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A retrospective review of unintentional opioid overdose risk and mitigating factors among acutely injured trauma patients

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Abstract

Background—Opioid medication to treat acutely injured patients is usual care in trauma settings. A higher prevalence of alcohol and other substance misuse in this population compared to the general population increases the vulnerability of such patients to both misuse of their prescribed opioids, and also unintentional opioid overdose. The primary purpose of this study was to assess the prevalence of substance use and unintentional opioid overdose risk among acutely injured trauma patients, and to examine the frequency and predictors of high opioid dose at discharge.

Methods—A retrospective electronic medical record (EMR) review of three-months of data from two Level 1 trauma centers. We assessed the prevalence of substance misuse, unintentional opioid overdose risk, and presence of documentation of clinical strategies to mitigate these risks, such as co-prescription of the opioid agonist naloxone.

Results—In total, 352 patient EMRs were examined. Over 40% of the patients reviewed had at least one indication of substance misuse (42.5% [95%CI: 37.3, 47.7]); at least 1 unintentional opioid overdose risk factor was identified in 240 EMR reviewed (68.2% [95%CI: 63.3, 73.1]).

Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention/the Agency for Toxic Substances and Disease Registry.

Contributors

Janette Baird contributed to the study design, study implementation, data analysis, and manuscript preparation. Mark Faul contributed to the data analysis, and manuscript preparation. Traci C. Green contributed to the study design, study implementation, and manuscript preparation. Jonathan Howland contributed to the study design, study implementation, and manuscript preparation. Charles A. Adams contributed to the study design and manuscript preparation. Ann George contributed to the study implementation and manuscript preparation. Michael J. Mello contributed to the study design, study implementation, data analysis, and manuscript preparation. All authors contributed to the original study design, development and writing of the submitted manuscript.

Conflict of interest

No conflict declared.

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Dose of opioid medication was not significantly different for patients with substance misuse versus those without. There was no co-prescription of naloxone for any of the discharged patients.

Conclusions—Our results indicate that despite the high rates of substance misuse, the potential for misuse, dependence and unintentional overdose risk from prescribed opioid medications are prevalent among acutely injured trauma patients. Prescribing after acute trauma care should address these risk factors.

Keywords

Alcohol and other substance use; Traumatic injury; Opioid medication; Risk factors

1. Introduction

The United States uses over 80% of all oxycodone manufactured in the world, and more than 90% of the world's manufactured hydrocodone (Manchikanti et al., 2012a), as demonstrated by the approximately 250 million prescriptions for opioids dispensed in 2013 (Centers for Disease Control and Prevention, 2016 Centers for Disease Control and Prevention (CDC), 2016). This level of consumption has been linked with unintentional opioid related deaths (Centers for Disease Control and Prevention, 2016), which are now at epidemic levels (Centers for Disease Control and Prevention, 2011; Manchikanti et al., 2012b; Volkow and McLellan, 2016), and has led to a discussion to educate both patients and physicians about risks that may be associated with medically indicated opioid prescriptions (Nelson and Perrone, 2012). The co-ingestion of opioids with psychoactive substances, such as alcohol and benzodiazepines, increases the risk of respiratory depression and death (Centers for Disease Control and Prevention, 2012; Webster et al., 2011; Dunn et al., 2010; Green et al., 2011; Silva et al., 2013). In addition to alcohol and medication use risks, there are acute and chronic diseases that have been associated with an increased likelihood of overdose, such as chronic obstructive pulmonary diseases, end stage liver and renal failure, and congestive heart failure (Webster et al., 2011).

