Annals of Surgery

DOI: 10.1097/SLA.0000000000004769

Outpatient Opioid Prescriptions are Associated with Future Substance Use Disorders and Overdose Following Adolescent Trauma

Teresa M. Bell, PhD[1,2], Jodi L. Raymond, MPH[3], Alejandro C. Mongalo, MS[4], Zachary W. Adams, PhD[5], Thomas M. Rouse, MD[3,4], LeRanna Hatcher, MD[6], Katie Russell, MD[1,2], and Aaron E. Carroll, MD[3,7]

1. University of Utah, School of Medicine, Department of Surgery, 30 N 1900 E, Room 2C340, Salt Lake City, Ut 84121
2. Intermountain Primary Children's Hospital, 100 N Mario Capecchi Dr, Salt Lake City, UT 84113
3. Indiana University Health Riley Hospital for Children, Indianapolis, IN 46202
4. Indiana University School of Medicine, Department of Surgery, 410 W 10th St, Suite 2000A, Indianapolis, IN 46202, USA
5. Indiana University School of Medicine, Department of Psychiatry, 410 W 10th St, Suite 2000A, Indianapolis, IN 46202, USA
6. Mayo Clinic College of Medicine and Science, Department of Anesthesiology, 200 First St SW, Rochester, MN 55905
7. Indiana University School of Medicine, Department of Pediatrics, 410 W 10th St, Suite 2000A, Indianapolis, IN 46202, USA

Corresponding Author:

Teresa Bell, Ph.D.

30 N 1900 E, Room 2C340

Salt Lake City 84121

Teresa.Bell@hsc.utah.edu

(317) 778-0012

Sources of Support: This study was supported by the following awards: NIH NCATS KL2 TR001106; NIH NCATS KL2 TR002530; NIH NCATS UL1 TR002529; NIH NICHD R21 HD097452; and the Indiana University Grand Challenges Program.

Conflicts of Interest: No conflicts of interest were declared by the authors.

MINI ABSTRACT

This retrospective cohort study examined 5 years of a regional health information exchange data to assess the relationship between post-discharge outpatient opioid prescriptions and future substance use disorders or overdoses in injured adolescents. Short-term prescribing was associated with new substance use disorder diagnoses, while long-term prescribing was associated with future overdoses.

STRUCTURED ABSTRACT

OBJECTIVE: This study aims to determine if outpatient opioid prescriptions are associated with future substance use disorder (SUD) diagnoses and overdose in injured adolescents five years following hospital discharge.

SUMMARY BACKGROUND DATA: Approximately, 1 in 8 adolescents are diagnosed with an SUD and 1 in 10 experience an overdose in the five years following injury. State laws have become more restrictive on opioid prescribing by acute care providers for treating pain, however, prescriptions from other outpatient providers are still often obtained.

METHODS: This was a retrospective cohort study of patients ages 12-18 admitted to two level I trauma centers. Demographic and clinical data contained in trauma registries were linked to a regional database containing five years of electronic health records and prescription data. Regression models assessed whether number of outpatient opioid prescription fills after discharge at different time points in recovery were associated with a new SUD diagnosis or overdose, while controlling for demographic and injury characteristics, as well as depression and PTSD diagnoses.

RESULTS: We linked 669 patients (90.9%) from trauma registries to a regional health information exchange database. Each prescription opioid refill in the first 3 months after discharge increased the likelihood of new SUD diagnoses by 55% (OR:1.55, CI:1.04-2.32). Odds of overdose increased with ongoing opioid use over 2-4 years post-discharge (p=0.016-0.025).

CONCLUSIONS: Short-term outpatient opioid prescribing over the first few months of recovery had the largest effect on developing an SUD, while long-term prescription use over multiple years was associated with a future overdose.

INTRODUCTION

Exposure to opioids during adolescence is a significant risk factor for developing a future substance use disorder (SUD).[1] During this critical period of development, adolescents are more likely to both try opioids nonmedically for the first time and are at the peak risk for becoming dependent on opioids between ages 14 and 16.[2-4] An injury or surgical procedure, which often involves both physical and psychological recovery, is frequently an adolescent patient's first exposure to opioids.[5-7] Additionally, studies have shown that injured adolescents are 56% more likely than uninjured adolescents to develop an SUD within 3 years of their injury.[8] Further, 1 in 8 adolescents hospitalized for injury are diagnosed with an SUD and 1 in 10 experience an overdose (OD) within 5 years of their injury.[9] This indicates that the adolescent trauma population is more vulnerable to SUD, however, it is uncertain whether this is due to exposure to trauma itself, how the injury is managed, or an inherent difference between the population of adolescents who sustain injuries and those who do not.

