Clinical/Basic Science Research Article

OPEN

Association between spine injury and opioid misuse in a prospective cohort of Level I trauma patients

Alyssa Shell Tilhou, MD, PhD[a,*], Joseph E. Glass, MSW, PhD[b], Scott J. Hetzel, MS[c], Ola Elizabeth Shana, BA[d], Tudor Borza, MD, MS[e], Amelia Baltes, MPH[f], Bri M.F. Deyo, MPH[f], Suresh Agarwal, MD, FACS, FCCM[g], Ann O'Rourke, MD, MPH, FACS[h], Randall T. Brown, MD, PhD, DFASAM[i]

Abstract

Objective: To explore patient and treatment factors explaining the association between spine injury and opioid misuse.

Design: Prospective cohort study.

Setting: Level I trauma center in a Midwestern city.

Participants: English speaking patients aged 18 to 75 on Trauma and Orthopedic Surgical Services receiving opioids during hospitalization and prescribed at discharge.

Exposure: Spine injury on the Abbreviated Injury Scale.

Main outcome measures: Opioid misuse was defined by using opioids: in a larger dose, more often, or longer than prescribed; via a non-prescribed route; from someone other than a prescriber; and/or use of heroin or opium. Exploratory factor groups included demographic, psychiatric, pain, and treatment factors. Multivariable logistic regression estimated the association between spine injury and opioid misuse when adjusting for each factor group.

Results: Two hundred eighty-five eligible participants consented of which 258 had baseline injury location data and 224 had follow up opioid misuse data. Most participants were male (67.8%), white (85.3%) and on average 43.1 years old. One-quarter had a spine injury (25.2%). Of those completing follow-up measures, 14 (6.3%) developed misuse. Treatment factors (injury severity, intubation, and hospital length of stay) were significantly associated with spine injury. Spine injury significantly predicted opioid misuse [odds ratio [OR] 3.20, 95% confidence interval [CI] (1.05, 9.78)]. In multivariable models, adjusting for treatment factors attenuated the association between spine injury and opioid misuse, primarily explained by length of stay.

Conclusion: Spine injury exhibits a complex association with opioid misuse that predominantly operates through treatment factors. Spine injury patients may represent a subpopulation requiring early intervention to prevent opioid misuse.

Keywords: abbreviated injury scale, length of stay, opioid-related disorders, risk factors, spine

1. Introduction

Opioid medications are often used in acute care settings to treat moderate to severe pain resulting from trauma or surgical interventions. Such use of opioid pharmacotherapy is frequently justified to relieve suffering and address pain, which can have negative consequences on health and recovery. However, opioid

Level of Evidence: Prognostic, Level III.

Funding comes from the University of Wisconsin School of Medicine and Public Health from the Wisconsin Partnership Program (Grant ID 3152). Joseph Glass was supported by the National Institute on Alcohol Abuse and Alcoholism under award K01AA023859. The authors have no conflicts of interest to declare.

Presented as an oral abstract at the 2021 AMERSA National Conference (11/2021).

Registered at clinicaltrials.gov: #NCT02861976.

[a] Department of Family Medicine, Boston University/Boston Medical Center, Boston, MA, [b] Kaiser Permanente Washington Health Research Group, Seattle, WA, [c] Department of Biostatistics and Medical Informatics, University of Wisconsin School of Medicine and Public Health, [d] University of Wisconsin School of Medicine and Public Health, [e] Departments of Urology and Surgery, University of Wisconsin School of Medicine and Public Health, [f] Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison, WI, [g] Department of Surgery, Duke University, Durham, NC, [h] Department of Surgery, University of Wisconsin School of Medicine and Public Health, [i] Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison, WI.

[*] Corresponding author. Address: 771 Albany St., Dowling 5 South, Rm 5507A, Boston, MA 02118. Tel: +608 263 6558; cell: +609 468 1277; fax: +608 263 5813. E-mail address: alyssa.tilhou@bmc.org (Alyssa Shell Tilhou).