High daily doses of opioids are also associated with increased risk of fatal opioid overdose (Dunn et al., 2010). While the definition of "high daily dose" is evolving, many considered daily intakes at or exceeding 100 morphine milligram equivalent doses (MME - the metric used to quantify the 24-h dose of opioid) as risky (Eder et al., 2005). Naloxone is a competitive antagonist (Helm et al., 2008) that binds to opioid receptors, and can reverse the effects of an overdose and is considered a key strategy in preventing opioid deaths (Bohnert et al., 2011; Walley et al., 2013). There are calls for increasing the availability of naloxone through provider opioid co-prescribing and dispensing at community pharmacies and other community health care and treatment settings. (Centers for Disease Control and Prevention, 2015; Davis et al., 2014; Doyon et al., 2014; Green et al., 2015; Green and Doe-Simkins, 2016). More recent opioid prescribing guidelines for chronic pain issued by the Centers for Disease Control and Prevention (CDC, 2016) recommend prescribing naloxone if the daily dose of opioids 50 MME, or when a patient is receiving both benzodiazepines and opioid medications, or when there is a patient history of substance use disorder (SUD). The maximum daily dose of opioid medication prescribed has been associated with both increased risk dependency and unintentional opioid overdose (Cheatle, 2015).

In the United States, there are annually 2.6 million trauma hospital admissions (Dowell et al., 2016), and opioid analgesia therapy is almost ubiquitous among these patients (Wunsch et al., 2016). While estimates of substance use vary in the general population from 2% of adults who report non-medical use of prescribed drugs to 10.1% who use any illicit drugs (Center for Behavioral Health Statistics and Quality, 2016), substance use, and substance misuse is much higher among the traumatically injured. Estimates of substance misuse among traumatically injured trauma patients has risen to between 40 and 60% (Rosenblatt and Mekhail, 2015). Field et al. (2014) reported on the non-medical use of prescription opioids for injured at-risk drinkers (defined by authors as an admission for an alcohol relate injury, or self-report of heavy drinking) up to 12 months following discharge from a Level 1 trauma care facility. They found that prior non-medical use of prescribed opioids and/or other drug use pre-admission was predictive of using non-prescribed of opioids following discharge (Field et al., 2014).

This concomitant concern of high opioid utilization in conjunction with the frequency of alcohol and other drug misuse, places injured trauma patients as a population vulnerable to the unintended negative consequences of prescription opioids. The challenge, for the health care professional, is to adequately control pain without increasing the burden of misuse, morbidity, and mortality among those prescribed opioid analgesics. This challenge is more difficult in a trauma care setting.

With many trauma patients receiving opioid prescriptions for pain control at discharge, and given the known increased misuse of substances among this population, it is critical to identify patients at risk for opioid overdose, and to assess the opportunities to introduce educational and clinical strategies to reduce those risks associated with prescription opioid medication. The purpose of the current study was to describe the frequency of unintentional opioid overdose risk among patients admitted to trauma service, and describe demographic characteristics associated with those risks. We also wanted to determine if receiving a high dose of discharge opioid medication (100 MME daily) was predicted by any patients' medical or demographic characteristics, and in particular if the presence of any unintentional opioid risk factor moderated the discharge dose.

2. Methods

2.1. Design

This was an observational study using retrospective electronic medical record (EMR) data. Patient data and reporting was handled in accordance with the guideline on Strengthening and Reporting of Observational Studies in Epidemiology (STROBE) (Noah, 2008).

2.2. Sample

The EMR of patients admitted to Level 1 trauma services at two urban academic hospitals in two states were included in the study. Site 1 admits over 2900 trauma patients annually and site 2 admits over 1800. Cases were identified using the trauma registry at each site. Criteria for inclusion were the admission to and discharge from the trauma services between July 1st 2014 and September 30th 2014; patient discharged to home; discharged with a prescription

for opioid pain medication; and patient age 18 years or older. The data reported on for this study were part of a larger study evaluating the effect of a safer opioid prescription protocol for discharged trauma patients. These data represent three-months of medical records for patients discharged from the trauma services prior to the implementation of the safer opioid prescription protocol. The Institutional Review Board at each hospital approved the study protocol and provided a waiver of informed patient consent.

