

Preface

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

Rachel Sayko Adams, PhD, MPH

BY THE TIME THE US Department of Health and Human Services declared the opioid epidemic a public health emergency in 2017,¹ prescription opioid rates had been declining for several years.² Yet, alarmingly, despite broad, multifaceted policy changes and interventions launched to curb the epidemic, opioid-related overdose deaths have increased by almost 5% from 2018 to 2019.^{3,4} Mortality associated with the opioid epidemic has been characterized by 3 waves,⁵ with the first wave fueled by increasing prescription opioid medications beginning in the 1990s, the second wave characterized by overdose deaths involving heroin starting around 2010, and the third wave driven by overdose deaths involving synthetic opioids (eg, fentanyl) starting in 2013.⁵

In recent years, traumatic brain injury (TBI) researchers, rehabilitation providers, funders, family members, and persons living with TBI have directed attention to understanding how the opioid epidemic has affected persons with TBI in the United States.⁶ There was speculation that persons with TBI may be at a greater risk for receiving prescription opioids due to secondary conditions common after injury (eg, pain)^{6,7};

however, systematic study was lacking. Recently, Drs Corrigan, Dams-O'Connor, and I published a commentary, “Opioid Use Among Individuals With Traumatic Brain Injury: A Perfect Storm?”⁸ in which we synthesized existing literature, highlighted gaps in knowledge, and posited that for some individuals with TBI, risk factors may converge to create a “perfect storm,” placing them at an increased risk for opioid use and associated consequences. We developed a 3-phase model for the “perfect storm,” which posits that there are cascading vulnerabilities that can make persons with TBI uniquely susceptible to devastating consequences from opioid use, with each phase increasing risk for progression to the next (see Figure 1). Briefly, phase I contends that persons with TBI have greater exposure to opioids. Phase II states that, given opioid exposure, persons with TBI have a greater risk for advancing to long-term opioid therapy (LTOT; a risk factor for overdose and development of dependence),^{9,10} opioid misuse, or opioid use disorder (OUD). Finally, phase III hypothesizes that if persons with TBI do develop OUD, they may face greater barriers to successfully engage in OUD treatment.

In **phase I**, we posited that persons with TBI are at an increased risk for opioid exposure due to several risk factors, the most significant of which is acute or chronic pain (including headaches) following TBI, which drives prescription opioid receipt. Studies indicate that more than 50% of individuals living with TBI have chronic pain.^{7,11,12} Other risk factors for prescription opioid receipt include reliance on opioids in the intensive care unit or during acute rehabilitation.¹³ To date, evidence has been strongest for phase I of the “perfect storm.” Most research focusing on prescription opioid receipt following a TBI diagnosis uses electronic medical record (EMR) data, largely with military/veteran populations.^{14–16} A new article by Kumar and

The author thanks Kristen Dams-O'Connor, PhD, for her thoughtful review and contributions to this Foreword.

This work was supported by a grant from the US Department of Health and Human Services (HHS), Administration for Community Living's (ACL's) National Institute for Disability, Independent Living, and Rehabilitation Research (NIDILRR) 90DPGE0007 (to Brandeis University, PI: Reif). The contents of this article do not necessarily represent the policy of NIDILRR, ACL, HHS, or the Veterans Health Administration, and you should not assume endorsement by the federal government.

The author declares no conflicts of interest.

DOI: 10.1097/HTR.0000000000000730

PERSONS WITH TBI MAY HAVE:

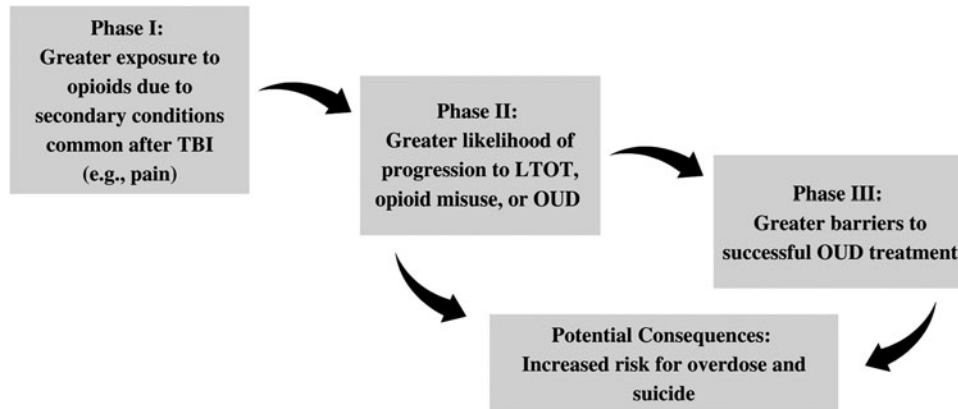


Figure 1. Cascade of vulnerabilities that create the “perfect storm.” LTOT indicates long-term opioid therapy; OUD, opioid use disorder; TBI, traumatic brain injury.

