Phenotypes of Comorbidity in Mild TBI: Development, Meaning and Utility for Use in Clinical Practice

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Disclaimer

I have no disclosures

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Our Journey Today

- What is a comorbidity trajectory and why study these trajectories?
- Trajectories of comorbidity in Post-9/11 Veterans with a history of TBI.
- Can comorbidity trajectories help predict outcomes?
- Is there clinical utility in these trajectories?
- What is our path forward?

Signature Injuries of War

Post-9/11 Conflicts

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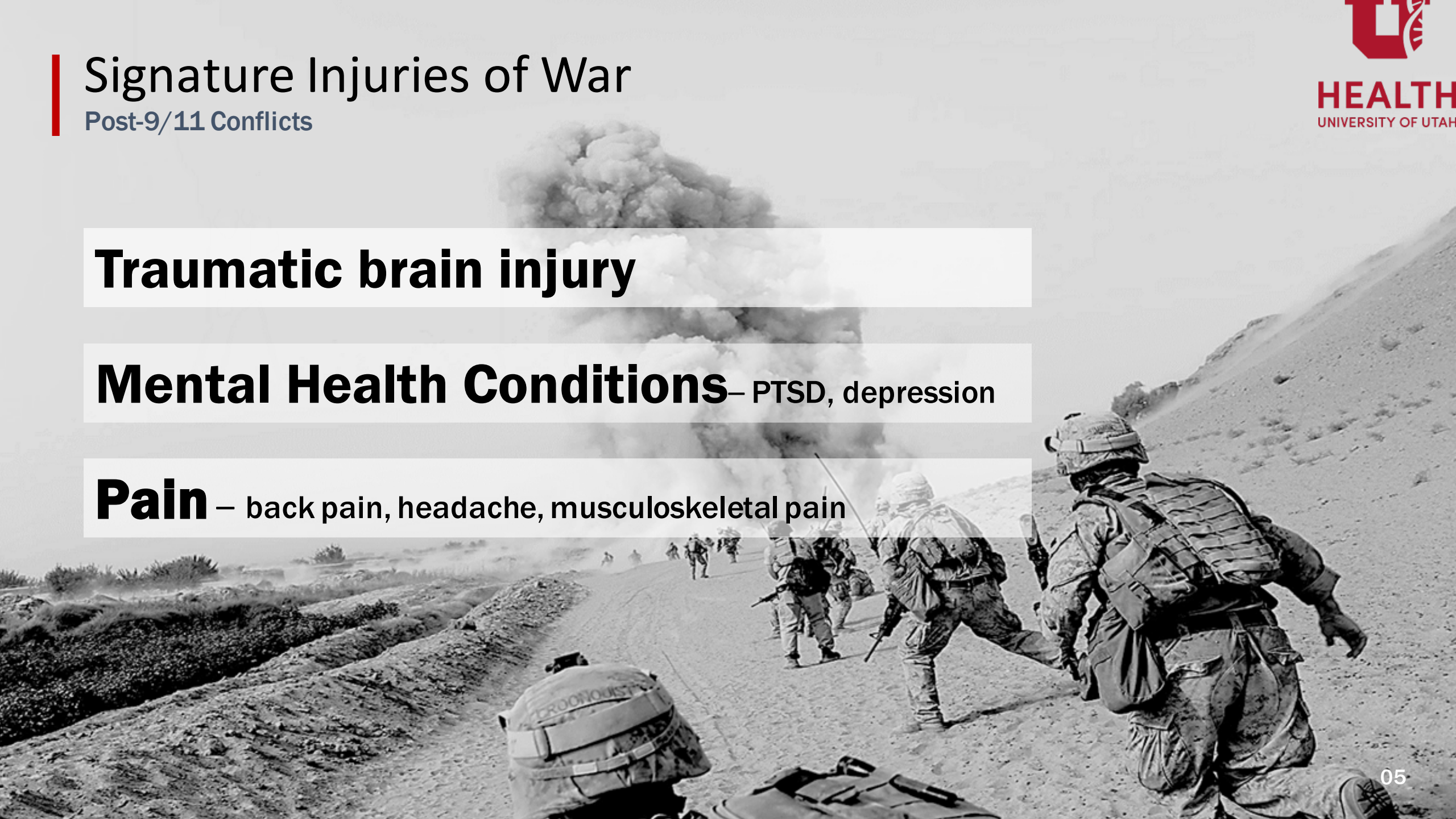
Traumatic brain injury

Mental Health Conditions– PTSD, depression

Pain – back pain, headache, musculoskeletal pain

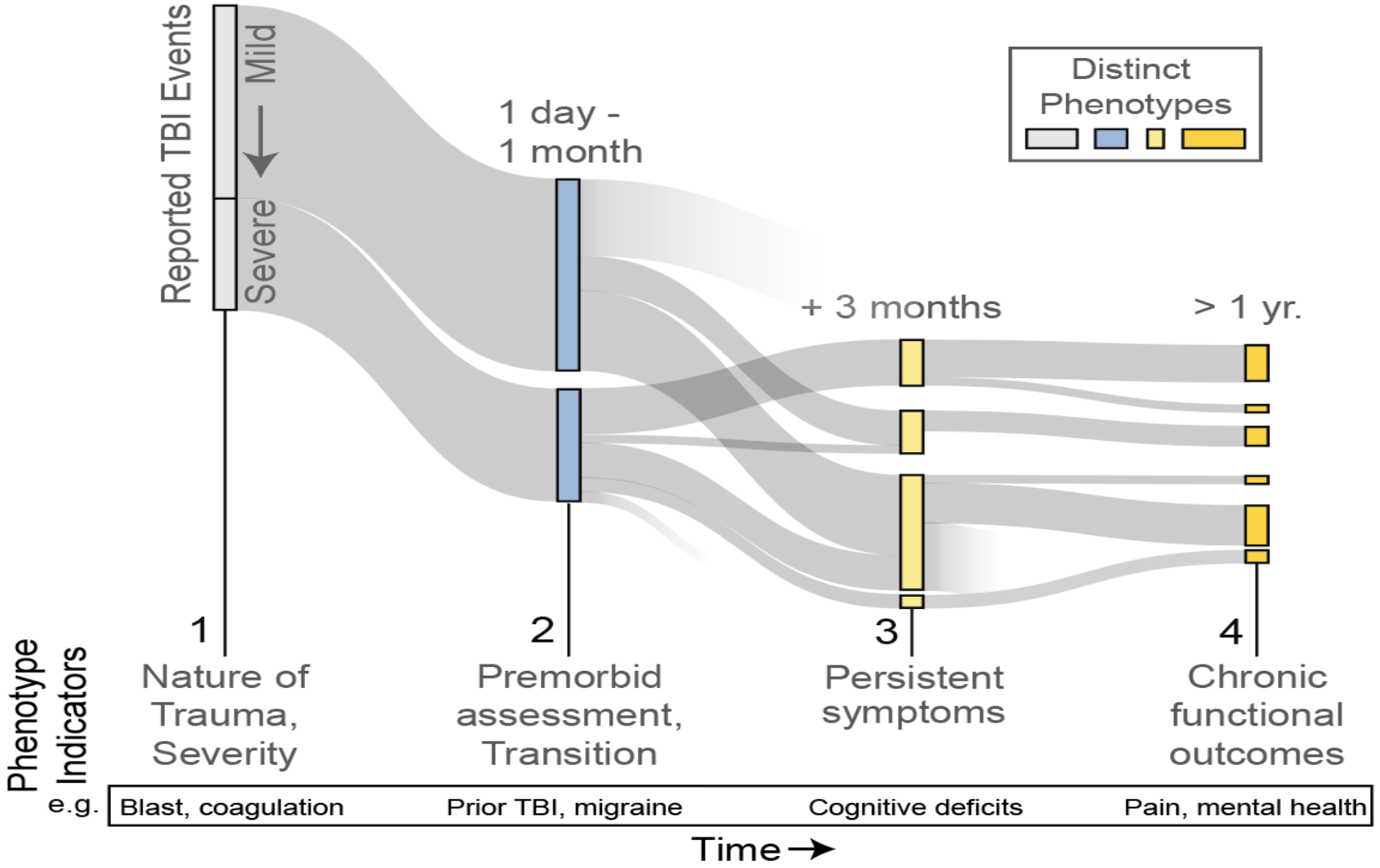


Why Trajectories of Recovery?

TBI is not just an event

TBI is a Chronic Disease…

Trajectories of Recovery in TBI



Objective

- Use longitudinal VA Health System data to examine patterns of comorbidity (comorbidity phenotypes) in Post-9/11 Veterans stratified by TBI severity during the first five years of VA care.

- Identify adverse outcomes associated with specific comorbidity phenotypes

Trajectory Analysis: Trajectories of Comorbidity

RESEARCH ARTICLE

Deployment, suicide, and overdose among comorbidity phenotypes following mild traumatic brain injury: A retrospective cohort study from the Chronic Effects of Neurotrauma Consortium

Mary Jo Pugh[1,2]*, Alicia A. Swan[3], Megan E. Amuan[1], Blessen C. Eapen[4,5], Carlos A. Jaramillo[6], Roxana Delgado[6], David F. Tate[7], Kristine Yaffe[8], Chen-Pin Wang[9]

PLOS ONE | https://doi.org/10.1371/journal.pone.0222674 September 20, 2019

Methods

- Retrospective Cohort Study
  - Cohort identified in VA data
  - Common post-concussion/post-deployment related symptoms/comorbidities identified each year for the first five years of VA care
- Latent class trajectory analysis of comorbidities over time stratified by TBI severity