OTA (2022) e205

Received: 26 September 2021 / Accepted: 20 March 2022

Published online 12 July 2022

http://dx.doi.org/10.1097/OI9.0000000000000205

exposure through prescription medications creates an opportunity for the development of opioid misuse. In 2019, approximately 10.1 million people in the United States reported misusing prescription opioids,[1] and prescription opioids have contributed significantly to overdose deaths.[2]

Survivors of traumatic injury are at increased risk of prolonged opioid use, misuse and addiction.[3] Among adults admitted to the hospital with traumatic injury, as many as 50% receive an opioid prescription at discharge[4] and up to 35% are still on opioid medications at 4 months after injury.[5] Short term opioid prescribing after injury can lead to long term opioid use and dependence, with significant consequences for individual health and societal costs.[6–10] Recent research suggests the rate of opioid misuse and addiction after traumatic injury may be as high as 5%.[11] Identifying risk factors for prolonged opioid use and opioid misuse and addiction can help clinicians and health systems risk stratify patients as they develop treatment plans following traumatic injury.

Spine injury may represent a significant risk factor for the development of prolonged opioid use.[9,12,13] A high proportion of persons living with traumatic spine injury use chronic prescription opioids, and their likelihood of using chronic opioids is significantly higher than matched controls.[14,15] While traumatic injuries are associated with pre- and post-injury risk factors for opioid misuse, these risk factors have yet to be disentangled in observational studies.[5,8–10,13,16–24] Identifying why patients with spine injury have a higher incidence of opioid misuse could inform opioid misuse prevention.

This paper explores the ways in which spine injury may contribute to the development of opioid misuse. First, we estimate the association between spine injury and opioid misuse in a sample of Level 1 adult trauma patients. Second, in exploratory analyses we sequentially examine whether 4 exploratory factor groups explain the association between spine injury and opioid misuse: demographic characteristics, preexisting psychiatric conditions, pain indicators and treatment factors. In this way, we aim to elucidate the relationship between spine injury and opioid misuse, and indicate directions for future research.

2. Materials and methods

Data for this analysis come from the Screening in Trauma for Opioid Misuse Prevention (STOMP) study,[3] reviewed and approved by the University of Wisconsin's Health Sciences Institutional Review Board. STOMP is a prospective cohort study of victims of traumatic injury recruited at an American College of Surgeons Level I trauma center. The primary aims of the study were to collect data on risk factors for and the development of opioid misuse and addiction in order to develop a novel opioid risk screening tool for pilot implementation at American College of Surgeons Level I and II trauma centers in Wisconsin. STOMP was funded by the University of Wisconsin School of Medicine from the Wisconsin Partnership Program. The sponsor had no role in the design and conduct of the study, or in the decision to submit this article for publication. Additional details about the background and methodology of STOMP can be found in the published protocol paper.[3]

2.1. Participants

Participants (n = 295) were enrolled from the University of Wisconsin Hospital Emergency Department and Trauma and Orthopedic Surgery services from February 2017 to December 2018. Of these, 285 eligible participants gave informed consent. Eligibility criteria included: primary admission diagnosis of traumatic injury, age 18 to 75, fluency in English language, anticipated need for post-discharge opioid analgesia, and anticipated post-discharge self-management of medications. Exclusion criteria included active opioid use disorder (OUD), ongoing participation in a treatment program for another substance use disorder, cancer diagnosis, inability to consent due to incapacitating injury or sedation, or planned discharge to a facility of any kind where medications are managed by people other than the participant.

2.2. Data collection

Data was collected at baseline (during hospitalization or within 1 week of discharge) and at 3 follow-up points: 4, 12, and 24 weeks after hospital discharge. Collected information included sociodemographic and health characteristics hypothesized to impact risk of OUD as well as indicators of opioid misuse or OUD. Baseline data were collected in person. Follow-up data were collected via mail, in person and/or by telephone. Participants received financial compensation for completion of each visit. Additional administrative data were collected from the electronic health record and the UW Health Trauma Registry. Data were managed using REDCap electronic data capture tools hosted at the University of Wisconsin-Madison, Department of Family Medicine and Community Health.[25] REDCap (Research Electronic Data Capture) is a secure, web-based software platform designed to support data capture for research studies.

2.3. Measures

The presence of a spine injury was assessed using the Abbreviated Injury Scale, an anatomical injury coding system that classifies each individual injury by body region and severity.[26] Using the abbreviated injury scale (AIS) classification system, participants with spine injuries were identified by AIS codes beginning with the number 6.[27,28] Opioid misuse was assessed at the final follow-up visit at 24 weeks by staff-administered survey items. Participants were asked if they had used opioids since hospital discharge (1) in larger amounts than prescribed, (2) more often than prescribed, (3) for longer than prescribed, (4) when not prescribed, (5) via a different route than prescribed (crushed, chewed, snorted, smoked, or injected), or if they had used (6) heroin or (7) opium. A positive response to 1 or more of these 7 items was defined as opioid misuse (dichotomized as yes/no).

