Predictors of new persistent opioid use after coronary artery bypass grafting

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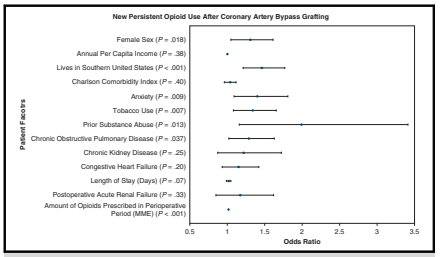
ABSTRACT

Objective: Deaths from prescription opioid overdose have quadrupled in the past 15 years, and no studies have evaluated appropriate opioid prescribing after cardiac surgery. The aim of this study is to quantify the amount of outpatient opioids prescribed to patients after coronary artery bypass grafting and determine the incidence and risk factors for new persistent opioid use after coronary artery bypass grafting.

Methods: Insurance claim data from privately insured opioid-naïve patients who underwent coronary artery bypass grafting from 2014 to 2016 were evaluated. New persistent opioid use was defined as patients who filled an opioid prescription in the perioperative period and filled opioid prescriptions between 90 and 180 days after surgery. Multivariable logistic regression was used to determine the preoperative and operative factors associated with new persistent opioid use.

Results: Among 7292 opioid-naïve patients undergoing coronary artery bypass grafting, 5628 (77.2%) filled opioid prescriptions in the perioperative period, and 590 (8.1%) had new persistent opioid use. Female gender (odds ratio [OR], 1.30; confidence interval [CI], 1.05-1.61; $P = .018$), anxiety (OR, 1.40; CI, 1.09-1.81; $P = .009$), tobacco use (OR, 1.34; CI, 1.08-1.65; $P = .007$), prior substance abuse (OR, 1.99; CI, 1.16-3.41; $P = .013$), chronic obstructive pulmonary disease (OR, 1.29; CI, 1.02-1.63; $P = .037$), living in the Southern United States (OR, 1.46; CI, 1.21-1.77; $P < .001$), and increased amount of opioids prescribed in the perioperative period (OR, 1.016; CI, 1.014-1.018; $P < .001$) were independently associated with new persistent opioid use.

Conclusions: New persistent opioid use after coronary artery bypass grafting is surprisingly common. Prospective studies are needed to determine the opioid requirements of patients after coronary artery bypass grafting to prevent opioid dependence. (J Thorac Cardiovasc Surg 2020;160:954-63)



Risk factors for new persistent opioid use after coronary artery bypass.

Central Message

New persistent opioid use occurs in 8.1% of opioid-naïve patients after CABG. Prospective studies are needed to determine the opioid requirements of patients after CABG to prevent opioid dependence.

Perspective

Opioid overdose deaths have quadrupled in the past 15 years, and few studies have evaluated appropriate opioid prescribing after cardiac surgery. Using insurance claim data, we found that 8.1% of opioid-naïve patients had new persistent opioid use after CABG. Opioid prescribing guidelines are needed to curtail opioid prescribing and possibly reduce new persistent opioid dependence in this population.

See Commentaries on pages 964 and 966.

More than 200,000 people died in the United States from prescription opioid overdoses from 1999 to 2016, and more than 46 people die every day.[1] New opioid addiction after surgical procedures contributes to this problem.[2-6] Brummett and colleagues[2] demonstrated that among 36,177 opioid-naïve

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Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
ICD-9 = International Classification of Diseases, Ninth Revision
ICD-10 = International Classification of Diseases, Tenth Revision
MME = morphine milligram equivalent
OR = odds ratio

patients who underwent minor or major surgery, 5.9% to 6.5% developed new persistent opioid use. Two Canadian studies reported that 3.1% of patients received opioids for more than 90 days after major elective surgery, and 10.3% of opioid-naïve patients received opioid prescriptions at 1 year after short-stay surgery.[5,6]

The challenge for providers is that there are no guidelines for outpatient perioperative opioid prescribing, and there are virtually no data to guide providers to estimate the postoperative opioid requirements for patients at the time of discharge to home. The US Centers for Disease Control and Prevention published opioid prescribing guidelines for long-term pain management, but there are no such guidelines for outpatient perioperative pain control.[7] Subsequently, the wide variety and excessive dosing of postoperative opioid prescriptions have been well documented in orthopedic and general surgical procedures.[8-10] The opioid requirements of patients who underwent cardiac surgery on discharge is unknown.

The aim of this study is to quantify the amount of outpatient opioids filled by patients after coronary artery bypass grafting (CABG) and determine the incidence and risk factors for new persistent opioid use after CABG. We hypothesized that new persistent opioid use would be a significant complication after CABG.

MATERIALS AND METHODS

Patient Population

The Johns Hopkins Medicine Institutional Review Board (Ref. IRB0038226) approved this study. Insurance claim data from opioid-naïve patients who underwent CABG from 2014 to 2016 were evaluated in the Truven Health Marketscan Database.[11] This claims database contains data from more than 250 million privately insured patients and approximately 100 insurance companies, but it does not include Medicare, Medicaid, or uninsured patients. Patients who underwent CABG were identified using International Classification of Diseases, Ninth Revision (ICD-9) and Tenth Revision (ICD-10) codes (Table E1). Patients were only included if they had continuous insurance enrollment for 1 year before surgery and 6 months after surgery, and this allowed quantification of preoperative comorbidities and opioid prescriptions. Patients with hospital length of stay greater than 30 days, discharge to hospice, death in hospital, or major surgical procedure within 6 months after their CABG were excluded (Figure 1). To exclude prior opioid users from the study, patients who filled opioid prescriptions 365 to 31 days before surgery were excluded.

