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Preoperative opioid use and postoperative pain associated with surgical readmissions

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ABSTRACT

Background: The extent of preoperative opioid utilization and the relationship with pain-related readmissions are not well understood.
Methods: VA Surgical Quality Improvement Program data on general, vascular, and orthopedic surgeries (2007–2014) were merged with pharmacy data to evaluate preoperative opioid use and pain-related readmissions. Opioid use in the 6-month preoperative period was categorized as none, infrequent, frequent, and daily.
Results: In the six-month preoperative period, 65.7% had no opioid use, 16.7% had infrequent use, 6.3% frequent use, and 11.4% were daily opioid users. Adjusted odds of pain-related readmission were higher for opioid-exposed groups vs the opioid-naïve group: infrequent (OR 1.17; 95% CI:1.04–1.31), frequent (OR 1.28; 95% CI:1.08–1.52), and daily (OR 1.49; 95% CI:1.27–1.74). Among preoperative opioid users, those with a pain-related readmission had higher daily preoperative oral morphine equivalents (mean 44.5 vs. 36.1, $p < 0.001$).
Conclusions: Patients using opioids preoperatively experienced higher rates of pain-related readmissions, which increased with frequency and dosage of opioid exposure.

Introduction

The opioid epidemic has reached a crisis level and garnered national attention with an estimated economic burden of approximately $78.5 billion annually.[1] Substantial increases in opioid prescribing, tripling from 1999 to 2015, paralleled the ongoing opioid epidemic with drastic increases in opioid abuse, dependency, and overdose rates.[2] Despite increased awareness to the potential risks associated with opioid use, a recent retrospective cohort study of 48 million commercially insured and Medicare Advantage beneficiaries found that the number of opioid prescriptions remained unchanged from 2007 to 2016.[3] A 2015 National Survey on Drug Use and Health (NSDUH) showed that more than one third of the US population used prescription opioids at some point during that year.[4] With such a high prevalence of opioid use, many surgical patients will have preoperative opioid exposure which may influence their outcomes. Published estimates vary widely reporting 7% to over 80% of surgical patients had

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preoperative opioid use, depending on surgical specialty and definition of preoperative use.[5–12]

In addition to the variation seen in the preoperative setting, recent studies have shown similar, wide variation in postoperative opioid prescribing practices.[13,14] Surgeons are now finding themselves and their prescribing patterns under scrutiny and are increasingly under pressure to reduce opioid prescriptions, while still adequately managing postoperative pain. Postoperative pain is a common reason for readmission following surgery and previous studies have demonstrated the importance of pain resolution due to the association with post discharge healthcare utilization.[15–18] While much emphasis has been placed on limiting opioids prescribed in the postoperative period, the question of how preoperative opioid use affects surgical outcomes has received much less attention.

The association between preoperative opioid use and increased postoperative healthcare utilization, including readmissions, has been studied independently in orthopedic,[7,19–21] abdominal,[5,22] and emergency general surgeries.[23] However, the extent of preoperative opioid utilization and the relationship to postoperative pain-related readmissions is unknown. The objective of this study is to examine the relationship between preoperative opioid use and the risk of pain-related postoperative readmissions in the Veterans Health Administration (VA) surgical population.

Methods

This is a retrospective cohort study of general, orthopedic, and peripheral vascular inpatient surgeries occurring in the VA between October 1, 2007 and September 30, 2014. The study was reviewed and approved with a waiver of informed consent by the VA Central Institutional Review Board.

Study population

The study population includes Veterans undergoing general, orthopedic, or peripheral vascular inpatient surgeries with a total length of hospital stay between 2 and 30 days. Patients were followed for 30 days after hospital discharge. Patients experiencing in-hospital death were excluded from the study population as were patients discharged to a location other than community. Due to our inability to assess quantities of outpatient opioid injections administered, 1,277 surgeries were also excluded due to evidence of outpatient prescriptions for injectable opioids. In the event of multiple surgeries during the study period, only information from the first surgery was included in this analysis.

Preoperative opioid exposure

Outpatient pharmacy data was obtained from the VA Corporate Data Warehouse (CDW) under the Outpatient Pharmacy Domain. The VA drug classification number for opioid analgesics (CN101) was used to identify outpatient opioid prescriptions filled in the 6 months prior to index hospital admission. The main exposure of interest was frequency of outpatient opioid usage in the preoperative period. Frequency of outpatient opioid usage was determined by the proportion of days covered (PDC) in the 6 months prior to hospital admission as calculated by the ReCOMP algorithm.[24] In brief, days covered was defined as the total day supply for the 6 months prior to surgery divided by 180. If a prescription was refilled before the end of a prior prescription, the remaining days of the previous prescription were not included in the calculation. For prescriptions filled before the start of the 6-month period but extending into the 6-month period, only the time covered in the 6-month period was included. Preoperative outpatient opioid usage was then determined by stratifying patients into four groups: no use, infrequent use ($\leq$2 prescription fills or < 30 days of supply), frequent but not daily use ($\geq$3 prescription fills with <80% PDC), and daily use ($\geq$3 prescription fills with $\geq$80% PDC).