The exploratory measures in this study fall into 4 groups. (1) *Demographic factors:* Demographic data including age, sex, and race/ethnicity were collected at baseline. (2) *Psychiatric factors:* To assess for preexisting symptoms of anxiety, depression and post-traumatic stress disorder (PTSD), the following validated self-report instruments were collected at baseline: the Generalized Anxiety Disorder-7 (GAD-7),[29] a 7-item measure of generalized anxiety symptoms and severity; the Patient Health Questionnaire-9 (PHQ-9),[30] a 9-item measure of depression symptoms and severity; and the Post-Traumatic Stress Disorder Checklist-5 (PCL-5),[31] a 20-item measure of PTSD symptoms and severity. Scores from the GAD-7 and PHQ-9 were operationalized as continuous variables while the PCL-5 was converted to a dichotomous variable at ≥33 to indicate likelihood of PTSD.[31] (3) *Pain factors:* Perceived pain was

assessed using the Brief Pain Inventory[32,33] at study intake and hospital discharge. This 7-item scale asks respondents to rate their current, average, minimum and maximum pain severity from 0 to 10. Responses are then averaged to yield a single score. To assess catastrophizing, the Pain Catastrophizing Scale (PCS)[34] was used, which consists of 13 items divided into 3 subscales each representing a unique dimension. The PCS was dichotomized at ≥30, consistent with thresholds used in the literature to indicate a clinically meaningful level of catastrophizing.[34] (4) *Treatment factors:* Injury severity was assessed using the Injury Severity Score, calculated from AIS codes, and dichotomized at ≤15 and >15 to match the literature.[4,26,35] Intubation was evaluated as an alternative measure of severity, and dichotomized as yes/no ever intubated during the index hospitalization. Hospital length of stay was calculated and then transformed into a dichotomous variable (<7 or ≥7 days) due to moderate skew.

2.4. Statistical analysis

All analyses were conducted using R.[36] Demographic and baseline characteristics are summarized as mean (standard deviation) or N (%) for the full sample and by presence of a spine injury. Characteristics were compared between those with and without a spine injury using *t* tests, Chi-square tests, or Fisher exact tests. A bivariate generalized logistic model estimated the relationship between spine injury and opioid misuse. In a subsequent series of multivariable models (generalized logistic models), groups of factors (demographic, psychiatric conditions, pain, and treatment factors) were entered sequentially to determine the impact of adjusting for each factor group on the relationship between spine injury and opioid misuse.

2.5. Role of the funding source

This research was funded by the University of Wisconsin School of Medicine and Public Health from the Wisconsin Partnership Program, which played no role in the analysis of data, the writing of this article or its submission for publication. In its utilization of REDCap, this project was supported by the Clinical and Translational Science Award program, through the National Institutes of Health (NIH) National Center for Advancing Translational Sciences, grant UL1TR002373. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

3. Results

A total of 1785 patients were examined for eligibility, of which 561 were deemed eligible. Two hundred ninety-five participants enrolled of which 10 withdrew consent or were screened out leaving 285 participants. Some participants (n = 27) did not have data on injury location and, therefore, could not be assessed for spine injury. Of the remaining 258, 224 participants completed survey items on opioid misuse at 24-week follow-up. Descriptive characteristics and results of bivariate tests are presented in Table 1. A total of 65 (25.2%) participants had a spine injury. Of participants completing follow-up, 14 (6.3%) developed opioid misuse. The sample was mostly male (67.8%), white (85.3%) and in their mid-40s (average age 43.1). Mean score on the GAD-7 and PHQ-9 were 3.7 and 3.9, respectively. Just over 10% reported enough symptoms on the PCL-5 to suggest likely diagnosis of PTSD. As expected, mean Brief Pain Inventory score on intake was higher than at hospital discharge (6.5 vs 4.0). Only 6% of the sample reported high pain catastrophizing on the PCS. Participants with a hospital length of stay of 7 days or more represented 30.2% of the sample. Only 7.8% of the sample required intubation during the index hospitalization but 26.7% had an Injury Severity Score of >15.