Data

OEF/OIF Roster

DoD Trauma Registry

VA Inpatient

VA Outpatient

VA Pharmacy

VA Comprehensive TBI Evaluation

DoD health system data for context

CENC Warrior Epidemiology Cohort

FY
’02
‘03
‘04
’05
’06
‘07
’08
‘09
’10
’11
‘12
’13
’14

Entered VA Care FY02-11 + 3 or more years of care prior to FY14

+ Received at least one year of VA care in 2007 or thereafter

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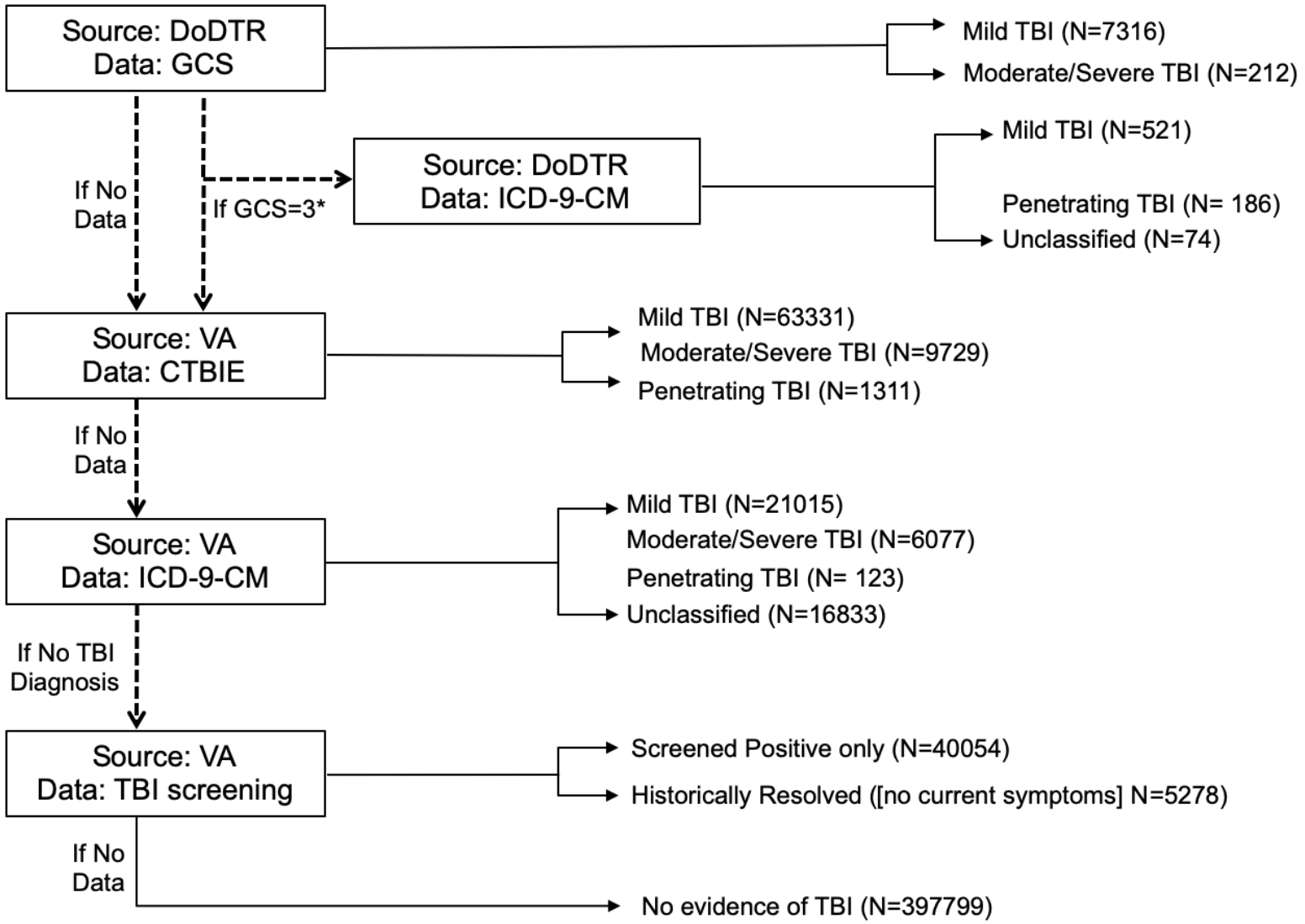
“All Sources” TBI Severity Algorithm



Measures

Comorbidity Conditions

Identified Using ICD-9 codes

Mental Health
PTSD, Substance Use Disorder (SUD), depression, anxiety

Possible TBI Sequelae
Tinnitus, hearing loss, vestibular, blurry vision, blind, cognitive, pituitary, seizure, cerebrovascular

Pain
Headache, neck pain, back pain, other pain

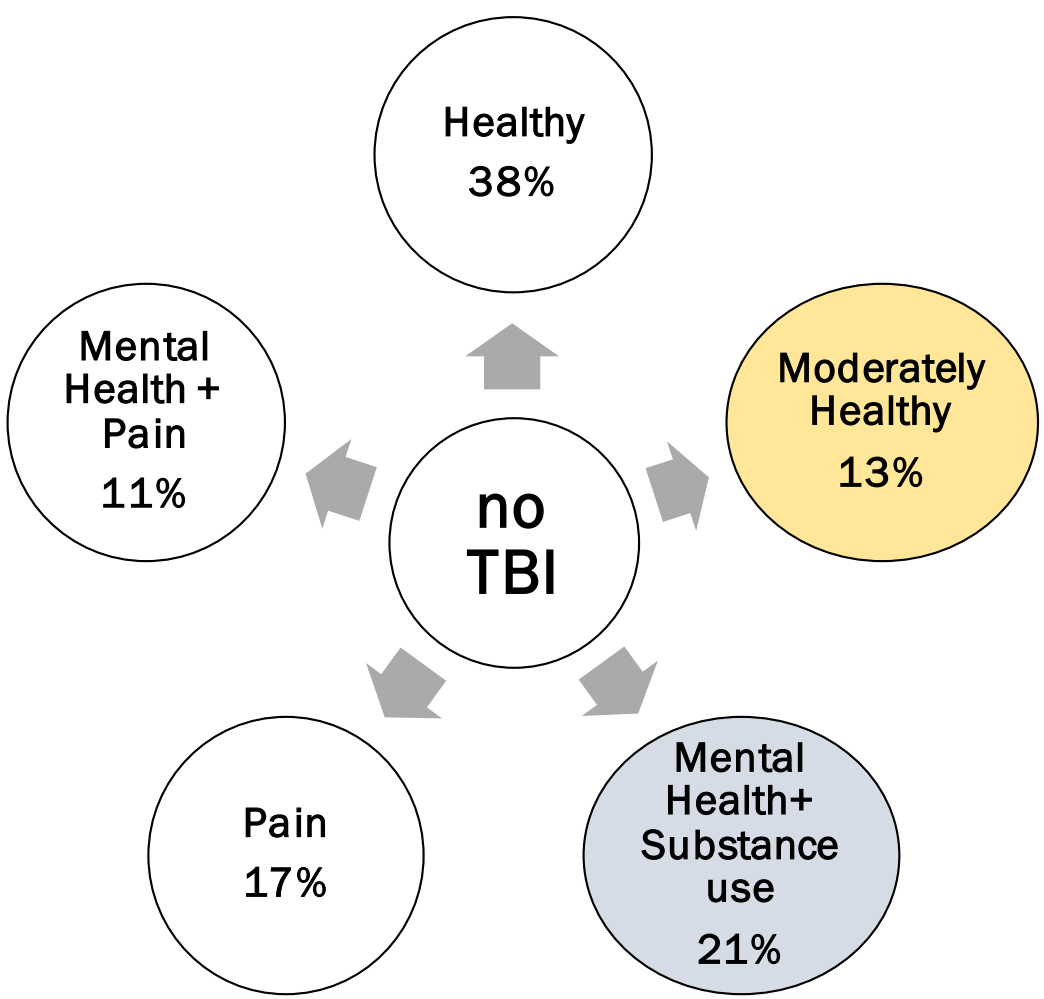
Weight & Sleep
Obesity, obstructive sleep apnea (OSA), insomnia, hypersomnia

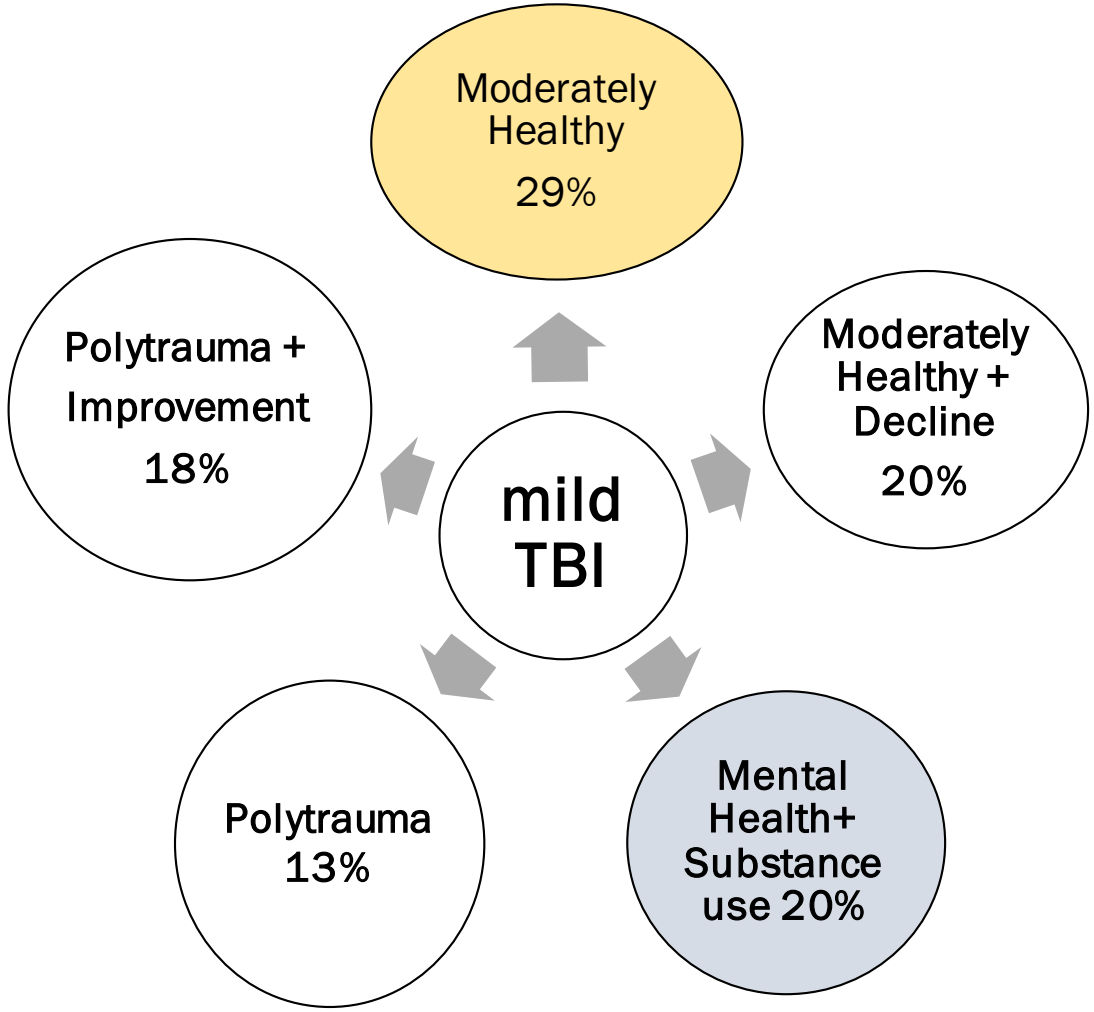
Latent Class [Trajectory] Analysis

Analysis

- Latent Class Trajectory Analysis
  - Conditions identified each year as diagnosed or not diagnosed
  - Analysis stratified by TBI severity to determine if there were similar or different comorbidity trajectories across TBI severity strata.
  - The class/trajectory analysis identified groups with similar patterns of comorbidity over time in each TBI strata