The link between developing an SUD and outpatient opioid prescribing following traumatic injury has not been established in the adolescent population. Prior studies have reported that 1 in 8 adolescents were still using prescription opioids 12 months after hospital discharge for injury.[9] Opioids are often prescribed by an emergency medicine physician or surgeon with the goal of short-term pain management.[10-13] However, acute care providers may be unaware when patients request additional opioid prescriptions from outpatient providers.[14] Further, providers may not know if a patient needs additional assessment and referral to treat ongoing psychological effects of injury.[15] Focusing on short-term pain management and physical functioning by acute care providers, who are most knowledgeable about a patient's injury, may make adolescents susceptible to requesting or inappropriately obtaining unnecessary pain medication from other providers or family members and misusing opioids to manage psychological symptoms of trauma, such as sleep disturbances or anxiety, which are prevalent after injury.[8,16-20]

This study aims to determine if outpatient opioid prescriptions are associated with future SUD diagnosis or OD in the 5-year period following hospital discharge. Understanding the association between opioid prescribing after injury and SUD development is important in that providers can modify how pain is treated post-discharge, both through prescribing and communication with outpatient providers who provide ongoing care.

METHODS

Data Source

This retrospective study was approved by the Indiana University Institutional Review Board prior to data acquisition. Our cohort consisted of 736 patients ages 12-18 admitted for trauma from 2011-2013. Two trauma centers contributed data, including the only level 1 pediatric trauma center in the state as well as an adult level 1 center. We examined up to 5 years of regional health information exchange records containing data on prescription drug and health service utilization (minimum length of follow-up was 53 months and 78% of the sample had complete 5 year follow-up). Demographic and clinical data contained in the trauma registries were linked to the Regenstrief Institute's Indiana Network for Patient Care (INPC), which

contains data on prescription fills and healthcare encounters across the state.[21,22] ICD-9 and 10 codes associated with inpatient, outpatient, and emergency department encounters were used to collect diagnosis information on patients for up to five years following hospital discharge for injury. The INPC contains prescription data filled by hospital pharmacies as well as from Surescripts, which includes data on prescriptions filled by major pharmacy chains such as Walgreens, CVS, and Rite Aid, among others.[23]

Variables

The primary independent variable was total number of outpatient opioid prescriptions filled post injury. Prescriptions filled by hospital pharmacies that were designated as outpatient as well as prescriptions filled by commercial pharmacies were categorized as outpatient prescriptions. The primary outcome variables were substance use disorder (SUD) and overdose (OD) diagnoses. We also examined mental health diagnoses including depression, anxiety, and PTSD. Diagnoses were based on ICD-9 and 10 codes associated with inpatient, outpatient, and emergency department encounters during the follow-up period. Due to data restrictions in the INPC research database, procedure and psychiatric diagnosis codes are not always linked to specific encounters. This is due to the fact that some health systems that contribute data do not allow for identifiers such as dates to be released for research purposes or mental health treatment data, which has additional privacy protections. In order to obtain this information, Regenstrief data brokers flagged cases with new onset mental health diagnoses post-discharge, although we did not have information on date of diagnosis or setting. They also included subsequent surgical procedures as a dichotomous variable for cases. Finally, we included demographic and injury data from the trauma registries including age, race, insurance status, rural/urban county of residence, injury severity score (classified as less than 15 or over 15), and injury mechanism (blunt, penetrating, or other). (**Figure 1**)

Analysis

Descriptive statistics of means and frequencies were calculated for demographic, outpatient prescription, and diagnostic outcomes of the cohort. We compared the mean number of outpatient opioid prescriptions in patients with and without diagnoses for SUD, OD, depression, PTSD, anxiety, and chronic pain using t-tests and ANOVA. In variables with more than one level, Bonferroni adjustments were applied and pairwise comparisons were made. All tests were two-sided and alpha was set and 0.05.

We used multivariable logistic regression to determine the odds of being diagnosed with SUD or OD based on the number of outpatient opioid prescriptions filled at 3, 6, 12, 24, 36, and 48 months. Separate models examining the total number of outpatient opioid prescriptions up to each time point were created. This allowed us to compare how the frequency and duration of opioid prescribing influenced SUD and OD outcomes. Models adjusted for age, race, injury severity, injury mechanism, insurance status, and residing in a rural or urban county at the time of injury. The models also included whether the patient underwent any surgical procedure or was diagnosed with depression or PTSD in the 5 years following discharge after hospitalization for injury. A diagnosis was considered present if at any point the patient had received a new diagnosis during the follow-up period, regardless of whether the model was examining the effects of opioid prescriptions at a shorter time point.

