

Opioid Use following TBI: The Creating and Dismantling of a perfect storm

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Disclosures

Grant # 1 U01 NS086625-01

National Institutes of Health (NIH)/National Institute of Neurological Disorders and Stroke (NINDS)

Grants # 1RF1NS115268-01, 1R01NS102646-01, U54 NS107201, 1R01 NS115268-01, U54 NS115322-01, U54 NS115266-01; National Institutes of Health (NIH)/National Institute of Neurological Disorders and Stroke (NINDS)

Grant # 1R01 AG061028-01

National Institutes of Health (NIH)/National Institute of Aging (NIA)

Grant #90DPTB0009-01-00

National Institute on Disability Independent Living and Rehabilitation Research (NIDILRR)

Grant #PCS-1604-35115

Patient Centered Outcome Research Institute (PCORI)

Grant # W81XWH-17-1-0330 Epidemiology of Military Risk Factors Award

Department of Defense CDMRP Peer Reviewed Alzheimer's Research Program

Grant # DVBIC-W91Y TZ-13-C-0015

Department of Defense – Defense and Veterans Brain Injury Center (DVBIC)

Grant # W81XWH-17-1-0330

Department of Defense CDMRP Peer Reviewed Alzheimer's Research Program

Grant # Pending (AZ170038) Research Partnership Award

Department of Defense CDMRP Peer Reviewed Alzheimer's Research Program

W81XWH-18-ERP-IDA

Department of Defense CDMRP Epilepsy Research Program

Grant #1K01HD074651-01A1

National Institutes of Health (NIH)/National Institute of Child Health and Development (NICHD)

Consulting: Brain Injury Association of America, Veterans Affairs Medical Centers, various law firms

Conflicts of interest: None.

Disclosure will be made when a product is discussed for an unapproved use. Commercial support was not received for this activity.

JOURNAL OF NEUROTRAUMA 37:211–216 (January 1, 2020)
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DOI: 10.1089/neu.2019.6451

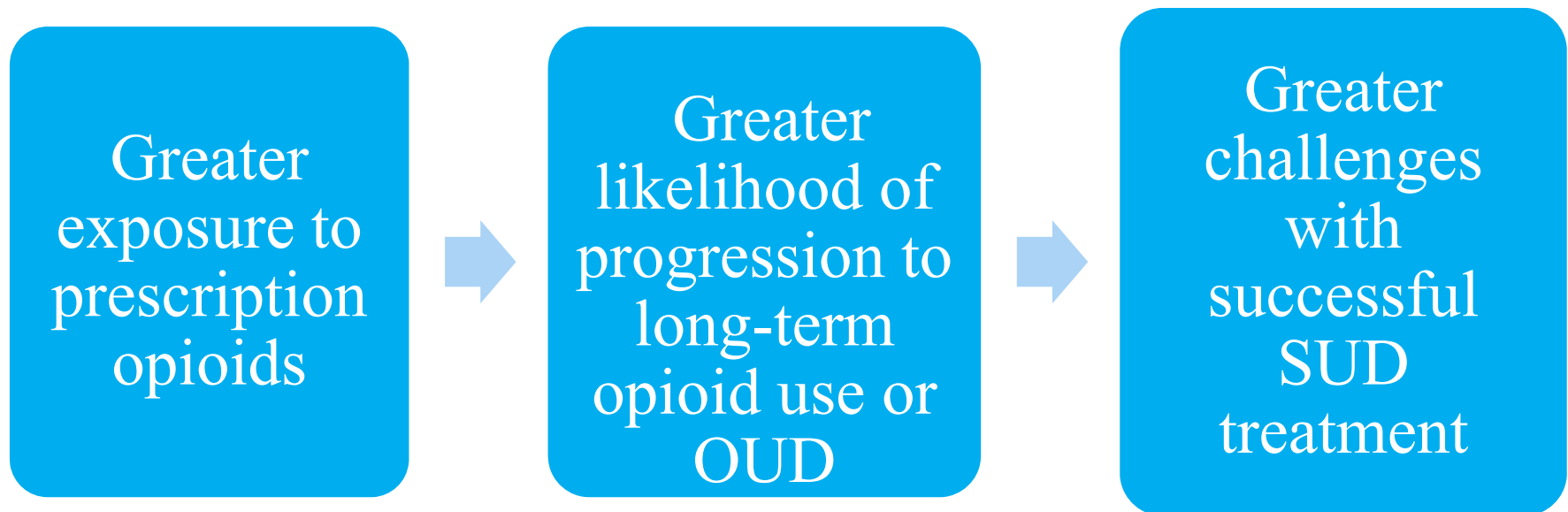
Short Communication

Opioid Use among Individuals with Traumatic Brain Injury: A Perfect Storm?

Rachel Sayko Adams,^{1,2} John D. Corrigan,³ and Kristen Dams-O'Connor^{4,5}

Cascade of vulnerabilities → “Perfect Storm”

Persons with TBI have:



The Perfect Storm - Vulnerability #1

Greater
exposure to
prescription
opioids

- Use of opioid medications during trauma/ICU care
- Use of opioid medications during acute rehabilitation
- Chronic pain
- Post-acute opioid use

Opioid use during Intensive Care

Nationwide cohort study of all ICU admissions 2010-2018 (van Oelreich 2020):

- 204,402 individuals survived the first two quarters after ICU admission and 22,138 developed chronic opioid use. (~11%)
 - Risk factors: OLDER age, female sex, disease comorbidity, preadmission opioid use, ICU LOS >2 days.

Opioid use during acute care for TBI: systematic review:

- Inclusion criteria: studies published in English, studies examining opioid prescription. The current review focused on those studies that examined opioid use during the acute medical treatment of TBI
- Exclusion criteria: Studies using animal models, populations with other acquired brain injury, and chronic management of brain injury
- 715 titles were screened, 227 abstracts reviewed, and 75 met eligibility criteria
- Conclusions: the longer-term implications of this opioid use in acute care for TBI are not well understood.

Opioid receipt during inpatient rehabilitation



Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2015;96(8 Suppl 3):S256-73



ORIGINAL RESEARCH

Psychotropic Medication Use During Inpatient Rehabilitation for Traumatic Brain Injury



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Ronald T. Seel, PhD,^e Thomas W. McAlister, MD,^b Darryl Kaelin, MD,^f David K. Ryser, MD,^g
John D. Corrigan, PhD,^d Nora Cullen, MD,^h Susan D. Horn, PhD^c

From the ^aCarolinas Rehabilitation, Charlotte, NC; ^bIndiana University School of Medicine, Indianapolis, IN; ^cInstitute for Clinical Outcomes Research, Salt Lake City, UT; ^dOhio State University, Columbus, OH; ^eCrawford Research Institute, Shepherd Center, Atlanta, GA; ^fUniversity of Louisville School of Medicine and Frazier Rehabilitation Institute, Louisville, KY; ^gIntermountain Medical Center, Salt Lake City, UT; and ^hToronto Rehabilitation Institute, Toronto, ON, Canada.