Demographic factors including age, gender, region of residence, type of health plan, and length of surgical admission were extracted from the Marketscan Database. Marketscan definitions of region of residence are

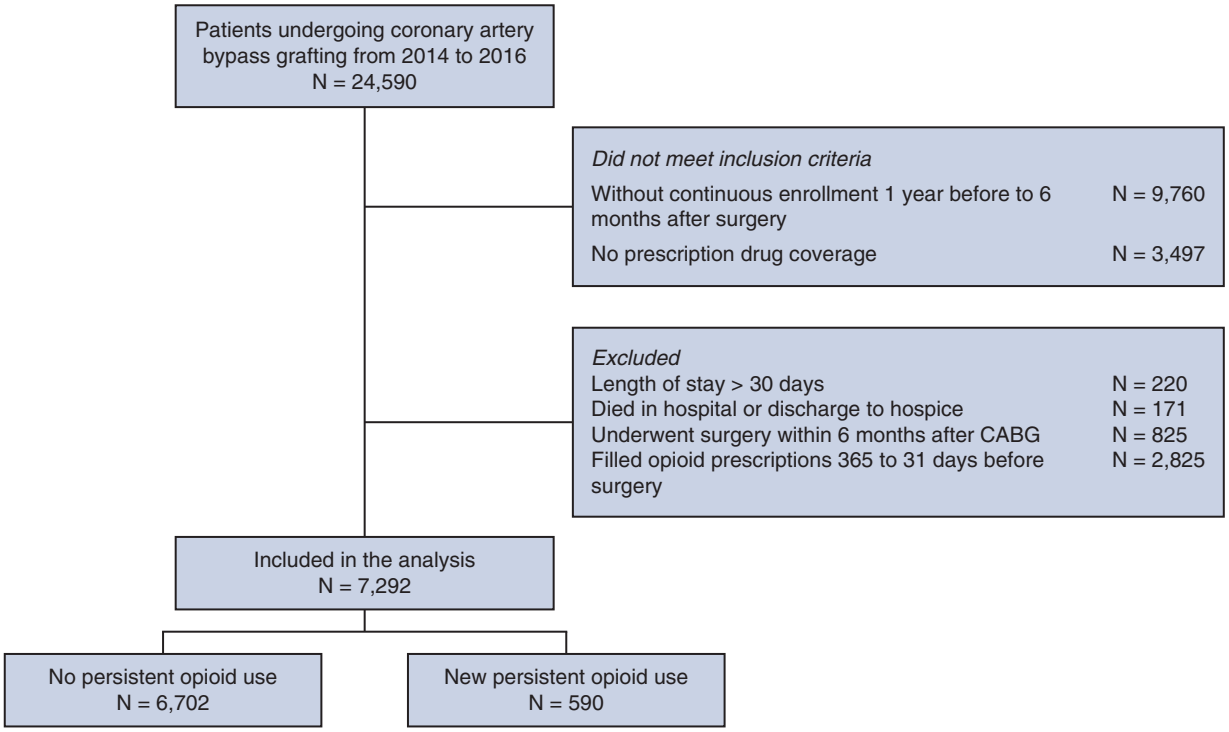


FIGURE 1. Flow diagram of patients included in the analysis. Among 7292 patients who underwent CABG and met inclusion criteria, 590 (8.1%) had new persistent opioid use. *CABG*, Coronary artery bypass grafting.

included in Table E2. Per capita annual income by metropolitan statistical area was calculated using data from the US Bureau of Economic Analysis.[12] Comorbidities were calculated with the Charlson Comorbidity Index, and this index predicts the risk of death within 1 year of hospitalization using ICD-9 and ICD-10 codes.[13] The Agency for Healthcare Research Clinical Classification Software was used to characterize specific preoperative risk factors such as anxiety, mood disorders, prior substance abuse, and chronic kidney disease.[14] This software categorizes ICD-9 and ICD-10 codes into approximately 700 more clinically relevant diagnoses for database research. The preoperative risk factor of prior substance abuse includes opioids, cannabis, benzodiazepines, cocaine, heroin, stimulants, and other hallucinogens, but prior substance abuse does not include tobacco or alcohol use. Postoperative complications including pneumonia, acute renal failure, and stroke were also identified using ICD-9 and ICD-10 codes from the Agency for Healthcare Research Clinical Classification Software. An unplanned reoperation during the index admission was identified using Current Procedural Terminology codes.

Opioid Calculations

According to the literature, the perioperative time period spanned from 30 days before surgery to 14 days after surgery.[2,15] New persistent opioid use was defined as a patient who filled an opioid prescription during the perioperative period and filled at least 1 opioid prescription between 90 and 180 days after surgery.[2,15] The quantity of opioids filled in the perioperative period, 30 to 90 days after surgery, 90 to 180 days after surgery, and 180 to 365 days after surgery were calculated in morphine milligram equivalents (MMEs).

Statistical Analysis

SPSS 25 (SPSS Inc, Chicago, Ill) was used for statistical analysis.[16] Continuous variables were reported as medians (interquartile range) and

TABLE 1. Characteristics of patients who underwent coronary artery bypass grafting