Outcome

The main outcome of interest for this study was the occurrence of an unplanned pain-related inpatient admission in the 30 days following the index hospital discharge. A readmission was defined as unplanned based on the current Centers for Medicare and Medicaid algorithm. Methods for this determination have been previously described.[25] Pain-related readmissions were defined using *International Classification of Disease, 9*th *Revision* (ICD9) pain-related diagnosis codes from administrative data (ICD9: 338.11, 338.12, 338.18, 338.19, 338.21, 338.22, 338.28, 338.29). An additional outcome of interest included all-cause unplanned inpatient readmission in the 30 days following the index hospital discharge.

Covariates

Characteristics of preoperative and postoperative opioid usage were obtained from the Outpatient Pharmacy domain as were prescriptions for nonsteroidal anti-inflammatory drugs, acetaminophen, and benzodiazepines. For all opioid prescriptions, total oral morphine equivalents (OMEs) were calculated by first multiplying the milligram strength of opioid per unit dispensed by the quantity dispensed and then multiplying the strength-quantity product by opioid-specific conversion factors. Average daily OMEs were then calculated by dividing the total OMEs for a prescription by the number of days supplied. Medications were considered active at admission if the prescription was filled prior to the index surgery date and overlapped with the admission based on the days supplied. Medications filled at discharge included prescriptions filled on the day prior to discharge through two days after discharge.

Additional covariates of interest were collected from both the VA CDW and the VA Surgical Quality Improvement Program (VASQIP) as previously described.[25] VASQIP data was primarily used for surgical specialty, patient demographics, and preoperative comorbidities. Codes from the *International Classification of Diseases, 9*th *Revision* in the VA CDW Inpatient and Outpatient domains were queried for additional information on marital status, mental health diagnoses, and prior healthcare utilization in the 6 months prior to surgery.

Statistical analyses

All data was cleaned and thoroughly checked for missing data elements and outliers. In keeping with the nature of administrative data, extreme values of opioid quantities were found for both preoperative and postoperative opioid fills. With no additional information on valid values, calculated OMEs in excess of the 99th percentile were marked as missing allowing an individual to be classified by preoperative opioid usage but eliminating the influence of potential administrative data errors. Univariate statistics were used to examine distributional assets of each variable prior to bivariate analyses.

Chi-square tests or analysis of variance was used to examine differences in covariates across the 4 groups of preoperative opioid usage. Chi-square tests and analysis of variance were also used to examine the association of opioid use with the outcome of pain-related readmission and all-cause unplanned readmission. After a thorough review of our findings in bivariate analyses, a multivariate model of pain-related readmission was constructed adjusting for factors found to be associated with pain-related readmission in

bivariate analyses. The three main covariates of interest in the multivariate model were frequency of preoperative opioid usage, the presence of opioids on hand at hospital admission, and the receipt of an opioid prescription at the time of hospital discharge.

Multivariate models were then stratified by surgical specialty in order to understand variation in opioid use and prescription patterns across surgical specialty. Lastly, the R-Program GGPLOT2 package was used to visualize smoothed trends in the association of preoperative daily OME and pain-related readmissions. Other analyses were conducted in SAS 9.4. An alpha of 0.05 was considered to be statistically significant.

Results

Patient and procedural characteristics

A total of 237,441 inpatient general, peripheral vascular or orthopedic surgical episodes in 198,979 patients were identified in the initial cohort. 29,474 surgical procedures were excluded because the patient was discharged to somewhere other than the community and another 1,277 surgical procedures were excluded due to evidence of outpatient prescriptions for injectable opioids. The final study population included 176,989 unique patients undergoing 206,720 surgical procedures. Surgical procedures included three broad categories: general surgery (42.9%), orthopedic (39.2%), and peripheral vascular. In the six months prior to surgery, 116,185 (65.7%) patients showed no evidence of opioid use, 29,460 (16.7%) were considered infrequent opioid users, 11,104 (6.3%) were frequent opioid users, and 20,240 (11.4%) were daily opioid users.

The demographic characteristics of the study population are shown in Table 1. Daily and frequent preoperative opioid use was more prevalent for patients undergoing orthopedic surgery. Patients with evidence of preoperative opioid use had a higher prevalence of psychiatric conditions (Depression: 22.5% vs. 13.3%, $p < 0.001$, Anxiety: 9.3% vs. 5.7%, $p < 0.001$), substance abuse (10.7% vs. 6.0%, $p < 0.001$), and history of chronic pain (6.1% vs. 1.2%, $p < 0.001$) than opioid naïve patients. Patients who were current smokers had increased preoperative opioid use (Table 1). Preoperative pain scores were higher for those with any preoperative opioid exposure as compared with opioid naïve patients (Mean: 4.1 vs. 3.1, $p < 0.001$, Table 1). Similarly, postoperative pain scores were higher for those with any preoperative opioid exposure as compared with opioid naïve patients (Mean: 4.6 vs. 3.6, $p < 0.001$). As shown in Table 1, both preoperative and postoperative pain scores were positively associated with increasing frequency of preoperative opioid use. Frequency of preoperative opioid use was also positively associated with higher rates of active prescriptions at the time of hospital admission for non-opioid analgesics (NSAIDs: 16.9% vs. 10.3%, $p < 0.001$ and acetaminophen: 34.2% vs. 12.0%, $p < 0.001$) and benzodiazepines (11.9% vs. 5.5%, $p < 0.001$).