- Narcotic analgesics (NA) were the most frequently administered psychotropic drugs: 72% were given opioids at *any time* during their inpatient stay.
- 45% were prescribed opioids during the *last 2 days* of their inpatient stay.
- Narcotics were consumed for an average of 16 days, accounting for a mean 65% of the RLOS administered.
- NA more likely in those with history of drug abuse, anxiety, or depression, and severe pain during rehabilitation

Acute & chronic pain are common after TBI

- Pain is most common medical condition among adults receiving rehabilitation for TBI (TBI Model Systems)
- Prevalence of chronic pain following TBI estimated to be over 50%
- Extracranial injuries following TBI may also contribute to pain
- Chronic pain following TBI is associated with functional disability and mood disorders
- **Acute and chronic pain have been drivers of prescription opioid receipt in the US**

Chronic pain in TBI vs Community Controls

TABLE 1. PERCENTAGE OF INDIVIDUALS WITH CHRONIC PAIN STRATIFIED BY AGE, SEX, AND TBI EXPOSURE

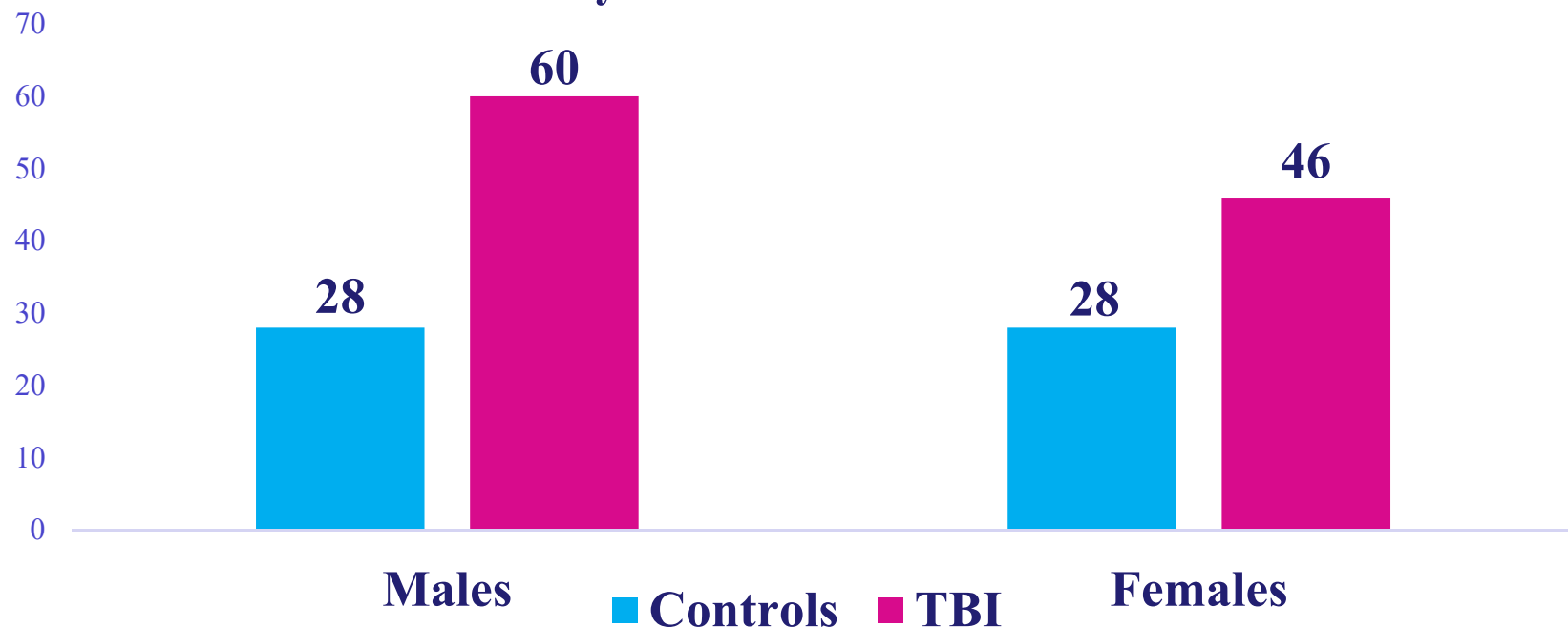
Age (years)	<i>TBI</i> (n = 205)			<i>Control</i> ^a (n = 5576)		
	<i>Total</i> (%)	<i>Male</i> (n = 119)	<i>Female</i> (n = 86)	<i>Total</i> (%)	<i>Male</i> (n = 2521)	<i>Female</i> (n = 3055)
		(%)	(%)		(%)	(%)
< 40 ^b	25	50	—	25.5	25.9	25.2
40–49	52.4	60.0	45.5	28.2	28.4	28.0
50–59	42.6	48.6	31.6	39.5	37.1	41.3
60–69	39.0	34.4	44.4	40.3	34.1	45.7
70–79	30.6	31.8	28.6	43.3	37.9	48.1
≥ 80	32.3	16.7	53.9	39.1	40.0	38.5

^aCommunity cohort data come from the Mid-life in the United States (MIDUS) study.³⁹

^bSample size <40 was insufficient to estimate stable rates.
TBI, traumatic brain injury.

Adults in their 40s with a history of TBI are at high risk for chronic pain

Percentage with Chronic Pain among Adults in the their 40s,
by Sex and TBI Status



Adams, Corrigan, and Dams-O'Connor, *Journal of Neurotrauma*, 2019

Headaches are common & contribute to pain following TBI

- Headache is one of the most common physical complaints following TBI
- Headache is a common symptom following deployment-related mild TBI
- Among adults with moderate/severe TBI, 33% reported new or worse headaches at both 1-year and 5-years post-injury
- **While opioids are not indicated for headaches, likelihood of opioid receipt may increase especially when pain is chronic**

Chronic Pain Opioid Use in TBI vs Controls

JOURNAL OF NEUROTRAUMA 38:1–7 (XXXX 00, 2021)
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DOI: 10.1089/neu.2020.7496

Original Article

Association between Lifetime History of Traumatic Brain Injury, Prescription Opioid Use, and Persistent Pain: A Nationally Representative Study

Raj G. Kumar,¹ Katherine A. Ornstein,^{2,3} John D. Corrigan,⁴
Rachel Sayko Adams,^{5,6} and Kristen Dams-O'Connor^{1,7}

Raj Kumar, PhD



Those with TBI had 52% increased risk for opioid use

TABLE 2. MULTI-VARIABLE LOGISTIC REGRESSION MODELS FOR PRESCRIPTION OPIOID MEDICATION USE AMONG ADULTS AGE 50+*

				<i>Prescription opioid use in last 3 months</i>	
<i>Models</i>		<i>TBI exposure classification</i>		<i>N, Weighted %[†]</i>	<i>RR (95% CI)</i>
Sensitivity analyses	Model 1	History of TBI	No history of TBI	76 (13.6)	Reference
			History of TBI	76 (19.7)	1.52 (1.11, 2.04)
	Model 2 [‡]	Years since most recent TBI	No history of TBI	76 (13.6)	Reference
			1–10	20 (38.1)	3.01 (1.57, 4.70)
			11–39	26 (19.6)	1.40 (0.91, 2.08)
			40+	28 (16.1)	1.29 (0.83, 1.92)
	Model 3 [‡]	Age at first TBI	No history of TBI	76 (13.6)	Reference
			<25	42 (18.9)	1.46 (0.99, 2.07)
			25–39	12 (18.1)	1.34 (0.66, 2.47)
			40+	20 (24.2)	1.98 (1.18, 3.04)
	Model 4	Number of lifetime TBIs	No history of TBI	76 (13.6)	Reference
			1	38 (16.0)	1.25 (0.83, 1.82)
			2+	38 (25.5)	2.00 (1.30, 2.90)