Table 1

Characteristics of adult Level 1 trauma patients with and without spine injuries.

Factor	All N = 258	No spine N = 193 (74.8%)	Spine N = 65 (25.2%)	*P*
N (%) or m (SD)				
Sociodemographic factors				
Age	43.1 (16.2)	43.3 (16.2)	42.3 (16.3)	.650
Sex				
Male	175 (67.8)	126 (65.3)	49 (75.4)	.176
Female	83 (32.2)	67 (34.7)	16 (24.6)	
Race				
White	220 (85.3)	166 (86.0)	54 (83.1)	.764
People of color	35 (13.6)	25 (13.0)	10 (15.4)	
Psychiatric factors				
GAD7	3.7 (4.8)	3.7 (4.5)	3.6 (5.4)	.804
PHQ	3.9 (4.6)	3.9 (4.4)	3.7 (5.2)	.779
PCL5				
<33	228 (88.4)	172 (89.1)	56 (86.2)	.734
≥33	27 (10.5)	19 (9.8)	8 (12.3)	
Pain factors				
BPI Intake	6.5 (2.5)	6.5 (2.5)	6.5 (2.5)	.988
BPI discharge	4.0 (2.4)	4.2 (2.3)	3.6 (2.4)	.134
Pain catastrophizing				
<30	241 (93.4)	180 (93.3)	61 (93.8)	1.000
≥30	16 (6.2)	12 (6.2)	4 (6.2)	
Treatment factors				
Length of stay				
<7	180 (69.8)	148 (76.7)	32 (49.2)	<.001
≥7	78 (30.2)	45 (23.3)	33 (50.8)	
Injury severity score				
≤15	189 (73.3)	159 (82.4)	30 (46.2)	<.001
>15	69 (26.7)	34 (17.6)	35 (53.8)	
Intubated				
no	238 (92.2)	183 (94.8)	55 (84.6)	.017
yes	20 (7.8)	10 (5.2)	10 (15.4)	
Opioid misuse at 24 weeks*				
No	210 (81.4)	160 (82.9)	50 (76.9)	.037
Yes	14 (5.4)	7 (3.6)	7 (10.8)	

BPI = Brief Pain Inventory; GAD7 = Generalized Anxiety Disorder-7; PCL5 = Post-Traumatic Stress Disorder Checklist-5; PHQ9 = Patient Health Questionnaire-9; SD = standard deviation.
* Thirty-four respondents did not have follow-up data on opioid misuse.

No demographic characteristics, pain factors or psychiatric comorbidities differed between participants with and without spine injury (Table 1). All 3 treatment factors exhibited a significant relationship with spine injury in bivariate analyses. Over 50% of patients with spine injuries experienced a long length of stay compared with less than 1-quarter of those without spine injuries (50.8% vs 23.3% with length of stay ≥7 days, $P < .001$). Participants with spine injuries also exhibited a greater percentage of high Injury Severity Scores compared with those without spine injuries (53.8% vs 17.6% with injury severity >15, $P < .001$). Finally, patients with spine injury were more likely to be intubated compared with patients without spine injuries (15.4% vs 5.2%, $P = .017$).

The results of multivariable logistic regression predicting opioid misuse are presented in Table 2. Model 1 shows the

Table 2

Multivariable regression models exploring the sequential effect of 4 factor groups on the association between spine injury and opioid misuse.

Factors	Model 1: Spine only OR (95% CI)	Model 2: Demographic factors OR (95% CI)	Model 3: Psychiatric factors OR (95% CI)	Model 4: Pain factors OR (95% CI)	Model 5: Treatment factors OR (95% CI)
Spine injury	3.20 (1.05,9.78)*	3.20 (0.95,10.89)	4.23 (1.14,16.78)*	3.36 (1.05,10.82)*	2.50 (0.73,8.59)
Sociodemographic					
Age		1.00 (0.96,1.04)			
Female		0.71 (0.17,2.49)			
People of color		11.20 (3.42,39.28)***			
Psychiatric					
GAD7			0.79 (0.62,.97)*		
PHQ9			1.37 (1.14,1.69)**		
PCL5 ≥ 33			9.25 (1.66,55.17)*		
Pain					
BPI intake				1.27 (0.97,1.76)	
BPI discharge				1.19 (0.93,1.55)	
PCS ≥ 30				2.71 (0.48,11.96)	
Treatment					
Length of stay ≥7					2.78 (0.83,9.53)
ISS>15					0.85 (0.22,2.97)
Intubated					1.04 (0.14,5.21)

BPI = Brief Pain Inventory; GAD7 = Generalized Anxiety Disorder-7; ISS = Injury Severity Score; PCL5 = Post-Traumatic Stress Disorder Checklist-5; PCS = Pain Catastrophizing Scale; PHQ9 = Patient Health Questionnaire-9.