Variable	All patients (N = 7292)	No persistent opioid use (N = 6702)	New persistent opioid use (N = 590)	*P* value
Age	58.0 (8.0)	58.0 (8.0)	58.0 (8.0)	.013
Male gender*	6065 (83.2)	5599 (83.5)	466 (79.0)	.005
Procedure type				.39
Isolated CABG	6822 (93.6)	6267 (93.5)	559 (94.7)	
CABG + aortic valve replacement	356 (4.9)	336 (5.0)	20 (3.4)	
CABG + mitral valve replacement	50 (0.7)	44 (0.7)	6 (1.0)	
CABG + mitral valve repair	45 (0.6)	41 (0.6)	4 (0.7)	
CABG + other procedure	15 (0.2)	14 (0.2)	1 (0.2)	
Per capita annual income in dollars*	45,508 (10,424)	45,722 (10,849)	44,658 (9531)	.002
Region*				<.001
Northeast	1216 (16.7)	1145 (17.1)	71 (12.0)	
North Central	1597 (21.9)	1481 (22.1)	116 (19.7)	
South	3610 (49.5)	3262 (48.7)	348 (59.0)	
West	807 (11.1)	760 (11.3)	47 (8.0)	
Unknown	62 (0.9)	54 (0.8)	8 (1.4)	
Type of health plan				.32
Preferred provider organization	4361 (59.8)	4011 (59.8)	350 (59.3)	
Consumer-directed health plans	781 (10.7)	710 (10.6)	71 (12.0)	
Health Maintenance Organization	640 (8.8)	588 (8.8)	52 (8.8)	
Point of service	546 (7.7)	504 (7.5)	42 (7.1)	
Other	964 (13.2)	889 (13.3)	75 (12.7)	
Charlson Comorbidity Index*	1 (1)	1 (1)	1 (1)	.002
Anxiety*	748 (10.3)	662 (9.9)	86 (14.6)	<.001
Mood disorder	638 (8.7)	583 (8.7)	55 (9.3)	.61
Alcohol use	214 (2.9)	193 (2.9)	21 (3.6)	.35
Tobacco use*	1361 (18.7)	1212 (18.1)	149 (25.3)	<.001
Prior substance abuse*	111 (1.5)	93 (1.4)	18 (3.1)	.002
Congestive heart failure	1711 (23.5)	1547 (23.1)	164 (27.8)	.010
Cerebrovascular disease	286 (3.9)	263 (3.9)	23 (3.9)	.98
Chronic obstructive pulmonary disease*	1005 (13.8)	891 (13.3)	114 (19.3)	<.001
Chronic kidney disease*	522 (7.2)	469 (7.0)	53 (9.0)	.073
Type II diabetes	3869 (53.1)	3539 (53.0)	320 (54.2)	.55

Continuous variables are shown as medians (interquartile range). Categoric variables are shown as counts (percentage). New persistent opioid use was defined as a patient who filled an opioid prescription during the perioperative period and filled at least 1 opioid prescription between 90 and 180 days after surgery. *CABG*, Coronary artery bypass grafting.
*Indicates variables included in the multivariable logistic regression.

compared with the Mann–Whitney *U* test. Categoric variables were reported as the count of patients (percentage) and compared with Pearson's chi-square test. A univariate analysis was performed to determine the characteristics of patients with no persistent opioid use versus new persistent opioid use. For the multivariable logistic regression, variables were included based on statistical significance (<0.10 in the univariate analysis) and clinical significance. Model fit was assessed by the Hosmer–Lemeshow test.

RESULTS

Among 7292 opioid-naïve patients, 590 (8.1%) had new persistent opioid use (Figure 1). The majority of the study cohort underwent isolated CABG (93.6%), and the second most common procedure was CABG and aortic valve replacement (4.9%) (Table 1). In the univariate analysis, younger age, female gender, lower annual income, living in the Southern United States, Charlson Comorbidity Index, anxiety, tobacco use, prior substance abuse, congestive heart failure, and chronic obstructive pulmonary disease were significantly associated with new persistent opioid use. There was no significant difference in the incidence of postoperative pneumonia, acute renal failure, stroke, unplanned reoperation, or discharge status between groups (Table 2).

Only 77.2% of all patients who underwent CABG filled at least 1 opioid prescription in the preoperative period (Table 3). New persistent opioid users were significantly more likely to fill prescriptions in the perioperative period for more total opioids (393 vs 263 MME, $P < .001$) and fill prescriptions with a greater day supply of opioids compared with nonpersistent users respectively (7 days vs 5 days, $P < .001$). When opioid-naïve users became new persistent users, they filled a median of 225 MME and 1 opioid prescription in the 90 to 180 days after surgery. To put this in perspective, this is equal to thirty 5 mg oxycodone tablets or forty-five 5 mg hydrocodone tablets. Furthermore, new persistent users were more likely to be readmitted to the hospital (15.8% vs 9.7%, $P < .001$) and visit the emergency department (40.8% vs 24.4%, $P < .001$) than patients without persistent opioid use in the 180 days after discharge. Of note, 36.8% of new persistent opioid users filled at least 1 more opioid prescription up to 1 year after discharge. The Southern United States had the highest percentage of patients who filled opioid prescriptions in the perioperative period (80.7%) and the highest incidence of new persistent opioid use (9.6%) (Figure 2). New persistent opioid use occurred even after receiving a single perioperative opioid prescription for 20 MME, and Figure E1 displays the rate of new persistent opioid use stratified by the amount of the perioperative opioids prescribed.

In the multivariable logistic regression, new persistent opioid use was independently associated with female gender (odds ratio [OR], 1.30; confidence interval [CI], 1.05-1.61; $P = .018$), anxiety (OR, 1.40; CI, 1.09-1.81; $P = .009$), tobacco use (OR, 1.34; CI, 1.08-1.65; $P = .007$), prior substance abuse (OR, 1.99; CI, 1.16-3.41; $P = .013$), chronic obstructive pulmonary disease (OR, 1.29; CI, 1.02-1.63; $P = .037$), living in the Southern United States (OR, 1.46; CI, 1.21-1.77; $P < .001$), and increased amount of opioids prescribed in the perioperative period (OR, 1.016; CI, 1.014-1.018; $P < .001$) (Table 4, Figure 3). The OR of opioids prescribed in the perioperative period reflects a 10 MME increase in opioids prescribed per 1% increase in new persistent opioid use. Thus, for every 13 additional 5 mg oxycodone tablets (~100 MMEs) prescribed, there is a 17.2% increased risk of new persistent opioid use. Factors not independently associated with new persistent opioid use included annual per capita income, congestive heart failure, chronic kidney disease, Charlson Comorbidity Index, postoperative acute renal failure, and surgical admission length of stay (all $P > .05$). The model

TABLE 2. Postoperative characteristics of patients who underwent coronary artery bypass grafting