colleagues¹² appears to be the first study to examine the association between lifetime history of TBI and prescription opioid receipt, using data from the nationally representative Health and Retirement Study. The authors found that older adults (aged 50+ years) with a lifetime history of TBI had a 52% increased risk for prescription opioid use in the past 3 months relative to those without a TBI history. Risk was highest among individuals with a recent TBI (1-10 years ago), first TBI after the age of 40 years, or 2+ lifetime TBIs.

There have been fewer studies directly exploring **phase II** of the “perfect storm.” Some studies have found that post-9/11 military members or veterans with a TBI diagnosis were at a greater risk for LTOT than those without TBI.^{14,15} Other studies examining self-reported TBI found an increased risk for prescription opioid misuse following injury; one among a small community-based sample of post-9/11 veterans reporting a deployment-related TBI,¹⁷ and the other among a sample of adults in Ontario reporting at least one lifetime injury (ie, knocked out for 5 minutes or longer or an overnight hospitalization).¹⁸ Lessons can be drawn from extensive literature on substance use following TBI. There is strong evidence that substance use is both a risk factor for TBI and that persons with TBI are at an elevated risk for postinjury substance use; thus, this cycle may be reinforcing.^{19,20} There is also growing evidence that experiencing a TBI during childhood may increase risk for late adolescent or adult substance use.^{21–23} While there has been little direct investigation into opioid misuse or OUD following childhood or lifetime TBI, there is reason to speculate that similar relationships would exist for opioids, which are uniquely addictive due to rapid development of dependence.²⁴ Unlike other illicit drugs, opioids are routinely prescribed to persons with TBI in the context of clinical care.¹³ Damage to reward circuitry from TBI may create a biological vulnerability,

while cognitive and neurobehavioral changes may serve as contributors to the development of prescription opioid misuse (eg, difficulty regulating impulsive behavior and emotions, memory problems leading to medication mismanagement, or taking extra prescription opioids to self-medicate).^{8,25}

For **phase III** of the “perfect storm,” we hypothesized that persons with TBI and OUD may face greater challenges accessing and successfully engaging in substance use disorder treatment due to neurobehavioral deficits or executive dysfunction following TBI.^{8,24,26} To date, there are no known studies examining experiences or outcomes of persons with TBI seeking treatment specifically for OUD. However, prior studies have shown that individuals with TBI may require accommodations in substance use disorder treatment settings to address TBI-related challenges.¹⁹ For instance, a randomized effectiveness trial within a trauma setting found that patients with TBI (vs no TBI) received less benefit from an evidence-based brief intervention for excessive alcohol use.²⁷

While research is still emerging, the potential consequences of this “perfect storm” can be dire and include nonfatal overdose, fatal overdose, and suicide risk.^{8,28–31} A study of post-9/11 veterans using the Veterans Health Administration (VHA) who received LTOT for treatment of chronic, noncancer pain found that veterans with TBI had a 3-fold increase in nonfatal opioid overdose compared with those without TBI.²⁸ Studies with both civilian^{30,32} and veteran²⁹ populations have found that individuals with TBI were more likely to die from a drug overdose than individuals without TBI. Furthermore, while studies with both military/veteran and civilian populations have found an increased risk for death by suicide among persons with TBI,^{33,34} one study of veterans using the VHA who were prescribed LTOT to treat chronic pain found that those with TBI were at an

increased risk for suicide attempt compared with those without TBI.³¹

Given the relatively nascent state of research systematically examining the relationship between TBI and opioid use and associated consequences, the current topical issue sought articles addressing this relationship broadly. This topical issue includes studies that provide further support for the “perfect storm,” while informing an agenda for future research. The majority of studies included in this topical issue examine prescription opioid receipt and use data from relatively recent years, contributing new knowledge about this topic after opioid prescriptions began to decrease in the United States around 2012.²