RESULTS

A total of 736 patients ages 12 to 18 who were admitted for trauma from 2011-2013 and discharged from the trauma service line alive were initially included in our cohort. The cohort has been described in previous publications.[9] Overall patients were predominantly white (70.5%), male (74.2%), were privately insured (43.8%), and lived in urban counties (58.4%). Approximately 85% of patients had an injury severity score below 15 and 18.1% experienced penetrating trauma. Over half of patients had a hospital length of stay of two days or more (53.8%) and 83.6% were discharged home with no services. (**Table 1**)

Prior to linking the cohort to the regional health information exchange, we further examined the data and excluded 23 patients who died after being discharged to another inpatient service line. We were able to link 669 patients (93.8%) to prescription drug data in the INPC, with 82.2% having data on opioid and/or non-opioid outpatient prescriptions (82 patients only had inpatient pharmacy prescription data from their initial hospitalization). This resulted in a final sample size of 587 patients. In the first month after discharge, 95.1% of patients filled at least 1 outpatient opioid prescription and 27.1% of patients received 2 or more opioid fills in the first three months after hospital discharge. Only 3.2% of patients had no outpatient opioid fills in the first three months after discharge. In the years following injury, approximately 35%, 17%, 15%, and 13% had 2 or more new outpatient opioid prescriptions per year (at 12, 24, 36, and 48 months). Only injury severity was associated with a greater mean number of opioid fills across the study period. (**Table 2**)

In a previous paper, we reported that 13.8% of patients had a diagnosis for substance use disorder in the 5 years following their injury.[9] Additionally, 7.6% had a diagnosis for overdose and 10.8% received an opioid antagonist injection during an emergency department encounter. We also found that approximately 6%, 2%, 11%, and 4% were diagnosed with depression, PTSD, anxiety, and chronic pain, respectively.[9] Approximately 2.2% of patients had a pre-existing diagnosis for either SUD, anxiety, depression, or PTSD. Patients with pre-existing diagnoses were still flagged as developing a new onset mental health condition if they received a diagnosis for a condition they did not have prior to injury. Patients with post-injury onset SUD, OD, and chronic pain diagnoses had a higher mean number of outpatient opioid prescriptions at nearly all time points. Patients with a new diagnosis of depression had a higher number of opioid prescriptions in the first three months after discharge, whereas patients with PTSD had a higher number of opioid fills at 6 and 12 months after discharge. Patients with post-injury anxiety diagnoses had a higher mean number of outpatient opioid fills at 6, 12, and 48 months. (**Table 3**)

Logistic regression analyses examined whether the total number of outpatient opioid prescriptions were predictive of SUD and OD outcomes. Separate models were run for each outcome examining the effect of total outpatient prescription opioid fills at 3, 6, 12, 36, and 48 months, while controlling for age, gender, race, insurance status, ISS, injury mechanism, rural/urban county of residence, and whether the patient had surgery. SUD models' c statistics ranged from 0.782-0.792 and the OD models' c statistics ranged from 0.841-0.854. Each prescription opioid fill in the first 3 months after discharge increased the likelihood of SUD diagnosis by 55% (OR:1.55, CI:1.04-2.32). Total opioid fills at 6 and 12 months were

not associated with SUD, however total fills at 24, 36, and 48 months increased the likelihood of SUD diagnosis (p=0.065, 0.066, <0.001, <0.001, and 0.004, respectively). Odds of OD were increased with each opioid refill at 24, 36, and 48 months (OR: 1.43, CI:1.07-1.90; OR:1.32, CI:1.05-1.66; and OR:1.19, CI:1.02-1.38, respectively). There was no association between outpatient opioid fills at 3 or 12 months. (**Figure 2**) Our models found several significant factors across SUD models and overdose models. For SUD specifically, we found undergoing additional surgery (OR 2.22-2.32, p 0.003-0.005), lower ISS score (OR 2.68-2.96, p 0.024-0.033), and living in a metro county (OR 2.37-2.46, p 0.008-0.010) increased the likelihood of SUD in all models (lowest and highest OR and p values indicated). Younger age at the time of injury (OR 0.47-0.48, p 0.01 all models) and being female (OR 0.42-0.48, p 0.021-.0.039) decreased the likelihood of SUD. PTSD (OR 4.97-5.89, p 0.020-0.031) and depression (OR 3.37-3.72, p 0.004-0.008) both increased the likelihood of SUD in all models. Race and insurance type were not associated with SUD outcomes in any model after controlling for rural/metro county. In the overdose models, surgery (OR 4.42-4.48, p <0.001 in all models), metro county (OR 2.56-2.77, p 0.047-0.051), and depression (OR 4.03-4.55, p 0.003-0.006) increased the likelihood of overdose. Younger age decreased the likelihood of overdose (OR 0.43-0.45, p 0.04-0.05). Race, gender, injury severity, insurance type, and PTSD were not significantly associated with overdose.

