

# Opioid Abuse or Dependence Increases 30-day Readmission Rates after Major Operating Room Procedures

## A National Readmissions Database Study

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### ABSTRACT

**Background:** Although opioids remain the standard therapy for the treatment of postoperative pain, the prevalence of opioid misuse is rising. The extent to which opioid abuse or dependence affects readmission rates and healthcare utilization is not fully understood. It was hypothesized that surgical patients with a history of opioid abuse or dependence would have higher readmission rates and healthcare utilization.

**Methods:** A retrospective cohort analysis was performed of patients undergoing major operating room procedures in 2013 and 2014 using the National Readmission Database. Patients with opioid abuse or dependence were identified using International Classification of Diseases codes. The primary outcome was 30-day hospital readmission rate. Secondary outcomes included hospital length of stay and estimated hospital costs.

**Results:** Among the 16,016,842 patients who had a major operating room procedure whose death status was known, 94,903 (0.6%) had diagnoses of opioid abuse or dependence. After adjustment for potential confounders, patients with opioid abuse or dependence had higher 30-day readmission rates (11.1% vs. 9.1%; odds ratio 1.26; 95% CI, 1.22 to 1.30), longer mean hospital length of stay at initial admission (6 vs. 4 days;  $P < 0.0001$ ), and higher estimated hospital costs during initial admission (\$18,528 vs. \$16,617;  $P < 0.0001$ ). Length of stay was also higher at readmission (6 days vs. 5 days;  $P < 0.0001$ ). Readmissions for infection (27.0% vs. 18.9%;  $P < 0.0001$ ), opioid overdose (1.0% vs. 0.1%;  $P < 0.0001$ ), and acute pain (1.0% vs. 0.5%;  $P < 0.0001$ ) were more common in patients with opioid abuse or dependence.

**Conclusions:** Opioid abuse and dependence are associated with increased readmission rates and healthcare utilization after surgery.

**Visual Abstract:** An online visual overview is available for this article at <http://links.lww.com/ALN/B704>. (**ANESTHESIOLOGY 2018; 128:880-90**)

UNPLANNED readmissions remain a significant component of healthcare expenditures<sup>1</sup> and were responsible for more than \$41 billion in hospital costs in 2011 alone.<sup>2</sup> In 2012, the Centers for Medicare and Medicaid Services imposed financial penalties on hospitals with high readmission rates for conditions such as heart failure and pneumonia. Surgical procedures such as elective total hip arthroplasty and coronary artery bypass graft were added in 2015 and 2017, respectively.<sup>3</sup> Previous work has demonstrated that one in seven patients hospitalized after major surgical procedures is readmitted,<sup>4</sup> and indications for readmission are more often related to perioperative complications rather than exacerbations of the presenting condition.<sup>5</sup>

Over the past decade, a dramatic increase in opioid use has driven a corresponding increase in opioid-related morbidity

#### What We Already Know about This Topic

- Limited studies have found greater readmission rates in opioid-tolerant compared to nontolerant patients
- However, these were not nationally representative studies and did not specifically target patients with opioid abuse or dependence

#### What This Article Tells Us That Is New

- The National Readmission Database for 2013 and 2014 was analyzed to compare readmission rates in patients with or without opioid abuse or dependence undergoing major operating room diagnostic or therapeutic procedures
- Patients with opioid abuse or dependence had higher 30-day readmission rates (11.1% vs. 9.1%)
- Readmissions for infection, opioid overdose, and acute pain were more common in patients with opioid abuse or dependence

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and mortality. From 2000 to 2014, deaths from overdoses involving opioids increased by 200%.<sup>6</sup> This increase in opioid-related complications has resulted not only from greater illicit opioid use but also from an increase in chronic opioid therapy. In December of 2016, the opioid misuse epidemic prompted the U.S. Surgeon General to issue a call to action, with guidelines targeted at curbing the use of opioids in the treatment of chronic pain.<sup>7</sup>

The increase in opioid consumption has several health-care-related implications. On average, inpatient stays related to opioid abuse or dependence have increased by 5% annually between 1993 and 2012.<sup>8</sup> Furthermore, patients with opioid abuse or dependence present several challenges for anesthesiologists in the perioperative period, including higher rates of psychologic disorders and an increased prevalence of hepatitis, human immunodeficiency virus, and other infectious diseases.<sup>9</sup> Compounding these challenges are findings that postoperative pain is often poorly controlled.<sup>10</sup>

For perioperative physicians such as anesthesiologists, an important question is whether perioperative opioid abuse or dependence affects clinical outcomes such as readmission or mortality. Current data support an effect of opioid misuse on surgical readmissions. A 2013 retrospective single-center study found an increased length of stay and a greater 30-day readmission rate in opioid-tolerant patients *versus* nontolerant controls.<sup>11</sup> Another 2017 study found an increase in readmission rates among patients on preoperative opioids who underwent elective abdominal surgery.<sup>12</sup> However, these studies were not nationally representative and did not specifically target patients with opioid abuse or dependence.

To examine the relationship between opioid abuse or dependence on perioperative outcomes, we retrospectively analyzed the National Readmission Database for 2013 and 2014. Patients who underwent a major operating room diagnostic or therapeutic procedure and who had opioid abuse or dependence codes according to the International Classification of Diseases, Ninth Revision, were compared to patients without those diagnoses who also underwent such procedures. We hypothesized that patients with opioid abuse or dependence would have higher readmission rates than patients without opioid abuse or dependence.