Starosta and colleagues³⁵ conducted a scoping review to systematically characterize existing literature on prescription and nonprescription opioid use among individuals with TBI. As of their search date (ie, January, 2020), 21 articles met study inclusion criteria: English language, adults with a stable TBI, and prescription opioid receipt or use after TBI (excluding those with acquired brain injury or focusing on acute management of TBI). Four studies were review articles, and more than half of the 17 original research articles examined military/veteran populations. Most studies used EMR data, largely within the VHA, to examine prescription opioid receipt among persons with a TBI diagnosis, with fewer relying on self-report of opioids or self-report of TBI. Preliminary findings from articles included in the scoping review support phase I of the “perfect storm.” Findings indicate that individuals with TBI have an increased likelihood of receiving prescription opioids and that opioid receipt is more common among those with comorbid pain and/or psychological health conditions in addition to TBI. The authors reported that few studies examined data from more recent years of the epidemic, a gap addressed by the studies in this topical issue as described as follows.

Adams and colleagues³⁶ examined the association of lifetime history of TBI with past year prescription opioid use and misuse among adults using data from the 2018 Ohio Behavioral Risk Factor Surveillance System survey. They found that adults with a lifetime history of TBI had 1.5 times the odds of past year prescription opioid use and 1.7 times the odds of past year prescription opioid misuse, compared with adults without TBI, controlling for sex, age, race/ethnicity, and marital status. This study was among the first to examine the relationship between lifetime history of TBI and opioid misuse. Study findings provide support for phases I and II of the “perfect storm” among an adult noninstitutionalized civilian population.

While prior studies examining opioid use following TBI have been conducted almost exclusively with adult populations, **Tham and colleagues**³⁷ conducted the first

study of TBI and opioids among a nationally representative sample of US adolescents. Using the 2019 Youth Risk Behaviors Survey, the authors found that the odds of prescription opioid misuse were 1.5 times higher for adolescents with a past year sports-related concussion than those without a past year concussion, controlling for sex, race/ethnicity, other substance use, and depressive symptoms. These results are consistent with a previous study of Canadian adolescents,³⁸ which found that self-report of lifetime history of TBI (ie, injury to the head resulting in loss of consciousness for 5+ minutes or a minimum 1-night hospital stay) was associated with 2.7 higher odds of past year prescription opioid misuse, controlling for grade and sex.

A series of articles in this issue examine prescription opioid receipt and consequences among military members and veterans with TBI who received care in the Military Health System or VHA, respectively. A study by **Hoover and colleagues**³⁹ examined risk factors of prescription opioid receipt among individuals who received an index TBI diagnosis in the Military Health System between 2016 and 2017. They found that 29% of military members with an index TBI diagnosis received prescription opioids in the year prior to their TBI diagnosis, and importantly, 84% of these individuals continued receiving prescription opioids after their injury. On the contrary, among those who did not receive a prescription opioid in the year prior to their TBI, only 20% received postinjury prescription opioids. Thus, prior prescription opioid receipt was a strong predictor of future opioid use. Both musculoskeletal conditions and behavioral health diagnoses (eg, mental health or substance use disorder) in the year prior to the index TBI were associated with an increased risk for prescription opioid receipt postinjury, similar to other studies.⁴⁰ Women with TBI were at an increased risk for postinjury opioid receipt compared with men with TBI. Other studies with military/veteran and civilian samples have found that women are at an increased risk for prescription opioid receipt compared with males,^{14,41,42} yet this appears to be the first study to examine this relationship in a population of persons with TBI.

A study by **Holmer and colleagues**⁴³ examined opioid and sedative-hypnotic prescription receipt and high-risk opioid outcomes among post-9/11 veterans with and without a TBI diagnosis treated in the VHA between 2012 and 2020. High-risk opioid outcomes included the following: LTOT, high-dose opioid therapy, and overlapping opioid prescriptions and benzodiazepine and/or nonbenzodiazepine sedative-hypnotic prescriptions—each of which increases risk for overdose and development of OUD.^{10,44} Among veterans with TBI, more than one-fourth subsequently received a

prescription opioid in the VHA. Among veterans with TBI who received opioids, 30.1% received a concurrent benzodiazepine, 36.0% received concurrent nonbenzodiazepine sedative-hypnotic prescriptions, and 26.3% used LTOT. This study was among the first to reveal that veterans with a moderate/severe TBI (compared with a mild TBI), and those who experienced blast exposure (compared with nonblast exposure), were more likely to have high-risk opioid use. **Ashraf and colleagues**⁴⁵ were the first to integrate VHA and non-VHA prescription opioid data to examine the prevalence and predictors of concurrent opioid and sedative-hypnotic prescriptions from VHA/non-VHA systems of care among post-9/11 veterans with TBI. They found that among veterans diagnosed with TBI in the VHA between 2014 and 2019 who received an opioid in the VHA, 20% received an overlapping opioid prescription from a non-VHA provider and 5.3% received overlapping benzodiazepines. These results imply that clinicians considering prescribing opioids to veterans with TBI in the VHA or in civilian settings may not have the complete picture of total opioid and/or benzodiazepine exposure and thereby fail to recognize the full risk for overdose or OUD.