Because patients who underwent additional surgery had a consistently higher likelihood of developing an SUD, we performed subgroup analyses on surgical and non-surgical patients. Because of the decrease in sample size, we controlled for race, gender, age, county, and injury severity in each model. We found that a higher number of outpatient opioid prescriptions increased the likelihood of SUD in non-surgical patients, but had no effect in surgical patients. (**Table 4**).

DISCUSSION

Our study found that the number of outpatient opioid prescriptions filled during an adolescent's acute recovery period from injury is predictive of developing a substance use disorder. In the first three months after injury, each additional outpatient opioid prescription increased the risk of developing an SUD by 55%. We also found that adolescent patients who fill prescription opioids for multiple years are more likely to experience an overdose. This is consistent with previous literature indicating that there is evidence of a dose response in adolescents, where taking 40 or more nonmedical opioid doses increases the likelihood of using heroin by 8700%.[24,25] A single exposure to an opioid can elicit changes in the brain and 30 days of continuous opioid use has been shown to result in permanent brain changes.[26] Therefore, limiting prescribing to reduce prescription misuse and nonmedical use in injured adolescents may be one way to reduce SUD in this high risk trauma subpopulation.

Studies in adults have indicated that the probability of refilling prescription opioids is not correlated to the amount and strength of opioids initially prescribed after surgery.[27] However, prolonged opioid use has been shown to be associated with other patient factors, such as younger age, lower income, chronic pain, and mental illness.[28-31] Additionally, most adolescents using opioids nonmedically report first being prescribed opioids by a doctor.[32] This suggests that a substance use disorder may develop after initially being treated for an injury, however, psychosocial factors and management of trauma post-discharge can likely increase or decrease the risk of developing an SUD.[33,34]

Considering most state laws have reduced the amount of opioids that can be prescribed by acute care providers, their role in reducing substance use in adolescent patients may go beyond limiting opioid prescriptions.[35] For example, improving the transfer of information around a patient's injury severity and recovery time, expected amounts of pain medication that should be needed, and education on the importance of assessing psychological effects of injury may help caregivers and other outpatient providers deliver better care to adolescents after trauma and reduce their risk of substance use disorder.[36] Additionally, post-discharge efforts to improve surveillance of substance disorders, PTSD, and depression in trauma centers has grown recently.[37,38] Improving the care transition of adolescent trauma patients by screening for psychological symptoms of trauma, educating their family members on appropriate pain medication usage, and connecting them to mental health providers or center-based interventions could also improve the long-term outcomes of patients.[39]

A major limitation of this study is that date information is not available for all variables and therefore longitudinal regression could not be applied. We attempted to address this by performing separate models looking at prescribing at different time points to assess whether pain management at the time of the injury impacts outcomes the same way as opioid prescribing beyond the acute recovery period, which likely takes place under the care of different providers. Additionally, although we are able to link the majority of patients in the trauma registry data to the INPC, we are unable to determine an exact denominator for outcome variables. The INPC is most complete in the central part of the state and therefore it is possible that patients from areas where fewer providers contribute data are more likely to be missing. Our study also does not have detailed information on prescribers available. We were unable to determine how many and what type of providers are prescribing opioids to adolescents in the outpatient setting. Our pharmacy data also contained information on the type of drug prescribed, however, a large number of pharmacy encounters did not include the strength of the medication, only the drug name, number of tablets, and instructions for use. We also examined opioid fills, which may not have been taken by the patient or they could have been diverted to other friends of family members. We assume most patients requesting refills do so because they have taken all of their previous medication, however it is possible medication was not used or diverted. Further, we do not know if patients in this cohort received prescription drugs from other members of their household or friends. We also do not know if they used any illicit drugs, which would increase the likelihood of SUD and overdose. Finally, it is important to note that the development of SUD is multifactorial and there are many psychosocial factors we were unable to account for using electronic health record data, particularly motivation for using prescription opioids.