Comorbidity Phenotypes

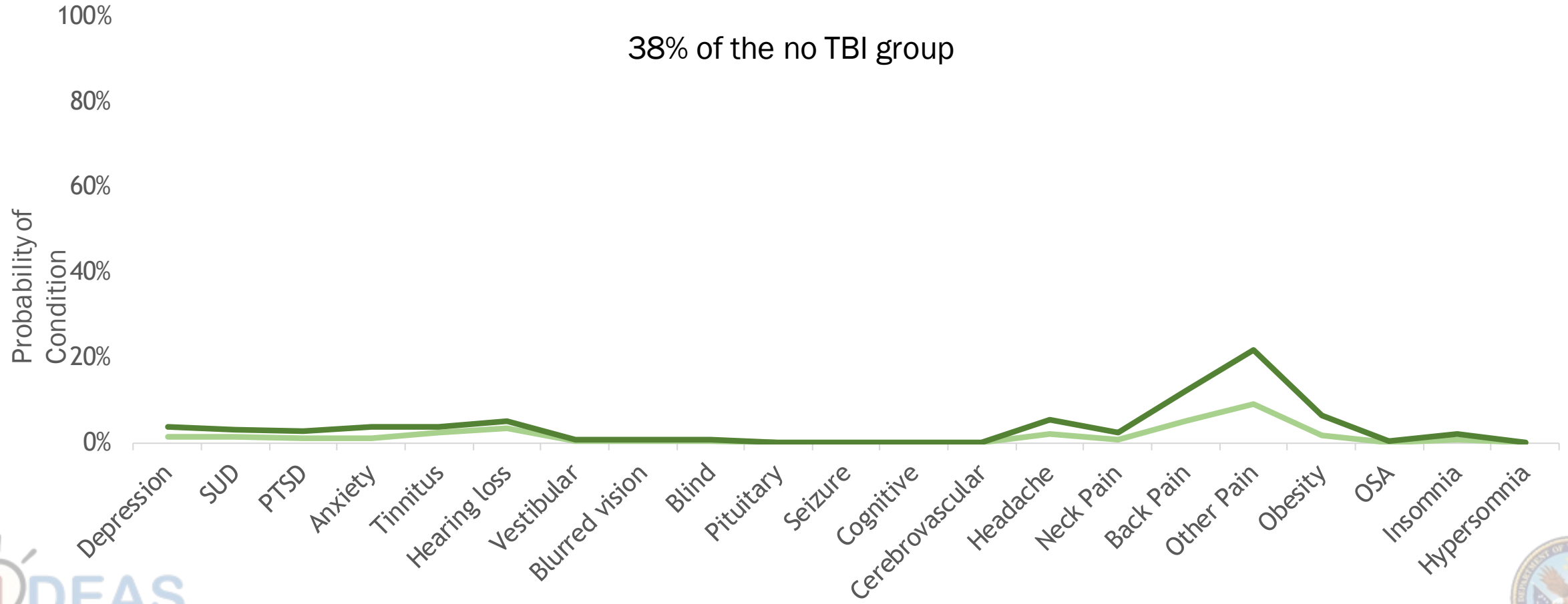




Healthy

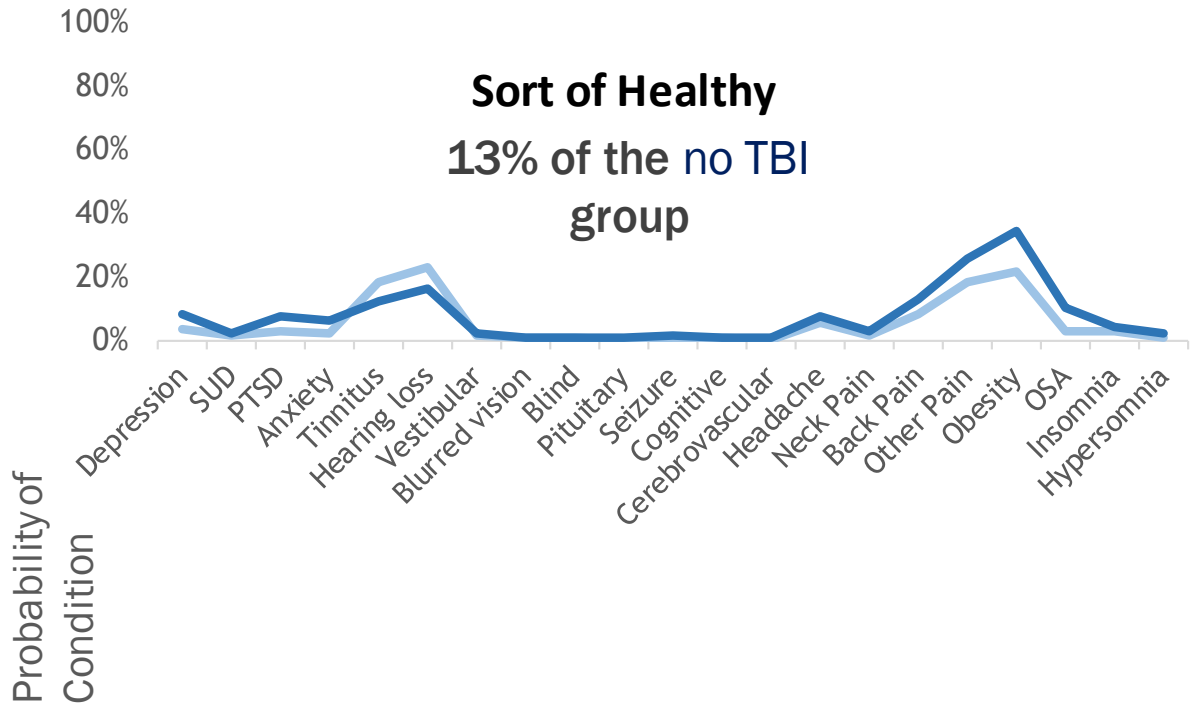
Year 1 v. Year 5

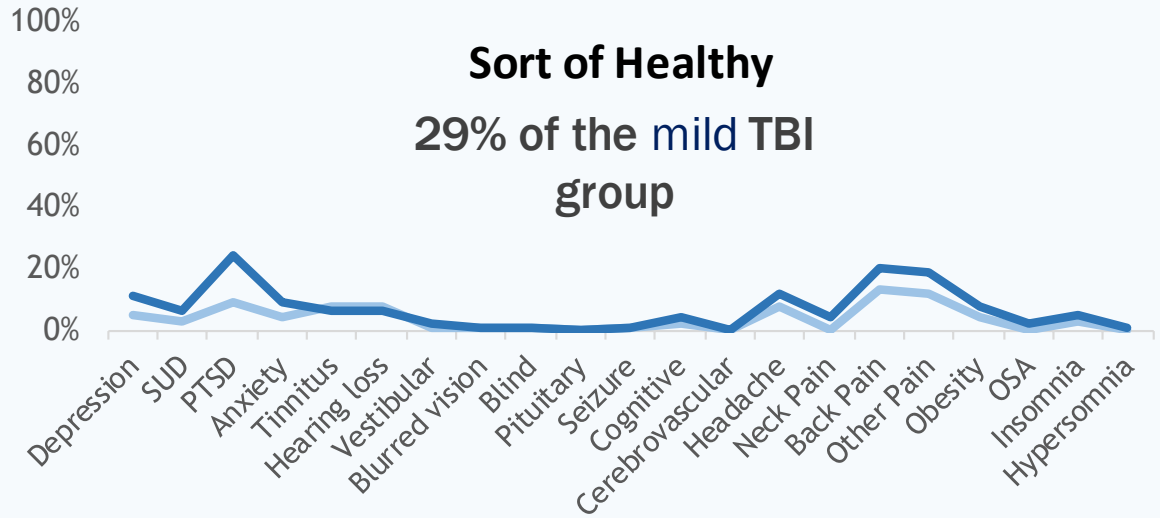
38% of the no TBI group

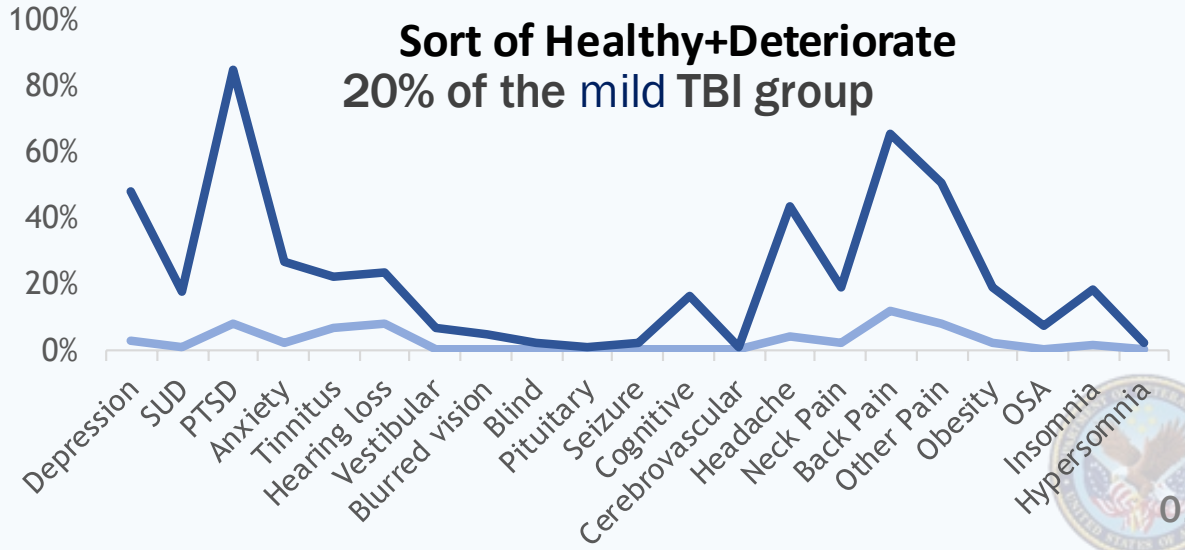


“Sort of Healthy”Phenotypes

Year 1 v. Year 5







Mental Health+Substance Use Disorder

Year 1 v. Year 5