## Materials and Methods

### Data Source

We performed a retrospective cohort study using the National Readmission Database from 2013 to 2014. The National Readmission Database is the largest U.S. readmissions database and is maintained by the Healthcare Cost and Utilization Project, a project sponsored by the Agency for

Healthcare Research and Quality. This database is abstracted from state inpatient databases of participating states and contains discharge level records from inpatients treated at U.S. academic medical centers and community hospitals, excluding federal hospitals, rehabilitation facilities, and long-term acute care facilities. Each database has about 14 million records representing about 50% of the U.S. population and can be weighted to produce estimates on 35 million discharges.<sup>13</sup> The National Readmission Database contains verified patient linkage numbers that can be used to track a patient across hospitals within a state but not from one year to the next. Each record also has a timing variable to help determine the chronologic order of admissions in an individual patient. Because the National Readmission Database has no patient identifiers, the institutional review board at the University of Chicago (Chicago, Illinois) declared this study exempt from review.

### Study Population

Our study population included patients who were 18 yr or older and had undergone a major operating room procedure. The Healthcare Cost and Utilization Project categorizes all procedures into one of four groups: major diagnostic, minor diagnostic, major therapeutic, and major therapeutic.<sup>14</sup> Any admission during which a patient had either a major diagnostic or major therapeutic procedure is considered to be an admission with a major operating room procedure. This categorization is currently being used by the Centers for Medicare and Medicaid Services for Hospital Readmissions Reduction Program for risk adjustment.<sup>15</sup> We excluded records where the discharge month was December (due to the inability to track 30-day readmission data across calendar years), where the death status was missing, or where the order of admissions could not be ascertained. Missing data comprised less than 0.5% of all observations for this cohort. In accordance with Healthcare Cost and Utilization Project methodology, the first admission was considered an “index” admission, and the second admission was considered a “readmission.” Subsequent admissions occurring within a 30-day period were not counted.

Patients with opioid abuse or dependence were identified *via* International Classification of Diseases, Ninth Revision, codes used by the Healthcare Cost and Utilization Project to identify opioid abuse or dependence (Supplemental Digital Content, table 1, <http://links.lww.com/ALN/B639>).<sup>16,17</sup> Although not explicitly validated as capturing opioid abuse or dependence, these codes have been used by other authors to identify opioid abuse or dependence,<sup>8,18–20</sup> and a retrospective 2016 cohort study found associations between the presence of International Classification of Diseases, Ninth Revision, codes for opioid use or dependence and opioid overprescription.<sup>21</sup>

### Combining Data Sets

Because linkage identifiers do not track the same patients from one year to another, readmissions were identified for the 2013 and 2014 data sets separately. The two data sets were then concatenated to produce the final study population.

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Before further analysis, we also verified that no two hospitals in the database were assigned the same hospital identifier.

### Patient and Hospital Characteristics

We collected data on patient demographics (e.g., age, sex, primary expected payer, and income quartile of zip code of patient's residence), comorbidities, and hospital characteristics (e.g., bed size, location, hospital control, and teaching status). International Classification of Diseases, Ninth Revision, codes were utilized to identify common operations performed in the United States, including spinal fusion, knee replacement, hip replacement, cholecystectomy, lysis of peritoneal adhesions, coronary artery bypass graft, colorectal resection, pneumonectomy, breast surgeries (including axillary lymph node dissection and reconstructive surgery), cesarean delivery, and operations for limb fractures (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/B639>).<sup>22</sup> Patients who had limb fracture operations as well as joint (hip or knee) replacement surgery during the same hospitalization were considered to only have had joint replacement surgery. In addition, we recorded data on discharge disposition and hospital charges. To estimate hospital costs, we used hospital-specific cost to charge ratio files provided by the Healthcare Cost and Utilization Project for use with the National Readmissions Database.<sup>23</sup>

### Outcomes

The primary outcome variable was 30-day readmission. Secondary outcomes were length of stay, estimated costs of hospital admission, and reasons for readmission.

### Statistical Analyses

We performed data analysis using SAS 9.4 (SAS Institute, USA) and SUDAAN 11.1 (Research Triangle Institute, USA). Discharges were weighted to get national estimates using the National Readmissions Database data. Weighting was calculated based on both patient and hospital characteristics.

To account for clustering, we used generalized estimating equations with robust variance estimates. Specifically, we modeled a two-level hierarchy with patients being level 1 and hospitals being level 2. This methodology thus accounts for both hospital and patient variance. The robust variance estimator used in this analysis is the Taylor linearization estimator.

Categorical variables are presented as proportions and compared using a chi-square test. Continuous variables are presented as means and 95% CIs. We calculated unadjusted and adjusted odds ratios for readmission and primary reasons for readmissions. The data are presented as odds ratios and 95% CIs. Model adjusted readmission rates were calculated using predicted marginal probabilities to accurately represent population-based estimates. Estimated costs were analyzed using a generalized linear model assuming  $\gamma$  distribution with log link function. This approach is consistent with that used by other investigators.<sup>24–27</sup> Length of stay was analyzed using analyzed negative binomial regression.<sup>28</sup> To correct for multiple comparisons, we used a Bonferroni adjusted *P* value

threshold of less than 0.01 for statistical significance. This threshold was calculated by dividing the maximum allowable false positive rate ( $\alpha$ ) of less than 0.05 by the number of outcomes reported in our study (readmission rate, length of stay at initial admission, length of stay at readmission, estimated costs at initial admission, and estimated costs at readmission). Although we identified our outcomes *a priori*, we did not publish these outcomes before accessing the data and did not calculate a minimum clinically important difference.