* $P < .05$.

** $P < .01$.

*** $P < .001$.

baseline relationship between spine injury and opioid misuse. Spine injury significantly increased the odds of having opioid misuse (odds ratio [OR] 3.20, 95% confidence interval [CI]: 1.05–9.78; $P = .037$). Models 2 to 4 sequentially introduced the 4 exploratory factor groups into the baseline model to test for attenuation of the effect of spine injury on opioid misuse. Model 2 results show that adding demographic factors did attenuate the effect of spine on misuse. However, the odds ratio of spine injury remained stable, suggesting that the attenuation was due to a decrease in power in a model with additional covariates rather than an explanatory role for race in the spine-misuse relationship.

Models 3 and 4 introduced psychiatric and pain factors, respectively. While a higher score on the GAD7, PHQ9, and PCL5 was associated with higher odds of misuse, adding these factors did not attenuate the effect of spine on opioid misuse. In contrast, adding pain factors did not predict misuse nor attenuate the spine-misuse relationship.

Finally, Model 5 incorporated treatment factors into the base spine-misuse model, which eliminated the statistically significant effect of spine injury on opioid misuse. Further analyses examined the individual impact of each treatment factor on the relationship between spine injury and opioid misuse. Adjusting for either intubation or injury severity only modestly attenuated the spine-misuse relationship, and neither factor alone predicted opioid misuse. In contrast, adjusting for length of stay substantially attenuated the spine-misuse relationship, and alone significantly predicted opioid misuse (OR 3.49, 95% CI:1.17, 11.03; $P = .026$).

4. Discussion

In a prospective cohort of adult victims of traumatic injury, spine injury increased the likelihood of developing opioid misuse at 24-week follow-up. Subsequently, we examined whether 4 exploratory factor groups explained the higher rates of opioid misuse among patients with traumatic spine injury. These multivariable regression models demonstrated that the difference in rates of opioid misuse between patients with and without spine injury was explained by treatment factors but not demographic factors, preexisting psychiatric conditions or pain measures. These findings suggest that the origins of opioid misuse for patients with spine injury may lie in the early treatment period following traumatic injury.

Further interpretation of these findings requires consideration of the individual treatment factors examined in this study: Injury Severity Score, hospital length of stay and intubation. We found that patients with spine injuries were more likely to have a long length of stay, a high Injury Severity Score and to be intubated compared with patients without spine injuries, and that these factors explained the spine-misuse relationship. These 3 factors align to suggest that patients with spine injuries experienced more severe injuries than those without spine injuries, and, therefore, that injury severity may explain the increased rates of opioid misuse among patients with spine injury. However, when evaluating their individual effects, we found that hospital length of stay explained substantially more of the spine-misuse relationship than injury severity or intubation. Furthermore, neither intubation nor injury severity alone predicted opioid misuse. One possible explanation is that these 3 factors—length of stay, Injury Severity Score and intubation—represent different aspects of related phenomena. For example, intubation may represent global criticalness of injury while the Injury Severity Score may represent the severity of coincident non-spine injuries or global injury burden. Beyond severity, hospital length of stay may reflect care complexity or logistical complexity (with regards to disposition after discharge). Longer length of stay could also increase exposure to intravenous and/or high potency opioids thereby creating a unique risk factor for opioid misuse. Additional research is needed to explore the pathways by which early treatment elements impact risk of opioid misuse and

addiction. In this vein, understanding the impact of distinct treatment elements by spine injury type will be important.

In line with prior literature, we found that preexisting symptoms of psychiatric conditions including anxiety, depression and PTSD predicted risk of opioid misuse.[19,37–39] However, these diagnoses did not explain the spine-misuse relationship suggesting that increased risk of opioid misuse among spine injury patients is not due to underlying psychological vulnerability.