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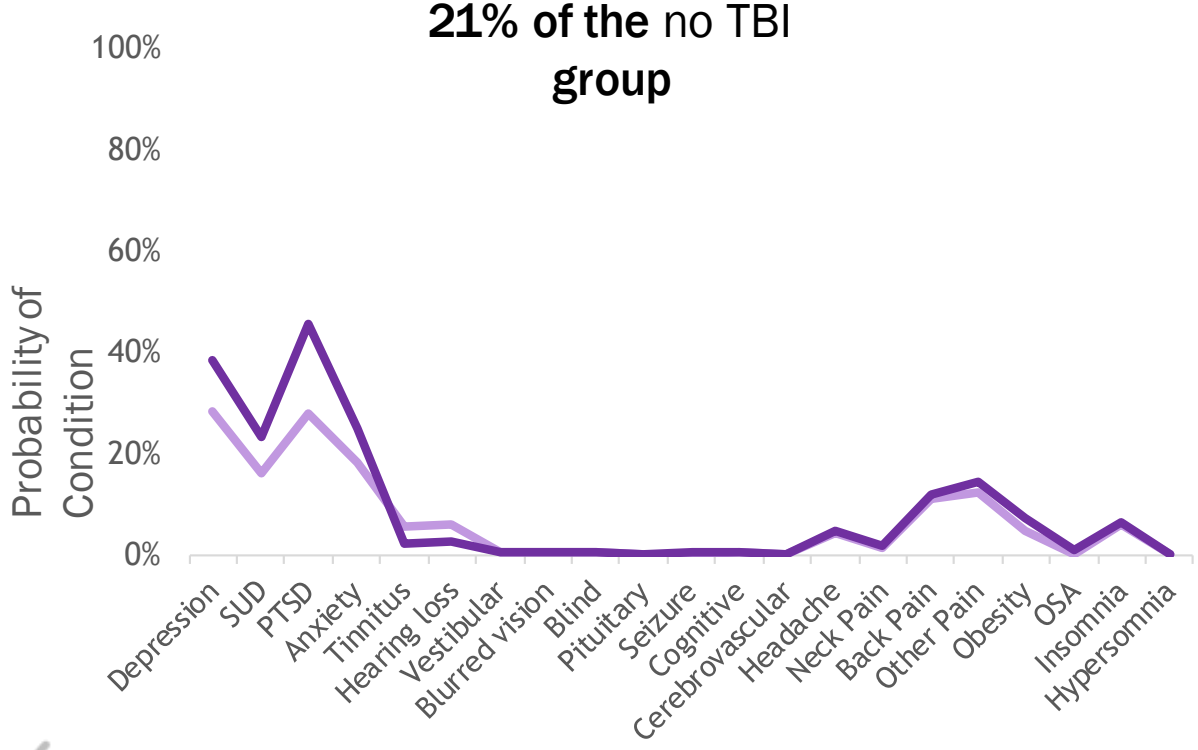
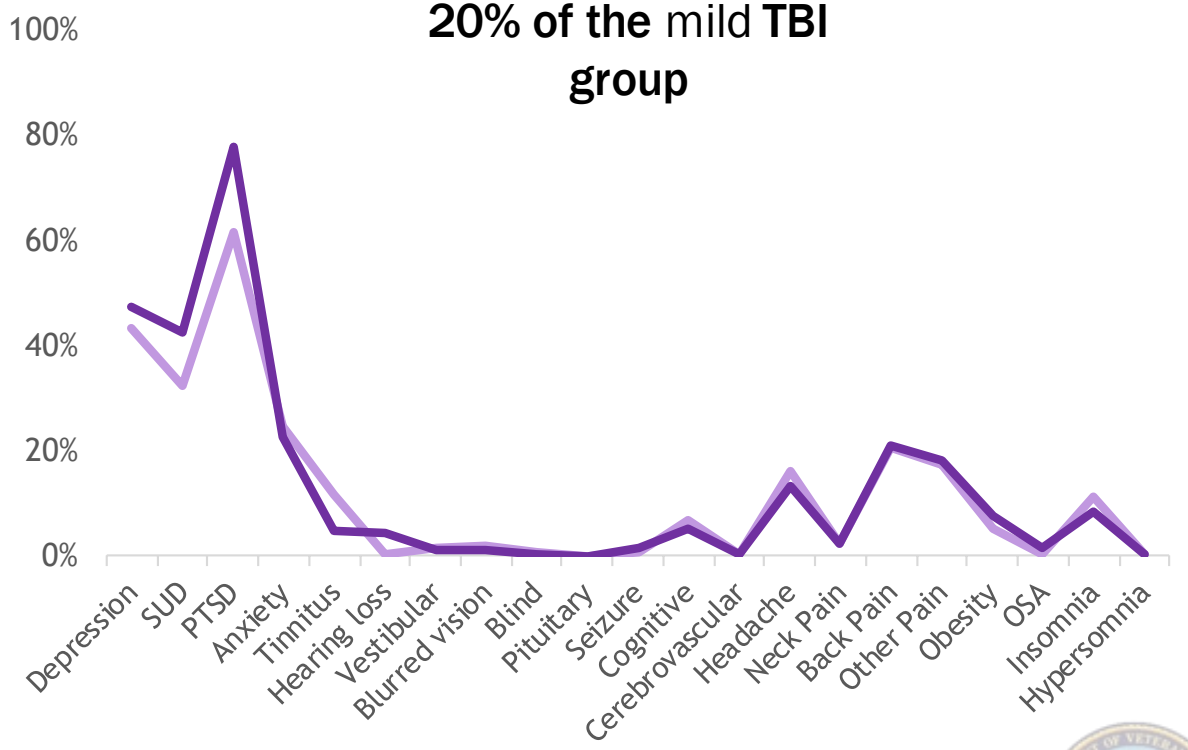
21% of the no TBI **group**



20% of the mild **TBI group**



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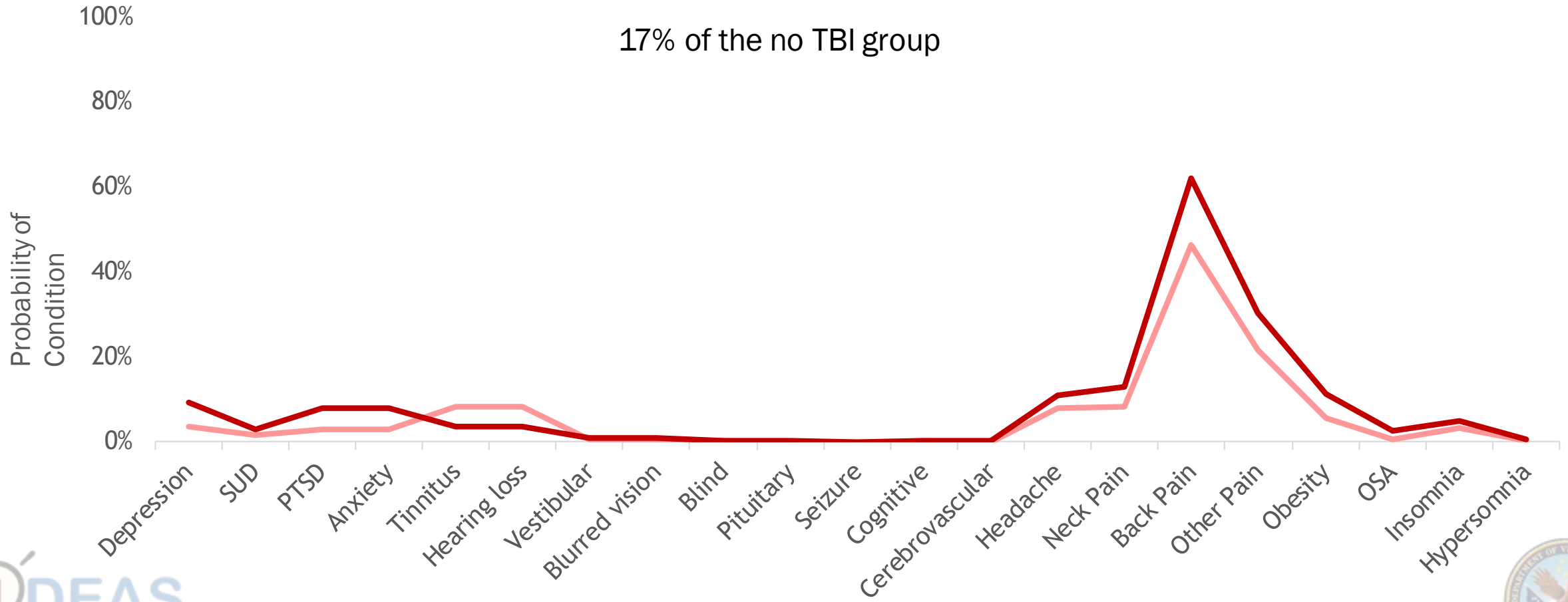
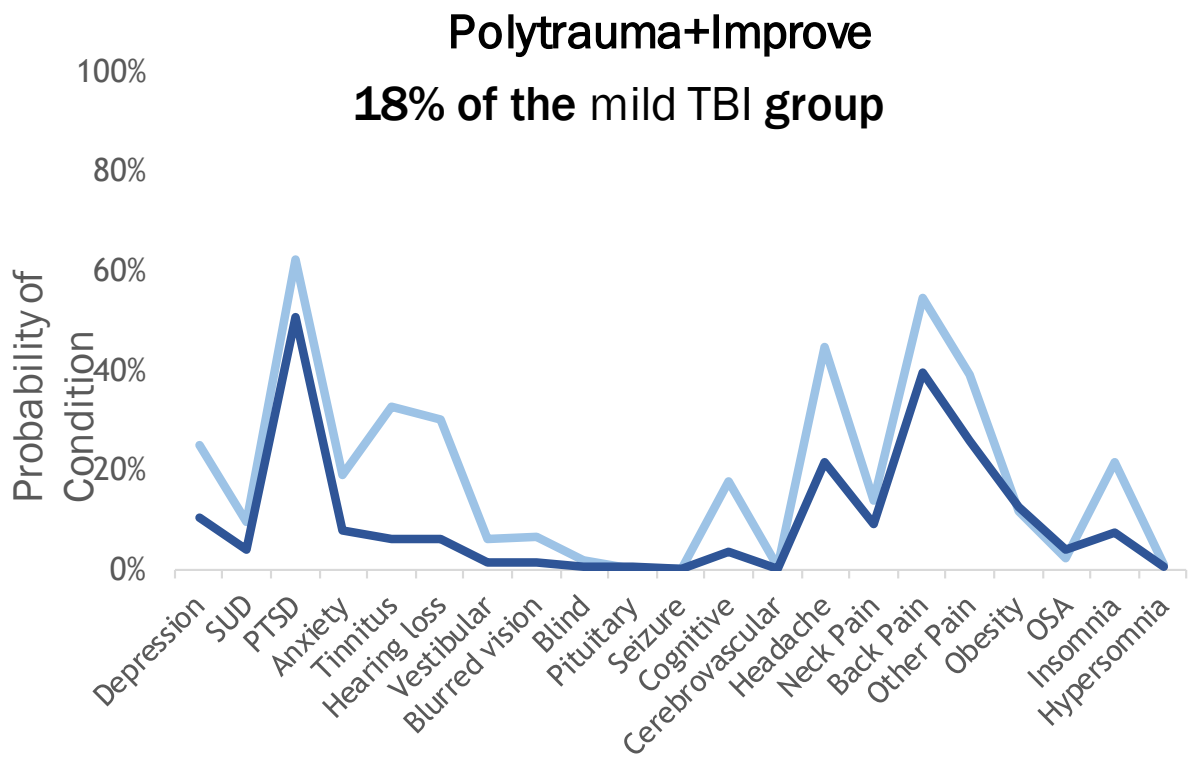
Pain

