Depression Increases Risk of Dementia Among Older Veterans



Depression aHR: 2.18, 95% CI: 2.08-2.28

PTSD Increases Risk of Dementia Among Older Veterans



PTSD aHR: 1.77 95% CI 1.70-1.85

PTSD & Prevalence/Incidence of Dementia

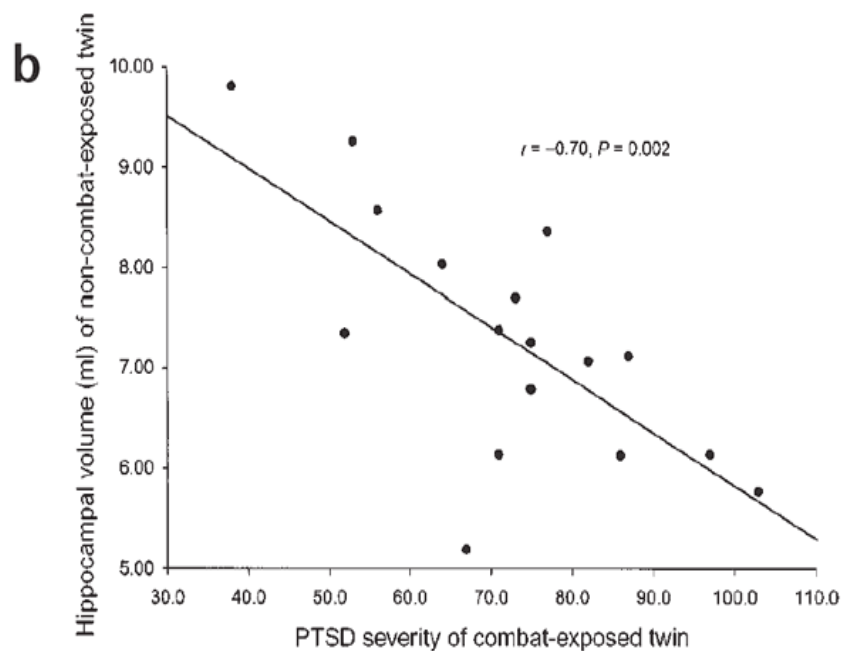
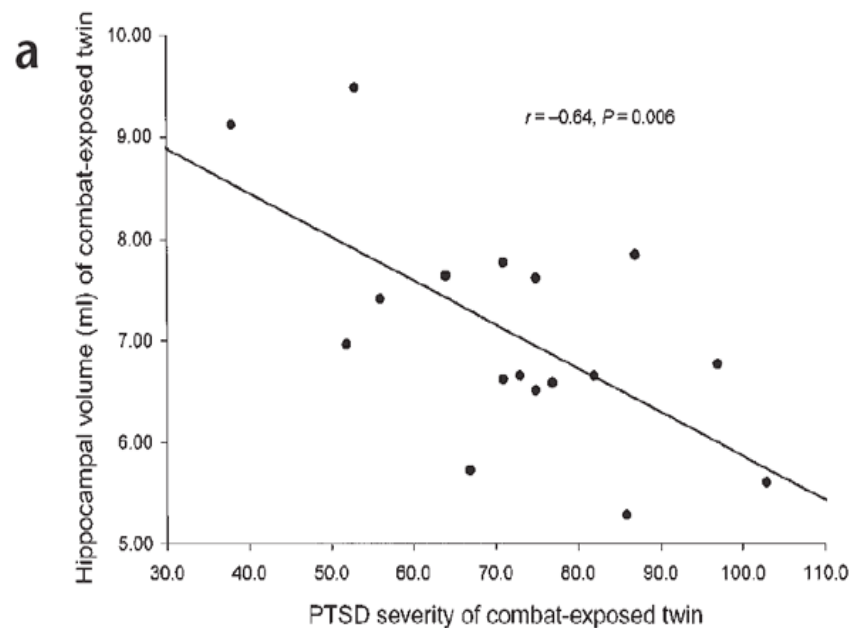
Veterans ≥ 65 years old from VISN 16

Comparisons	Dementia Prevalence OR* (95% CI)	Dementia Incidence OR* (95% CI)
PTSD+/PH- vs PTSD-/PH-	2.3 (2.0–2.7)	2.2 (1.8–2.6)
PTSD+/PH- vs PTSD-/PH+	2.0 (1.6–2.5)	1.7 (1.4–2.2)

PTSD in older veterans associated with dementia prevalence and incidence compared to those without PTSD and compared to those with combat related trauma

PTSD Symptoms and Hippocampal Volume in Vietnam Twin Pairs Discordant for Warzone Service

- Hippocampal volume in non-exposed twin predicts PTSD symptom severity
- Suggests hippocampal volume loss is a pre-existing vulnerability trait



National Academies Gulf War and Health : Updates Related to Cognitive Aging

- Gulf war illness shares many similar symptoms to PTSD and depression and affects multiple systems
- Need to investigate link between body and brain
- Limited data on risk of neurologic outcomes
- Too early for manifestation of neurodegenerative diseases in Gulf War veterans so more follow up needed

Summary

- Evidence for TBI, PTSD, and other military exposures as risk factors for dementia is increasing
- In addition, veterans are at risk for accelerated cognitive aging because they have a greater burden of medical and psychiatric risk factors
- Need continued investigation of modifiable risk factors in veterans to understand the interplay of these associations
- Explore specific exposures of Gulf War veterans
- Develop a multi-domain framework for research, prevention, and intervention for cognitive aging in veterans

Acknowledgements

Funders

- NIA
- NIDDK
- NHLBI
- Department of Defense
- Veterans Administration
- Sierra-Pacific Mental Illness Research, Education, and Clinical Center

Collaborators

- Deborah Barnes
- Amy Byers
- Raquel Gardner
- Allison Kaup
- Joel Kramer
- Carrie Peltz
- Karen Seal

USUHS

- Ramon Diaz Arrastia
- Kimbra Kenney

Chronic Effects of Neurotrauma Consortium (CENC)

- David Cifu
- Mary Jo Pugh