2.3. Data extracted

Medical data were extracted from the patients' EMR for the following main categories of data: demographics, admission history, medication, and comorbid medical conditions. The content for each of these categories is shown in Fig. 1. The MME dose was calculated for the discharge opioid dose by multiplying the frequency of daily dose by the strength of dose (or maximum if a range of frequency was recorded). Naloxone prescriptions at discharge were recorded. We also recorded if any recorded instruction on safe opioid use (i.e., use as prescribed, do not use with alcohol) and safe storage was given to the patient. Most of the data was abstracted from the medical record, which included details on the prescribed opioids following a discharge.

A classification system for drug types (opioid pain medication, benzodiazepines, other sedatives, and non-opioid pain medication) was developed by the research study pharmacist.

2.4. Data extraction protocol and training

The data extraction protocol was developed by the study research investigators, and research assistants were trained in the protocol. The explicit EMR data extraction protocol included reviewing the same 10 patient charts independently, and discussing with the research team any issues of ambiguous or conflicting medical record documentation for any data. The research assistants conducting the chart review data abstraction were not blinded to the study objectives. Relevant data were extracted from the EMR and entered into a Microsoft Excel file at each study site, and later merged into one database. As part of the data extraction protocol, 10% of all medical records were reviewed to assess data extraction and rater reliability by an independent rater not involved with the initial medical record data extraction. When the rater agreement analysis was conducted, data disagreements were reviewed by the study investigators at each site, the individual EMR was re-reviewed by the research assistant and the investigator, and the corrected entry was included in the analyses.

2.5. Opioid overdose risk factor composite score

Using opioid risk factors identified from the research literature (Dunn et al., 2010; Green et al., 2011; Silva et al., 2013; Webster et al., 2011), a composite score for opioid overdose risk factors was developed from the EMR data. A score (1 v. 0) was applied to each of the following seven risk factors: a.) relevant comorbid medical condition (any one of the following: COPD, congestive heart failure, end stage renal or liver disease); b.) home opioid/and benzodiazepine medication; c.) discharge benzodiazepine co-prescription; d.) discharge opioid medication 100 MME; e.) positive alcohol or illicit drug screen on admission; f.) prior treatment for SUD in past 12 months; g.) opioid overdose in the past 12

months. The summed composite score across all seven indicator variables ranged from 0 to 7.

2.6. Substance use disorder

The substance use disorder (SUD) status of the patient was categorized as: positive as identified through trauma service standardized screening, and/or toxicology results indicating use of illicit substances or medication not prescribed on admission, and/or prior treatment in the past 12 months for substance misuse, and/or opioid overdose in the past 12 months; or negative if none of these indications were present.

2.7. Data analysis approach

A power analysis was conducted based on the expectation that 30% of the reviewed charts would have at least one identified opioid overdose risk factor. We estimated that we would have to review a minimum of 322 charts to determine that 30% of charts would have at least one indicated risk factor, assuming a 5% error in our estimated proportion.

The data were formatted into Statistical Analysis Software (SAS) (Version 9.2, Carey, NC) for statistical analyses. Descriptive data analyses were conducted with means, counts and proportions reported with 95% confidence intervals (CIs), and medians with relevant interquartile range (IQR). Comparisons between the two sites were conducted using Wilcoxon Signed Ranks test for non-normal continuous data, and a binomial test of proportions and Pearson's Chi-square test for categorical data. The inter-rater reliability of the medical data extracted was calculated using Cohen's Kappa. The coefficient agreement between raters was reported for six identified categories: patient demographics, comorbid medical conditions, positive toxicology or substance use screen, home medication, discharge medications, and discharge opioid medication MME. These agreement rates are reported with 95% CIs.

A hierarchical model with log link function (SAS Proc glimmix) was conducted to determine the relative risk of opioids overdose risk associated with patient level characteristics. The trauma center site was the nesting variable for patients. Based on the distribution of opioid overdose risks, the outcome variable was dichotomized into no versus at least 1 identified risk factor. Participant predictor variables were gender, race (White, African-American/other) ethnicity, age (median centered).

In the second predictive model second model we examined predictors of the discharge dose medication strength, dichotomized as < 100MME daily and 100MME daily. Patient demographic and medical characteristics were entered as predictors. Specifically; any medication risk factor (we combined home opioid or benzodiazepine, or discharge coprescription of benzodiazepine), SUD status, and co-morbid disorders.