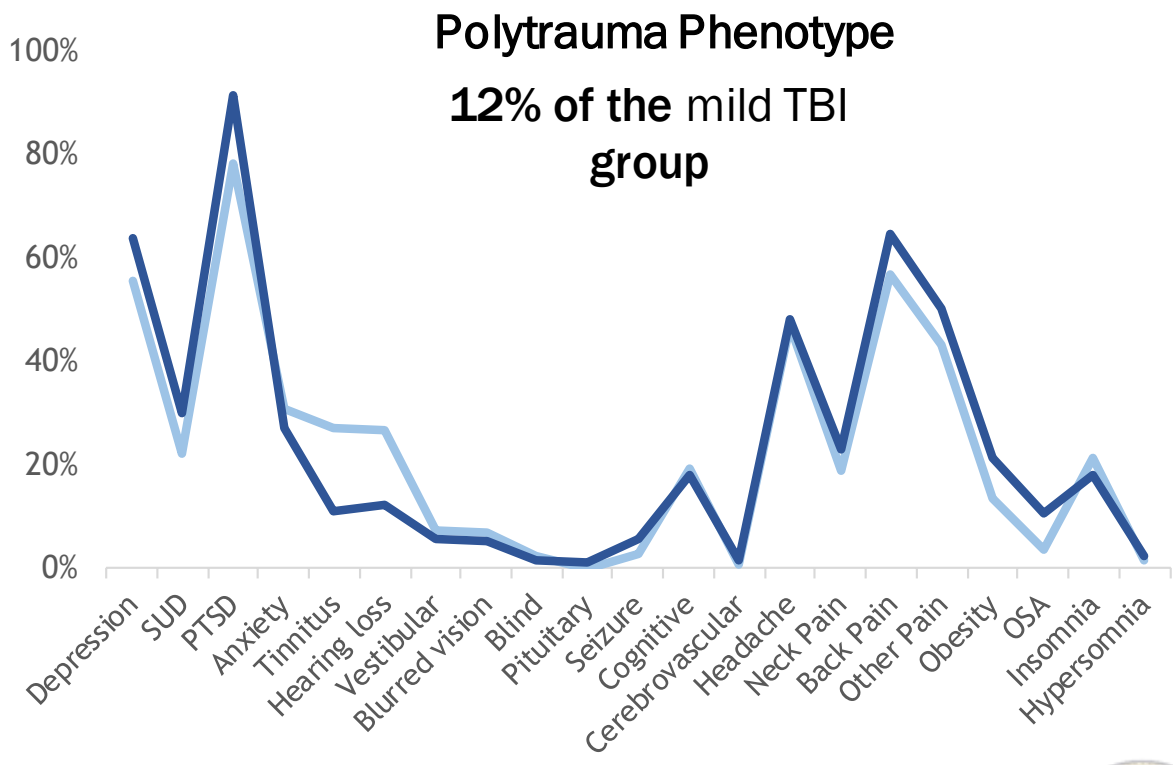
Year 1 v. Year 5



Polytrauma Phenotypes

Year 1 v. Year 5





Differences in DoD Characteristics Among Key Comorbidity Phenotypes

Moderately Healthy + Deteriorate
vs.
Sort of Healthy

Deterioration phenotype

- **Less likely to have**
  - Guard/Reserve service
  - Multiple deployments
- **More likely to have**
  - DoD TBI diagnosis
  - DoD Mental Health diagnosis
  - 5 or more CNS active medications/year

Polytrauma vs.
Polytrauma+Improvement

Improvement phenotype

Less likely to have

- DoD TBI diagnosis
- DoD Mental Health diagnosis
- 5 or more CNS active medications/year

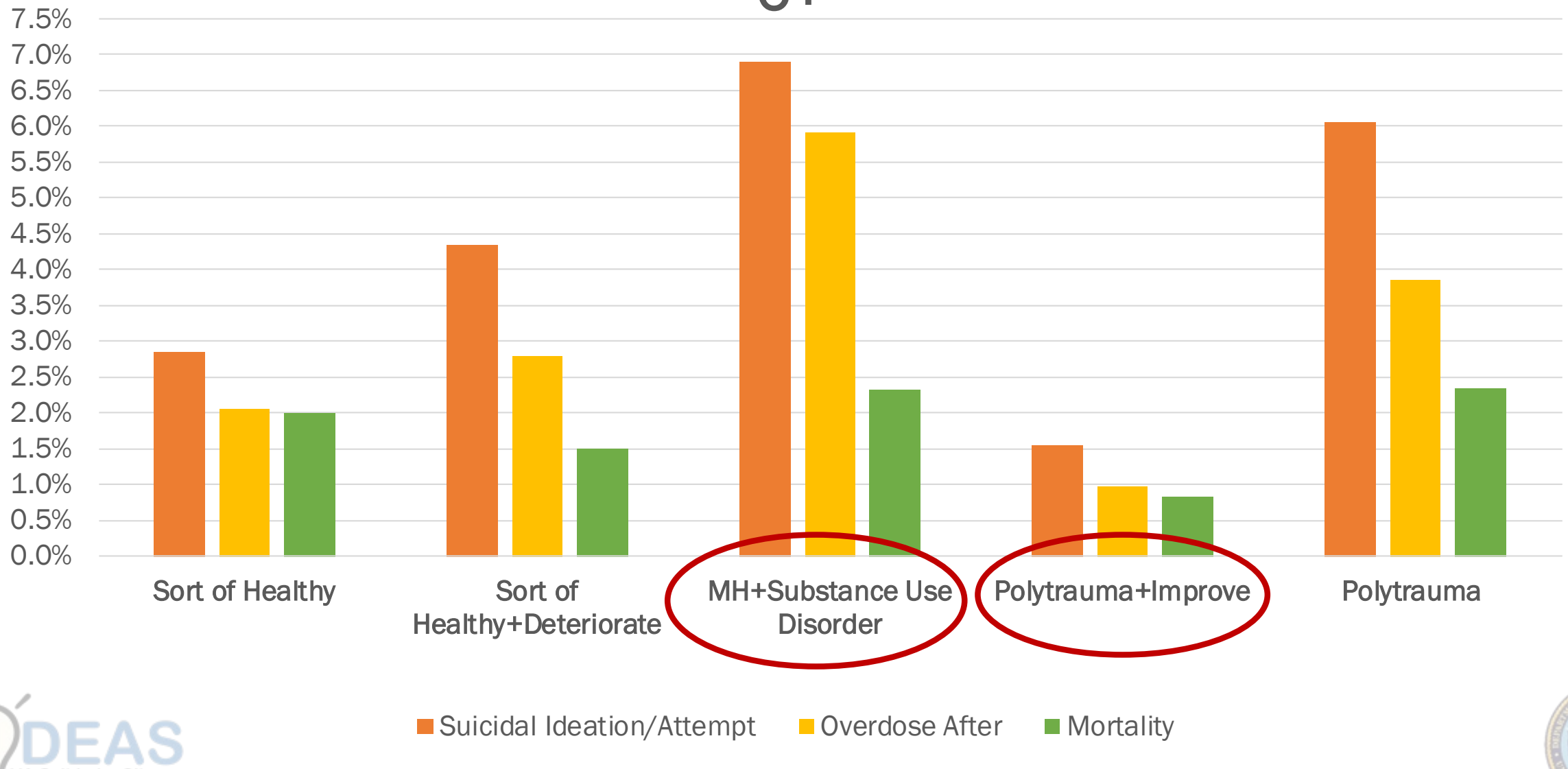
- **More likely to have**
  - Multiple deployments


SO WHAT?

Identified Adverse Outcomes

- Suicidal Ideation
- Suicide Attempt
- Homelessness
- Mortality

Adverse Outcomes Among mTBI Phenotypes Year 6+



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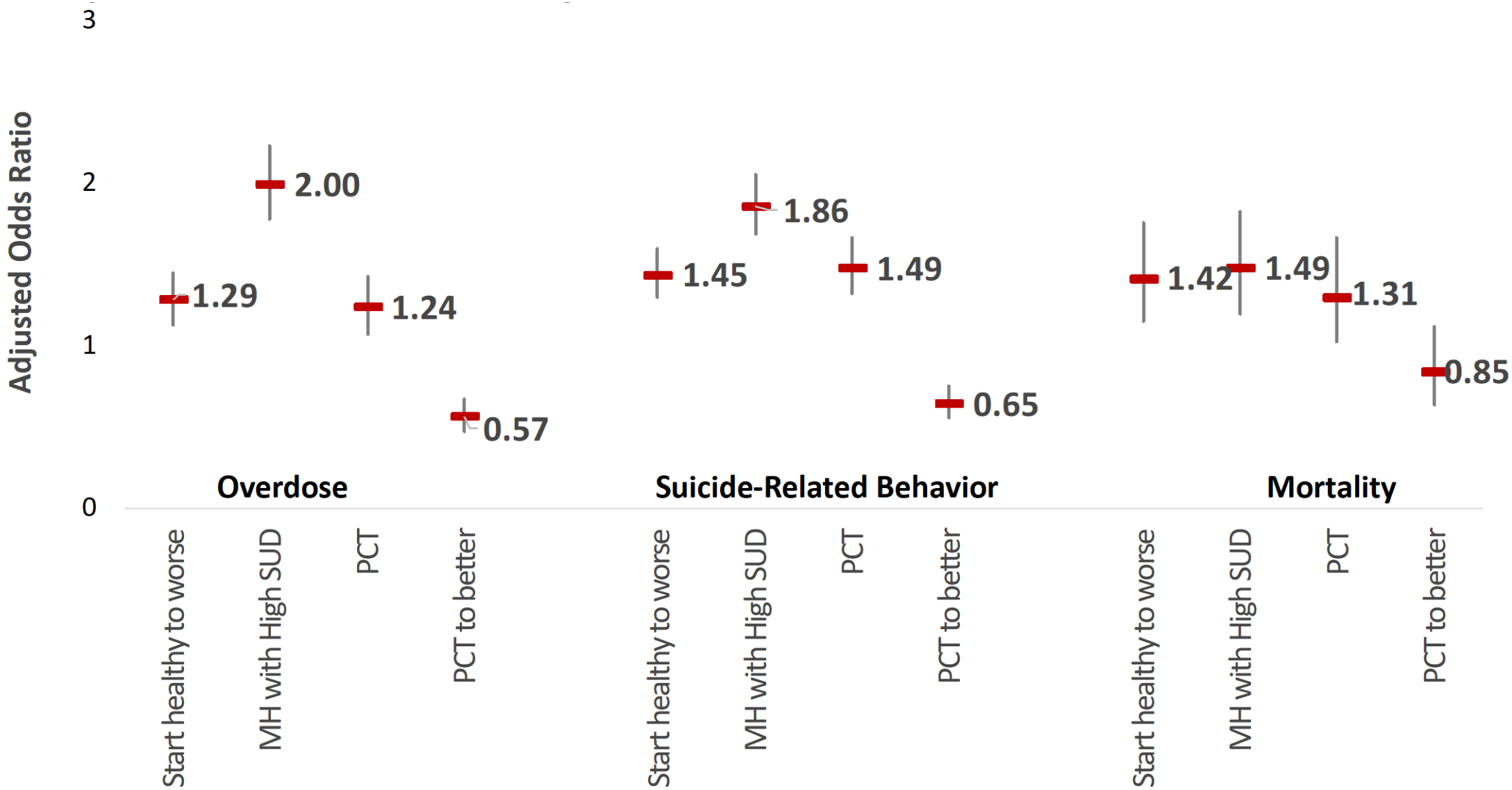
Adverse Outcomes in Mild TBI Phenotypes
Comparator: Moderately Healthy



Sub Analysis With More Clinical Detail

J Head Trauma Rehabil

Health Phenotypes and Neurobehavioral Symptom Severity Among Post-9/11 Veterans With Mild Traumatic Brain Injury: A Chronic Effects of Neurotrauma Consortium Study

Erin D. Bouldin, PhD, MPH; Alicia A. Swan, PhD; Rocio S. Norman, PhD; David F. Tate, PhD; Christa Tumminello, BS; Megan E. Amuan, MPH; Blessen C. Eapen, MD; Chen-Pin Wang, PhD; Amira Trevino, BS; Mary Jo Pugh, PhD, RN