For the adjusted analysis, we inserted all potential confounders of association of opioid abuse or dependence with readmission into our model. These included age, surrogates for socioeconomic status such as payer status and income quartile of zip code of residence, hospital characteristics, other (non-opioid) drug abuse status, length of stay at initial admission, all Elixhauser comorbidities (except drug abuse), need for ventilatory support more than 96h, need for whole blood, packed red blood cells, plasma or platelet transfusion (except autologous blood transfusion), and diagnoses of acute myocardial infarction, acute renal failure, deep vein thrombosis, pneumonia, sepsis, or respiratory failure during initial admission (Supplemental Digital Content, table 3, <http://links.lww.com/ALN/B639>). Because readmission rates may also depend on the specific surgical procedure performed, we also adjusted for common procedures.

### Sensitivity Analyses

Because some studies have also included opioid abuse and/or dependence in remission codes (Supplemental Digital Content, table 4, <http://links.lww.com/ALN/B639>) in their definition of opioid abuse or dependence, we also performed a *post hoc* sensitivity analysis to see whether inclusion of these codes would alter our primary outcome. In addition, because we adjusted for common procedures (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/B639>), we performed a sensitivity analysis to determine whether restricting the cohort to patients who had undergone these procedures would alter our results.

Finally, to verify that opioid abuse or dependence was an independent risk factor for readmission, as well as hospital length of stay and estimated costs, we calculated those parameters for patients with and without opioid abuse or dependence who had high-risk attributes (younger, male, on Medicaid, presenting to a large metropolitan teaching hospital, and residing in zip codes with lower-quartile incomes).

### Disposition

Because the National Readmissions Database does not classify transfers from a rehabilitation facility, skilled nursing facility, or long-term acute care facility to a hospital as a readmission, we analyzed our cohort to calculate rates of discharge to such facilities in both groups.

## Results

### Demographics and Patient Characteristics

We identified 16,019,086 patients who were 18 yr or older and had a major operating room procedure. Of these, 16,016,842

had a known death status; 94,903 (0.6%) of these patients met our definition of opioid abuse or dependence, as depicted in figure 1. Patients with opioid abuse or dependence were more likely to be younger, male, on Medicaid, and reside in zip codes with incomes in lower quartiles. Patients with opioid abuse or dependence were also more likely to present to a large, metropolitan teaching hospital on initial presentation. Patient and hospital characteristics are shown in table 1.

**Patient Comorbidities and Operating Room Procedure Characteristics**

The prevalence of relevant comorbidities and complications for both groups of patients are shown in table 2. Opioid abuse or dependence patients had a higher prevalence of acquired immunodeficiency syndrome, psychoses, alcohol abuse, depression, chronic lung disease, and liver disease. Patients without a history of opioid abuse or dependence had higher rates of hypertension, obesity, and renal failure. Opioid abuse or dependence patients were also more likely to have needed perioperative ventilatory support for more than 96h, to have needed blood transfusion (whole blood, packed red cells, plasma, platelets excluding autologous blood transfusion), and to have diagnoses of acute renal failure, acute respiratory failure, pneumonia, sepsis, or deep vein thrombosis on initial admission. Patients with opioid abuse or dependence were less likely to have undergone cholecystectomy, colorectal surgery, coronary artery bypass graft, hip replacement, hysterectomy, knee replacement, and breast surgery. No differences were observed between groups for rates of pneumonectomy,

lysis of adhesions, spinal fusion, or cesarean delivery. Rates of common procedures in the two groups are shown in table 3.

**Readmissions**

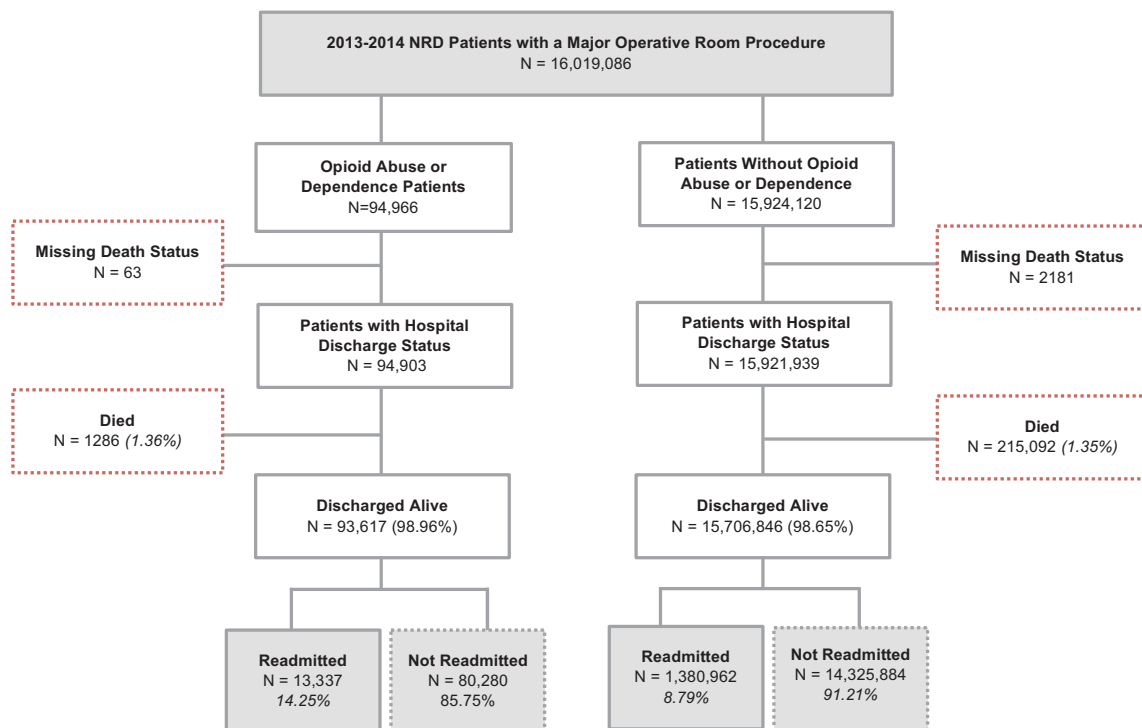
Opioid abuse or dependence patients had higher 30-day readmission rates than patients without these diagnoses (14.3% vs. 8.8%; odds ratio 1.72; 95% CI, 1.67 to 1.78;  $P < 0.0001$ ). This association persisted after adjustment for all relevant confounders (11.1% vs. 9.1%; odds ratio 1.26; 95% CI, 1.22 to 1.30;  $P < 0.0001$ ; table 4).