3. Results

3.1. Interrater reliability

During the three-month trauma admission period in which the medical record review data were collected, 210 admitted patients were discharged from site one and 261 from site two.

Of these patients, 191 (91%) at Site 1 and 160 (62%) from site 2 were discharged to home with one or more prescriptions for opioid pain medication, and therefore eligible for study inclusion. The initial inter-rater percent agreement was: a. patient descriptive data = 100%; b. comorbid medical conditions = 93% (95% CI 89.4, 96.6); c. positive substance use screen = 83% (95% CI 77.7, 88.3); d. home medications = 94% (95% CI 90.6, 97.6); e. discharge medications = 100%; f. MME > 100 = 89% (95% CI 84.6, 93.4).

3.2. Patient characteristics

Table 1 reports on the demographic characteristics of the included medical record review patient sample. Across both sites, most patients were male, White and non-Hispanic. Site 1 patients were on average older than those at site 2 (43 years versus 32.5 [p < 0.001]), and were less likely to be African-American (13.1% versus 46% [p < 0.001]). The average length of stay was similar at both sites (site 1 = 4.6 days [95% CI: 3.9, 5.3]; site 2 = 4.4 days [95% CI: 3.4, 5.3]).

3.3. Substance use

A toxicology screen for drug use on admission was conducted more frequently in site 1 (120/191 = 62.8%) compared to site 2 (n = 72/161 = 44.7%). Among those who were tested at both sites, 143/192 (74.5%; 95% CI: 68.3, 80.7) screened positive for any substance. Table 2 indicates the main drugs detected in the toxicology screens conducted. Opioids were the most common positive drug screen, and documentation of prescribed use (i.e., used in the trauma care of the patient in the pre-hospital setting, or that the patient was prescribed opioids as a home medication), being found for just over half of these patients (53%). Among patients who screened positive for drugs on admission; 69.9% were positive for one drug, 22.4% for 2 drugs and 7.7% for 3 or 4 drugs. A consult from hospital substance misuse services (social work or psychiatric services) was requested for 86 patients. Patients who were male, were more likely, if screened, to be positive for alcohol (males = 45.2% [95% CI: 38.8, 52.0]; females = 22.9% [95% CI: 10.8, 34.1]), but not for other drugs (males = 76.3%[95% CI: 69.6, 82.8]; females = 66.7% [95% CI: 52.3, 82.1]). Rates of SUD were calculated from the criteria explained in the Methods section. In total 149 participants (42.5% [95%CI: 37.3, 47.7]) were categorized as having a SUD; the proportion was approximately equal for each site.

3.4. Prescribed opioid medications

Oxycodone was the most frequently prescribed opioid at discharge 299/352 (84.9%). Typically this was a daily 5 mg dose with 1–2 tablets per dose (n = 258/299, 86.3%); the remaining patients had a higher dosage. Across the types of opioid medication prescribed at discharge, frequency of dose ranged from 1 to 8 times a day, with the most frequent being twice a day (77.6%). The mean days of prescribed dosing was 13.9 days (SD = 8.7) with a median of 12 days (IQR = 7.5–16). At discharge, the median discharge 24-h maximum dose prescribed was 90 MME, however, high doses of 100 MME was comparatively common in site 1 (39% [95% CI: 25.3, 38.5]), compared to site 2 2.5% [95% CI: 0.88, 4.91]. There were no differences in MME of discharge opioid dose for patients who had were classified as SUD versus those who did not. Twenty-six patients (7.4%) were co-prescribed a benzodiazepine with opioid medication at discharge.

3.5. Opioid overdose risk factors

Table 3 presents the frequency of risk factors identified from the EMR review. At least 1 opioid overdose risk factor was identified in 240 patient EMR (68.2% [95% CI: 63.3, 73.1]), with a range of 0–5 factors identified. More patients in site 1 (117/191 [61.2%; 95% CI: 54.4, 68.2]) had identified overdose risk factors than in site 2 (22/161 [13.7%; 95% CI: 8.4, 19.0]). On admission, home sedating medications and positive drug/alcohol screenings were the most commonly identified risk factors.