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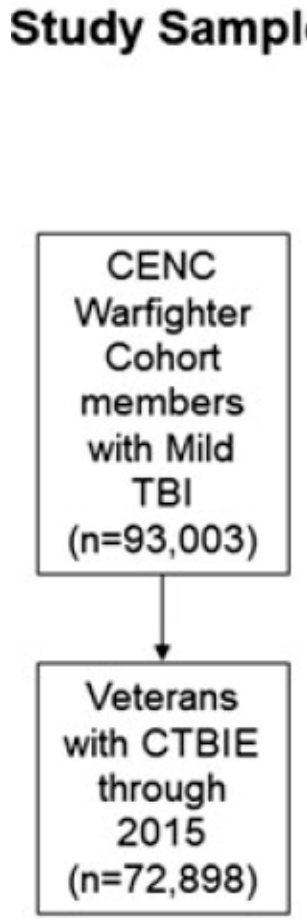
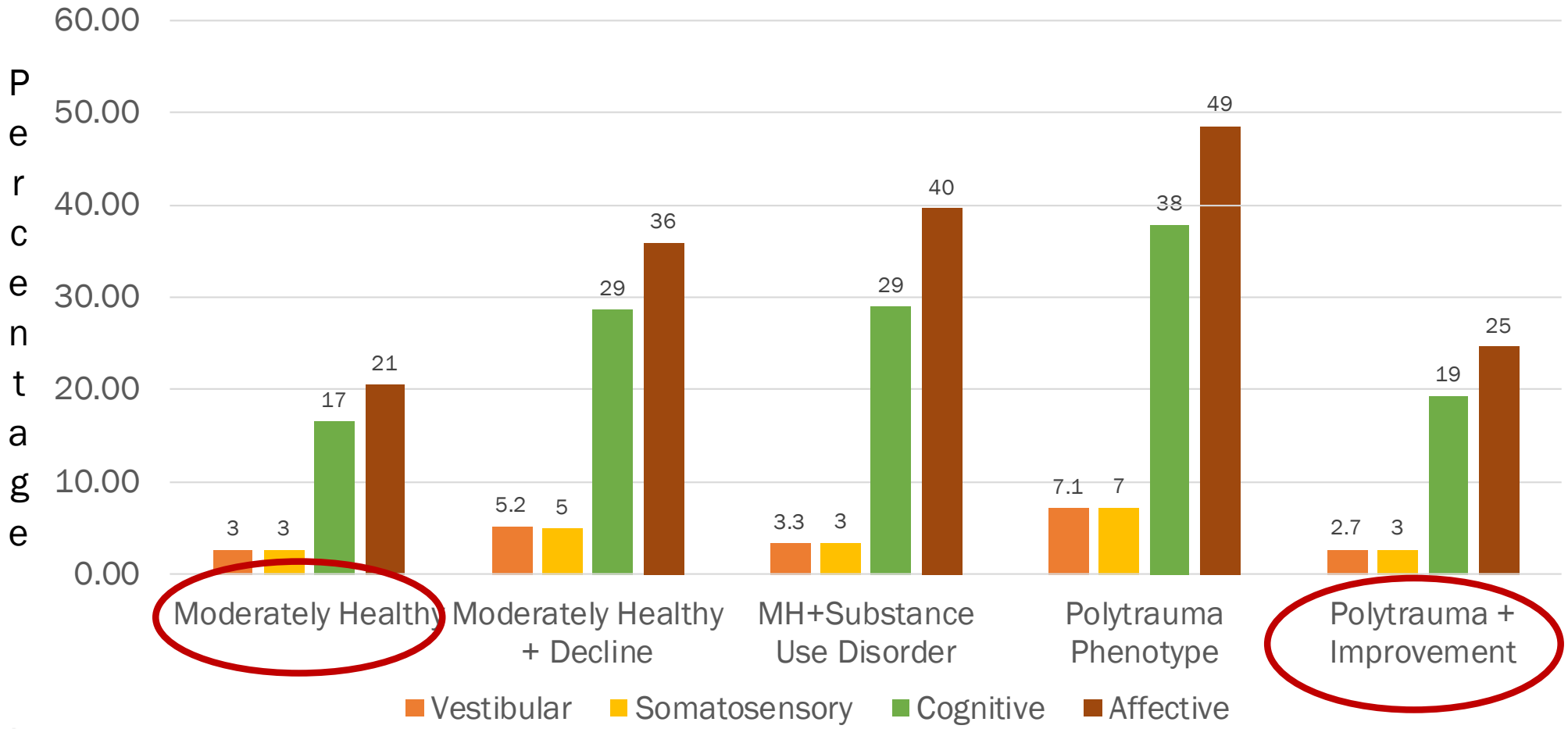
Examination of Neurobehavioral Symptoms



- Neurobehavioral Symptom Inventory 22: 22 Items
- 4 subscales
  - Affective
  - Cognitive
  - Vestibular
  - Somatic/Sensory
- 1 item: Interference
- Severity of each symptom rated 0 (none) to 4 (very severe) during TBI evaluation.
- High Burden: Mean of ≥ 3

High Neurobehavioral Symptom Burden by mTBI Phenotypes



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Adjusted Odds of High Burden NSI Scales

TABLE 3 *Logistic regression results estimating the association between Neurobehavioral Symptom Inventory subscale scores and group membership*[a]

	Severe or very severe symptoms (Average scaled NSI score ≥3.0)				
	Vestibular	Somatosensory	Cognitive	Affective	Interference
Comorbidity phenotype	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
Moderately healthy	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Moderately healthy + decline	**2.1**[b] **(1.8-2.4)**	**2.0**[b] **(1.8-2.3)**	**2.0**[b] **(1.9-2.1)**	**2.2**[b] **(2.0-2.3)**	*1.9*[b] *(1.8-2.0)*
Polytrauma + improvement	1.2 (1.0-1.4)	1.2 (1.1-1.4)	1.2[b] (1.2-1.3)	1.3[b] (1.2-1.4)	1.3[b] (1.3-1.4)
Polytrauma phenotype	***2.9***[b] ***(2.6-3.3)***	***2.9***[b] ***(2.6-3.3)***	***3.0***[b] ***(2.9-3.2)***	***3.6***[b] ***(3.4-3.8)***	***2.8***[b] ***(2.7-3.0)***
Mental health	*1.5*[b] *(1.3-1.7)*	*1.5*[b] *(1.4-1.8)*	**2.1**[b] **(2.0-2.3)**	***2.6***[b] ***(2.5-2.8)***	**2.1**[b] **(2.0-2.2)**

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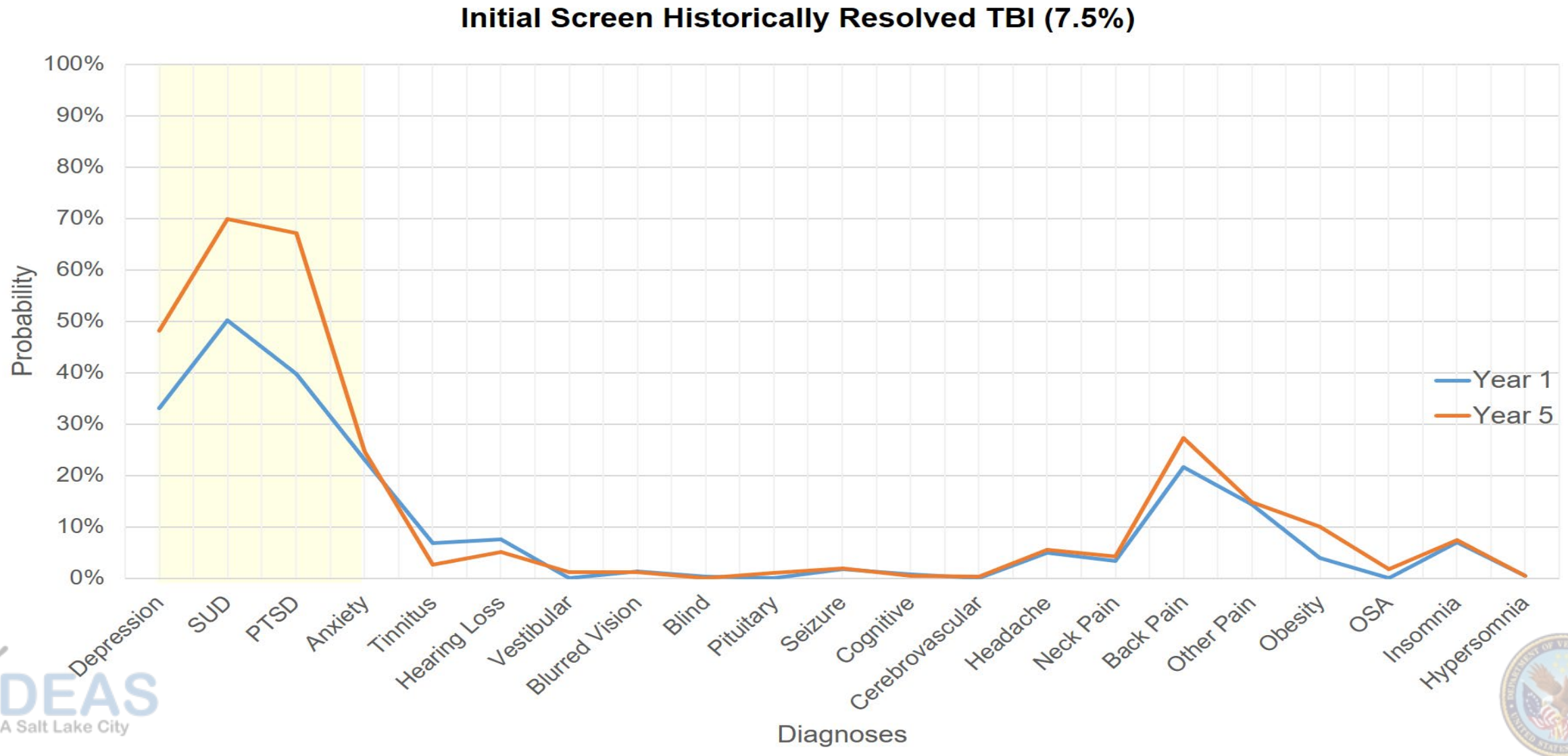
Are these Trajectories Similar Across TBI Severity Strata?