**Reasons for Readmission**

The most common reason for readmission in both groups was infection. However, infections were a more common reason for readmission in opioid abuse or dependence patients (27.0% vs. 18.9%;  $P < 0.0001$ ). Certain infections were more common in patients with opioid abuse or dependence, namely cellulitis and other subcutaneous infections, bone and joint infections, endocarditis, and central nervous system abscesses. In contrast, rates of device- and procedure-related infections, pneumonia, abdominal abscess, and peritonitis were similar in both groups. Opioid abuse or dependence patients also had higher rates of psychiatric diagnoses, acute pain, opioid dependence, opioid overdose, nonopioid overdose, and drug withdrawal (table 5).

**Length of Stay and Cost Analyses**

The mean hospital length of stay was longer in opioid abuse or dependence patients at initial admission (10 vs. 5 days;  $P < 0.0001$ ; table 6) and readmission (7 vs. 6 days;  $P < 0.0001$ ;



**Fig. 1.** Consolidated Standards of Reporting Trials diagram depicting the study flow for patients in the National Readmission Database (NRD) who were admitted with and without opioid abuse or dependence. Overall, 14.3% of patients with opioid abuse or dependence were readmitted, compared to 8.8% of patients without opioid abuse or dependence.

**Table 1.** Demographics of Patients Having Major Operating Room Procedures at Initial Admission

	Patients with Opioid Abuse or Dependence (N = 94,903)	Patients without Opioid Abuse or Dependence (N = 15,921,938)	P Value
<b>Patient characteristics</b>			
Female sex	50,347 (53.1)	9,550,354 (60.0)	< 0.0001*
Age category (yr)			
18–39	36,602 (38.6)	3,871,996 (24.3)	< 0.0001*
40–64	47,384 (49.9)	5,918,612 (37.2)	
65–74	7,767 (8.2)	3,209,660 (20.2)	
75+	3,150 (3.3)	2,921,669 (18.4)	
Zip code income quartile			
Yr 2013	Yr 2014		< 0.0001*
\$1–37,999	\$1–39,999	3,979,265 (25.4)	
\$38,000–47,999	\$40,000–50,999	4,253,156 (27.1)	
\$48,000–\$63,999	\$51,000–65,999	3,909,321 (24.9)	
\$64,000+	\$66,000+	3,540,772 (22.6)	
Insurance status			
Medicare	13,639 (28.4)	6,603,802 (41.6)	< 0.0001*
Medicaid	37,144 (39.2)	2,211,298 (13.9)	
Private insurance	17,094 (18.0)	5,831,954 (36.7)	
Self-pay	7,644 (8.1)	518,664 (3.3)	
No charge	1,284 (1.4)	76,235 (0.5)	
Other	4,642 (4.9)	655,811 (4.1)	
Elective admission to the hospital	28,600 (30.2)	8,462,272 (53.3)	< 0.0001*
Patient’s residence and hospital are in same state	91,543 (96.5)	14,920,645 (93.7)	< 0.0001*
<b>Hospital characteristics</b>			
Teaching status			
Metropolitan nonteaching	26,495 (27.9)	4,808,216 (30.2)	0.001*
Metropolitan teaching	62,402 (65.8)	9,900,494 (62.2)	
Nonmetropolitan hospital	6,007 (6.3)	1,213,229 (7.6)	
Hospital location			
Large metropolitan area > 1 million residents	60,417 (63.7)	8,831,853 (55.5)	< 0.0001*
Small metropolitan area < 1 million residents	28,479 (30.0)	5,876,857 (36.9)	
Metropolitan area	5,017 (5.3)	984,759 (6.2)	
Nonurban area	990 (1.0)	228,470 (1.4)	
Hospital bed size			
Small	9,906 (10.4)	2,079,152 (13.1)	< 0.0001*
Medium	21,714 (22.9)	3,916,048 (24.6)	
Large	63,284 (66.7)	9,926,738 (62.4)	
Hospital control			
Government, nonfederal	13,757 (14.5)	1,831,873 (11.5)	0.0003*
Private nonprofit	70,001 (73.8)	11,922,077 (74.9)	
Private investor–owned	11,146 (11.7)	2,167,988 (13.6)	

The data are presented as N (%).

\*Significant P value of less than 0.01.

table 7). These differences persisted after adjustment for relevant covariates at both initial admission (6 vs. 4 days;  $P < 0.0001$ ) and readmission (6 vs. 5 days;  $P < 0.0001$ ). Estimated costs at initial admission were higher in patients with opioid abuse or dependence (\$27,422 vs. \$19,409;  $P < 0.0001$ ; table 6). This difference persisted after adjustment for relevant covariates (\$18,528 vs. \$16,617;  $P < 0.0001$ ). Estimated costs at readmission did not differ between groups after adjustment (\$12,258 vs. \$12,220;  $P = 0.79$ ; table 7).

**Sensitivity Analyses**

Readmission rates were similar ( $P = 0.31$ ) for patients who had only opioid abuse or dependence codes (14.3%), only opioid abuse or dependence in remission codes (13.2%), or

both (14.5%). Restricting our cohort to patients who had undergone common procedures that we specifically controlled for (Supplemental Digital Content, table 2, <http://links.lww.com/ALN/B639>) also resulted in higher 30-day readmission rates among patients with opioid abuse or dependence (odds ratio 1.39; 95% CI, 1.31 to 1.46). Patients who had undergone these procedures comprised 58% of the full cohort.