Variable	All patients (N = 7292)	No persistent opioid use (N = 6702)	New persistent opioid use (N = 590)	*P* value
Postoperative pneumonia	222 (3.0)	199 (3.0)	23 (3.9)	.21
Postoperative acute renal failure*	550 (7.5)	494 (7.4)	56 (9.5)	.061
Postoperative stroke (ischemic or hemorrhagic)	140 (1.9)	131 (2.0)	9 (1.5)	.47
Unexpected return to the operating room	88 (1.2)	77 (1.1)	11 (1.9)	.13
Length of surgical admission, d	7.0 (4.0)	7.0 (4.0)	7.0 (4.0)	.069
Discharge status				.18
Discharged to home	4467 (61.3)	4093 (61.1)	374 (63.4)	
Discharged to home with home health	2146 (29.4)	1978 (29.5)	168 (28.5)	
Discharged to skilled nursing facility	140 (1.9)	134 (2.0)	6 (1.0)	
Discharged to inpatient rehabilitation	106 (1.5)	98 (1.5)	8 (1.4)	
Other	433 (5.9)	399 (6.0)	34 (5.8)	

Continuous variables are shown as medians (interquartile range). Categoric variables are shown as counts (percentage). New persistent opioid use was defined as a patient who filled an opioid prescription during the perioperative period and filled at least 1 opioid prescription between 90 and 180 days after surgery. *Indicates variable included in the multivariable logistic regression.

TABLE 3. Opioid prescriptions and outcomes for patients who underwent coronary artery bypass grafting

Time frame	Variable	All patients (N = 7292)	No persistent opioid use (N = 6702)	New persistent opioid use (N = 590)	*P* value
Perioperative	No. of patients who filled opioid prescriptions	5628 (77.2)	5038 (75.2)	590 (100.0)	<.001
	Total amount of opioids filled in perioperative period (MME)	300 (315)	263 (397)	393 (375)	<.001
	Day supply of the initial opioid prescription (MME)	5 (5)	5 (7)	7 (5)	<.001
	No. of opioid prescriptions filled	1 (0)	1 (0)	1 (1)	<.001
30-90 d after discharge	No. of patients who filled an opioid prescription	928 (12.7)	687 (10.3)	241 (40.8)	<.001
	Amount of opioids filled (MME)	0 (0)	0 (0)	0 (375)	<.001
	No. of opioid prescriptions filled	0 (0)	0 (0)	0 (1)	<.001
90-180 d after discharge	Amount of opioids filled by new persistent opioid users	N/A	N/A	225 (379)	<.001
	No. of opioid prescriptions filled by new persistent opioid users	N/A	N/A	1 (1)	
180-365 d after discharge	No. of new persistent opioid users Who filled an opioid prescription	N/A	N/A	217 (36.8)	
	Amount of opioids filled by new persistent opioid users	N/A	N/A	0 (296)	
	No. of opioid prescriptions filled by new persistent opioid users	N/A	N/A	0 (1)	
0-180 d after discharge	Readmissions	741 (10.2)	648 (9.7)	93 (15.8)	<.001
	Emergency department visits	1877 (25.7)	1636 (24.4)	241 (40.8)	<.001
	No. of patients with an insurance Claim for opioid dependence	8 (0.1)	8 (0.1)	0 (0)	.40

Perioperative time period spanned from 30 days before surgery to 14 days after surgery. New persistent opioid use was defined as a patient who filled an opioid prescription during the perioperative period and filled at least 1 opioid prescription between 90 and 180 days after surgery. Continuous variables are shown as medians (interquartile range). *MME*, Morphine milligram equivalent; *N/A*, not applicable.

correctly predicted 91.9% of cases, and model fit was determined with the Hosmer–Lemeshow test ($P = .115$). When perioperative opioids were analyzed by quartile, the top quartile of perioperative opioids prescribed was associated with a 27-fold increased odds of new persistent opioid use (OR, 27.97; CI, 15.19-51.50; $P < .001$) (Table E3).

Comment

In summary, among 7292 opioid-naïve patients undergoing CABG, 5628 (77.2%) filled opioid prescriptions in the perioperative period, and 590 (8.1%) had new persistent opioid use. New persistent opioid users filled prescriptions in the perioperative period for significantly more total opioids and with a greater day supply of opioids compared with nonpersistent users. New persistent opioid users also had more hospital readmissions and emergency department visits in the 180 days after the index admission. Independent risk factors for new persistent opioid use included female gender, anxiety, tobacco use, prior substance abuse, chronic obstructive pulmonary disease, living in the Southern United States, and increased amount of opioids prescribed in the perioperative period. These results are summarized in the graphical abstract (Figure 4). For every 100 MME increase in opioids prescribed, there was a 17.2% increased risk of new persistent opioid use. New persistent opioid use was highest in the Southern United States, and this is consistent with the fact that these states have the highest rate of opioid prescriptions and the highest number of opioid deaths after adjusting for age and population size.[17,18] This present study provides a unique contribution to the literature because it is the largest database study of opioid use in patients undergoing CABG.

A single-center analysis of 330 patients who underwent CABG in the Partners Healthcare System in Boston, Massachusetts, determined that chronic opioid dependence occurred in 21.7% of opioid-exposed versus 3.2% of opioid-naïve patients.[19] In our analysis, the risk of new persistent opioid use was 6.6% in Massachusetts, 5.8% in the Northeast Region, and 8.1% in the United States. The design of the Partners study also focused on comparing characteristics of opioid-exposed versus opioid-naïve patients in contrast to this present study, which focused on predictors of new persistent opioid use in opioid-naïve patients. Overall, both studies highlight the alarming incidence of chronic opioid use after CABG.