Some but not all

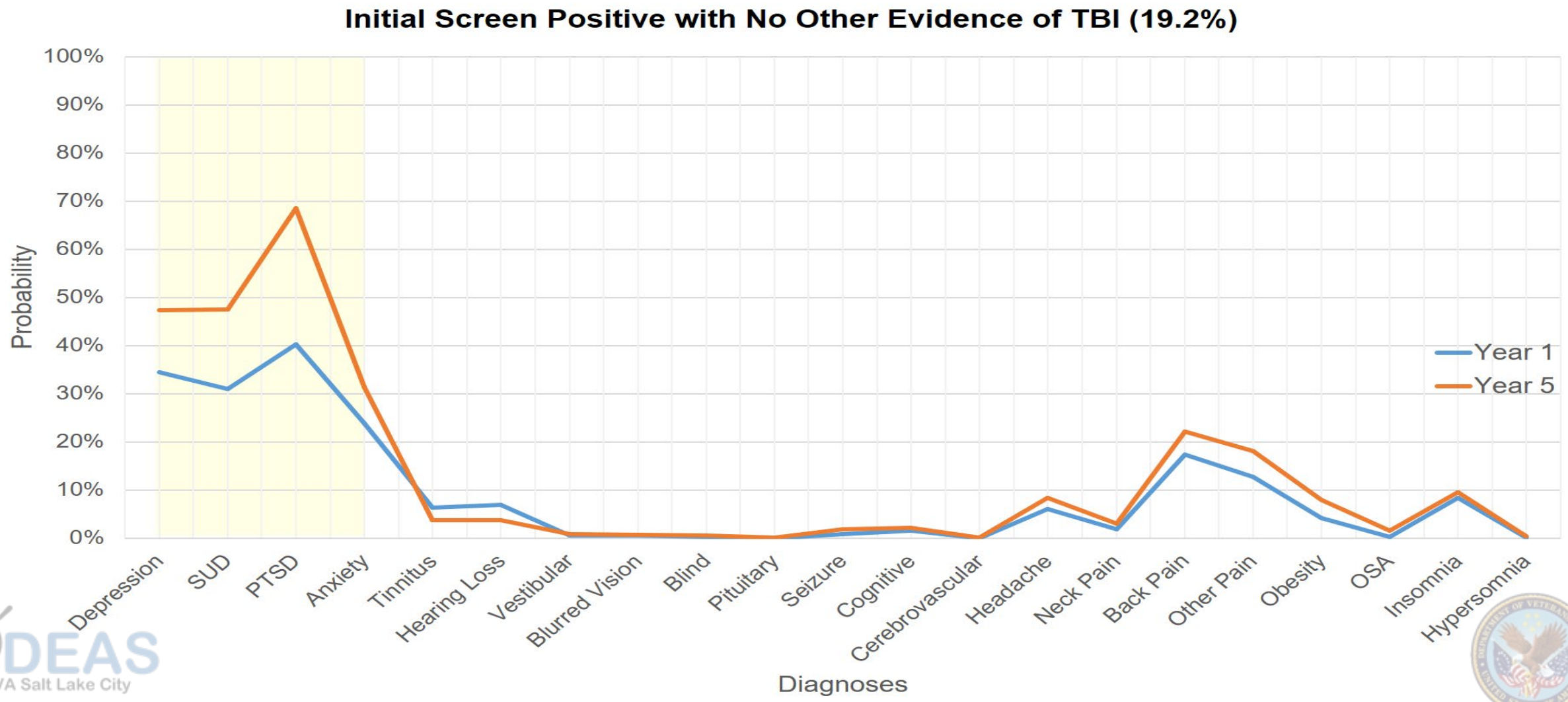
5 Comorbidity Trajectories by TBI Strata

Penetrating (n=1,632)	Mod/Severe (n=16,751)	Mild (92,183)	Unclassified (n=17,410)	Screen Positive (n=40,062)	Historical Resolved (n=5,280)
Moderately Healthy	**Moderately Healthy**	**Moderately Healthy**	**Moderately Healthy**	**Moderately Healthy**	**Moderately Healthy**
Mod Healthy+Decline		Mod Healthy+Decline	Mod Healthy+Decline		
High SUD	**High SUD**	**High SUD**	**High SUD**	**High SUD**	**High SUD**
Polytrauma	Polytrauma	Polytrauma	Polytrauma	Polytrauma	
	Polytrauma + improve	Polytrauma + improve	Polytrauma + improve		
	Insomnia + Decline				
Neurodegeneration					
				Pain	Pain
				Mental Health	Mental Health
					Pain + Mental Health

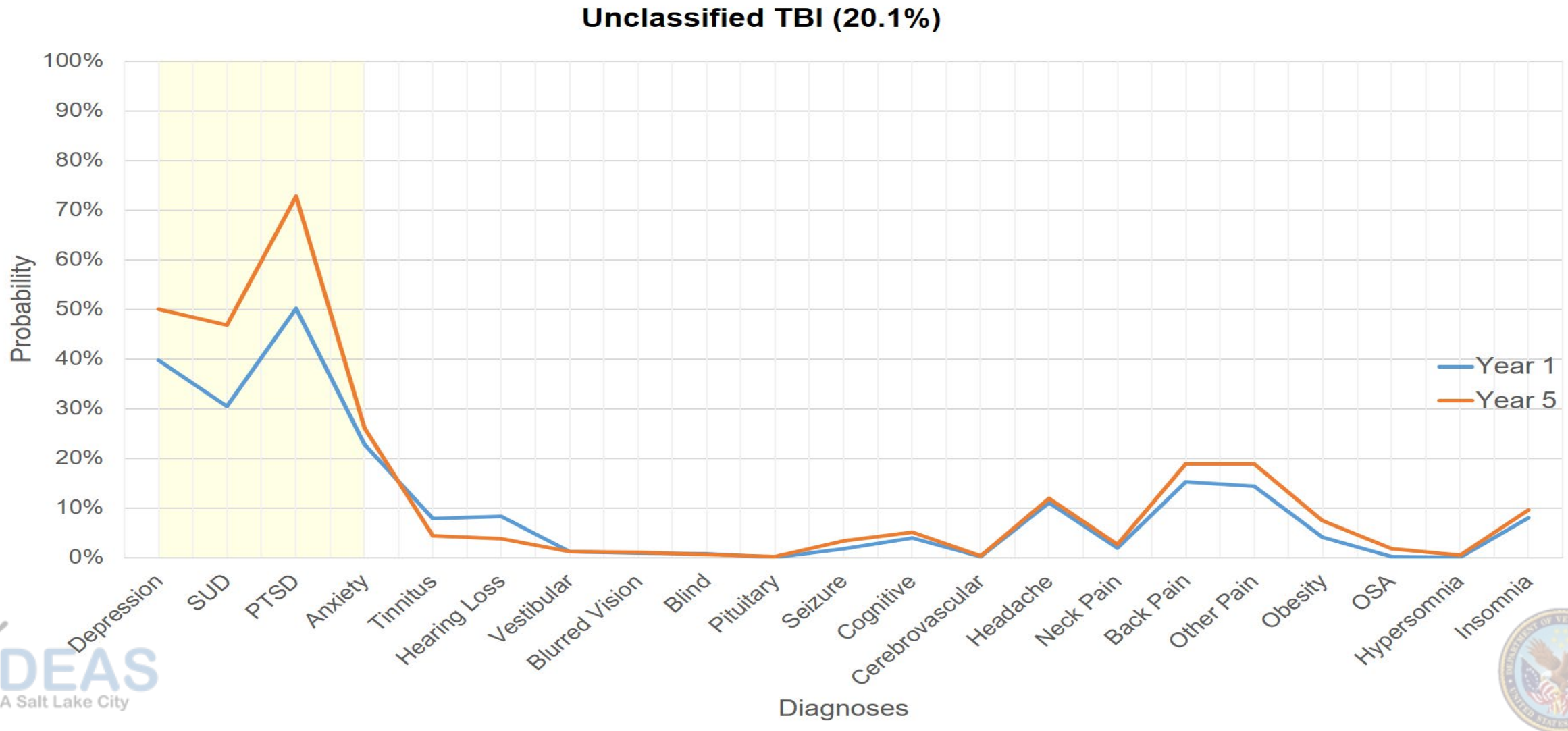
Historically Resolved mTBI (total N=5,278)



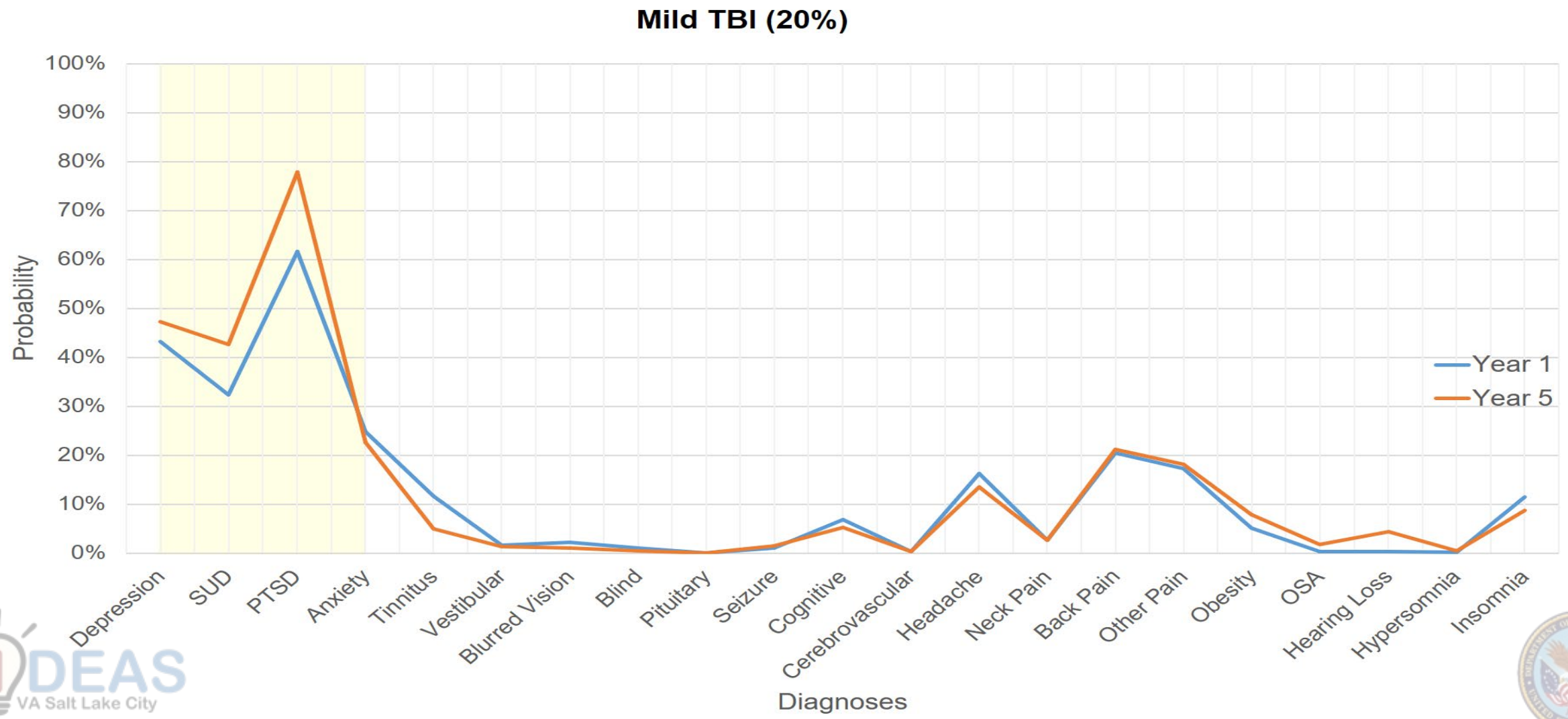
Screen Positive, No TBI Diagnosis (Total N=40,062)