Within the cohort that had high risk attributes (younger, male, on Medicaid, presenting to a large metropolitan teaching hospital, and residing in zip codes with lower-quartile incomes), patients with opioid abuse or dependence had higher readmission rates (18.6 vs. 11.7%;  $P = 0.001$ ), higher costs (\$36,249 vs. \$28,902;  $P < 0.001$ ), and longer lengths of stay on initial hospitalization (14 [13 to 16] vs. 9 [9 to 9];  $P < 0.001$ ).

**Table 2.** Comorbidities of Patients with Major Operating Room Procedures at Initial Admission

Comorbidities	Patients with Opioid Abuse or Dependence (N = 94,903)	Patients without Opioid Abuse or Dependence (N = 15,921,938)	P Value
Acquired Immunodeficiency Syndrome	528 (0.6)	15,642 (0.1)	< 0.0001*
Alcohol abuse	11,292 (11.9)	385,357 (2.4)	< 0.0001*
Deficiency anemias	19,909 (21.0)	2,197,766 (13.8)	< 0.0001*
Connective disease	3,328 (3.5)	420,335 (2.6)	< 0.0001*
Chronic blood loss anemia	4,167 (4.4)	557,540 (3.5)	< 0.0001*
Congestive heart failure	4,311 (4.5)	697,776 (4.4)	0.22
Chronic lung disease	20,772 (21.9)	2,419,134 (15.2)	< 0.0001*
Coagulopathy	6,500 (6.9)	694,546 (4.4)	< 0.0001*
Depression	19,284 (20.3)	1,587,130 (10.0)	< 0.0001*
Diabetes mellitus uncomplicated	9,953 (10.5)	2,560,099 (16.1)	< 0.0001*
Diabetes mellitus with complications	5,870 (6.2)	687,717 (4.3)	< 0.0001*
Hypertension	36,270 (38.2)	7,725,052 (48.5)	< 0.0001*
Hypothyroidism	6,944 (7.3)	1,651,251 (10.4)	< 0.0001*
Liver disease	10,624 (11.2)	353,794 (2.2)	< 0.0001*
Fluid/electrolyte disorders	24,580 (25.9)	2,506,768 (15.7)	< 0.0001*
Neurologic disorders other than paralysis	7,069 (7.5)	739,568 (4.6)	< 0.0001*
Obesity	13,071 (13.8)	2,386,039 (15.0)	0.001*
Paralysis/stroke	2,622 (2.8)	286,284 (1.8)	< 0.0001*
Peripheral vascular disease	6,043 (6.4)	1,024,239 (6.4)	0.70
Psychoses	12,238 (12.9)	439,917 (2.8)	< 0.0001*
Renal failure	6,894 (7.3)	1,385,453 (8.7)	< 0.0001*
Peptic ulcer without bleeding	60 (0.1)	4,789 (0.03)	0.01
Valvular disease	2,624 (2.8)	464,447 (2.9)	0.08
Weight loss	7,390 (7.8)	581,183 (3.7)	< 0.0001*
Acute myocardial infarction	2,805 (3.0)	754,418 (4.7)	< 0.0001*
Acute renal failure	9,316 (9.8)	1,109,014 (7.0)	< 0.0001*
Respiratory failure	10,020 (10.6)	1,013,734 (6.4)	< 0.0001*
Pneumonia	5,560 (5.9)	469,809 (3.0)	< 0.0001*
Sepsis	11,309 (11.9)	601,875 (3.8)	< 0.0001*
Deep vein thrombosis	2,248 (2.4)	230,277 (1.5)	< 0.0001*
Need for ventilatory support > 96 h	2,793 (2.9)	224,166 (1.4)	< 0.0001*
Blood transfusion	12,605 (13.3)	1,526,420 (9.6)	< 0.0001*

The data are presented as N (%).

\*Significant P value of less than 0.01.

**Table 3.** Common Major Operating Room Procedures at Initial Admission

Procedure Categories	Patients with Opioid Abuse or Dependence (N = 94,903)	Patients without Opioid Abuse or Dependence (N = 15,921,938)	P Value
Cholecystectomy	3,612 (3.8)	694,907 (4.4)	< 0.0001*
Colorectal surgery	1,871 (2.0)	561,748 (3.5)	< 0.0001*
Coronary artery bypass graft	918 (1.0)	371,621 (2.3)	< 0.0001*
Hip replacement	3,796 (4.0)	962,015 (6.0)	< 0.0001*
Hysterectomy	671 (0.7)	471,902 (3.0)	< 0.0001*
Spinal fusion	5,609 (5.9)	816,022 (5.1)	0.01
Knee replacement	4,249 (4.5)	1,393,654 (8.8)	< 0.0001*
Lysis of adhesions	1,608 (3.4)	573,026 (3.6)	0.10
Pneumonectomy	834 (0.9)	160,508 (1.0)	0.02
Limb fracture surgery	8,073 (8.5)	947,378 (6.0)	< 0.0001*
Cesarean delivery	12,607 (13.3)	2,238,576 (14.1)	0.09
Breast surgery	249 (0.3)	152,265 (1.0)	< 0.0001*

The data are presented as N (%).

\*Significant P value of less than 0.01.

**Disposition**

More patients with a history of opioid abuse or dependence underwent discharge to rehabilitation, skilled nursing facility, or long-term acute care facility after initial hospitalization (38.5% vs. 33.1%; *P* < 0.0001).