To investigate potential explanations for sleep-related disorders that are common following TBI, **Martin and colleagues**⁴⁶ examined the association between prescription opioid receipt during acute inpatient rehabilitation for moderate/severe TBI with sleep parameters (eg, quality, architecture, respiration) during 2017-2019; a quarter of the sample used a VHA facility. They found that prescription opioid receipt early after TBI was associated with impaired sleep parameters and sleep-related respiration outcomes (eg, increased frequency of central sleep apnea events during total and non-REM [rapid eye movement] sleep; higher frequency of obstructive sleep apnea events during REM sleep). This is among the first studies to consider the implications for sleep-related outcomes from opioid use during acute rehabilitation for TBI, expanding the scope of potential adverse outcomes associated with the “perfect storm.”

Finally, an article by **Herrera and colleagues**⁴⁷ used EMR data from 2011-2015 to examine how prescription opioid receipt was associated with risk for TBI among community-dwelling Medicare beneficiaries aged 65+ years. Among Medicare beneficiaries who received an index TBI diagnosis during the study period, 16.2% were prescribed opioids in the 7 days preceding the TBI diagnosis. Prescription opioid use independently increased the odds of TBI by 30% compared with nonusers. This study highlights that prescription opioid use may ultimately increase risk for future TBI; thus, the pattern of risk may be cyclical once someone has either experienced a TBI or initiated opioids. These findings buttress previously recognized concerns

that the opioid epidemic may be contributing to additional brain injuries, as anoxic or hypoxic brain damage can occur during a nonfatal overdose.²⁴ As we saw in Hoover and colleagues,³⁹ prescription opioid use prior to TBI increases risk for continuation of opioid use postinjury. Thus, older adults who are using prescription opioids in the months prior to a new TBI may be at a greater risk for continuing opioids after injury and advancing to LTOT, accelerating into phase II of the “perfect storm.”

Together, the original research articles in this topical issue contribute new knowledge about risk for prescription opioid use, misuse, and other negative outcomes among persons with TBI. These studies rely on recently collected data, reflecting risks that endure after the reduction in opioid prescribing that started circa 2012.² Since then, clinical practice guidelines have been introduced to reduce high-risk opioid receipt, particularly among individuals with chronic pain,^{10,48} and to caution against prescribing opioids to military members/veterans with a mild TBI⁴⁹; yet, findings from this topical issue suggest that persons with TBI remain at an elevated risk for prescription opioid receipt and high-risk use or misuse of prescription opioids. The findings presented emanate from diverse populations of persons with TBI (ie, civilians, adolescents, military members, and veterans). These studies provide further evidence to support phases I and II of the “perfect storm”—that persons with TBI are at a greater risk for opioid exposure and, given exposure, they are at a greater risk for opioid misuse and high-risk opioid receipt (eg, LTOT, overlapping opioids and benzodiazepines) and adverse consequences (ie, adverse sleep-related outcomes).

Although the original data used in the studies in the topical issue were collected during the second and third waves of the opioid epidemic, no study investigated illicit opioid use following TBI or how prescription opioid use may be a pathway to illicit opioid use. This aspect remains a high-priority research area. More research is needed to understand patterns of prescription opioid use and associated outcomes following TBI for those with and without preinjury opioid use. In general, women are less likely to advance to LTOT or experience opioid misuse or OUD^{14,42}; yet, sex differences in opioid use remain largely unexplored among persons with TBI. This is an important area for future research, as gender or sex can impact outcomes following TBI.^{50,51} Given high rates of pain following TBI,^{7,11,12} alternative pain management options are urgently needed. Evaluation of nonpharmacological treatments of chronic pain is underway in other populations⁵² and should be examined in populations of individuals with TBI and comorbid pain to minimize adverse outcomes in this high-risk group. Clinicians considering tapering opioid prescriptions for their patients with TBI should use

caution and provide careful oversight, as reports of increased suicide risk following forced tapering have been observed in the United States.⁵³