Those with TBI reported more pain

TABLE 3. MULTI-NOMIAL REGRESSION MODEL FOR MODERATE-SEVERE PAIN IN 2014 (T1) AND 2016 (T2) AMONG ADULTS 50+*

	<i>No pain (T1 and T2) N (%)[†]</i>	<i>Intermittent pain (T1 or T2) N (%)[†]</i>	<i>Persistent pain (T1 and T2) N (%)[†]</i>
No history of TBI	434 (70.7)	127 (18.6)	79 (10.7)
History of TBI	164 (48.1)	80 (22.5)	114 (29.4)
	OR (95% CI)	OR (95% CI)	OR (95% CI)
History of TBI vs. no history of TBI	Reference	1.89 (1.33, 2.68)	4.93 (3.43, 7.08)

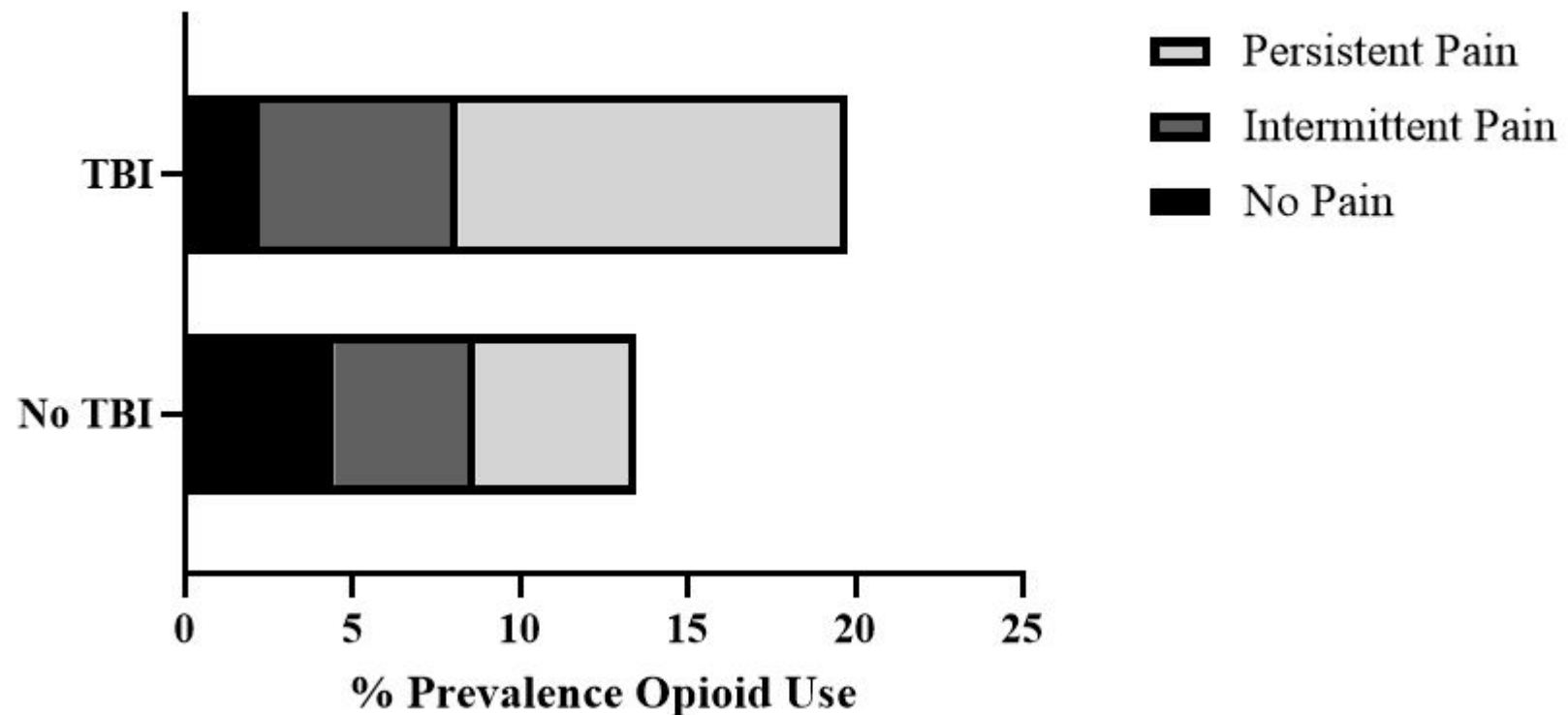
TBI, traumatic brain injury; OR, odds ratio; CI, confidence interval.

*Multinomial Regression Model adjusted for age, sex, and race.

[†]Percentages adjusted for 2016 Health and Retirement Study complex survey design weights to be representative of the United States; row percentages reported; N = 15 individuals had a survey weight of 0 and were dropped from weighted analysis; some individuals (N = 9) did not have pain data available in 2014 and 2016 and were not included in this analysis.