Our study is also consistent with reports of new persistent opioid use in other surgical subspecialties, and these studies are summarized in Table E4.[3,4,15,20-22] As in the present

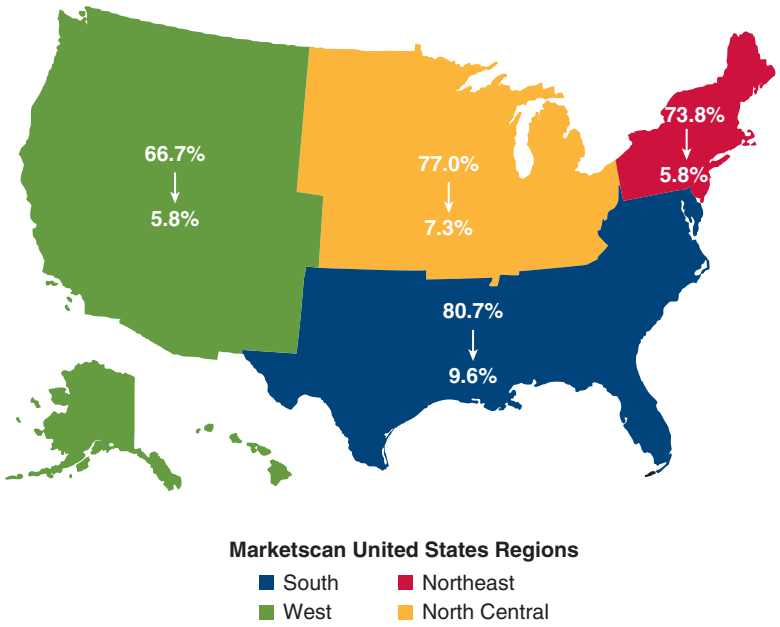


FIGURE 2. New persistent opioid use by regions in the United States. The percentage above the arrow is the percent of patients who filled opioid prescriptions in the perioperative period in the region. The percentage below the arrow is the incidence of new persistent opioid use in the region. Patients who underwent CABG in the Southern United States were significantly more likely to fill a perioperative opioid prescription and have new persistent opioid use.

study, preoperative anxiety, prior substance abuse, and multiple comorbidities are independently associated with increased new persistent opioid use after surgical procedures in the literature.[2,4,20,21] The present study found that female gender was a risk factor for new persistent opioid use after CABG. Although female gender has not been consistently reported as a risk factor for new persistent opioid use, a review of more than 22,000 German surgical patients demonstrated that female patients consistently endorse higher postoperative pain scores than men after 30 different surgical procedures.[23] However, few other studies evaluate patients who underwent cardiothoracic surgery with the exception of the studies by Brescia and colleagues,[3] which reported a 14% risk of new persistent opioid use after lung cancer resection, and Clarke and colleagues,[6] which reported a 3.3% risk of new persistent opioid after isolated CABG in Canada.

Given this risk of opioid addiction after surgical procedures, it is prudent to develop strategies to reduce opioid use during the surgical admission and more judiciously prescribe

TABLE 4. Multivariable logistic regression of variables associated with new persistent opioid use

Variable	Odds ratio	Lower 95% CI	Upper 95% CI	*P* value
Prior substance abuse	1.99	1.16	3.41	.013
Lives in Southern United States	1.46	1.21	1.77	<.001
Anxiety	1.40	1.09	1.81	.009
Tobacco use	1.34	1.08	1.65	.007
Female sex	1.30	1.05	1.61	.018
Chronic obstructive pulmonary disease	1.29	1.02	1.63	.037
Chronic kidney disease	1.22	0.87	1.72	.25
Postoperative acute renal failure	1.17	0.85	1.62	.33
Congestive heart failure	1.15	0.93	1.42	.2
Charlson Comorbidity Index	1.04	0.96	1.12	.4
Length of stay (d)	1.02	0.99	1.05	.07
Amount of opioids prescribed in perioperative period (MME)	1.016	1.014	1.018	<.001
Annual per capita income	1.00	1.00	1.00	.38

The OR for opioids prescribed in the perioperative period reflects the effect of a 10 MME increase in opioids prescribed. Southern United States includes the following states: District of Columbia, Delaware, Florida, Georgia, Maryland, North Carolina, South Carolina, Virginia, West Virginia, Alabama, Kentucky, Mississippi, Tennessee, Arkansas, Louisiana, Oklahoma, and Texas. *CI*, Confidence interval; *MME*, morphine milligram equivalent.