More research is needed to fully understand the association of high-risk opioid use with adverse outcomes among TBI survivors. As noted earlier, studies indicate that persons with TBI who engage in LTOT are at an increased risk for overdose (nonfatal and fatal) and suicide attempt.^{8,28–31} A recent study that used machine learning to reveal sex-specific predictors of suicide among persons with substance use disorders in Denmark revealed that prior poisoning (ie, overdose) was among the most important predictors of suicide death, particularly among women, and that this risk could extend for many years after the poisoning.⁵⁴ Investigation of this dynamics among persons with TBI is warranted, as persons with TBI are at an elevated risk for suicide,^{33,34,55} and prior overdose may help identify those at even a greater risk of suicide.

Phase III of the “perfect storm,” which hypothesizes that persons with TBI who develop OUD may face greater challenges successfully accessing and engaging in OUD treatment, remains unstudied specific to OUD. This gap in knowledge is critical, as studies in the topical issue found additional evidence that persons with TBI are at a greater risk for opioid misuse, increasing their likelihood of developing OUD and risk for morbidity and mortality. While examination of barriers to substance use disorder treatment following TBI, and outcomes of such treatment, has been limited to date, prior studies indicate that persons with TBI face greater barriers and do not benefit as much as persons without TBI in standard substance use

disorder treatments.^{19,27,56} Evaluation of how individuals with TBI are able to access and benefit from evidence-based interventions and treatments of OUD is of the utmost importance.³⁵ Substance use disorder treatment providers should be trained to screen for lifetime history of TBI, as evidence is mounting that a large portion of persons seeking substance use disorder treatment have a history of TBI.⁵⁷ These providers should be trained to recognize and accommodate cognitive and other neurobehavioral consequences of TBI in their practice.¹⁹

Empirical investigation into each element of the “perfect storm” is needed to identify treatment targets and prevention opportunities. This research will require investment in longitudinal studies that allow assessment of lifetime history of TBI, exposure to prescription and nonprescription opioid use, and long-term morbidity and mortality outcomes. As research progresses to address gaps in knowledge highlighted herein, prevention strategies inclusive of nonpharmacological pain management interventions and evidence-based treatments of OUD incorporating accommodations for persons with TBI should be implemented to prevent future morbidity and mortality.

Rachel Sayko Adams, PhD, MPH

*Institute for Behavioral Health
Heller School for Social Policy & Management
Brandeis University
Waltham, Massachusetts
Rocky Mountain Mental Illness Research Education and
Clinical Center
Veterans Health Administration
Aurora, Colorado*

REFERENCES

1. US Department of Health and Human Services. HHS Acting Secretary declares public health emergency to address national opioid crisis. Published 2017. Accessed February 6, 2021. <https://www.hhs.gov/about/news/2017/10/26/hhs-acting-secretary-declares-public-health-emergency-address-national-opioid-crisis.html>
2. Schuchat A, Houry D, Guy GP Jr. New data on opioid use and prescribing in the United States. *JAMA*. 2017;318(5):425–426. doi:10.1001/jama.2017.8913
3. Centers for Disease Control and Prevention. *Wide-Ranging Online Data for Epidemiologic Research (WONDER)*. CDC National Center for Health Statistics; 2020. Accessed February 1, 2021. <http://wonder.cdc.gov>
4. Rudd RA, Seth P, David F, Scholl L. Increases in drug and opioid-involved overdose deaths—United States, 2010–2015. *MMWR Morb Mortal Wkly Rep*. 2016;65(50/51):1445–1452. doi:10.15585/mmwr.mm655051e1
5. Centers for Disease Control and Prevention. *Understanding the Epidemic*. National Center for Injury Prevention and Control; 2021. Accessed June 14, 2021. <https://www.cdc.gov/drugoverdose/epidemic/index.html#three-waves>
6. National Institute on Disability, Independent Living, and Rehabilitation Research. *Summary of Responses From a Request for Information: People With Disabilities and Opioid Use Disorder*. Administration for Community Living; 2018.
7. Nampiaparampil DE. Prevalence of chronic pain after traumatic brain injury: a systematic review. *JAMA*. 2008;300(6):711–719. doi:10.1001/jama.300.6.711
8. Adams RS, Corrigan JD, Dams-O'Connor K. Opioid use among individuals with traumatic brain injury: a perfect storm? *J Neurotrauma*. 2020;37(1):211–216. doi:10.1089/neu.2019.6451
9. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a National Institutes of Health Pathways to Prevention Workshop. *Ann Intern Med*. 2015;162(4):276–286. doi:10.7326/M14-2559
10. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *JAMA*. 2016;315(15):1624–1645. doi:10.1001/jama.2016.1464
11. Cifu DX, Taylor BC, Carne WF, et al. Traumatic brain injury, posttraumatic stress disorder, and pain diagnoses in OIF/OEF/OND veterans. *J Rehabil Res Dev*. 2013;50(9):1169–1176. doi:10.1682/JRRD.2013.01.0006