Greater pain ↔ more opioid use among persons with TBI

Pain Groups Among Opioid Users by TBI Exposure



Remote TBI confers increased risk for Prescription Opioid Use

J Head Trauma Rehabil
Vol. 36, No. 5, pp. 328–337
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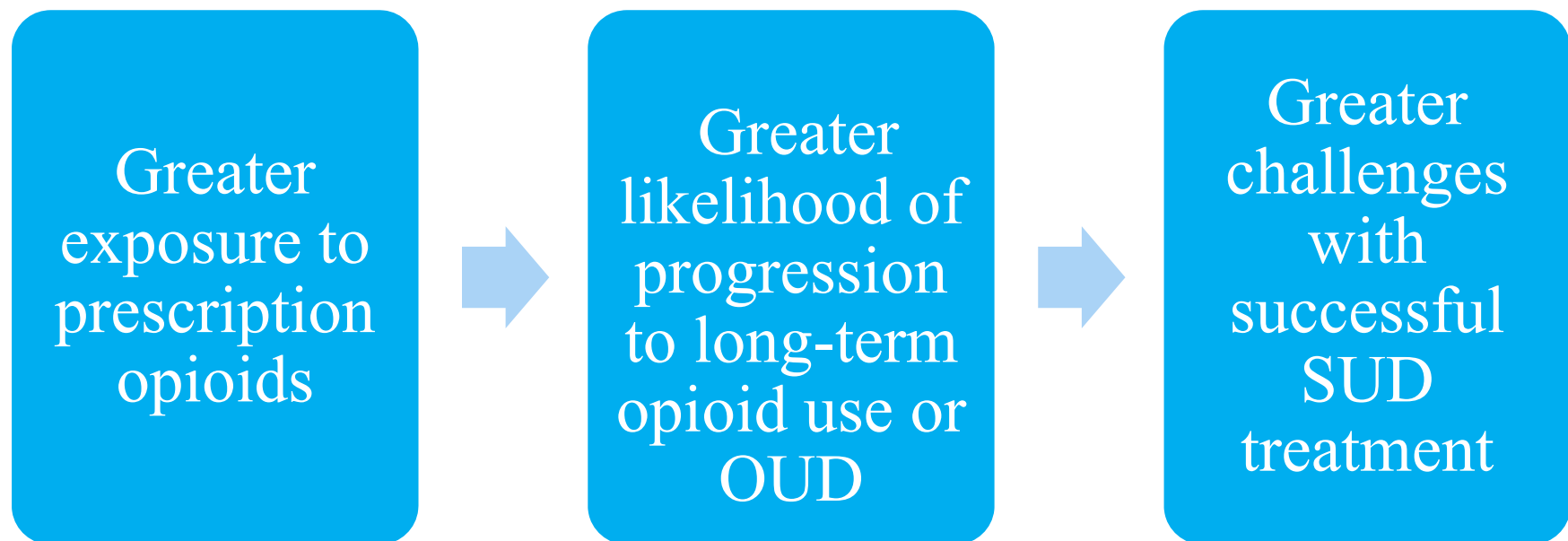
Association of Lifetime History of Traumatic Brain Injury With Prescription Opioid Use and Misuse Among Adults

*Rachel Sayko Adams, PhD, MPH; John D. Corrigan, PhD; Grant A. Ritter, PhD;
Abby Hagemeyer, PhD, MPH; Madeline B. Pliskin; Sharon Reif, PhD*

Objective: To investigate associations of lifetime history of traumatic brain injury (TBI) with prescription opioid use and misuse among noninstitutionalized adults. **Participants:** Ohio Behavioral Risk Factor Surveillance System (BRFSS) participants in the 2018 cohort who completed the prescription opioid and lifetime history of TBI modules ($n = 3448$). **Design:** Secondary analyses of a statewide population-based cross-sectional survey. **Main Measures:** Self-report of a lifetime history of TBI using an adaptation of the Ohio State University TBI-Identification Method. Self-report of past year: (1) prescription pain medication use (ie, prescription opioid use); and (2) prescription opioid misuse, defined as using opioids more frequently or in higher doses than prescribed and/or using a prescription opioid not prescribed to the respondent. **Results:** In total, 22.8% of adults in the sample screened positive for a lifetime history of TBI. A quarter (25.5%) reported past year prescription opioid use, and 3.1% met criteria for prescription opioid misuse. A lifetime history of TBI was associated with increased odds of both past year prescription opioid use (adjusted odds ratio [AOR] = 1.52; 95% CI, 1.27-1.83; $P < .01$) and prescription opioid misuse (AOR = 1.65; 95% CI, 1.08-2.52; $P < .05$), controlling for sex, age, race/ethnicity, and marital status. **Conclusion:** Results from this study support the “perfect storm” hypothesis—that persons with a history of TBI are at an increased risk for exposure to prescription opioids and advancing to prescription opioid misuse compared with those without a history of TBI. Routine screening for a lifetime history of TBI may help target efforts to prevent opioid misuse among adults. **Key words:** *Ohio, opioid misuse, prescription opioids, traumatic brain injury*

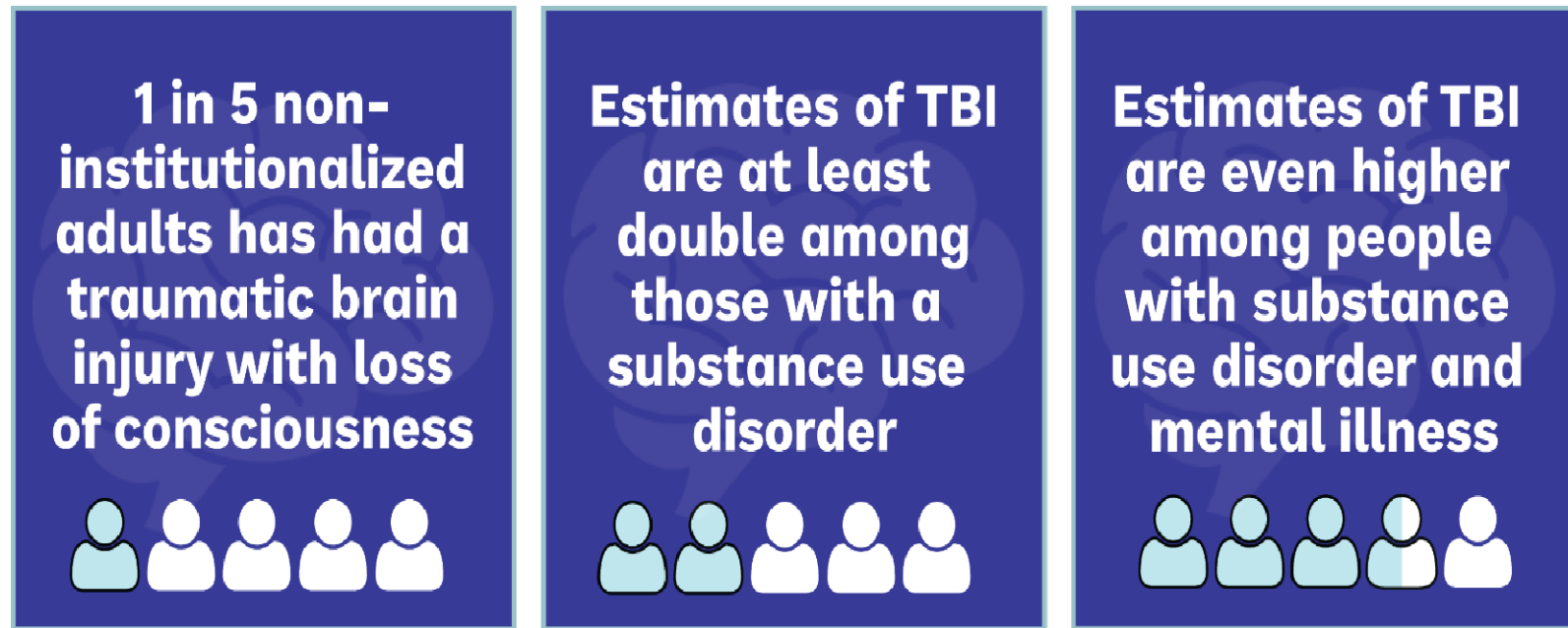
The Perfect Storm - Vulnerability #2

Persons with TBI have:



Vulnerability #2

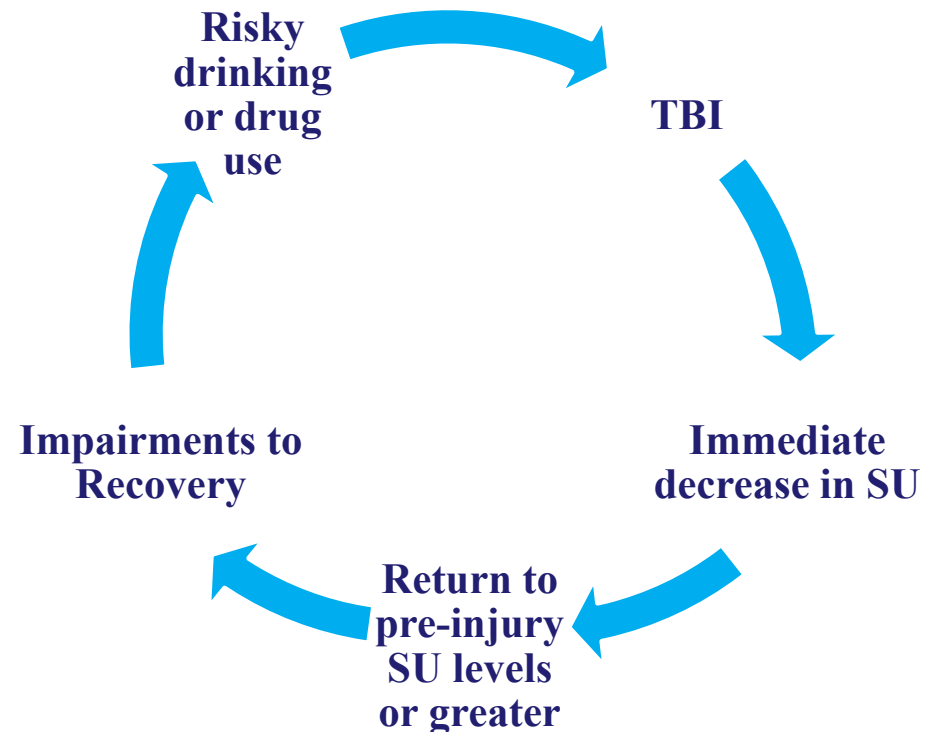
History of TBI is common among persons with a SUD



Corrigan et al., 2017; Whiteneck et al., 2016; <https://heller.brandeis.edu/ibh/research/inroads/index.html>

Substance use and TBI are often interrelated

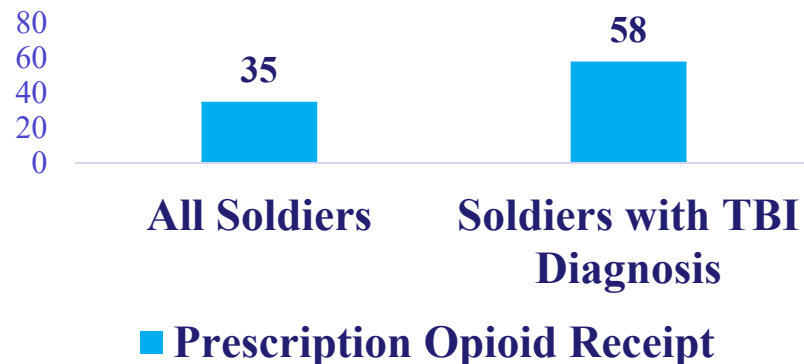
- Substance use is a risk factor for TBI
- Post-TBI, some reduce or stop their drinking, yet many resume pre-injury drinking levels 1-2 years post-injury
- Substance use may reduce brain healing, impede rehabilitation, and increase risk for future TBIs
- **Cycle has not been studied specifically for opioids**



Weil et al., 2016; Corrigan & Cole 2008

Combat Veterans with TBI are more likely to advance to high-risk opioid use

Percent of Soldiers with Prescription Opioid Receipt in Postdeployment Year

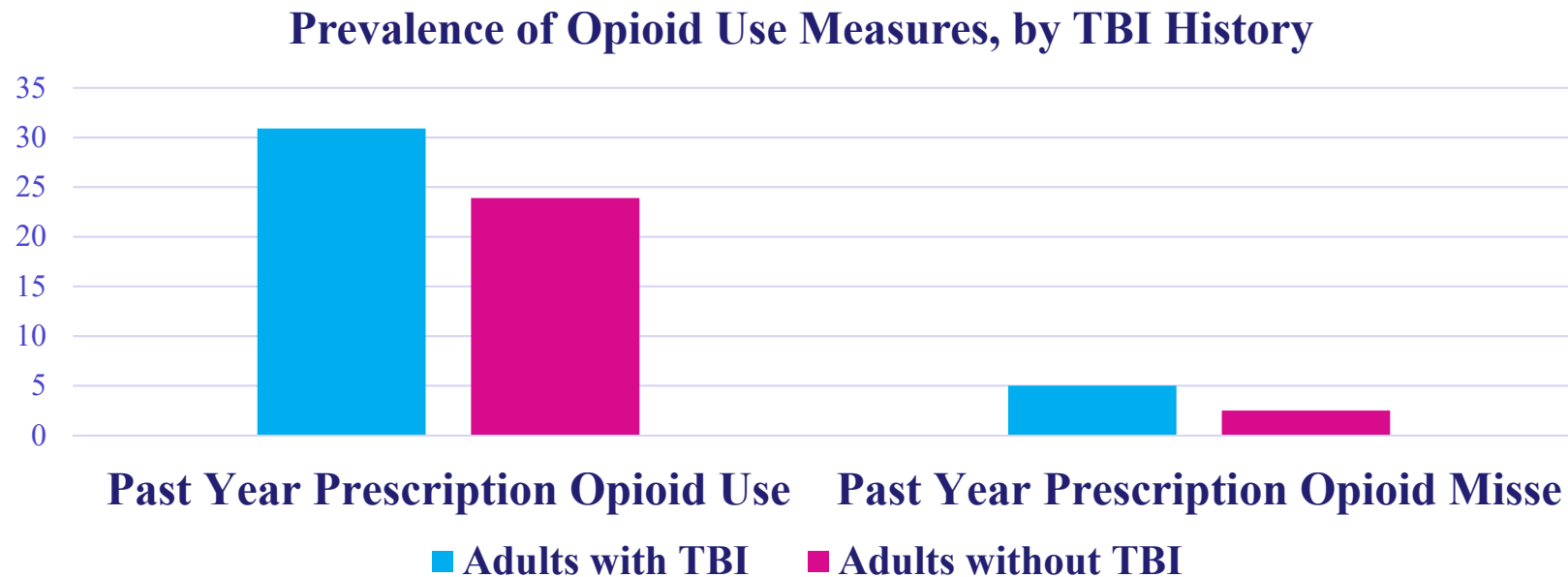


Rachel Sayko Adams, PhD

- ▶ Among Afghanistan/Iraq Veterans using the Veterans Health Administration with a TBI diagnosis
 - More likely to use opioids long-term
- ▶ Increased risk for concurrent benzodiazepine and opioid use due to mental health comorbidities
 - Can increase overdose risk

Adams et al., *Military Medicine*, 2018; Bertenthal et al., 2018; Hudson et al., 2018; Carlson et al., 2018