Interestingly, measures of pain and pain catastrophizing did not predict risk of opioid misuse. Furthermore, they did not explain the spine-misuse relationship. These findings align with literature suggesting that pain severity does not predict opioid misuse[20] despite contributing to prolonged opioid use.[5,40] The irrelevance of pain to the spine-misuse relationship may also reflect the unique nature of pain associated with spine injuries: limited evidence demonstrates efficacy of opioid medications in treating neuropathic pain disorders.[41] Alternatively, our data only assessed pain and pain catastrophizing during the index hospitalization, while understanding the relationship between pain and substance misuse may require attention to the more complex and longitudinal nature of pain trajectories after trauma.

While other research has demonstrated associations between demographic characteristics, like age and sex, and traumatic injury[22,23] and prolonged opioid use,[9,13,21,42] we found that these factors did not predict opioid misuse or explain the spine-misuse relationship. One explanation might be that pathways to misuse vary more than risk across these groups. For example, age may operate through prolonged use in older patients[9,21] but prior substance use in younger patients.[43] Being of color did predict opioid misuse, but did not explain the spine-misuse relationship. However, our data are limited by the small sample size of participants of color. Given well-documented racial disparities in access to adequate pain treatment[44] and OUD addiction services,[45] it is important that future research examine how opioid misuse develops after traumatic injury in communities of color.

An important limitation of this study is the low event rate of developing opioid misuse. Inadequate variation in opioid misuse across the exploratory factors of interest could disguise their true relationship. The low event rate also limited our ability to build more complex models to control for potential confounders. In particular, we were not able to control for, or investigate, medical comorbidity. A second limitation pertains to misuse measurement. This study relied on self-reported opioid misuse, which could have contributed to underreporting.[46] However, self-report via timeline follow-back has been shown to be an acceptable method for assessing illicit substance use in clinical research, including for opiates, specifically.[47] Additional research is needed to assess the validity of self-reported prescribed and illicit opioid misuse. Third, we do not distinguish between specific spine injury types such as spinal cord injuries, bony fractures, or contusions, among others. Understanding how and why spine injuries impact risk of opioid misuse may require further spine injury characterization. Fourth, a substantial proportion of eligible patients did not participate in the study. It is possible that risk factors for misuse operate differently among individuals who choose not to participate in research studies. Finally, analyses were limited by missing baseline data on body injury location and missing follow up data on opioid misuse. However, STOMP's prospective cohort design represents a unique strength in this field. Results from this study should be taken as preliminary, and future research should aim to replicate these findings in other samples to confirm the associations observed here.

While opioid medications offer potent and effective means of controlling pain following traumatic injury, opioid misuse and addiction pose a national health crisis that continues to rise.[48] It is critical that we better understand risk factors for misuse in settings where exposure to opioids is often required, such as after traumatic injury. This study demonstrates that traumatic spine injury may increase risk for opioid misuse. In this way, injury body region may offer a novel lens through which to risk stratify patient populations and deliver targeted interventions to prevent opioid misuse. Furthermore, features of the early treatment period captured by hospital length of stay explain the higher rate of opioid misuse in this patient population. These findings suggest that the origins of opioid misuse may lie in the early treatment period for patients with spine injury. These exploratory findings call for additional research on the way management of spine injuries may translate into risk of opioid misuse. Confirming the role of treatment-related factors could provide an exciting opportunity for hospital systems to mitigate risk for opioid misuse while the patient is still in acute care.

Acknowledgments

The authors would like to extend thanks to the Trauma and Orthopedic clinical teams at University of Wisconsin Hospital including Kelly Laishes advanced practice nurse prescriber (APNP), Amy Stacy APNP, Tatum Curry APNP, Jen Yeager NP, Shea Lues APNP, and Kimberly Williams NP. Rebecca Turpin MA, Injury Prevention Coordinator at UW Hospital, assisted in communications and study implementation.