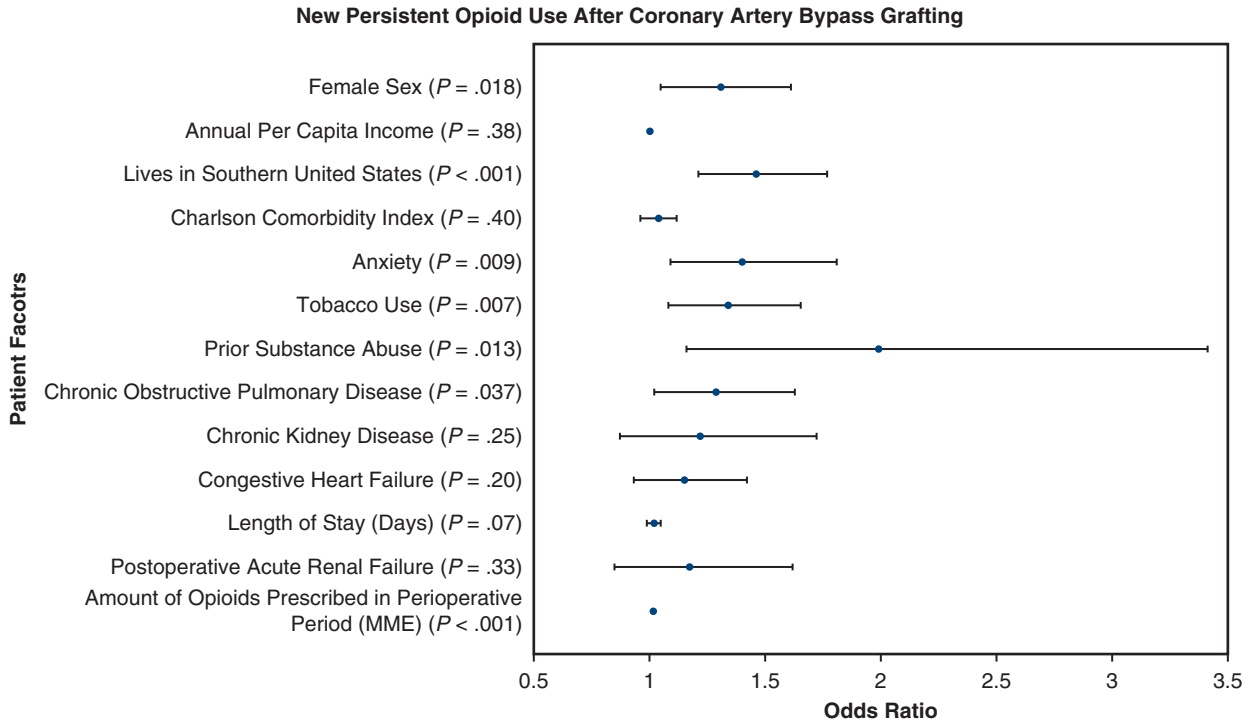


FIGURE 3. Multivariable logistic regression to determine the predictors of new persistent opioid use after CABG. Points represent the OR, and brackets show the lower and upper 95% CIs for each variable. Female sex, living in the Southern United States, tobacco use, prior substance abuse, chronic obstructive pulmonary disease, and the amount of opioids prescribed in the perioperative period were significant risk factors for new persistent opioid use. The OR for opioids prescribed in the perioperative period reflects the effect of a 10 MME increase in opioids prescribed. *MME*, Morphine milligram equivalent.

opioids upon discharge.[9] Multimodal pain therapy including nonsteroidal anti-inflammatory drugs, acetaminophen, gabapentin, and regional analgesia effectively reduce pain scores and opioid use in cardiac surgery recipients and may reduce the risk of chronic poststernotomy pain.[24-26] However, the US Food and Drug Administration issued a black box warning for nonsteroidal anti-inflammatory drugs after CABG in 2005.[27] In addition, a recent study demonstrated

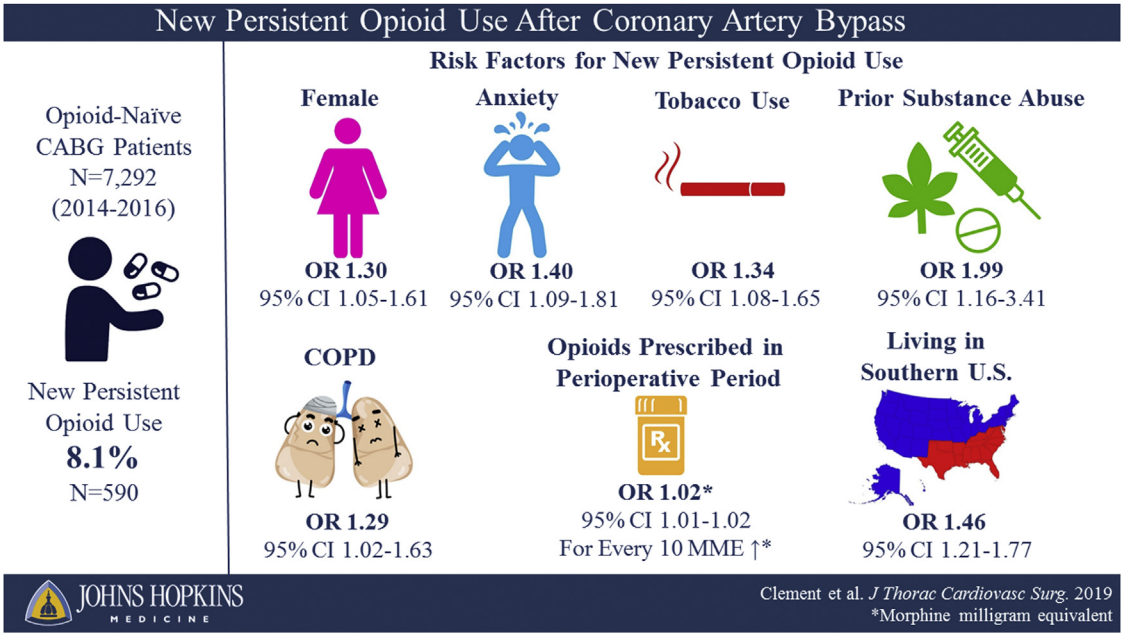
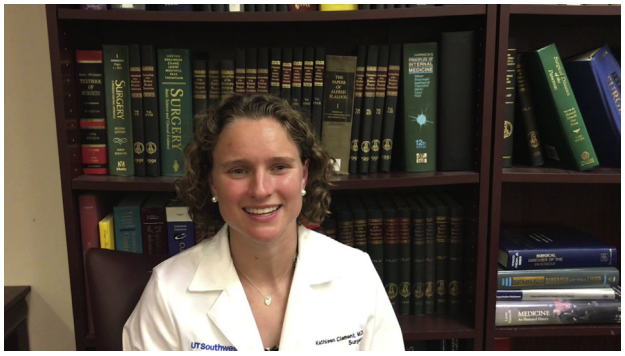


FIGURE 4. The incidence and risk factors for new persistent opioid use after CABG. *CABG*, Coronary artery bypass grafting; *OR*, odds ratio; *CI*, confidence interval; *MME*, morphine milligram equivalent.