3.5.1. Predicting opioid overdose risk factors and MME discharge dose—Table 4 shows the relative risk ratios (with 95% CI s) for an unintentional opioid overdose risk from the patient demographic characteristics entered into first model. The known site differences between the two Level 1 trauma sites were adjusted for in these hierarchical models. In the first model, having a risk factor versus not having one could not be predicted by any of the patients' characteristics. The calculated intraclass correlation (ICC) was 0.24; which indicates that 24% of the variability in predicting the overdose risk factors was due to trauma site variability. In model 2 we examined the relative risk of being prescribed a high potency discharge opioid dose (i.e. 100 MME). Due to low frequency we created a medication risk (combination of either benzodiazepine prescribed at discharge, or home opioid, or benzodiazepines), SUD status (as described in Methods), and co-morbidity risk, and used these composite variables as predictors with the other variables shown in model 2 on Table 4. No predictor variable was significant in this model. The ICC was 0.28.

3.5.2. Naloxone co-prescription—There were no prescriptions for naloxone given at either site for any patients in this record review

4. Discussion

Patients in our study had received prescription opioid medications during their admission and were discharged to home with opioid medications to control their pain. Prior research has shown that individuals who are prescribed opioids in high doses, with a co-prescription of benzodiazepines, or who have a medical comorbidity, or, and substance use disorders have an elevated risk of an unintentional opioid overdose (Centers for Disease Control and Prevention, 2012; Webster et al., 2011; Dunn et al., 2010; Green et al., 2011; Silva et al., 2013). These risk factors were identified in over 68% of the trauma patient charts reviewed. The presence of these risk factors was not associated with a lower likelihood of having a higher potency prescribed daily dose of opioids (100 MME) at discharge, and we found no individual patient characteristics that were associated with these risks, which would indicate that more universal approaches to identifying those are risk for an unintentional opioid overdose are needed. We also found that a large variability of prescribing across the two sites studied, which is likely due to localized prescribing practices.

There were no documented prevention strategies initiated by clinicians; including no prescriptions provided for naloxone for patients who we identified as being at risk for an unintentional opioid overdose. Recent clinical guidelines issued by the Centers for Disease Control and Prevention (2016), do recommend that prescribers consider co-prescription of naloxone when daily doses of opioids exceed 50 MME, or the patient is co-prescribed

benzodiazepines. The lack of any naloxone prescribing among the medical records reviewed is concerning and suggests that prescribers need to be educated about the unintentional opioid overdose risk their patients face, and the role of naloxone in overdose prevention. Alternatively, risk factors may have been considered for some patients who were discharged from these trauma services without prescribed opioid pain medications (whose data was not included in this study); these potential risk factors may have been important in considering whether or not to prescribe an opioid analgesic medication.

In conducting the EMR review we found the ease of extracting the indicators of unintentional opioid overdose risk varied enormously. Some data were well documented and easily retrievable from one or two sources in the EMR, others were not. Data on discharge and home medications tended to be contained within easily designated areas in the EMR, data on past treatment for SUD was not consistently documented or documented in any one section of the EMR. Our sole purpose of the extraction were to find these risk factors, for the busy clinician about to discharge a patient, finding these sources of patient medical information would require time and effort, which maybe not feasible given the demands of clinical care in a trauma setting. The EMR is a powerful tool that could be used to collate and highlight important patient medical information that the clinician could use in deciding the patient's discharge medication dose and potential need for naloxone.