CONCLUSION

Overall, short-term outpatient opioid prescribing was the strongest predictor of developing a substance use disorder. Each refill in the three months following hospital discharge increases the likelihood of developing an SUD by 55%. In contrast, long-term outpatient opioid prescribing was predictive of experiencing an overdose, with the cumulative number of fills reaching significance two years post-injury. Future studies would further understanding on how trauma relates to the development of SUD by examining populations from other states and include patient data on social and genetic risk factors for substance use.

ACKNOWLEDGEMENTS

We would like to acknowledge Katie Bickett-Burkhart of the Regenstrief Institute for extracting data from the INPC database used in the study.

REFERENCES

1. McCabe SE, West BT, Veliz P, McCabe VV, Stoddard SA, Boyd CJ. Trends in Medical and Nonmedical Use of Prescription Opioids Among US Adolescents: 1976-2015. *Pediatrics.* 2017;139(4).
2. Meier EA, Troost JP, Anthony JC. Extramedical use of prescription pain relievers by youth aged 12 to 21 years in the United States: national estimates by age and by year. *Archives of pediatrics & adolescent medicine.* 2012;166(9):803-807.
3. Parker MA, Anthony JC. Epidemiological evidence on extra-medical use of prescription pain relievers: transitions from newly incident use to dependence among 12-21 year olds in the United States using meta-analysis, 2002-13. *PeerJ.* 2015;3:e1340.
4. Blakemore SJ, Robbins TW. Decision-making in the adolescent brain. *Nature neuroscience.* 2012;15(9):1184-1191.
5. Vibhakar V, Allen LR, Gee B, Meiser-Stedman R. A systematic review and meta-analysis on the prevalence of depression in children and adolescents after exposure to trauma. *Journal of affective disorders.* 2019;255:77-89.
6. BL Zarzaur TB. Trajectory Subtypes After Injury and Patient Centered Outcomes. *Journal of Surgical Research.* 2016;Accepted.
7. Cron DC, Lee JS, Dupree JM, et al. Provider Characteristics Associated With Outpatient Opioid Prescribing After Surgery. *Annals of Surgery.* 2020;271(4).
8. Zatzick DF, Grossman DC. Association between traumatic injury and psychiatric disorders and medication prescription to youths aged 10-19. *Psychiatr Serv.* 2011;62(3):264-271.
9. Bell TM, Raymond J, Vetor A, et al. Long-term Prescription Opioid Utilization, Substance Use Disorders, and Opioid Overdoses after Adolescent Trauma. *J Trauma Acute Care Surg.* 2019.
10. Barnett ML, Olenski AR, Jena AB. Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use. *The New England journal of medicine.* 2017;376(7):663-673.
11. Chou R, Qaseem A, Snow V, et al. Diagnosis and treatment of low back pain: a joint clinical practice guideline from the American College of Physicians and the American Pain Society. *Annals of internal medicine.* 2007;147(7):478-491.
12. 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. *Annals of internal medicine.* 2015;162(4):276-286.
13. Larach DB, Waljee JF, Hu H-M, et al. Patterns of Initial Opioid Prescribing to Opioid-Naive Patients. *Annals of Surgery.* 2020;271(2).

14. Morris BJ, Zumsteg JW, Archer KR, Cash B, Mir HR. Narcotic Use and Postoperative Doctor Shopping in the Orthopaedic Trauma Population. *J Bone Joint Surg Am.* 2014;96(15):1257-1262.

15. deRoon-Cassini TA, Hunt JC, Geier TJ, et al. Screening and treating hospitalized trauma survivors for posttraumatic stress disorder and depression. *J Trauma Acute Care Surg.* 2019;87(2):440-450.

16. Zatzick DF, Jurkovich GJ, Fan MY, et al. Association between posttraumatic stress and depressive symptoms and functional outcomes in adolescents followed up longitudinally after injury hospitalization. *Archives of pediatrics & adolescent medicine.* 2008;162(7):642-648.

17. Trevino CM, Essig B, deRoon-Cassini T, Brasel K. Chronic pain at 4 months in hospitalized trauma patients: incidence and life interference. *Journal of trauma nursing : the official journal of the Society of Trauma Nurses.* 2012;19(3):154-159.