Characteristics of opioid use

The average number of days' supply dispensed (or number of days covered) during the six-month preoperative period was 31.4 days (SD = 27.0) for infrequent opioid users, 95.4 days (SD = 32.0) for frequent opioid users, and 138.0 days (SD = 37.3) daily opioid users. For patients with three or more opioid fills in the preoperative period, the average PDC for frequent opioid users was 62.7% (SD = 13.1) and 93.8% (SD = 5.9) for daily opioid users. Among patients with opioid use in the 6 months prior to surgery, the average OME per day was 36.1 OME (SD = 31.4); 7.6% of patients with ≤10 OME per day, 34.9% with >10 to 25 OME per day, 36.6% with >25 to 50 OME per day, and 16.1% with >50 to 100 OME per day. Only 4.3% of patients averaged more than 100 OME per day in the six months prior to surgery and 8.3% of patients had an active opioid prescription at the time of surgery with more than 100 OME per day.

Association between preoperative opioid use and pain-related readmissions

Within 30-days post-discharge, 1.5% of patients experienced a pain-related readmission. Pain-related readmission was highest for daily preoperative opioid users (2.5%) as compared to frequent (2.2%), infrequent (1.7%), and patients with no evidence of preoperative opioid use (1.2%, $p < 0.001$). In unadjusted analysis, every 10-unit increase in daily preoperative OME was associated with a 7% increase in odds of pain-related readmission (OR 1.07, 95% CI: 1.05–1.08). When compared to the overall cohort of preoperative opioid users, those with a pain-related readmission had higher OME per day preoperatively (mean 44.5 vs. 36.1, $p < 0.001$, Table 2). Patients with higher preoperative and postoperative pain scores were also more likely to be readmitted for pain-related reasons (preoperative mean: 4.0 vs. 3.4, $p < 0.001$ and postoperative mean: 4.5 vs. 3.9, $p < 0.001$).

Prior to adjustment, any preoperative opioid use was associated with a 74% increase in odds of pain-related readmission (OR 1.74; 95% CI: 1.61–1.88, Table 3). After adjusting for patient and procedure characteristics, including closest preoperative pain score and highest postoperative pain score, patients with any evidence of preoperative opioid use were 31% more likely to experience a pain-related readmission within 30 days following discharge (OR 1.31, 95% CI: 1.18–1.46). As shown in Table 3, the adjusted odds of a pain-related readmission within 30 days of discharge were significantly higher for all groups of preoperative opioid user: daily (OR 1.49; 95% CI: 1.27–1.74), frequent (OR 1.28; 95% CI: 1.08–1.52), and infrequent (OR 1.17; 95% CI: 1.04–1.31). While a history of preoperative opioid use in the six-months preoperative period was associated with pain-related readmissions, having an active prescription at the time of admission was not significantly associated (OR 1.15; 95% CI: 1.00–1.31) but filling an opioid prescription at discharge was significantly associated with increased odds of pain-related readmissions when compared to those not filling an opioid prescription at discharge (OR 1.13; 95% CI: 1.04–1.23).

Surgical specialty variation in pain related readmissions

As shown in Fig. 1, the adjusted odds of pain-related readmission by preoperative opioid use also varied by surgical specialty. Any history of preoperative opioid use was associated with pain-related readmissions for general surgeries (OR 1.37, 95% CI: 1.19–1.57), but not for vascular (OR 1.28, 95% CI: 0.96–1.71) and orthopedic surgeries (OR 0.96, 95% CI: 0.78–1.19). Among general surgery patients, there is also a substantial increase in pain-related readmissions as the average daily preoperative OME increases (Fig. 2). In contrast, patients undergoing orthopedic surgery were more likely to experience a pain-related readmission if they had an active opioid prescription at index admission (OR 1.40; 95% CI: 1.10–1.79) or filled an opioid prescription at discharge (OR 1.24; 95% CI: 1.07–1.45).

Discussion

Our study compared the association of pain-related postoperative readmission based on preoperative opioid use across a broad group of inpatient surgical procedures in the Veterans Healthcare System. We found that patients with prior opioid exposure were at greater risk for pain-related readmission compared to opioid naïve patients, even after controlling for

Table 1
Characteristics by preoperative opioid use pattern.