**Discussion**

In this study, we report an association between opioid abuse or dependence and readmission rates after perioperative hospitalizations in the 2013 and 2014 National Readmissions Database. This association remained significant after controlling for

relevant patient and surgical factors. Hospital length of stay was higher at initial admission and at readmission for patients with opioid abuse and dependence. Estimated hospital costs for the initial hospitalization were also higher in this group.

Previous studies have also found an association between preoperative opioid use with increased mortality,<sup>20</sup> morbidity,<sup>12,20,29</sup> length of stay,<sup>11,12,20,29,30</sup> and costs.<sup>12,29</sup> Two retrospective 2017 studies also observed higher readmission rates in patients with preoperative opioid use who underwent elective abdominal surgery.<sup>12,29</sup> Our study expands on these findings because it included all patients undergoing a major operating room procedure in a nationally representative database.

**Table 4.** Odds Ratio of the Multivariable Model Predicting Readmission

Variable	Odds Ratio (95% CI)	
Opioid abuse or dependence	1.26 (1.22–1.30)	
Patient characteristics		
Female sex	0.95 (0.94–0.95)	
Age category (yr)		
18–39	1.00 (reference)	
40–64	1.16 (1.15–1.18)	
65–74	1.04 (1.02–1.06)	
75+	1.20 (1.18–1.22)	
Zip income quartile		
Yr 2013	Yr 2014	
\$1–37,999	\$1–39,999	1.00 (reference)
\$38,000–47,999	\$40,000–50,999	0.97 (0.96–0.97)
\$48,000–63,999	\$51,000–65,999	0.96 (0.95–0.97)
\$64,000+	\$66,000+	0.93 (0.92–0.95)
Insurance status		
Medicare	1.00 (reference)	
Medicaid	0.98 (0.96–0.99)	
Private insurance	0.71 (0.70–0.72)	
Self-pay	0.69 (0.67–0.71)	
No charge	0.74 (0.71–0.78)	
Other (e.g., TRICARE)	0.72 (0.70–0.74)	
Hospital characteristics		
Hospital ownership		
Government	1.00 (reference)	
Private nonprofit	0.99 (0.96–1.02)	
Private investor-owned	1.07 (1.04–1.11)	
Hospital bed size		
Small	1.00 (reference)	
Medium	1.09 (1.06–1.12)	
Large	1.13 (1.10–1.16)	
Teaching status		
Metropolitan nonteaching	1.00 (reference)	
Metropolitan teaching	1.10 (1.08–1.12)	
Nonmetropolitan hospital	0.84 (0.81–0.86)	
Hospital location		
Large metropolitan area > 1 million residents	1.00 (reference)	
Small metropolitan area < 1 million residents	0.93 (0.91–0.95)	
Micropolitan area	1.00 (1.00–1.00)	
Nonurban area	0.96 (0.90–1.01)	

(Continued)

**Table 4.** (Continued)

Variable	Odds Ratio (95% CI)
Comorbidities/complications	
Acquired Immunodeficiency Syndrome	1.32 (1.24–1.41)
Alcohol abuse	1.05 (1.03–1.07)
Deficiency anemias	1.19 (1.18–1.20)
Connective tissue disease	1.17 (1.15–1.19)
Chronic blood loss anemia	1.04 (1.02–1.06)
Congestive heart failure	1.25 (1.23–1.26)
Chronic lung disease	1.21 (1.20–1.22)
Coagulopathy	1.11 (1.10–1.13)
Depression	1.11 (1.10–1.12)
Diabetes mellitus (uncomplicated)	1.14 (1.13–1.15)
Diabetes mellitus with complications	1.29 (1.27–1.31)
Drug use other than opioids	1.19 (1.16–1.21)
Hypertension	1.02 (1.01–1.03)
Hypothyroidism	1.02 (1.01–1.03)
Liver disease	1.27 (1.24–1.30)
Fluid/electrolyte disorders	1.26 (1.25–1.27)
Neurologic disorders other than paralysis	1.15 (1.14–1.17)
Obesity	1.04 (1.03–1.05)
Paralysis	1.03 (1.01–1.05)
Peripheral vascular disease	1.21 (1.19–1.22)
Psychoses	1.23 (1.21–1.26)
Renal failure	1.37 (1.35–1.38)
Peptic ulcer	1.28 (1.13–1.44)
Valve disease	1.05 (1.04–1.07)
Weight loss	1.22 (1.20–1.24)
Acute myocardial infarction	1.03 (1.01–1.05)
Acute renal failure	1.17 (1.15–1.18)
Respiratory failure	1.17 (1.15–1.18)
Pneumonia	1.15 (1.13–1.17)
Sepsis	1.11 (1.09–1.13)
Deep vein thrombosis	1.34 (1.31–1.36)
Need for ventilatory support > 96 h	0.67 (0.65–0.69)
Transfusion	1.38 (1.36–1.39)
Procedures	
Coronary artery bypass graft	0.83 (0.81–0.85)
Cholecystectomy	0.80 (0.78–0.81)
Colorectal surgery	1.12 (1.11–1.14)
Hip replacement	0.54 (0.54–0.56)
Hysterectomy	0.61 (0.60–0.63)
Knee replacement	0.41 (0.40–0.42)
Lysis of adhesions	1.21 (1.19–1.23)
Pneumonectomy	0.83 (0.80–0.86)
Spinal fusion	0.60 (0.58–0.61)
Limb fracture surgery	0.67 (0.66–0.68)
Cesarean delivery	0.28 (0.27–0.28)
Breast surgery	0.71 (0.68–0.73)

Although infections were the most common reason for readmission in both groups, we found that infections overall, as well as specific infections (endocarditis, central nervous system abscesses, cellulitis and other subcutaneous infections, and bone and joint infections), were more common reasons for readmission in the opioid abuse or dependence group. In contrast to our findings, a recent 2017 study found similar reasons for readmission among preoperative opioid