VIDEO 1. Dr Kathleen C. Clement explains the methods, importance, and limitations of the work. Video available at: https://www.jtcvs.org/article/S0022-5223(19)32169-5/fulltext.

that an enhanced recovery after cardiac surgery program significantly reduced opioid use in the first 24 hours postoperatively, intensive care unit length of stay, and hospital length of stay.[28] However, it is unknown if the reduction of short-term opioid use in the intensive care unit will translate to less opioids prescribed on discharge and reduced new persistent opioid use. Educational interventions directed at surgical residents, attendings, and associate providers significantly reduced the amount of opioids prescribed on discharge after general surgery procedures and may be a potential solution to unintended opioid over-prescribing after cardiac surgery.[8,29]

Study Limitations

This study has certain limitations given its retrospective nature. The Marketscan database is limited to patients with private insurance and does not include Medicaid, Medicare, and uninsured patients. Privately insured patients only account for approximately 37.6% of all patients undergoing CABG, and private insurance is associated with decreased mortality, length of stay, and total costs compared the Medicare, Medicaid, and uninsured patients.[30] Although this study adjusted for age, annual income by metropolitan statistical area, gender, and region of residence for each patient, Marketscan does not contain race and ethnicity data because they are not routinely collected by health insurers. Marketscan is also unable to capture information regarding deep sternal wound infections, prolonged intubation, and long-term mortality. This claims database permits the quantification of filled opioid prescriptions, but this is not always equivalent to the amount of opioids taken by the patient. A recent study in the general surgery literature demonstrated that only 28% of prescribed opioid pills were taken after outpatient general surgery procedures,[8] and this discrepancy between opioids filled and taken also likely occurs in patients undergoing cardiothoracic surgery. Furthermore, this study may underestimate the incidence of new persistent opioid use if patients obtain prescription opioids from family members, friends, and by other means not linked to insurance claim data.

CONCLUSIONS

New persistent opioid use occurs in 8.1% of privately insured patients after CABG. Opioid prescribing guidelines may curtail excessive opioid prescribing in patients who undergo cardiac surgery and may reduce the risk of new persistent opioid use in this population. To determine opioid prescribing guidelines for cardiac surgery, a future prospective study is needed to evaluate the opioid requirements upon discharge to home of patients who have undergone cardiac surgery. Further studies are also needed to determine if prescribing less opioids on discharge reduces new persistent opioid use or leads to increased pain or other consequences such as anxiety or depression. While awaiting these prospective studies, we recommend that providers judiciously prescribe outpatient opioids on the basis of the patient's daily opioid use in the hospital before discharge instead of prescribing the same amount of opioid tablets for every patient. Furthermore, providers need to be aware of regional differences in opioid prescribing and new persistent opioid use after CABG and curtail their opioid prescribing accordingly (Video 1).

Webcast

You can watch a Webcast of this AATS meeting presentation by going to: https://aats.blob.core.windows.net/media/19%20AM/Saturday_May4/202AC/S27%20-%20Minimizing%20Opioids%20to%20enhance/S27_2_webcast_114651166.mp4.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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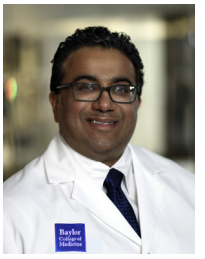
Key Words: opiod dependence, coronary artery bypass

Discussion



Dr Subhasis Chatterjee *(Houston, Tex)*. Dr Clement and colleagues from Johns Hopkins should be congratulated on a meaningful analysis on the prevalence of opioid dependence after CABG. Typically, we have focused on opioid use as a risk factor in our infective endocarditis surgical population, but this is a thoughtful investigation into our responsibility in exacerbating this problem. Dr Clement and colleagues' central finding was in an opioid-naive group of patients who underwent CABG, and 8% of patients developed persistent opioid use defined as still using opioids 3 to 6 months after surgery. I have 3 questions for you.

The first is regarding prevention. There are 2 potential opportunities and strategies to limit opioid use in patients undergoing surgery. One is to identify preoperatively patients at higher risk of developing prolonged opioid use. Are there strategies such as counseling that could offer help to reduce this? And another might be at the 30- or 90-day mark when people have already had their surgery and appear to be using more opioids than expected. Are there strategies that could limit the use or risk of developing opioid dependence in this group of patients?

Dr Kathleen C. Clement *(Baltimore, Md)*. The big thing is patient education. With a lot of these enhanced recovery after cardiac surgery protocols, the reason why they are successful is you tell your patients ahead of time, you are going to experience pain and this is what we are going to expect. So I think we should educate patients in the preoperative phase that, hey, there is a risk to getting addicted to opioids after surgery and let people know about that. I think that's incredibly important.

Also, as people have alluded to, postoperatively the enhanced recovery after cardiac surgery protocols are incredibly helpful in using multimodal pain therapy such as acetaminophen and gabapentin, and there are a lot of intraoperative interventions that our team at Johns Hopkins is using to try to minimize opioid use postoperatively.

Dr Chatterjee. Second is physician or surgeon responsibility. There is a concept known as high-risk prescribing. For providers who are prescribing higher dosages or longer durations, does this analysis allow you to track specific physicians who are writing the prescriptions? Is there an opportunity to identify physicians by prescribing patterns and intervene?

Dr Clement. Unfortunately in this database, no, because it is not provider linked. However, at Johns Hopkins we have an opioid dashboard that was developed that identified the opioid prescribing patterns per surgeon and per

physician provider, which is helpful. The other thing, too, is the Kaiser Family Foundation publishes the amount of opioid prescriptions per 100 US residents per state, and you can actually see statewide variations in opioid prescriptions. It turns out it's also highest in the South, too.

Dr Chatterjee. Third, there is a recent study from Dartmouth on approximately 20,000 patients that showed approximately 13% of patients were opioid users, and they were also 30% more likely to provide positive patient satisfaction scores. In our healthcare system, much of our financial incentives and bonuses are structured around patient satisfaction scores. How do we address the fact that our patients love us more when we are more generous with opioid prescribing?

Dr Clement. That's a big challenge, because right now we are all talking about it; we need to design ways to prescribe less opioids. I think the big albatross in the room is, first, we are worried about getting called. We get called about a lot of things postoperatively. The last thing we want to be called about is a patient who needs pain medication 1 or 2 weeks out of surgery because they didn't get enough pain medication. So I think that's why we also prescribe in excess, because it prevent calls.