	Overall	Preoperative Opioid Use (6 Months Prior)				
		No Opioids	Infrequent	Frequent	Daily	P-Value
N	176,989	116,185	29,460	11,104	20,240	
%		65.7%	16.7%	6.3%	11.4%	
Surgical Specialty, %						<.001
General	42.9%	46.8%	38.9%	33.2%	31.8%	
Orthopedic	39.2%	34.6%	43.2%	51.3%	53.3%	
Peripheral Vascular	17.9%	18.7%	17.9%	15.5%	15.0%	
Demographics						
Age, Mean (SD)	63.5 (11.4)	64.4 (11.6)	62.3 (11.3)	61.7 (10.6)	60.7 (9.6)	<.001
BMI, Mean (SD)	28.7 (6.5)	28.6 (6.5)	28.8 (6.4)	29.0 (6.5)	29.1 (6.5)	<.001
Male, %	94.4%	94.9%	93.9%	93.6%	93.7%	<.001
Race, %						<.001
White	77.6%	78.5%	73.8%	73.9%	80.3%	
Black or African American	16.5%	15.2%	20.7%	21.2%	14.8%	
American Indian or Alaska Native	0.7%	0.7%	0.7%	0.7%	0.9%	
Native Hawaiian or other Pacific Islander	0.3%	0.4%	0.3%	0.2%	0.1%	
Asian	0.7%	0.7%	0.7%	0.9%	0.8%	
Unknown	4.2%	4.5%	3.8%	3.1%	3.1%	
Social/Behavioral Factors						
Marital Status, %						<.001
Married	47.8%	48.3%	47.0%	45.9%	46.6%	
Divorced	29.9%	29.0%	30.4%	31.6%	33.2%	
Widowed	8.3%	8.9%	7.6%	7.6%	6.3%	
Separated	3.8%	3.4%	4.4%	4.9%	4.7%	
Single	10.3%	10.4%	10.6%	10.0%	9.3%	
Depression Diagnosis, %	16.5%	13.3%	18.5%	24.6%	27.2%	<.001
Anxiety Diagnosis, %	6.9%	5.7%	7.6%	9.7%	11.3%	<.001
Bipolar Disorder Diagnosis, %	2.2%	1.7%	2.5%	3.3%	3.7%	<.001
Etoh >2 Drinks/Day; 2 wks Before Admission, %	8.2%	8.7%	8.0%	7.2%	6.3%	<.001
Current Smoker Within 1 Year, %	33.2%	30.7%	34.9%	37.3%	42.8%	<.001
Evidence of Substance Abuse, %	7.6%	6.0%	9.4%	11.9%	11.9%	<.001
History of Chronic Pain, %	2.9%	1.2%	3.4%	7.1%	9.4%	<.001
Preoperative Healthcare Utilization and Comorbidities						
Functional Health Status, %						<.001
Independent	92.2%	92.3%	92.2%	91.5%	91.9%	
Partially/Totally Dependent	7.8%	7.7%	7.8%	8.5%	8.1%	
Prior ER Visits w/in 6 Months, Mean (SD)	0.7 (1.5)	0.6 (1.2)	1.1 (1.8)	1.3 (2.3)	0.8 (1.8)	<.001
Prior Inpatient Admissions w/in 6 Months, Mean (SD)	0.5 (1.4)	0.4 (1.1)	0.8 (1.7)	1.0 (2.3)	0.6 (1.6)	<.001
ASA Classification, %						<.001
1-2	19.7%	20.7%	19.6%	16.7%	15.8%	
3	68.7%	67.8%	68.6%	70.9%	72.6%	
4-5	11.6%	11.5%	11.8%	12.4%	11.6%	
Operative Characteristics						
Emergency procedure, %	8.8%	9.8%	7.2%	6.6%	6.7%	<.001
Operative Time, Hours, Mean (SD)	2.5 (1.5)	2.5 (1.5)	2.5 (1.6)	2.5 (1.5)	2.5 (1.5)	0.001
Work RVU, Mean (SD)	19.7 (7.5)	19.8 (7.5)	19.5 (7.9)	19.7 (7.4)	19.9 (7.2)	<.001
Pain, Mean (SD)						
Closest Preoperative	3.4 (3.1)	3.1 (3.0)	3.7 (3.2)	4.1 (3.2)	4.5 (3.2)	<.001
Closest Postoperative	3.9 (3.2)	3.5 (3.1)	4.1 (3.2)	4.7 (3.2)	5.0 (3.2)	<.001
Opioid Usage						
Active at Admission, %	20.8%		27.7%	64.7%	81.7%	<.001
Filled on Discharge, %	46.6%	37.7%	48.9%	52.9%	55.5%	<.001
OME at Discharge, Mean (SD)	602.7 (748.5)	505.1 (463.3)	571.7 (674.2)	694.1 (836.6)	974.7 (1,337.6)	<.001
Day Supply at Discharge, Mean (SD)	16.4 (9.7)	15.5 (9.3)	16.6 (10.3)	17.7 (9.8)	19.3 (10.1)	<.001
Average OME/day at Discharge, Mean (SD)	38.9 (26.8)	36.6 (24.2)	38.0 (25.6)	41.1 (27.9)	47.7 (34.5)	<.001
Average OME per day						
Preoperative, Mean (SD)	36.1 (31.4)		26.0 (20.1)	33.1 (26.5)	53.3 (39.7)	<.001
Postoperative, Mean (SD)	37.7 (30.2)	31.8 (22.6)	31.2 (23.8)	36.3 (28.3)	54.7 (40.1)	<.001
Number of Prescription Fills						
Preoperative, Mean (SD)	3.6 (2.8)		1.4 (0.7)	4.4 (1.8)	6.3 (2.4)	<.001
Postoperative, Mean (SD)	3.4 (2.8)	2.1 (1.8)	2.7 (2.2)	4.1 (2.7)	5.9 (3.0)	<.001
Other Medications						
Nonsteroidal Anti-inflammatory						
Active at Admission, %	12.7%	10.3%	14.1%	18.4%	20.1%	<.001
Filled on Discharge, %	2.3%	2.2%	2.5%	2.9%	2.5%	<.001
Acetaminophen						
Active at Admission, %	20.6%	12.0%	24.3%	36.7%	47.2%	<.001
Filled on Discharge, %	60.1%	63.0%	60.0%	55.5%	50.4%	<.001
Benzodiazepines						
Active at Admission, %	7.8%	5.5%	7.3%	12.0%	18.4%	<.001
Filled on Discharge, %	2.5%	1.9%	2.8%	3.6%	5.0%	<.001

SD: Standard Deviation, ASA: American Society of Anesthesiologists, COPD: Chronic Obstructive Pulmonary Disorder, OME: Oral Morphine Equivalent.
* Preoperative infrequent opioid use was defined is 2 or fewer fills in the 6 months preceding hospital admission independent of the proportion of days covered.