Trauma patients may also be a particularly vulnerable group for misusing prescription opioids; given the higher SUD rates (Field et al., 2014) than in the general population (Alam et al., 2012). Prior research has reported that among trauma patients with a history of risky drinking, pre-admission illicit use of prescription opioids and other drugs is predictive of long-term opioid use and misuse (King et al., 2014). Comprehensive screening for SUD is common in trauma centers, and is required as part of the accreditation process to become a Level 1 trauma center. Of the trauma patient's EMRs we reviewed, over 40% screened positive for substance use either by toxicology screen or by a standardized assessment tool, and had the potential for SUD. Of these patients, 86 received a consult for their substance use. However, the lack of toxicology screens documented in approximately 25% of reviewed medical charts does suggest that SUD may be under-reported in this population. Increasing screening to identify trauma patients whose substance use history elevates their likelihood of misusing their opioid medications, may be another effective strategy to address the crisis we currently face of opioid medication misuse, dependency, and overdose. This underscores the need for appropriate treatment options, such as medication assisted therapies, as well as behavioral counseling.

Central to improving opioid medication safety are multi-level interventions that not only target those at high risk, but also primary prevention to promote safer opioid use for all patients. Prevention interventions regarding opioid misuse and overdose risk may disrupt the continuum of use, risk for misuse, and probability of overdose (Dunn et al., 2010; Manchikanti et al., 2012a; Webster et al., 2011). The Food and Drug Administration (FDA) has stated that the misuse of prescription opioids can be mitigated in part by educating patients about the safe use, storage and disposal of their opioid pain medications (FDA, 2011). A recent pilot study demonstrated the feasibility and short-term effect of delivering a web-based education intervention on the safe use, storage and disposal of prescription opioid

pain medications for adult patients attending an outpatient pain management clinic (McCauley et al., 2013). There is a growing recognition among clinicians of the importance of education to increase patient safety around their prescribed opioid use (American Hospital Association, 2016), and to promote the role of naloxone in reducing unintentional opioid overdose risk.

As the data gathered here represent patients admitted to only two Level 1 trauma center sites in the Northeast of the United States, it may not be generalizable to other trauma center sites. There were important differences between the sites that may have accounted for the observed difference in frequency and dose of opioids prescribed to trauma patients at discharge. Site 1 is the only level 1 trauma center in the region whereas site 2 is one of several level 1 trauma centers within the same city; this may result in more severely injured patients being admitted at site 1 with a greater corresponding need for opioid medication. Across both sites, the EMR was only reviewed for patients who were discharged to home with an opioid, so we have no comparative data for patients not discharged to home with opioids, whose rate of SUD and opioid overdose risk factors may be as great as what we report. Also, discussion about safer opioid medication use, storage and disposal may have occurred between patient, nurse, and/or physician, but not recorded.

The Department of Health and Human Services (2015) listed education of providers around opioid medication prescription practices and availability of naloxone, as two of three national priority areas for reducing opioid abuse and overdose. Our results indicate that there are opportunities for engaging with prescribers to inform them of the evidence-based opioid overdose risk factors among their acutely injured patients, especially those who may have a SUD and receive advanced care at a trauma center.

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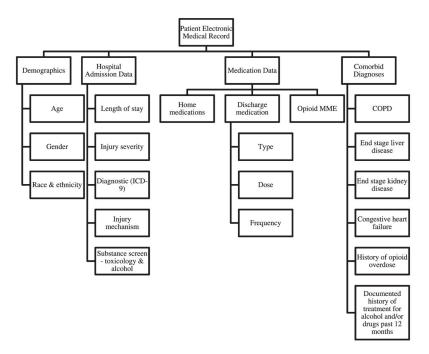


Fig. 1. Schematic of the extracted electronic medical record review categories and content.

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Table 1

Description of Patients Sample at Two Trauma Center Sites.

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Demographic characteristics	Site 1 n = 191	Site 2 n = 160	
Median age, years (IQR)	43 (31)	32.5 (15)	
Range	18–96	18-80	
	n (%; 95%CI)	n (%)	
Gender			
Female	43 (22.5; 16.5, 28.4)	32 (20.5; 14.3, 26.7)	
Male	148 (77.5; 71.6, 83.4)	128 (79.5; 76.3, 85.7)	
Ethnicity			
Hispanic	22 (11.5; 6.97, 16.0)	25 (16.1; 10.4, 21.8)	
Non-Hispanic	168 (88.0; 83.4, 92.6)	135 (83.9; 78.2, 89.6)	
Not documented	1 (0.52; 0, 1.3)	0	
Race			
White	161 (84.3; 79.1, 89.5)	54 (34.2; 26.9, 41.5)	
Black/African-American	25 (13.1; 8.31, 17.9)	74 (46.0; 38.3, 53.7)	
Asian	2 (1.1; 0.0, 2.5)	3 (1.9; 0, 4.01)	
Other	22 (11.5; 7.0, 16.0)	29 (18.0; 12.07, 23.9)	

CI = Confidence interval; IQR = inter quartile range.