References

1. What is the U.S. Opioid Epidemic? [Internet]. U.S. Department of Health and Human Services. Available at: https://www.hhs.gov/opioids/about-the-epidemic/index.html. Accessed March 5, 2021.
2. Compton WM, Jones CM, Baldwin GT. Relationship between nonmedical prescription-opioid use and heroin use. *N Engl J Med* 2016; 374:154–163.
3. Brown R, Deyo B, Riley C, et al. Screening in Trauma for Opioid Misuse Prevention (STOMP): study protocol for the development of an opioid risk screening tool for victims of injury. *Addict Sci Clin Pract* 2017; 12:1–9.
4. Chaudhary MA, Schoenfeld AJ, Harlow AF, et al. Incidence and predictors of opioid prescription at discharge after traumatic injury. *JAMA Surg* 2017; 152:930–936.
5. Rosenbloom BN, McCartney CJ, Canzian S, et al. Predictors of prescription opioid use 4 months after traumatic musculoskeletal injury and corrective surgery: a prospective study. *J Pain* 2017; 18:956–963.
6. Lawal OD, Gold J, Murthy A, et al. Rate and risk factors associated with prolonged opioid use after surgery: a systematic review and meta-analysis. *JAMA Netw Open* 2020; 3:e207367–e1207367.
7. Levy N, Quinlan J, El-Boghdadly K, et al. An international multidisciplinary consensus statement on the prevention of opioid-related harm in adult surgical patients. *Anaesthesia* 2020; 76:520–536.
8. Mohamadi A, Chan JJ, Lian J, et al. Risk factors and pooled rate of prolonged opioid use following trauma or surgery: a systematic review and meta-(regression) analysis. *JBJS* 2018; 100:1332–1340.
9. Von Oelreich E, Eriksson M, Brattström O, et al. Risk factors and outcomes of chronic opioid use following trauma. *J Br Surg* 2020; 107:413–421.
10. Beyer CA, Poltavskiy E, Walker LE, et al. Persistent opioid use after combat injury and subsequent long-term risk of abuse: a retrospective cohort study. *Ann Surg* 2019; 274:e957–e965.
11. Brown R, Deyo B, Nicholas C, et al. Screening in Trauma for Opioid Misuse Prevention (STOMP): Results from a prospective cohort of victims of traumatic injury. *Drug Alcohol Depend* 2022; 109286.
12. Schoenfeld AJ, Jiang W, Chaudhary MA, et al. Sustained prescription opioid use among previously opioid-naive patients insured through TRICARE (2006-2014). *JAMA Surg* 2017; 152:1175–1176.
13. Daoust R, Paquet J, Moore L, et al. Incidence and risk factors of long-term opioid use in elderly trauma patients. *Ann Surg* 2018; 268:985–991.
14. Guilcher SJ, Hogan M-E, Guan Q, et al. Prevalence of prescribed opioid claims among persons with traumatic spinal cord injury in Ontario,