Table 2
Opioid use by any unplanned readmission and pain-related readmission.

	Overall	Readmission			
		Any Unplanned	P-Value	Pain-Related	P-Value
N	176,989	16,193		2,595	
%		9.2%		1.5%	
Preoperative Opioid Use, %			<.001		<.001
No Opioids	65.7%	8.7%		1.2%	
Infrequent	16.7%	10.0%		1.7%	
Frequent	6.3%	10.6%		2.2%	
Daily	11.4%	9.7%		2.5%	
Postoperative Opioid Use, %			<.001		<.001
No Opioids	57.7%	7.8%		0.9%	
Infrequent	22.4%	10.8%		1.9%	
Frequent	13.0%	13.0%		2.8%	
Daily	11.1%	9.6%		2.5%	
Pain, Mean (SD)					
Closest Preoperative	3.4 (3.1)	3.4 (3.3)	0.95	4.0 (3.3)	<.001
Closest Postoperative	3.9 (3.2)	3.9 (3.3)	0.63	4.5 (3.3)	<.001
Opioid Usage					
Active at Admission, %	20.8%	20.0%	<.001	28.2%	<.001
Filled on Discharge, %	46.6%	40.4%	<.001	48.8%	<.001
OME at Discharge, Mean (SD)	602.7 (748.5)	620.50 (852.6)	0.02	712.4 (1,052.4)	<.001
Day Supply at Discharge, Mean (SD)	16.4 (9.7)	16.0 (9.8)	<.001	16.7 (10.1)	0.33
Average OME/day at Discharge, Mean (SD)	38.9 (26.8)	38.9 (26.7)	0.99	41.8 (30.8)	<0.001
Among Opioid Users					
Average OME per day					
Preoperative, Mean (SD)	36.1 (31.4)	37.4 (31.8)	<.001	44.5 (38.0)	<.001
Postoperative, Mean (SD)	37.7 (30.2)	39.6 (3.16)	<.001	44.6 (34.7)	<.001
Number of Prescription Fills					
Preoperative, Mean (SD)	3.6 (2.8)	3.7 (2.9)	0.02	4.3 (3.2)	<.001
Postoperative, Mean (SD)	3.4 (2.8)	3.5 (3.0)	<.001	4.2 (3.4)	<.001
Other Medications					
Nonsteroidal Anti-inflammatory					
Active at Admission, %	12.7%	10.0%	<.001	12.4%	0.78
Filled on Discharge, %	2.3%	2.2%	0.24	3.3%	<.001
Acetaminophen					
Active at Admission, %	20.6%	21.1%	<.001	25.4%	<.001
Filled on Discharge, %	60.1%	56.1%	<.001	58.4%	0.02
Benzodiazepines					
Active at Admission, %	7.8%	8.9%	<.001	10.8%	<.001
Filled on Discharge, %	2.5%	3.1%	<.001	4.1%	<.001

important confounding variables. Furthermore, this association was dose dependent-like, both in the frequency of preoperative exposure and the quantity of opioid use, adding to the strength of our findings.

Approximately one-third of our cohort of VA patients with surgeries between fiscal years 2007 and 2014 had evidence of at least one opioid prescription in the six months prior to their surgery. In this cohort, preoperative and postoperative pain scores increased with more frequent preoperative opioid use. As opioid use is associated with analgesic tolerance and opioid-induced hyperalgesia, it is not surprising that preoperative opioid use is associated with pain-related outcomes.[26] As clinicians and policy makers continue to balance pain management and opioid use, this evidence is essential to consider when setting opioid guidelines and limits.

Providing adequate analgesia for opioid tolerant patients is challenging and lack of recognition for pre-surgical baseline opioid use can lead to uncontrolled pain. A concerted effort must be made to balance adequate pain control and overprescribing of opioids. While a number of institutional clinical pathways and procedure-specific approaches have been published in recent years to assist clinicians in determining an appropriate prescribing amount for opioid naïve patients, there remains a lack of knowledge on how to best manage postoperative pain for opioid tolerant patients.[13,14,27,28] Protocols and programs that limit opioid use postoperatively with a blanket guide of number of pills per procedure may not provide sufficient pain control. For patients using opioids chronically before surgery, consultative expertise for help managing postoperative pain and alternative strategies like multimodal pain management are necessary. A previous study found that multimodal postoperative pain management therapy, including opioids in combination with NSAIDs and acetaminophen, was associated with a significant reduction in follow-up pain scores and 30-day all cause readmissions when compared to opioids alone.[29] With the increasing use of multimodal pain management therapy secondary to efforts to decrease opioid use, future studies should examine postoperative outcomes of these opioid-sparing protocols stratified by preoperative opioid utilization.

When stratified by surgery type, we found differences in both the frequency of preoperative opioid use and the risk of pain-related readmissions. Daily and frequent preoperative opioid use was more prevalent for patients undergoing orthopedic surgery, where patients may have been using opioids to treat longstanding musculoskeletal problems, including pain, that required surgical intervention. Although preoperative opioid use was more prevalent in orthopedic patients, any history of preoperative opioid use was only associated with pain-related readmissions for general surgery patients. In contrast, pain-related readmissions among orthopedic patients was driven more by opioids on hand at the time of admission and filling opioids at the time of discharge. We hypothesize that these differences reflect procedure factors, including surgical diagnosis, complexity of operation, and surgical technique.