12. Kumar RG, Ornstein KA, Corrigan JD, Adams RS, Dams-O'Connor K. Association between lifetime history of traumatic brain injury, prescription opioid use, and persistent pain: a nationally representative study. *J Neurotrauma*. Published online March 11, 2021. doi:10.1089/neu.2020.7496
13. Hammond FM, Barrett RS, Shea T, et al. Psychotropic medication use during inpatient rehabilitation for traumatic brain injury. *Arch Phys Med Rehabil*. 2015;96(8)(suppl):S256–S263.e14. doi:10.1016/j.apmr.2015.01.025
14. Adams RS, Thomas CP, Ritter GA, et al. Predictors of postdeployment prescription opioid receipt and long-term prescription opioid utilization among Army active duty soldiers. *Mil Med*. 2019;184(1/2):e101–e109. doi:10.1093/milmed/usy162
15. Bertenthal D, Yaffe K, Barnes DE, et al. Do postconcussive symptoms from traumatic brain injury in combat veterans predict risk for receiving opioid therapy for chronic pain? *Brain Inj*. 2018; 32(10):1188–1196. doi:10.1080/02699052.2018.1493535
16. Seal KH, Bertenthal D, Barnes DE, et al. Traumatic brain injury and receipt of prescription opioid therapy for chronic pain in Iraq and Afghanistan veterans: do clinical practice guidelines matter? *J Pain*. 2018;19(8):931–941. doi:10.1016/j.jpain.2018.03.005
17. Golub A, Bennett AS. Prescription opioid initiation, correlates, and consequences among a sample of OEF/OIF military personnel. *Subst Use Misuse*. 2013;48(10):811–820. doi:10.3109/10826084.2013.796988
18. Ilie G, Adlaf EM, Mann RE, et al. Associations between a history of traumatic brain injuries and current cigarette smoking, substance use, and elevated psychological distress in a population sample of Canadian adults. *J Neurotrauma*. 2015;32(14):1130–1134. doi:10.1089/neu.2014.3619
19. Corrigan J, Adams R, Dams O'Connor K. At-risk substance use and substance use disorders. In: Zasler N, Katz D, Zafonte R, eds. *Brain Injury Medicine: Principles and Practice*. 3rd ed. Springer Publishing Company LLC; 2021.
20. Beaulieu-Bonneau S, St-Onge F, Blackburn MC, Banville A, Paradis-Giroux AA, Ouellet MC. Alcohol and drug use before and during the first year after traumatic brain injury. *J Head Trauma Rehabil*. 2018;33(3):E51–E60. doi:10.1097/HTR.0000000000000341
21. Cannella LA, McGary H, Ramirez SH. Brain interrupted: early life traumatic brain injury and addiction vulnerability. *Exp Neurol*. 2019;317:191–201. doi:10.1016/j.expneurol.2019.03.003
22. Corrigan JD, Bogner J, Mellick D, et al. Prior history of traumatic brain injury among persons in the Traumatic Brain Injury Model Systems National Database. *Arch Phys Med Rehabil*. 2013;94(10): 1940–1950. doi:10.1016/j.apmr.2013.05.018
23. Weil ZM, Karelina K, Corrigan JD. Does pediatric traumatic brain injury cause adult alcohol misuse: combining preclinical and epidemiological approaches. *Exp Neurol*. 2019;317:284–290. doi:10.1016/j.expneurol.2019.03.012
24. Corrigan JD, Adams RS. The intersection of lifetime history of traumatic brain injury and the opioid epidemic. *Addict Behav*. 2019;90:143–145. doi:10.1016/j.addbeh.2018.10.030
25. Dams-O'Connor K, Landau A, Hoffman J, St De Lore J. Patient perspectives on quality and access to healthcare after brain injury. *Brain Inj*. 2018;32(4):431–441. doi:10.1080/02699052.2018.1429024
26. Corrigan JD, Cole TB. Substance use disorders and clinical management of traumatic brain injury and posttraumatic stress disorder. *JAMA*. 2008;300(6):720–721. doi:10.1001/jama.300.6.720
27. Zatzick D, Donovan DM, Jurkovich G, et al. Disseminating alcohol screening and brief intervention at trauma centers: a policy-relevant cluster randomized effectiveness trial. *Addiction*. 2014;109(5):754–765. doi:10.1111/add.12492