Adults with a history of TBI at increased risk for opioid misuse



**2018 Ohio Behavioral Risk Factor
Surveillance Survey**

Adams et al., *Under Review*

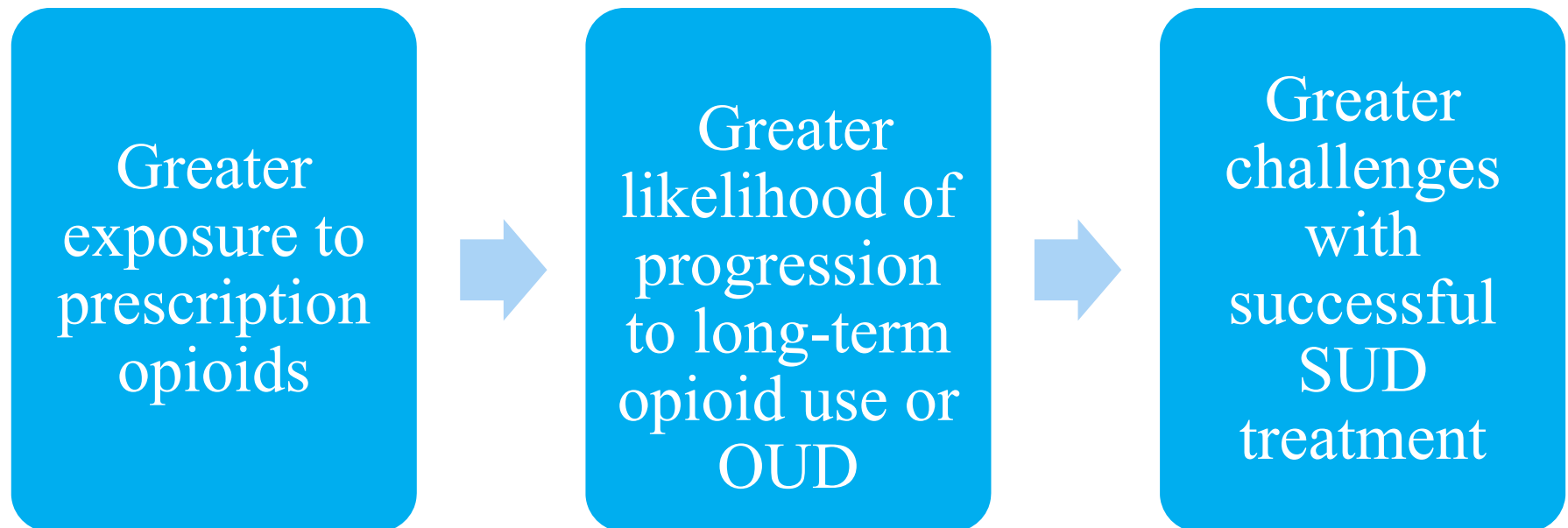
Neurobehavioral changes may → risk for risky substance use

- Cognitive deficits (e.g., memory problems, executive functioning limitations)
 - Medication mismanagement and poor adherence to prescribed dosing
- Mood disorders (e.g., depression, anxiety), sleep disturbance, traumatic stress
 - Risk factors for at-risk substance use
- Prefrontal cortex damage may increase impulsive behavior
 - More difficult to self-regulate substance use
- **Neurobehavioral changes may converge post-TBI to increase risk for opioid misuse or OUD**

Dams-O'Connor et al., 2018; Ashman et al., 2006; Adams et al., 2019

The Perfect Storm - Vulnerability #3

Persons with TBI have:



Vulnerability #3

Reasons for less successful SUD treatment

1. Neurobehavioral impairments undermine ability to participate and benefit from conventional treatment
2. Greater co-occurring psychiatric disorders among those with TBI
3. Lowered ability to sustain improvements without external structure

The potential consequences of the “perfect storm” are dire

Consequences beyond dependence or addiction:

- Increased risk for non-fatal overdose
- Increased risk for overdose death
- Additional contribution to risk for death by suicide

TBI is associated with increased risk for non-fatal opioid overdose among Veterans receiving long-term opioid therapy

- ▶ Post-9/11 Veterans receiving care at the VHA between 2007-2012
- ▶ Age 18-40 receiving long-term opioid treatment for chronic, non-cancer pain
- ▶ Veterans with TBI had more than a 3-fold increase in opioid overdose compared to those without TBI
 - Association was attenuated in mediation analyses for any co-occurring psychiatric condition, but remained significant (HR 1.77)

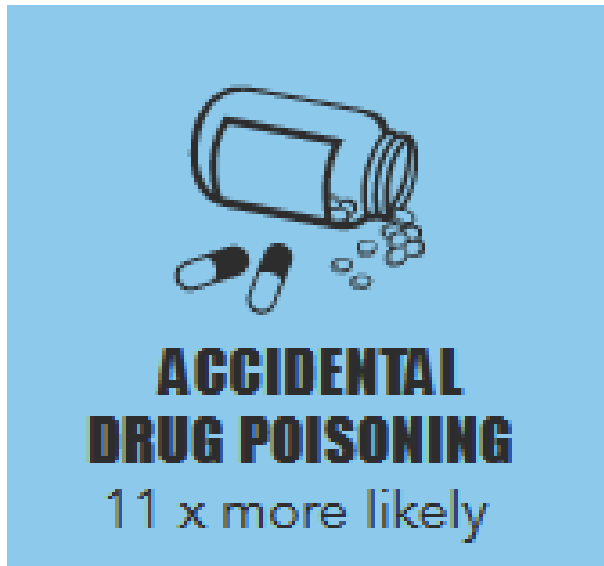
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Traumatic Brain Injury and Opioid Overdose Among Post-9/11 Veterans With Long-Term Opioid Treatment of Chronic Pain

Jennifer R. Fonda, PhD; Jaimie L. Gradus, DSc; Susan B. Brogly, PhD;
Regina E. McGlinchey, PhD; William P. Milberg, PhD; Lisa Fredman, PhD