Table 3
Model of post-discharge readmission within 30 days.

	Pain-Related Readmission			
	Unadjusted		Adjusted[a]	
	OR	(95% CI)	OR	(95% CI)
Preoperative Opioids				
No Opioids	Ref.		Ref.	
Infrequent	1.34	(1.22–1.47)	1.17	(1.04–1.31)
Not Daily	1.58	(1.40–1.79)	1.28	(1.08–1.52)
Daily	1.79	(1.63–1.97)	1.49	(1.27–1.74)
On Hand at Admission	1.57	(1.45–1.70)	1.15	(1.00–1.31)
Post-Discharge Opioids				
Filled at Discharge	1.22	(1.13–1.37)	1.13	(1.04–1.23)

[a] All models are adjusted for closest preoperative pain, highest postoperative pain, age, gender, race, marital status, body mass index, depression, anxiety, bipolar disorder, recent alcohol use, smoking status, substance abuse, history of chronic pain, functional health status, prior emergency department and inpatient admissions, ASA classification, hypertension, diabetes, history of COPD, chronic steroid use, current dialysis, work relative value unit (RVU), and operative time.

Pain management after discharge following surgery will always present a challenge to clinicians. Even among patients who were not taking preoperative opioids, we found one of eight readmissions were associated with pain, compared to one in four for daily preoperative opioid users. The development of pain, or pain that persists longer than expected, can be a meaningful indicator of conditions needing further assessment and possible alternate/additional intervention. For both patients with and without preoperative opioid use, setting expectations related to pain control should be done prior to surgery and may reduce unnecessary utilization. Opioid use is only one risk factor among many for pain-related readmission. Still, understanding how the magnitude of opioid use before surgery affects readmissions will help us optimize pain care for this vulnerable population.

With the increased scrutiny of opioid use, this study has notable clinical implications. Predicting readmission is the first step to identifying interventions to reduce unnecessary utilization. Given that preoperative opioid use is associated with an absolute increase of 1–2% of pain related readmissions following surgery, interventions can begin prior to the surgical episode. Since the risk of pain-related readmissions were found to vary by frequency of preoperative opioid exposure and surgical specialty, our findings highlight the importance of collecting a comprehensive medication history rather than only an assessment of chronic opioid use or medications on hand.

Limitations

This study is not without limitations. We were unable to account for the variability in procedure related pain or account for possible complications that resulted in pain. By restricting our analysis to patients with at least a 2 day stay, we eliminated many outpatient procedures with uncomplicated recoveries. We acknowledge that surgical procedures are increasingly performed in the outpatient setting and future research should address whether similar patterns are seen in patients undergoing outpatient surgery. Although we were able to include extensive clinical, demographic, and pharmacy patient-level data because of VA's robust integrated electronic medical record, we were unable to account for any medications filled outside of the VA system, including opioids and over-the-counter pain relievers and analgesics. While there is some evidence from the medical record of patients' self-reported non-VA prescriptions, we expect these data are incomplete based on the self-reported nature of the information and the lack of standardization around provider reporting. Additionally, we were unable to assess whether medications that were filled prior to index admission and considered active at admission were being used at admission or if the medication was intended for postoperative pain management. Furthermore, PDC calculations may overestimate the

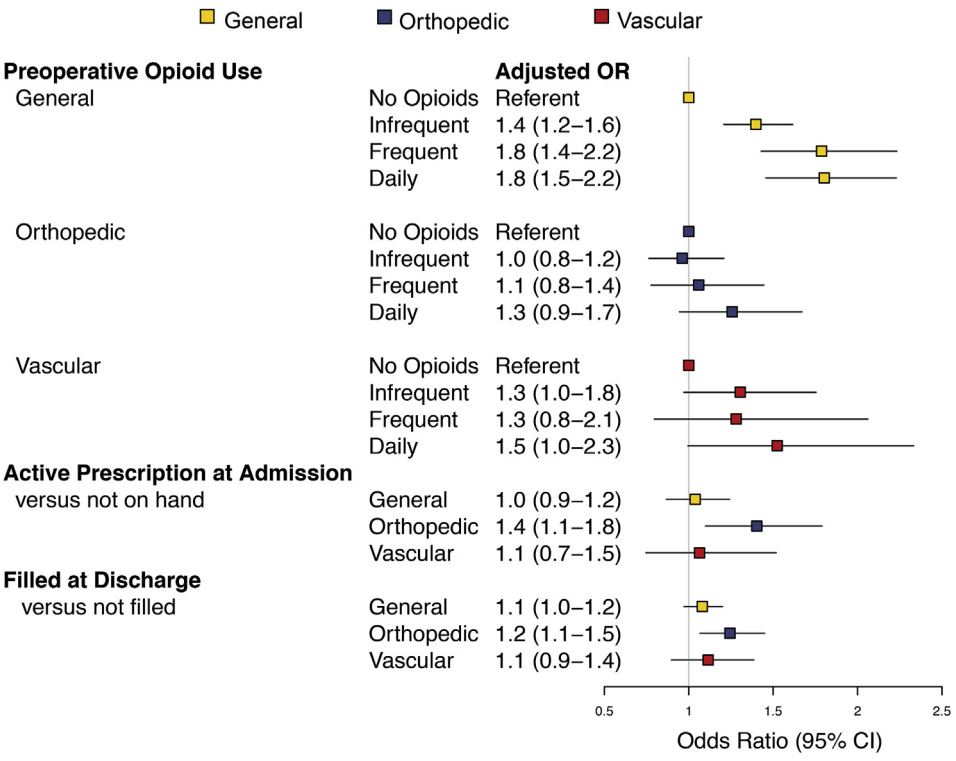

Fig. 1. Adjusted* model of post-discharge pain-related readmission within 30 days.