28. Fonda JR, Gradus JL, Brogly SB, McGlinchey RE, Milberg WP, Fredman L. Traumatic brain injury and opioid overdose among post-9/11 veterans with long-term opioid treatment of chronic pain. *J Head Trauma Rehabil*. 2020;35(3):209–217. doi:10.1097/HTR.0000000000000546
29. Byers AL, Li Y, Barnes DE, Seal KH, Boscardin WJ, Yaffe K. A national study of TBI and risk of suicide and unintended death by overdose and firearms. *Brain Inj*. 2020;34(3):328–334. doi:10.1080/02699052.2019.1701708
30. Harrison-Felix C, Pretz C, Hammond FM, et al. Life expectancy after inpatient rehabilitation for traumatic brain injury in the United States. *J Neurotrauma*. 2015;32(23):1893–1901. doi:10.1089/neu.2014.3353
31. Im JJ, Shachter RD, Oliva EM, et al. Association of care practices with suicide attempts in US veterans prescribed opioid medications for chronic pain management. *J Gen Intern Med*. 2015;30(7): 979–991. doi:10.1007/s11606-015-3220-y
32. Hammond FM, Ketchum J, Dams-O'Connor K, et al. Mortality secondary to unintentional poisoning after inpatient rehabilitation among individuals with moderate to severe traumatic brain injury. *J Neurotrauma*. 2020;37(23):2507–2516. doi:10.1089/neu.2020.7038
33. Hostetter TA, Hoffmire CA, Forster JE, Adams RS, Stearns-Yoder KA, Brenner LA. Suicide and traumatic brain injury among individuals seeking Veterans Health Administration services between fiscal years 2006 and 2015. *J Head Trauma Rehabil*. 2019;34(5):E1–E9. doi:10.1097/HTR.0000000000000489
34. Madsen T, Erlangsen A, Orlovskaya S, Mofaddy R, Nordentoft M, Benros ME. Association between traumatic brain injury and risk of suicide. *JAMA*. 2018;320(6):580–588. doi:10.1001/jama.2018.10211
35. Starosta AJ, Adams RS, Marwitz JH, et al. Scoping review of opioid use after traumatic brain injury. *J Head Trauma Rehabil*. 2021;36(5): 310–327. doi:10.1097/HTR.0000000000000721
36. Adams RS, Corrigan JD, Ritter GA, Hagemeyer A, Pliskin MB, Reif S. Association of lifetime history of traumatic brain injury with prescription opioid use and misuse among adults. *J Head Trauma Rehabil*. 2021;36(5):328–337. doi:10.1097/HTR.0000000000000729
37. Tham SW, Palermo TM, Chrisman S, Groenewald CB. Prescription opioid misuse and sports-related concussion among high school students in the United States. *J Head Trauma Rehabil*. 2021; 36(5):338–344. doi:10.1097/HTR.0000000000000706
38. Ilie G, Mann RE, Hamilton H, et al. Substance use and related harms among adolescents with and without traumatic brain injury. *J Head Trauma Rehabil*. 2015;30(5):293–301. doi:10.1097/HTR.0000000000000101
39. Hoover P, Johnson D, Wu T, French LM, Caban J. Risk factors associated with the prescription of opioids among service members following a first mild traumatic brain injury (mTBI). *J Head Trauma Rehabil*. 2021;36(5):345–353. doi:10.1097/HTR.0000000000000711
40. Adams RS, Larson MJ, Meerwijk EL, Williams TV, Harris AH. Postdeployment polytrauma diagnoses among soldiers and veterans using the Veterans Health Affairs polytrauma system of care and receipt of opioids, nonpharmacologic, and mental health treatments. *J Head Trauma Rehabil*. 2019;34(3):167–175. doi:10.1097/HTR.0000000000000481
41. Toblin RL, Quartana PJ, Riviere LA, Walper KC, Hoge CW. Chronic pain and opioid use in US soldiers after combat deployment. *JAMA Intern Med*. 2014;174(8):1400–1401. doi:10.1001/jamainternmed.2014.2726
42. Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription opioid use, misuse, and use disorders in US adults:

- 2015 National Survey on Drug Use and Health. *Ann Intern Med.* 2017;167(5):293–301. doi:10.7326/M17-0865
43. Holmer HK, Gilbert TA, Ashraf AJ, O'Neil ME, Carlson KF. Opioid and sedative-hypnotic prescriptions among post-9/11 veteran VA users nationwide with traumatic brain injury, 2012–2020. *J Head Trauma Rehabil.* 2021;36(5):354–363. doi:10.1097/HTR.0000000000000712
 44. Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort study of the impact of high-dose opioid analgesics on overdose mortality. *Pain Med.* 2016;17(1):85–98. doi:10.1111/pme.12907
 45. Ashraf AJ, Gilbert TA, Holmer HK, Cook LJ, Carlson KF. Receipt of concurrent VA and non-VA opioid and sedative-hypnotic prescriptions among post-9/11 veterans with traumatic brain injury. *J Head Trauma Rehabil.* 2021;36(5):364–373. doi:10.1097/HTR.0000000000000728
 46. Martin AM, Almeida EJ, Starosta AJ, et al. The impact of opioid medications on sleep architecture and nocturnal respiration during acute recovery from moderate to severe traumatic brain injury (TBI): a TBI Model Systems study. *J Head Trauma Rehabil.* 2021;36(5):374–387. doi:10.1097/HTR.0000000000000727
 47. Herrera AV, Wastila L, Brown JP, Chen H, Gambert SR, Albrecht JS. Effects of prescription opioid use on traumatic brain injury risk in older adults. *J Head Trauma Rehabil.* 2021;36(5):388–395. doi:10.1097/HTR.0000000000000716
 48. Department of Veterans Affairs and Department of Defense. VA/DoD clinical practice guideline for the management of opioid therapy for chronic pain—clinician summary. Published 2017. Accessed April 14, 2017. <https://www.healthquality.va.gov/guidelines/Pain/cot>
 49. Department of Veterans Affairs and Department of Defense. VA/DoD Clinical Practice Guideline for Management of Concussion/Mild Traumatic Brain Injury. Version 2.0. The Management of Concussion/mTBI Working Group; 2016.
 50. Colantonio A. Sex, gender, and traumatic brain injury: a commentary. *Arch Phys Med Rehabil.* 2016;97(2)(suppl):S1–S4. doi:10.1016/j.apmr.2015.12.002
 51. Valera EM, Joseph A-LC, Snedaker K, et al. Understanding traumatic brain injury in females: a state-of-the-art summary and future directions. *J Head Trauma Rehabil.* 2021;36(1):E1–E17. doi:10.1097/HTR.0000000000000652
 52. Meerwijk EL, Larson MJ, Schmidt EM, et al. Nonpharmacological treatment of army service members with chronic pain is associated with fewer adverse outcomes after transition to the Veterans Health Administration. *J Gen Intern Med.* 2020;35(3):775–783. doi:10.1007/s11606-019-05450-4
 53. Darnall BD, Juurlink D, Kerns RD, et al. International stakeholder community of pain experts and leaders call for an urgent action on forced opioid tapering. *Pain Med.* 2019;20(3):429–433. doi:10.1093/pm/pty228
 54. Adams RS, Jiang T, Rosellini AJ, et al. Sex-specific risk profiles for suicide among persons with substance use disorders in Denmark. *Addiction.* Published online February 23, 2021. doi:10.1111/add.15455
 55. Teasdale TW, Engberg AW. Suicide after traumatic brain injury: a population study. *J Neurol Neurosurg Psychiatry.* 2001;71(4):436–440. doi:10.1136/jnnp.71.4.436
 56. West SL, Graham CW, Cifu DX. Rates of alcohol/other drug treatment denials to persons with physical disabilities: accessibility concerns. *Alcohol Treat Q.* 2009;27(3):305–316. doi:10.1080/07347320903008190
 57. Dams-O'Connor K, Cantor JB, Brown M, Dijkers MP, Spielman LA, Gordon WA. Screening for traumatic brain injury: findings and public health implications. *J Head Trauma Rehabil.* 2014;29(6):479–489. doi:10.1097/HTR.0000000000000099