18. Aitken LM, Chaboyer W, Kendall E, Burmeister E. Health status after traumatic injury. *J Trauma Acute Care Surg.* 2012;72(6):1702-1708.

19. Bell TM, Vetor AN, Zarzaur BL. Prevalence and treatment of depression and posttraumatic stress disorder among trauma patients with non-neurological injuries. *J Trauma Acute Care Surg.* 2018;85(5):999-1006.

20. Nguyen AP, Glanz JM, Narwaney KJ, Binswanger IA. Association of Opioids Prescribed to Family Members With Opioid Overdose Among Adolescents and Young Adults. *JAMA Network Open.* 2020;3(3):e201018-e201018.

21. Bell TM, Gilyan D, Moore BA, et al. Long-term evaluation of a hospital-based violence intervention program using a regional health information exchange. *J Trauma Acute Care Surg.* 2018;84(1):175-182.

22. McDonald CJ, Overhage JM, Barnes M, et al. The Indiana network for patient care: a working local health information infrastructure. An example of a working infrastructure collaboration that links data from five health systems and hundreds of millions of entries. *Health affairs.* 2005;24(5):1214-1220.

23. The Surescripts Network Alliance https://surescripts.com/. Accessed April 2, 2020.

24. Palamar JJ, Shearston JA, Dawson EW, Mateu-Gelabert P, Ompad DC. Nonmedical opioid use and heroin use in a nationally representative sample of us high school seniors. *Drug Alcohol Depend.* 2016;158:132-138.

25. Kelley-Quon LI, Cho J, Strong DR, et al. Association of Nonmedical Prescription Opioid Use With Subsequent Heroin Use Initiation in Adolescents. *JAMA Pediatrics.* 2019;173(9):e191750-e191750.

26. Sprenger C, Eichler IC, Eichler L, Zollner C, Buchel C. Altered Signaling in the Descending Pain-modulatory System after Short-Term Infusion of the mu-Opioid Agonist Remifentanil. *The Journal of neuroscience : the official journal of the Society for Neuroscience.* 2018;38(10):2454-2470.

27. Sekhri S, Arora NS, Cottrell H, et al. Probability of Opioid Prescription Refilling After Surgery: Does Initial Prescription Dose Matter? *Ann Surg.* 2018;268(2):271-276.

28. Clarke H, Soneji N, Ko DT, Yun L, Wijeysundera DN. Rates and risk factors for prolonged opioid use after major surgery: population based cohort study. *BMJ.* 2014;348:g1251.

29. Page MG, Kudrina I, Zomahoun HTV, et al. A Systematic Review of the Relative Frequency and Risk Factors for Prolonged Opioid Prescription Following Surgery and Trauma Among Adults. *Ann Surg.* 2019.

30. Harbaugh CM, Lee JS, Hu HM, et al. Persistent Opioid Use Among Pediatric Patients After Surgery. *Pediatrics.* 2018;141(1).

31. Donohoe GC, Zhang B, Mensinger JL, Litman RS. Trends in Postoperative Opioid Prescribing in Outpatient Pediatric Surgery. *Pain Med.* 2019.

32. McCabe SE, West BT, Boyd CJ. Leftover prescription opioids and nonmedical use among high school seniors: a multi-cohort national study. *J Adolesc Health.* 2013;52(4):480-485.

33. Neuman MD, Bateman BT, Wunsch H. Inappropriate opioid prescription after surgery. *Lancet.* 2019;393(10180):1547-1557.

34. Rosenbloom BN, McCartney CJL, Canzian S, Kreder HJ, Katz J. Predictors of Prescription Opioid Use 4 Months After Traumatic Musculoskeletal Injury and Corrective Surgery: A Prospective Study. *J Pain.* 2017;18(8):956-963.

35. Guy GP, Jr., Zhang K, Bohm MK, et al. Vital Signs: Changes in Opioid Prescribing in the United States, 2006-2015. *MMWR Morb Mortal Wkly Rep.* 2017;66(26):697-704.

36. Weinberg JA, Shehada MZ, Chapple KM, et al. The Health Literacy of Hospitalized Trauma Patients: We Should Be Screening for Deficiencies. *J Trauma Acute Care Surg.* 2019.

37. Hungerford DW. Recommendations for trauma centers to improve screening, brief intervention, and referral to treatment for substance use disorders. *J Trauma.* 2005;59(3 Suppl):S37-42.