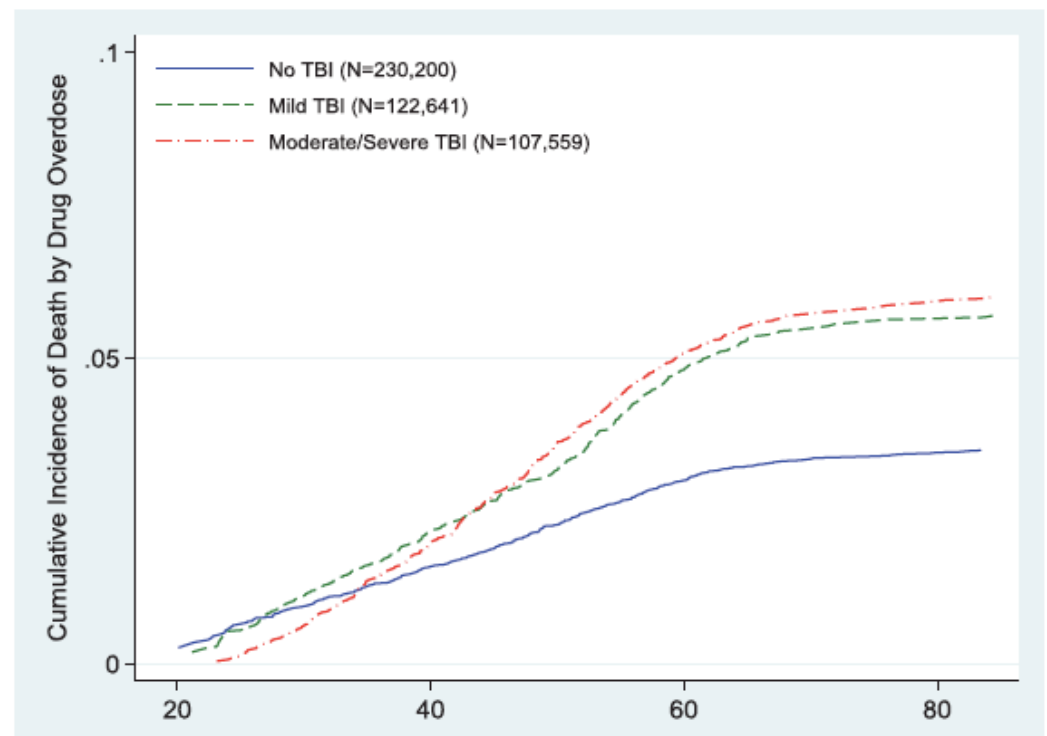
TBI is associated with increased risk for overdose deaths

TBI Model Systems



Hammond et al. 2020 - 90% of accidental overdose deaths were drug related (predominantly opioids)

VHA study



Hammond et al., 2020; CDC/NIDILRR Fact Sheet; Byers et al., 2019

TBI + Opioids may → Suicide risk

- ▶ Several studies have found an association between TBI and increased risk for death by suicide
- ▶ Long-term opioid therapy and OUD also increase risk for suicide
- ▶ VHA study found, among Veterans prescribed long-term opioid therapy to treat chronic pain, those with TBI were at increased risk for suicide attempt compared to those without TBI (Im et al., 2015)

Summary

Persons with TBI are:

1. receiving more exposure to opioids than people without,
2. more likely to use opioids long-term, to misuse opioids, and to develop addiction, and
3. To face additional barriers accessing and receiving quality substance use disorder treatment

The potential consequences of this “perfect storm” are dire, and include increased morbidity and mortality

Opioid use following TBI remains poorly understood

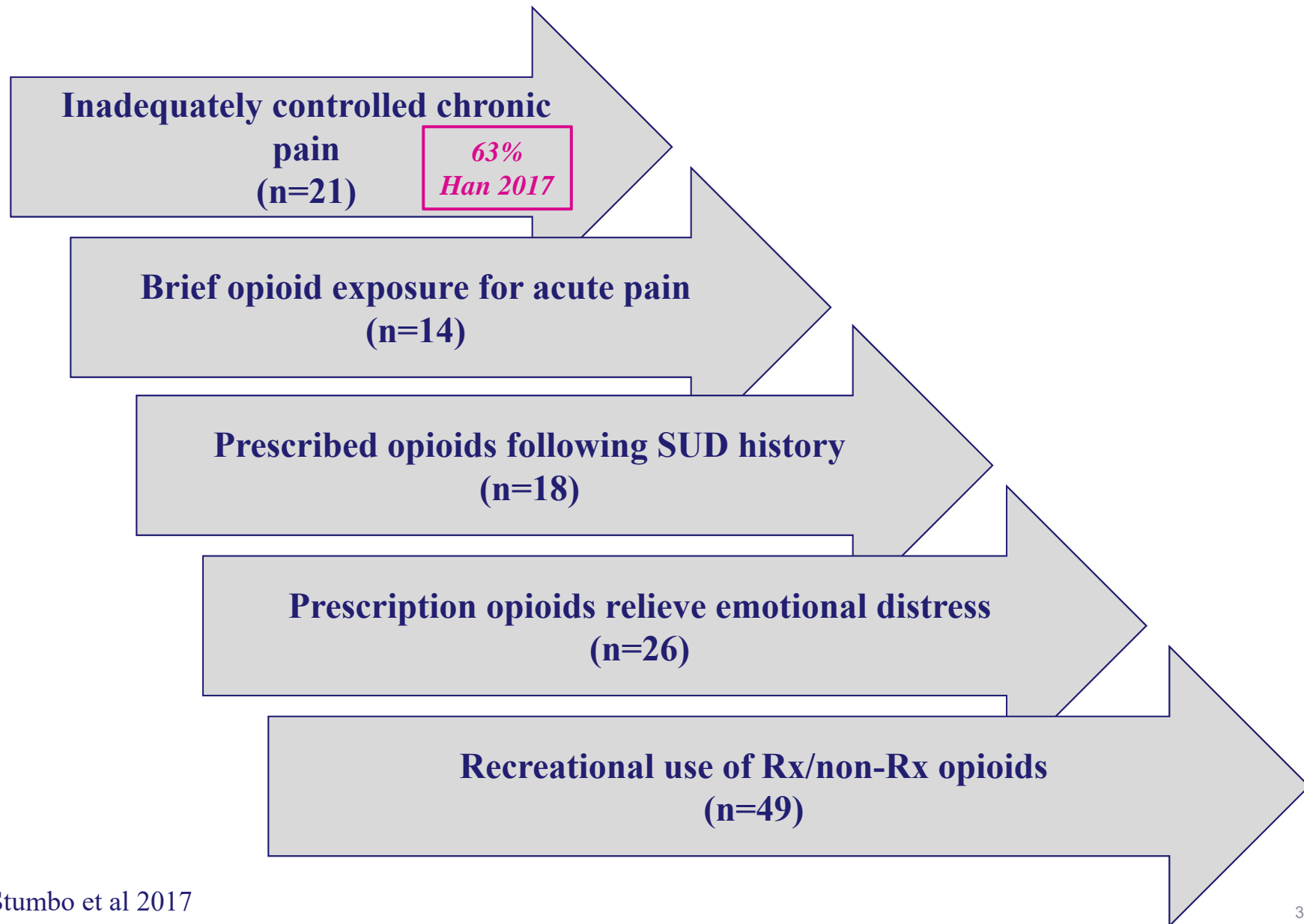
Scoping Review of Opioid Use after TBI

- Inclusion criteria: English language, Adults w stable TBI, rx opioid receipt or use after TBI.
- Exclusion criteria: Animal models, other ABI, acute TBI management, non-peer-reviewed papers.
- 771 abstracts were screened, 183 full texts were reviewed, and 21 met eligibility criteria.
- Most studies used administrative/EMR data from military samples. Prescription opioid receipt is associated with psychological symptoms. No studies evaluated interventions to reduce opioid use or risk in TBI.
- **Despite growing concerns about opioid use following TBI, very few studies have directly investigated opioid use or consequences in this population.**

Recommendations for People with TBI and Families

- ▶ Monitor opioid use, early and often
- ▶ Seek alternative pain management approaches
- ▶ Consider what opioids are treating.
 - Seek treatments/supports that align with needs
- ▶ Advocate for treatment plans that minimize risk and maximally address individual treatment needs.