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**Table 5.** Reasons for Readmission

	Patients with Opioid Abuse or Dependence (N = 13,337)	Patients without Opioid Abuse or Dependence (N = 1,380,962)	P Value
Acute respiratory failure	129 (1.0)	15,288 (1.1)	0.29
Acute heart failure	99 (0.7)	21,763 (1.6)	< 0.0001*
Acute renal failure	260 (2.0)	32,404 (2.4)	0.10
Infections	3,542 (27.0)	261,485 (18.9)	< 0.0001*
Device- and procedure-related infections	1,110 (8.3)	106,194 (7.7)	0.10
Sepsis	919 (6.9)	90,402 (6.6)	0.32
Cellulitis and other subcutaneous infections	659 (4.9)	17,239 (1.3)	< 0.0001*
Bone and joint infections	371 (2.8)	7,185 (0.5)	< 0.0001*
Pneumonia	278 (2.1)	32,855 (2.4)	0.16
Central nervous system abscess	88 (0.7)	1,690 (0.1)	< 0.0001*
Endocarditis	61 (0.5)	634 (0.1)	< 0.0001*
Abdominal abscess and peritonitis	48 (0.4)	5,677 (0.4)	0.48
Nonhealing wounds/dehiscence	223 (1.7)	20,520 (1.5)	0.27
Psychiatric disorders	371 (2.8)	8,152 (0.6)	< 0.0001*
Opioid-related			
Opioid dependence	60 (0.5)	144 (0.01)	< 0.0001*
Other drug dependence	21 (0.2)	130 (0.01)	0.01
Opioid overdose	135 (1.0)	1,563 (0.1)	< 0.0001*
Drugs other than opioids			
Overdose of other drugs	66 (0.5)	1,342 (0.1)	< 0.0001*
Drug withdrawal (except alcohol)	154 (1.2)	704 (0.05)	< 0.0001*
Drug mental disorders	24 (0.2)	376 (0.03)	0.07
Pain diagnoses			
Acute pain	129 (1.0)	6,638 (0.5)	< 0.0001*

The data are presented as N (%).

\*Significant P value of less than 0.01.

**Table 6.** Length of Stay and Hospital Costs at Initial Admission

Outcome	Patients with Opioid Abuse or Dependence (N = 94,903)	Patients without Opioid Abuse or Dependence (N = 15,921,938)	P Value
Unadjusted			
Length of stay on initial admission, days	10 (10–10)	5 (5–5)	< 0.0001*
Cost of stay on initial admission, \$	27,422 (27,214–27,634)	19,409 (19,398–19,421)	< 0.0001*
Adjusted†			
Length of stay on initial admission, days	6 (6–6)	4 (4–4)	< 0.0001*
Cost of stay on initial admission, \$	18,528 (18,424–18,632)	16,617 (16,610–16,624)	< 0.0001*

The values are presented as means (95% CI).

†Significant P value of less than 0.01. †The values are adjusted for patient demographics, hospital characteristics, comorbidities, prolonged ventilation, transfusion, procedures, acute myocardial infarction, acute renal failure, pneumonia, acute respiratory failure, deep vein thrombosis, and sepsis (all at initial admission).

users and nonusers.<sup>12</sup> This difference may be due to a wider spectrum of operating room procedures in our study and our identification of patients with opioid abuse or dependence rather than preoperative opioid use, as the group of interest. Previous studies have identified a link between opioid dependence and endocarditis<sup>31</sup> and opioid and amphetamine dependence and methicillin-resistant *Staphylococcus aureus* infections.<sup>32</sup> A National Inpatient Sample study found that over a 10-yr period, rates of serious bacterial infection (endocarditis, osteomyelitis, septic arthritis, and epidural abscess) were two times higher among patients with opioid abuse or dependence.<sup>33</sup> Two population-based studies also found significant associations between serious bacterial infections

with periods of oral opioid intake in elderly patients<sup>34</sup> and in patients with rheumatoid arthritis.<sup>35</sup> Because our study was retrospective, however, we cannot determine whether the association between opioid misuse and infection rates that we observed is a direct causal effect.

A higher proportion of patients in the opioid abuse or dependence group had psychiatric diagnoses, opioid overdose, nonopioid overdose, drug withdrawal, opioid dependence, and acute pain diagnoses as reasons for readmission. The increased prevalence of these diagnoses emphasizes a link between the presence of opioid abuse or dependence and a heightened risk of readmission related to these disorders and is consistent with previous data finding high



**Table 7.** Length of Stay and Hospital Costs at Readmission

Outcome	Patients with Opioid Abuse or Dependence (N = 13,337)	Patients without Opioid Abuse or Dependence (N = 15,921,938)	P Value
Unadjusted			
Length of stay on readmission, days	7 (7–7)	6 (6–6)	< 0.0001*
Cost of stay on readmission, \$	15,248 (14,898–15,606)	14,564 (14,532–14,597)	0.01
Adjusted†			
Length of stay on readmission, days	6 (5–6)	5 (5–5)	< 0.0001*
Cost of stay on readmission, \$	12,258 (11,978–12,545)	12,220 (12,185–12,256)	0.79

The values are presented as means (95% CI).