38. Love J, Zatzick D. Screening and Intervention for Comorbid Substance Disorders, PTSD, Depression, and Suicide: A Trauma Center Survey. *Psychiatr Serv.* 2014;65(7):918-923.

39. Quinn PD, Hur K, Chang Z, et al. Association of Mental Health Conditions and Treatments With Long-term Opioid Analgesic Receipt Among Adolescents. *JAMA Pediatrics.* 2018;172(5):423-430.

FIGURE LEGENDS

Figure 1. Study Variables Available by Timepoint. Outcome variables included substance use disorder or overdose diagnosis after discharge. Independent variables included the number of outpatient opioid fills post-discharge. AA – African American, ISS – Injury Severity Score, PTSD – Posttraumatic Stress Disorder, HIE – Health Information Exchange, Dx – Diagnosis.

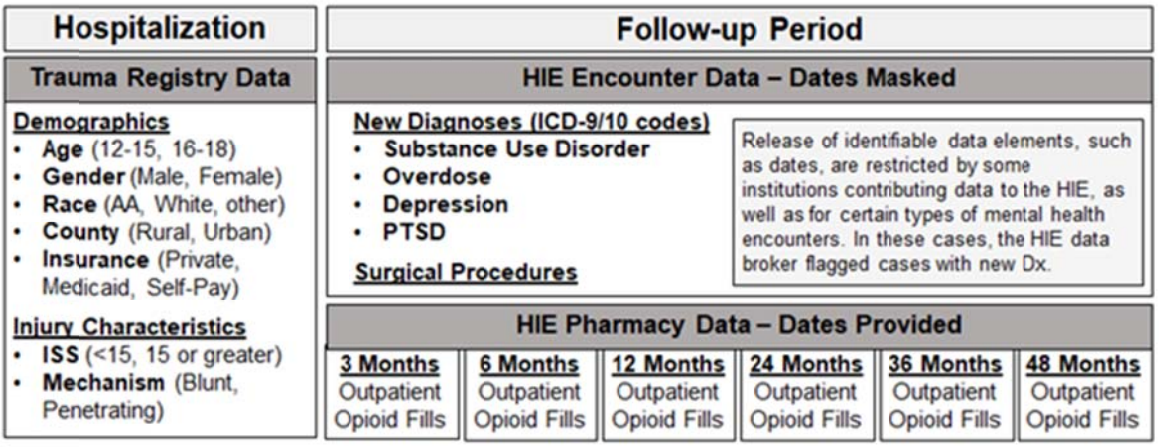
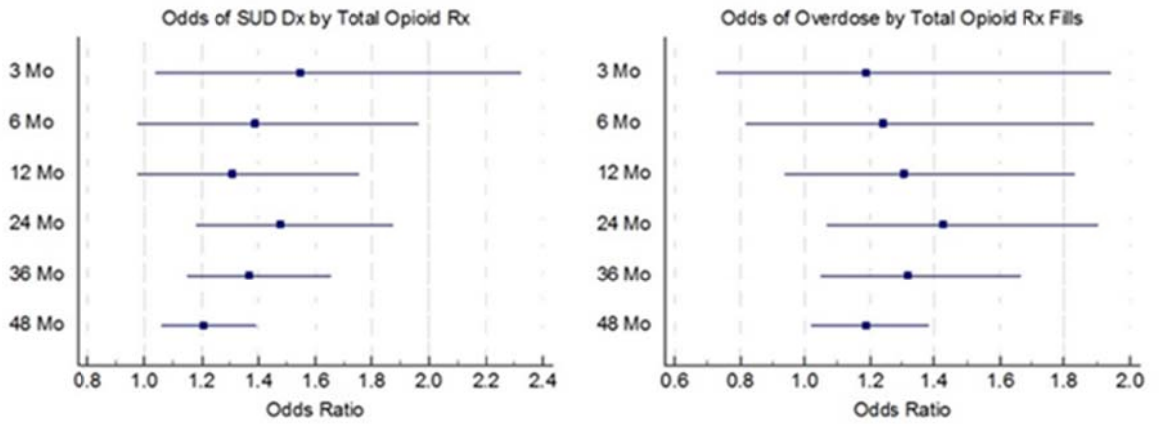


Figure 2. Likelihood of SUD and OD by Total Number of Outpatient Opioid Rx Fills. Logistic regression models adjusted for age, race, insurance, injury severity/type, post-discharge surgery, urban/rural county of residence, PTSD diagnosis, and depression diagnosis.