Pathways to Opioid Use Disorders



Recommendations for SUD and TBI Treatment Providers

- ▶ Screen for lifetime history of TBI
- ▶ Identify and accommodate neurobehavioral deficits
- ▶ Address co-morbid interactions (e.g., depression, anxiety, pain, sleep, sensory/motor deficits)
- ▶ Create formal and/or informal supports needed during and after treatment completion
- ▶ Medication-based treatments are safe and effective and can be used with other methods to reduce cue sensitivity
- ▶ Consider patients' full care team and prescription sources

Our recent publications in this area



J Head Trauma Rehabil


Vol. 36, No. 5, pp. 303–309

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Preface

Traumatic Brain Injury and Opioid Use: Additional Evidence Supporting the “Perfect Storm” of Cascading Vulnerabilities

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Thank You

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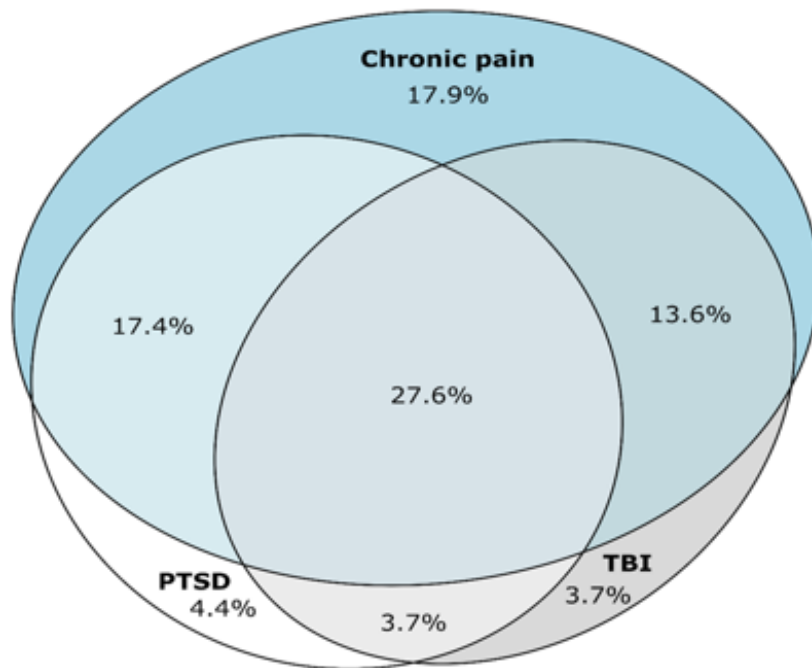
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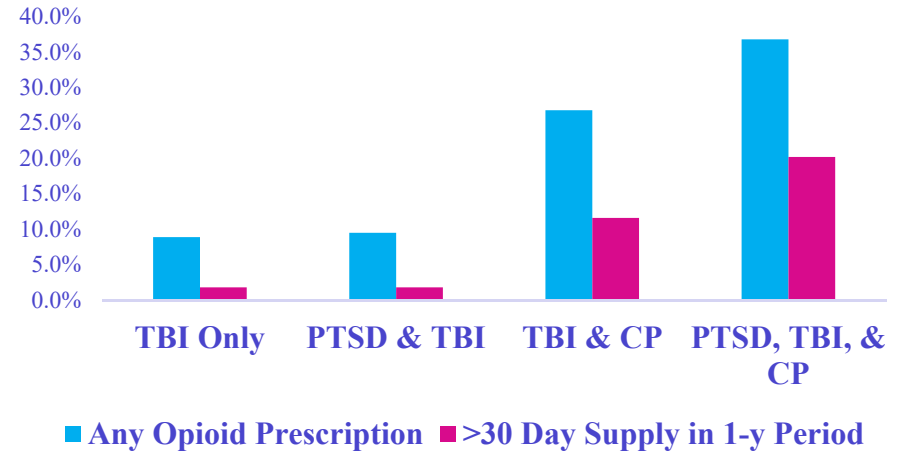
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Military TBI Polytrauma: opioid use increases with comorbidity

“polytrauma clinical triad”

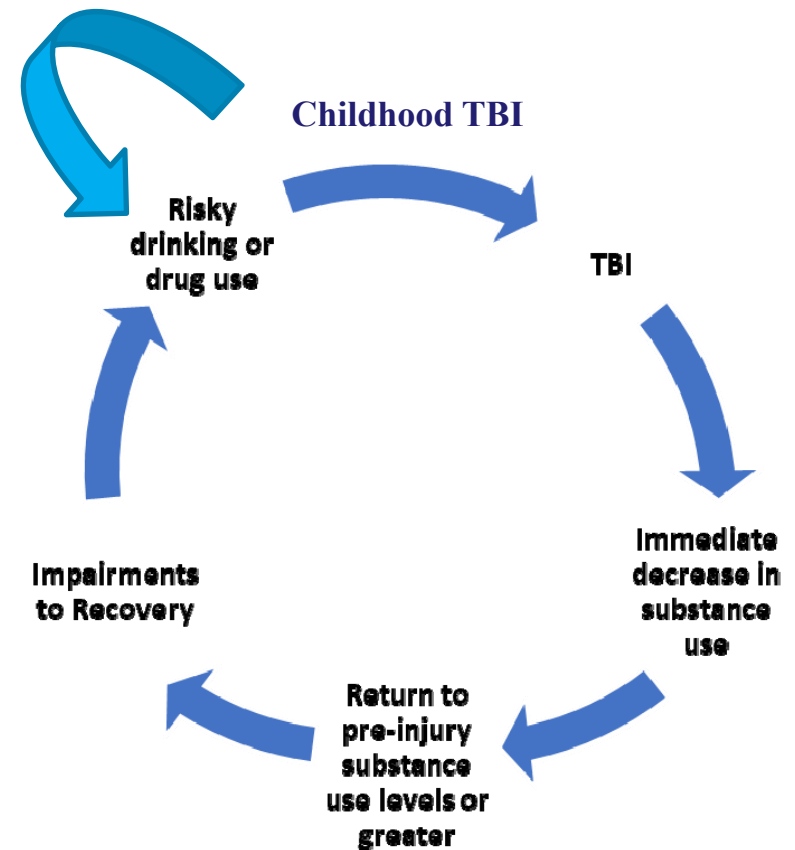


Increase in opioid use as comorbidities increase



Childhood TBI may increase risk for future substance use problems

- Association between childhood TBI and increased likelihood of substance use problems
- Adults with TBI before age 6 more likely to misuse alcohol or use illicit drugs following new adult TBI (TBI Model Systems)
- Childhood TBI before age 12 associated with increased binge drinking post-deployment
- **This relationship has not been studied specifically for opioids**



McKinlay et al., 2002; Corrigan et al., 2013; Kennedy et al., 2017;
Adams, Campbell-Sills et al., 2019; Weil, Karelina, and Corrigan, 2019