\*Significant *P* value of less than 0.01. †The values are adjusted for patient demographics, hospital characteristics, comorbidities, prolonged ventilation, transfusion, procedures, acute myocardial infarction, acute renal failure, pneumonia, acute respiratory failure, deep vein thrombosis, and sepsis (all at initial admission).

readmission rates in patients admitted for psychiatric disorders and substance-related disorders.<sup>36,37</sup>

Our study does have several limitations. Our results depended on the use of diagnoses (International Classification of Diseases, Ninth Revision) and procedure codes to identify a cohort of patients with opioid abuse and/or dependence who underwent surgical procedures. Because our study involved a retrospective database review, we cannot verify the accuracy of diagnoses coded and cannot estimate what proportion of patients with opioid abuse and dependence were captured by the diagnosis codes used. The prevalence of opioid abuse or dependence in our study was similar to that in other administrative database studies.<sup>38,39</sup> However, our results may underestimate the true prevalence due to provider reluctance to assign such diagnoses to patients, reimbursement considerations, and a lack of recognition of opioid abuse or dependence.<sup>20,38,40</sup> Such an underestimation may have caused patients with a history of opioid abuse or dependence to be incorrectly assigned to the group without these diagnoses, potentially reducing the effect size we observed.

Furthermore, even though we accounted for relevant patient and surgical factors, we cannot account for unmeasured covariates, which may have contributed to the differences in readmission rates we observed. We controlled for common procedures but did not restrict our cohort to the subset of patients who had undergone procedures that were controlled for to avoid limiting generalizability. In our sensitivity analysis, however, we found the increased risk of readmission within 30 days to persist even among this smaller cohort. In addition, we considered all patients discharged alive from initial admission to be at risk for readmission. However, because the National Readmissions Database cannot be linked to the National Death Index, we could not ascertain how many patients died after initial discharge in each group and thus were no longer at risk for readmission. Finally, a lower proportion of patients with opioid abuse or dependence were discharged home rather than to rehabilitation, skilled nursing facility, or long-term acute care facility. Because the National Readmissions Database does not classify transfers back from such facilities to a hospital as a readmission, the readmission rate calculated may be falsely low.

Despite these limitations, however, our use of a large, nationally representative database that captures data from over half of all admissions in the United States and includes patients who are uninsured, privately insured, and on Medicaid/Medicare allows us a widely generalizable result and a more complete analysis of risk factors. Our data suggest that patients with a history of opioid abuse or dependence have a higher baseline risk for readmission and may benefit from interventions targeted at minimizing their readmission risk.

In conclusion, in this retrospective analysis of the National Readmissions Database we describe an association between a history of opioid abuse or dependence and increased risk of readmission after perioperative hospitalization. Future work is needed to identify causative factors and develop perioperative interventions to minimize the risk of readmissions and opioid-related complications in patients with opioid abuse or dependence.

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## Competing Interests

The authors declare no competing interests.

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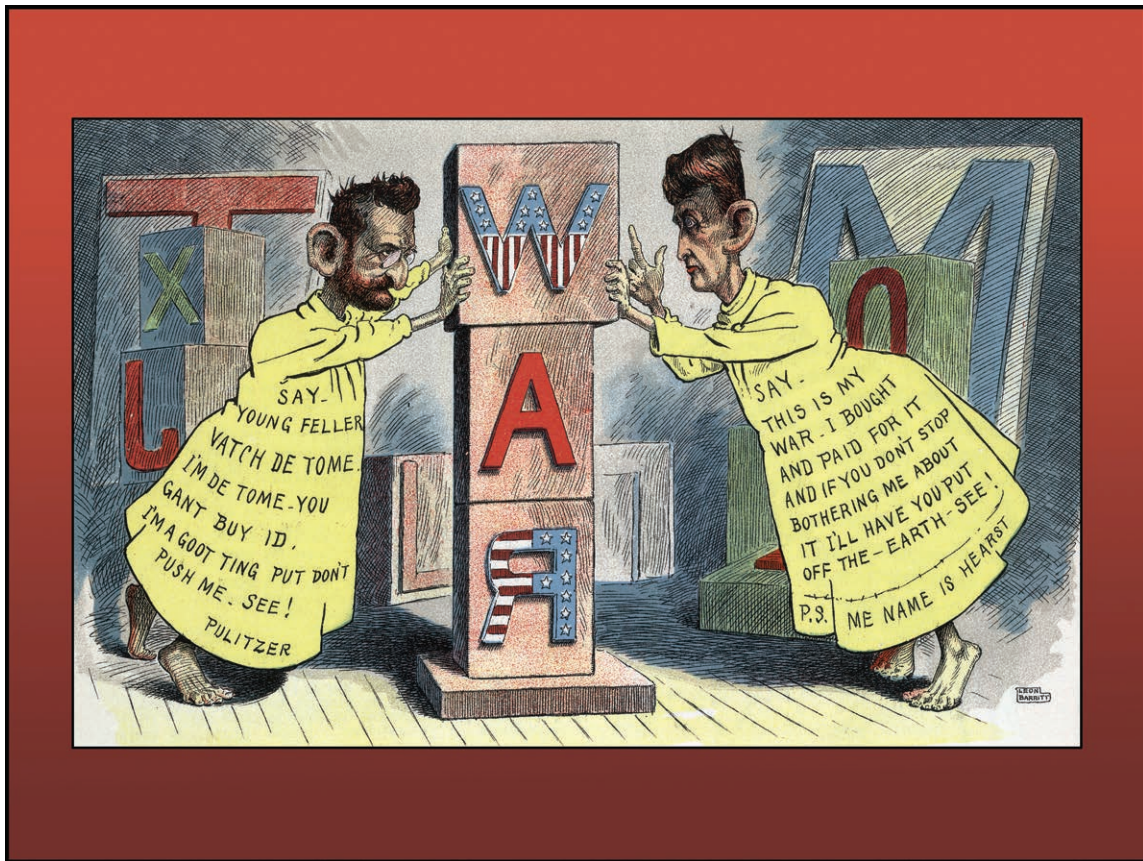
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