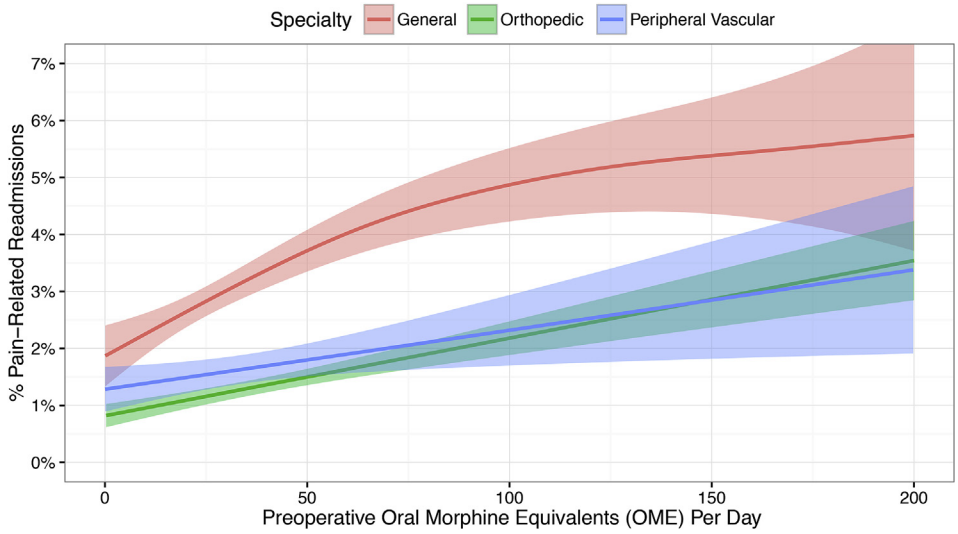

Fig. 2. Average daily preoperative OME and pain-related readmission stratified by specialty.

frequency of opioid use as we cannot ascertain whether medications were taken, only that they were dispensed. Lastly, this study was limited to a veteran population and may not be generalizable to other populations.

Conclusions

Pain and opioid exposure are common following inpatient surgery. Patients using opioids preoperatively experienced higher rates of postoperative readmissions, particularly those related to pain. This relationship was dependent both on the frequency and dosage of opioid use and varied by surgical specialty. This work suggests that clinicians need to adequately assess and respond to preoperative opioid exposure.

Meeting presentation

This study was presented at the Association for Academic Surgery/Society of University Surgeons' 13th Annual Academic Surgical Congress; February 1, 2018; Jacksonville, Florida.

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We explored the association between preoperative opioid utilization and 30-day unplanned readmissions related to pain following surgery. Those with prior opioid exposure were at greater risk for pain-related readmission compared to opioid naïve patients. This association was dose dependent-like, both in the frequency of preoperative exposure and the quantity of opioid use, and varied by surgical specialty. Clinicians need to adequately assess and respond to preoperative opioid exposure to optimize patient outcomes.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2019.02.033.

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References

1. Florence CS, Zhou C, Luo F, Xu L. The economic burden of prescription opioid overdose, abuse, and dependence in the United States, 2013. *Med Care*. 2016;54(10):901–906. https://doi.org/10.1097/MLR.0000000000000625.
2. Guy GP, 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. https://doi.org/10.15585/mmwr.mm6626a4.
3. Jeffery MM, Hooten WM, Henk HJ, et al. Trends in opioid use in commercially insured and Medicare Advantage populations in 2007-16: retrospective cohort study. *BMJ*. 2018;362. https://doi.org/10.1136/bmj.k2833.
4. Han B, Compton WM, Blanco C, Crane E, Lee J, Jones CM. Prescription opioid use, misuse, and use disorders in U.S. Adults: 2015 national survey on drug use and health. *Ann Intern Med*. 2017;167(5):293. https://doi.org/10.7326/M17-0865.
5. Cron DC, Englesbe MJ, Bolton CJ, et al. Preoperative opioid use is independently associated with increased costs and worse outcomes after major abdominal surgery. *Ann Surg*. 2017;265(4):695–701. https://doi.org/10.1097/SLA.0000000000001901.
6. Kim SC, Choudhry N, Franklin JM, et al. Patterns and predictors of persistent opioid use following hip or knee arthroplasty. *Osteoarthritis Cartilage*. 2017;25(9):1399–1406. https://doi.org/10.1016/j.joca.2017.04.002.
7. Rozell JC, Courtney PM, Dattilo JR, Wu CH, Lee G-C. Preoperative opiate use independently predicts narcotic consumption and complications after total joint arthroplasty. *J Arthroplasty*. 2017;32(9):2658–2662. https://doi.org/10.1016/j.arth.2017.04.002.
8. Armaghani SJ, Lee DS, Bible JE, et al. Preoperative opioid use and its association with perioperative opioid demand and postoperative opioid independence in patients undergoing spine surgery. *Spine*. 2014;39(25):E1524–E1530. https://doi.org/10.1097/BRS.0000000000000622.
9. Hilliard PE, Waljee J, Moser S, et al. Prevalence of preoperative opioid use and characteristics associated with opioid use among patients presenting for surgery. *JAMA Surg*. 2018;153(10):929. https://doi.org/10.1001/jamasurg.2018.2102.
10. Westermann RW, Anthony CA, Bedard N, et al. Opioid consumption after rotator cuff repair. *Arthroscopy*. 2017;33(8):1467–1472. https://doi.org/10.1016/j.arthro.2017.03.016.
11. Namba RS, Inacio MCS, Pratt NL, et al. Postoperative opioid use as an early indication of total hip arthroplasty failure. *Acta Orthop*. 2016;87(sup1):37–43. https://doi.org/10.1080/17453674.2016.1181820.