Canada: a population-based retrospective cohort study. *Arch Phys Med Rehabil* 2021; 102:35–43.
15. Hand BN, Krause JS, Simpson KN. Dose and duration of opioid use in propensity score–matched, privately insured opioid users with and without spinal cord injury. *Arch Phys Med Rehabil* 2018; 99:855–861.
16. Zwisler ST, Hallas J, Larsen MS, et al. Opioid prescriptions before and after high-energy trauma. *J Opioid Manag* 2015; 11:313–318.
17. Harvin JA, Green CE, Allen L, et al. Opioid exposure after injury in United States trauma centers: a prospective, multicenter observational study. *J Trauma Acute Care Surg* 2020; 88:816–824.
18. Armaghani SJ, Lee DS, Bible JE, et al. Preoperative opioid use and its association with perioperative opioid demand and postoperative opioid independence in patients undergoing spine surgery. *Spine* 2014; 39: E1524–E1530.
19. Schoenfeld AJ, Nwosu K, Jiang W, et al. Risk factors for prolonged opioid use following spine surgery, and the association with surgical intensity, among opioid-naive patients. *JBJS* 2017; 99:1247–1252.
20. Turk DC, Swanson KS, Gatchel RJ. Predicting opioid misuse by chronic pain patients: a systematic review and literature synthesis. *Clin J Pain* 2008; 24:497–508.
21. Riva JJ, Noor ST, Wang L, et al. Predictors of prolonged opioid use after initial prescription for acute musculoskeletal injuries in adults: a systematic review and meta-analysis of observational studies. *Ann Intern Med* 2020; 173:721–729.
22. DiMaggio C, Ayoung-Chee P, Shinseki M, et al. Traumatic injury in the United States: in-patient epidemiology 2000-2011. *Injury* 2016; 47:1393–1403.
23. Hasler RM, Exadaktylos AK, Bouamra O, et al. Epidemiology and predictors of cervical spine injury in adult major trauma patients: a multicenter cohort study. *J Trauma Acute Care Surg* 2012; 72:975–981.
24. Berecki-Gisolf J, Collie A, McClure RJ. Prescription opioids for occupational injury: results from workers' compensation claims records. *Pain Med* 2014; 15:1549–1557.
25. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009; 42:377–381.
26. Palmer CS, Gabbe BJ, Cameron PA. Defining major trauma using the 2008 Abbreviated Injury Scale. *Injury* 2016; 47:109–115.
27. Doud AN, Weaver AA, Talton JW, et al. Has the incidence of thoracolumbar spine injuries increased in the United States from 1998 to 2011? *Clin Orthop Relat Res* 2015; 473:297–304.
28. Tafida MA, Wagatsuma Y, Ma E, et al. Descriptive epidemiology of traumatic spinal injury in Japan. *J Orthop Sci* 2018; 23:273–276.
29. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006; 166:1092–1097.
30. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med* 2001; 16:606–613.
31. VISN 4 MIRECC. PCL-5 Assessment Resources [Internet]. Available at: https://www.mirecc.va.gov/cih-visn2/Documents/Clinical/PCL-5_with_Info_Sheet.pdf. Accessed April 14, 2021.
32. Cleeland CS, Ryan KM. Pain assessment: global use of the Brief Pain Inventory. *Ann Acad Med Singap* 1994; 23:129–138.
33. Archer KR, Castillo RC, Wegener ST, et al. Pain and satisfaction in hospitalized trauma patients: the importance of self-efficacy and psychological distress. *J Trauma Acute Care Surg* 2012; 72:1068–1077.
34. Sullivan MJ, Bishop SR, Pivik J. The pain catastrophizing scale: development and validation. *Psychol Assess* 1995; 7:524.
35. Baker SP, O'Neill B, Haddon WJr, et al. The injury severity score: a method for describing patients with multiple injuries and evaluating emergency care. *J Trauma Acute Care Surg* 1974; 14:187–196.
36. Team RC. R Core Team (2017). R: A language and environment for statistical computing. R Found Stat Comput Vienna Austria. 2017. https://www.R-project.org/
37. Hassan AN, Le Foll B, Imtiaz S, et al. The effect of post-traumatic stress disorder on the risk of developing prescription opioid use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. *Drug Alcohol Depend* 2017; 179:260–266.
38. Armaghani SJ, Lee DS, Bible JE, et al. Preoperative narcotic use and its relation to depression and anxiety in patients undergoing spine surgery. *Spine* 2013; 38:2196–2200.
39. Sullivan MD. Depression effects on long-term prescription opioid use, abuse, and addiction. *Clin J Pain* 2018; 34:878–884.
40. Clarke H, Soneji N, Ko DT, et al. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ* 2014; 348:g1251.
41. McNicol ED, Midbari A, Eisenberg E. Opioids for neuropathic pain. *Cochrane Database Syst Rev* 2013; 8:(CD006146.
42. Dong XS, Brooks RD, Cain CT. Prescription opioid use and associated factors among US construction workers. *Am J Ind Med* 2020; 63:868–877.
43. Schrager SM, Kecojevic A, Silva K, et al. Correlates and consequences of opioid misuse among high-risk young adults. *J Addict* 2014; 2014:156954.
44. Meghani SH, Byun E, Gallagher RM. Time to take stock: a meta-analysis and systematic review of analgesic treatment disparities for pain in the United States. *Pain Med* 2012; 13:150–174.
45. Hadland SE, Wharam JF, Schuster MA, et al. Trends in receipt of buprenorphine and naltrexone for opioid use disorder among adolescents and young adults, 2001-2014. *JAMA Pediatr* 2017; 171:747–755.
46. Clark CB, Zyambo CM, Li Y, et al. The impact of non-concordant self-report of substance use in clinical trials research. *Addict Behav* 2016; 58:74–79.
47. Hjorthøj CR, Hjorthøj AR, Nordentoft M. Validity of timeline follow-back for self-reported use of cannabis and other illicit substances—systematic review and meta-analysis. *Addict Behav* 2012; 37:225–233.
48. Baumgartner J, Radley D. The Spike in Drug Overdose Deaths During the COVID-19 Pandemic and Policy Options to Move Forward [Internet]. To the Point. 2021 [cited 2021 Apr 30]. Available at: https://www.commonwealthfund.org/blog/2021/spike-drug-overdose-deaths-during-covid-19-pandemic-and-policy-options-move-forward. Accessed April 30, 2021.