 Table 2

 Screening Test Results for Presence of Alcohol, Prescribed and Illicit Substances on Admission.

Drug Screen Type	a Positive Screen n (%)	b Prescribed n (%)
Opioids	102 (53)	54 (53)
Cannabinoid	45 (23)	2 (4)
Benzodiazepines	30 (16)	13 (43)
Cocaine	29 (15)	-
Amphetamines	7 (4)	4 (57)
Barbiturates	3 (2)	3 (100)
Methadone	1 (< 1)	1 (100)

 $^{^{}a}$ N = 192 received toxicology screening for drugs.

^bOf those with positive toxicology screen for substance.

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Table 3

Identified Opioid Overdose Risk Factors Among the Trauma Patients.

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Risk Factors	N = 351 n (%; 95%CI)		
Co-morbidity			
Respiratory Disease	21 (6.0; 3.5, 8.4)		
Renal Disease	4 (1.1; 0.0, 2.2)		
Cardiac Disease	7 (2.0; 0.6, 3.4)		
Liver Disease	14 (4.0; 1.9, 6.0)		
Medication			
Home			
Rx opioid home	29 (8.2; 5.4, 11.1)		
Rx benzodiazepine home	6 (1.7; 0.40, 3.1)		
Discharge			
Rx benzodiazepine	26 (7.4; 4.7, 10.1)		
Rx opioid dose > 100 MME	61 (31.9; 27, 36.8)		
Admission Substance Screen			
Alcohol Positive	110 (31.3; 26.5, 35.1)		
Alcohol Negative	157 (44.7; 39.5, 50.2)		
Alcohol Not Documented	85 (24.2; 19.7, 28.7)		
Drug Positive	143 (40.7; 35.6, 45.8)		
Drug Negative	49 (14.0; 11.6, 17.6)		
Drug Not documented	160 (45.6; 40.4; 50.7)		
Substance Misuse			
Tx alcohol/substance abuse (last 12 months)	12 (3.4; 1.5, 5.3)		
Prior opioid overdose (last 12 months)	3 (< 1)		

 $Tx = treatment; \ Rx = Prescription; \ MME = Morphine \ Milligram \ Equivalent; \ CI = Confidence \ interval.$

Table 4

Hierarchical Regression Models Predicting Relative risk for Opioid Overdose Risk Opioid Risk Factors and Opioid Prescribed Discharge Dose 100 MME.

Model 1	Identified Opioid Overdose Risk Factor				
	Predictors		95%CI		
	Gender (Female = referent)		0.07, 19.9		
	Race (White = referent) Ethnicity (Hispanic = referent)		0.02, 17.5		
			0.30, 57.1		
	Age (median = 36)	1.30	0.11, 15.1		
Model 2	Discharge Opioid Medication Daily Dose	100 MME			
	Predictors	RR	95%CI		
	Gender (Female = referent)	0.74	0.02, 44.7		
	Race (White = referent)	1.90	0.003, > 100		
Ethnicity (non-Hispanic = referent)		0.66	0.001, > 100		
	Age (median = 36)	0.87	0.04, 18.4		
	Medication risk factor (0 = referent)	0.65	0.02, 20.1		
	Substance use disorder risk (0 = referent)	0.79	0.004, 13.92		
	Medical comorbidity (0 = referent)	1.83	0.004, > 100		

 $MME = Morphine \ Milligram \ Equivalent; \ RR = Relative \ risk \ ratios; \ CI = confidence \ intervals.$