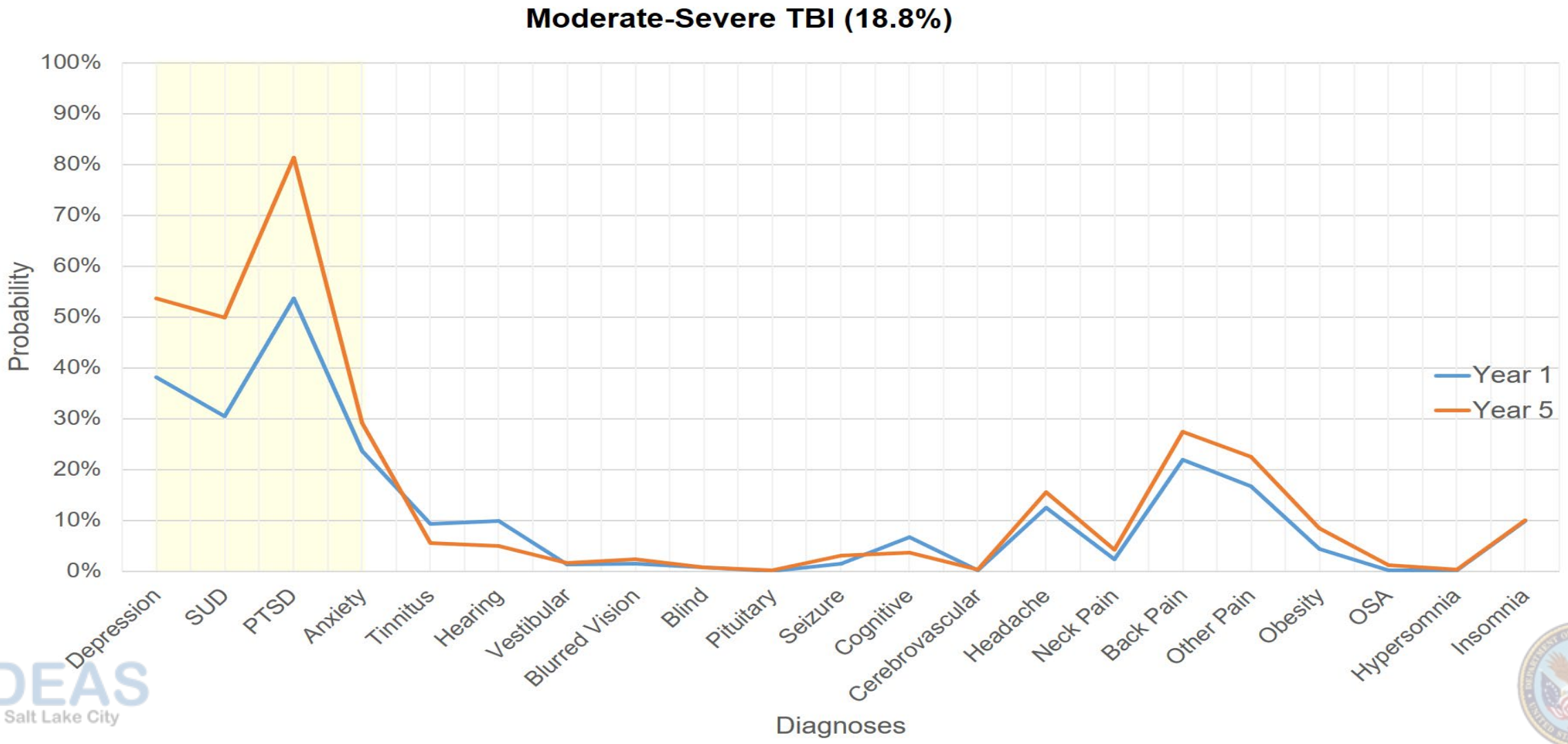
Unclassified TBI (Total N=17,410)



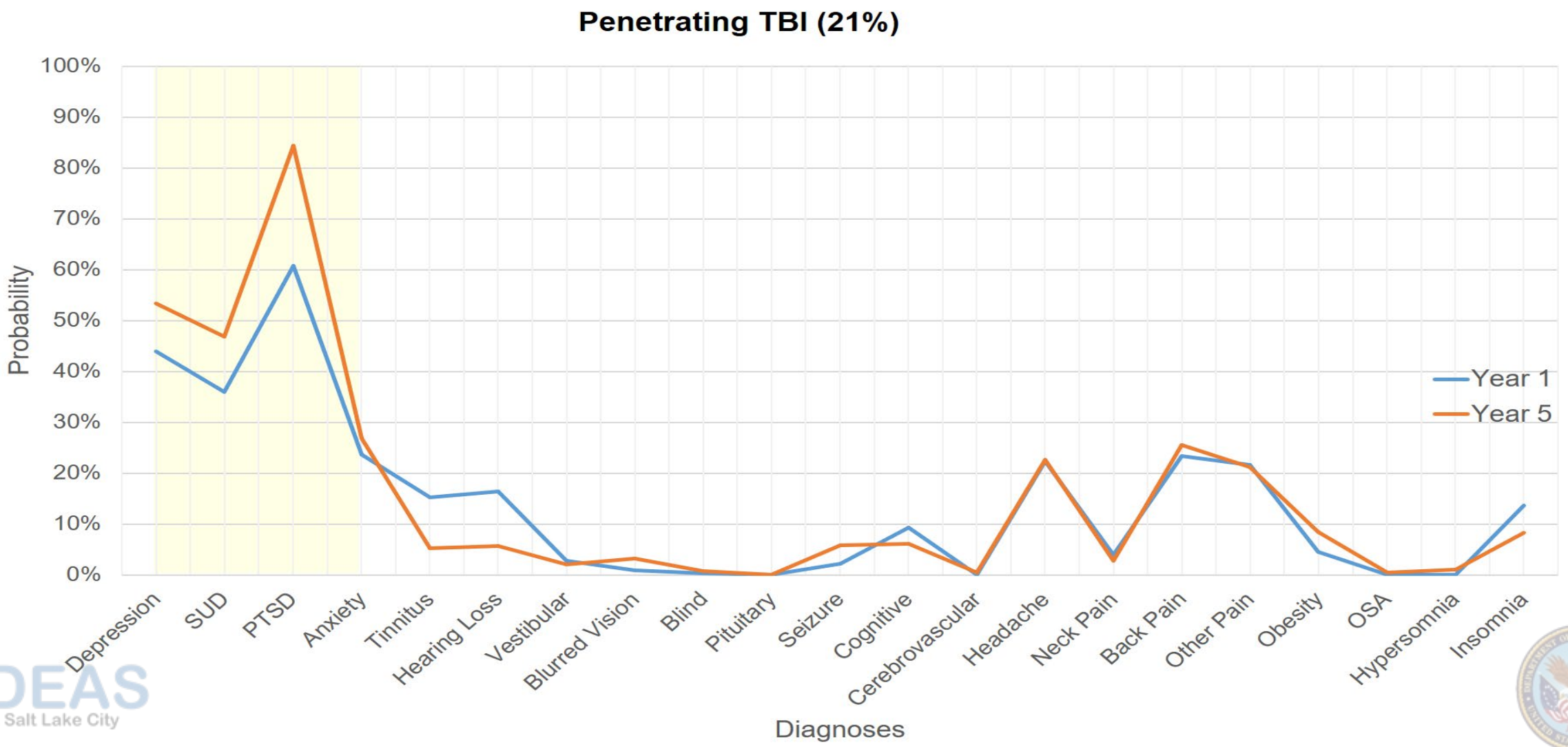
Mild TBI (Total N=92,183)



Moderate/Severe TBI (Total N=16,751)



Penetrating (Total N=1,632)



What Does This Mean Clinically?

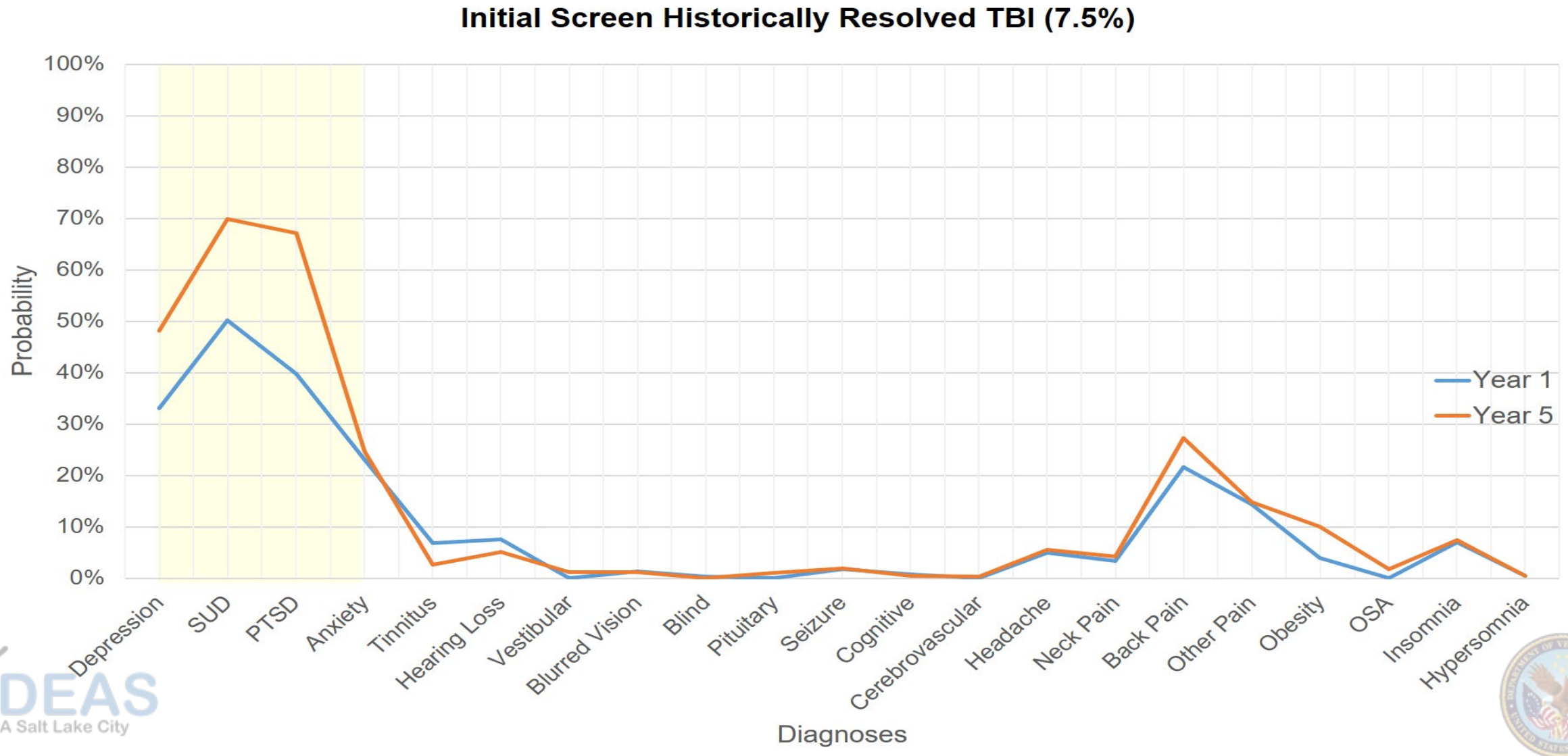
Raises more questions than it answers…

TBI severity and SUD trajectory

- All are associated with high probability of PTSD
  - Does treatment of PTSD/depression mitigate SUD risk?

- Historically Resolved: TBI exposure and initial symptoms that resolve
  - Have a small group with the highest probability of SUD over time (50% year 1; 70% year 5).

Does the TBI screening/evaluation process help mitigate emergence of SUD (by initiating PTSD/depression treatment) in those who either screen positive or have diagnosed TBI?



Conclusion

- Using longitudinal health system data can help us understand trajectories of TBI comorbidity.
  - Some show improvement and are associated with better outcomes
  - Some show deterioration and are associated with adverse outcomes
  - There is meaningful variation by TBI severity

- This is just a first step

Limitations

- Trajectories developed using
  - Only VA data
  - Only diagnosis data
  - Focused solely on deployment-related TBI
  - Results are descriptive

Next: Long-term Impact of Military Relevant Brain Injury Consortium (LIMBIC)

Questions/Discussion

- Thank you!
- Questions?
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  - Maryjo.pugh@hsc.Utah.edu