TABLES

Table 1. Cohort Characteristics, n=736 (%)

Age, mean	14.55
Gender	
Male	74.2%
Female	25.8%
Race	
White	70.5%
Black	22.9%
Other/Unknown	6.6%
County	
Urban	58.4%
Rural	41.4%
Injury Type	
Blunt	75.1%
Penetrating	18.1%
Other	6.8%
Injury Severity	
Minor/Moderate	85.3%
Major	14.7%
Routine Discharge	83.6%
Length of Stay	
<2 Days	44.9%
2-7 Days	42.9%
Week or More	10.9%
Insurance Status	
Medicaid	36.3%
Self-pay	19.1%
Private	43.8%

Table 2. Mean Outpatient Opioid Rx Fills by Patient Demographic and Injury Characteristics

		Mean Total Fills					
		3 Months	6 Months	12 Months	24 Months	36 Months	48 Months
Age	12 to 15	1.28	1.32	1.42	1.59	1.75	**1.90**
	16 to 18	1.30	1.40	1.53	1.71	1.88	**2.19***
Gender	Female	1.31	1.38	1.50	1.74	1.94	2.15
	Male	1.28	1.35	1.45	1.60	1.74	1.96
Race	White	1.30	1.37	1.48	1.68	1.83	2.01
	Black	1.23	1.29	1.39	1.50	1.66	2.02
	Other or Unknown	1.30	1.33	1.45	1.64	1.88	2.00
County of Residence	Rural	1.32	1.37	1.48	1.65	1.77	1.98
	Metro	1.27	1.35	1.45	1.63	1.81	2.02
Insurance	Medicaid	**1.32***	1.38	1.50	1.69	1.85	2.09
	Private	**1.29**	1.35	1.45	1.60	1.76	1.93
	Self-pay	**1.28**	1.38	1.47	1.70	1.87	2.09
Injury Severity	Mild/Moderate	**1.26**	**1.31**	**1.41**	**1.60**	1.77	1.97
	Major	**1.48***	**1.63***	**1.77***	**1.89***	2.01	2.35
Injury Mechanism	Blunt	1.28	1.34	1.45	1.65	1.81	2.01
	Penetrating	1.33	1.44	1.53	1.59	1.74	2.10

Tests of ANOVA adjusted for all pairwise comparisons using the Bonferroni Correction. Significant differences are in bold with the higher value indicated by an asterisk.

Table 3. Mean Outpatient Opioid Rx Fills by Diagnosis Outcomes

		Mean Total Fills											
		3 Months	p value	6 Months	p value	12 Months	p value	24 Months	p value	36 Months	p value	48 Months	p value
Substance Use Disorder	No	1.26	<0.001	1.33	0.001	1.43	0.005	1.58498	0.474	1.73	0.016	1.92	0.003
	Yes	1.43		1.50		1.64		1.975		2.21		2.56	
Overdose	No	1.28	0.028	1.34	0.004	1.44	<.001	1.60	0.015	1.75	0.004	1.94	0.007
	Yes	1.39		1.55		1.75		2.09		2.32		2.80	
Depression	No	1.27	0.025	1.34	0.084	1.44	0.758	1.62	0.085	1.76	0.739	1.96	0.146
	Yes	1.51		1.6		1.7		2		2.2		2.7	

	s			0		1				6		1	
PTSD	No	1.28	0.061	1.34	<0.001	1.45	0.001	1.62	0.096	1.78	0.122	1.99	0.266
	Yes	1.67		2.08		2.17		2.50		2.67		3.08	
Chronic Pain	No	1.28	0.013	1.35	0.034	1.45	0.165	1.62	0.234	1.77	0.041	1.95	<0.001
	Yes	1.38		1.46		1.71		2.13		2.38		3.21	
Anxiety	No	1.29	0.231	1.38	0.006	1.45	0.034	1.62	0.093	1.77	0.110	1.95	0.001
	Yes	1.27		1.39		1.52		1.79		2.02		2.47	

Table 4. Comparison of Odds of SUD between Patients Undergoing Additional Surgery Post-discharge and Patients Not Undergoing Additional Surgery

	Non-Surgical Patients		Surgical Patients	
Total Opioid Rx Fills	OR	P	OR	P
3 Month	2.61	0.008	1.22	0.359
6 Month	1.92	0.044	1.18	0.371
12 Month	1.64	0.074	1.17	0.315
24 Month	1.69	0.004	1.24	0.115
36 Month	1.48	0.004	1.19	0.111
48 Month	1.35	0.005	1.22	0.359