12. Mudumbai SC, Oliva EM, Lewis ET, et al. Time-to-cessation of postoperative opioids: a population-level analysis of the veterans affairs health care system. *Pain Med*. 2016;17(9):1732–1743. https://doi.org/10.1093/pm/pnw015.
13. Scully RE, Schoenfeld AJ, Jiang W, et al. Defining optimal length of opioid pain medication prescription after common surgical procedures. *JAMA Surg*. 2018;153(1):37. https://doi.org/10.1001/jamasurg.2017.3132.
14. Thiels CA, Anderson SS, Ubl DS, et al. Wide variation and overprescription of opioids after elective surgery. *Ann Surg*. 2017;266(4):564–573. https://doi.org/10.1097/SLA.0000000000002365.
15. Hernandez-Boussard T, Graham LA, Desai K, et al. The fifth vital sign: postoperative pain predicts 30-day readmissions and subsequent emergency department visits. *Ann Surg*. 2017;266(3):516–524. https://doi.org/10.1097/SLA.0000000000002372.
16. Wu CL, Berenholtz SM, Pronovost PJ, Fleisher LA. Systematic review and analysis of postdischarge symptoms after outpatient surgery. *Anesthesiology*. 2002;96(4):994–1003. https://doi.org/10.1097/00000542-200204000-00030.
17. Mattila K, Toivonen J, Janhunen L, Rosenberg PH, Hynynen M. Postdischarge symptoms after ambulatory surgery: first-week incidence, intensity, and risk factors. *Anesth Analg*. 2005;101(6):1643–1650. https://doi.org/10.1213/01.ANE.0000184189.79572.28.
18. Brix LD, Bjørnholdt KT, Thillemann TM, Nikolajsen L. Pain-related unscheduled contact with healthcare services after outpatient surgery. *Anaesthesia*. 2017. https://doi.org/10.1111/anae.13876.
19. Zywiel MG, Stroh DA, Lee SY, Bonutti PM, Mont MA. Chronic opioid use prior to total knee arthroplasty. *J Bone Jt Surg Am*. 2011;93(21):1988–1993. https://doi.org/10.2106/JBJS.J.01473.
20. Ben-Ari A, Chansky H, Rozet I. Preoperative opioid use is associated with early revision after total knee arthroplasty a study of male patients treated in the veterans affairs system. *J Bone Jt Surg Am*. 2017;99(1):1–9. https://doi.org/10.2106/JBJS.16.00167.
21. Pivec R, Issa K, Naziri Q, Kapadia BH, Bonutti PM, Mont MA. Opioid use prior to total hip arthroplasty leads to worse clinical outcomes. *Int Orthop*. 2014;38(6):1159–1165. https://doi.org/10.1007/s00264-014-2298-x.
22. Waljee JF, Cron DC, Steiger RM, Zhong L, Englesbe MJ, Brummett CM. Effect of preoperative opioid exposure on healthcare utilization and expenditures following elective abdominal surgery. *Ann Surg*. 2017;265(4):715–721. https://doi.org/10.1097/SLA.0000000000002117.
23. Kim Y, Cortez AR, Wima K, et al. Impact of preoperative opioid use after emergency general surgery. *J Gastrointest Surg*. 2018;22(6):1098–1103. https://doi.org/10.1007/s11605-017-3665-x.
24. Bryson CL, Au DH, Young B, McDonell MB, Fihn SD. A refill adherence algorithm for multiple short intervals to estimate refill compliance (ReComp). *Med Care*. 2007;45(6):497–504. https://doi.org/10.1097/MLR.0b013e3180329368.
25. Morris MS, Graham LA, Richman JS, et al. Postoperative 30-day readmission: time to focus on what happens outside the hospital. *Ann Surg*. 2016;264(4):621–631. https://doi.org/10.1097/SLA.0000000000001855.
26. Hayhurst CJ, Durieux ME. Differential opioid tolerance and opioid-induced hyperalgesia: a clinical reality. *Anesthesiology*. 2016;124(2):483–488. https://doi.org/10.1097/ALN.0000000000000963.
27. Hill MV, McMahon ML, Stucke RS, Barth RJ. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg*. 2017;265(4):709–714. https://doi.org/10.1097/SLA.0000000000001993.
28. Hill MV, Stucke RS, McMahon ML, Beeman JL, Barth RJ. An educational intervention decreases opioid prescribing after general surgical operations. *Ann Surg*. 2018;267(3):468–472. https://doi.org/10.1097/SLA.0000000000002198.
29. Desai K, Carroll I, Asch SM, et al. Utilization and effectiveness of multimodal discharge analgesia for postoperative pain management. *J Surg Res*. 2018;228:160–169. https://doi.org/10.1016/j.jss.2018.03.029.