The second thing is patient satisfaction. We are not only monitored by the Society of Thoracic Surgeons database in terms of outcomes but also by patient-reported outcomes. The risk is, if we are going to implement these protocols, we also need to get buy-in from the patients so they are aware when they are doing these Press Ganey scores and things that they a part of the process and not negatively affect these protocols that we are implementing.

Dr Judson B. Williams *(Raleigh, NC).* This was a fantastic presentation, and congratulations to the Johns Hopkins group for this important work. Raleigh, North Carolina, is on I95, halfway between Miami and New York, and our region is a hotbed for trafficking of narcotics along that corridor. When we have addressed this issue locally, community advocates, orthopedic surgeons, and others have asked, well, if you are not prescribing these in a controlled way and owning it as the surgeons and the clinicians, well, the patients are just going to buy it somewhere else. What do you think about that?

Dr Clement. Unfortunately, that is a challenge we cannot completely control, but that's true. For a majority of patients, hopefully they are not getting drugs off the street to fulfill prescriptions. But in other locations such as Johns Hopkins and other areas with good patient education and good pain control with perioperative and multimodal pain therapy, hopefully we can avoid patients needing to seek pain medications outside of the traditional prescription realms.

The challenge with all these databases I used has been reported. You can't account for the patients who are taking opioids from their grandma or parents who have had prescriptions from their last surgery, and that's a huge amount, and the problem is we can't account for those in these studies.

Dr Michael C. Grant *(Baltimore, Md).* With respect to the concept of patient satisfaction scores, the anesthesia literature has done a nice job of articulating the link between patient satisfaction and pain management. It is adequate pain management that leads to the highest satisfaction rather than the implication that it has to be opioid based. So although that study you referred to is an important one, and it tells us a lot about how we currently manage pain, what we now know is Press Ganey scores, as you mentioned, are a bit more closely linked to whether or not people have been adequately assessed for pain and whether or not it has been addressed in a formal fashion rather than whether opioids in particular were provided.

Dr Daniel T. Engelman *(Springfield, Mass).* Have you looked at all at disposal of opioids, that maybe at the first postoperative visit we should have our patients bring in their unused opioids and count them, use that to tailor our prescription habits, and then dispose of them to keep family members and others from accessing them?

Dr Clement. We have not specifically looked at that, but at Johns Hopkins, well, I can mention this now. We are institutional review board approved for a prospective opioid study to implement an opioid-prescribing protocol for patients undergoing cardiac surgery. We are going to call patients 1 week and 2 weeks postoperatively and do a pill count to compare how many pills they are actually taking, what are their side effects, do they need more medication, so we can get a better grasp of how many pills patients actually need when they go home.

Dr Engelman. It would be nice to dispose of them, also, because a big problem is that family members are accessing them. There are some real cheap opioid-disposable ways of doing that now in the office.

Unidentified Speaker. I was just wondering for opioids prescribed in the perioperative period, it makes total sense to model it as a continuous variable. Did you happen to look at that relationship and how linear it was, whether in percentiles or quartiles, or at what point did the rate of new persistent use really jump up by prescription size, if that's available?

Dr Clement. That's a great idea, but we did not basically look at the analysis based on quartiles or 10% and such. We just looked at it as a continuous variable. And the reason why is the opioid prescribing was so different based on region and it was so non-normally distributed, that's why we decided to leave it as it was.

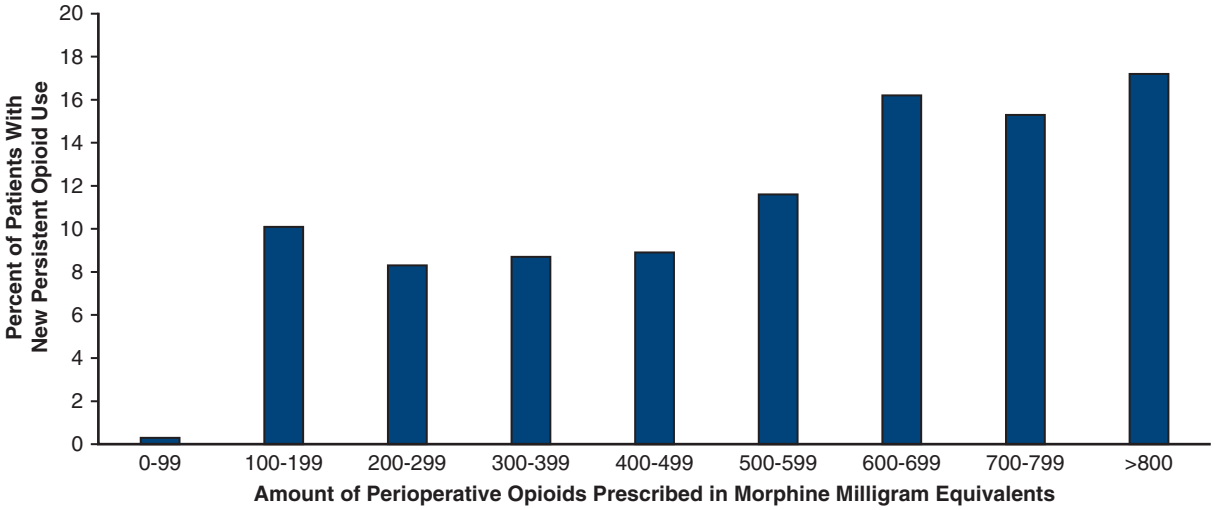


FIGURE E1. New persistent opioid use after CABG stratified by amount of perioperative opioids prescribed.

TABLE E1. International Classification of Diseases, Version 9 and 10 codes

CABG ICD-9 codes	CABG ICD-10 codes	AVR ICD-9 codes	AVR ICD-10 codes	MVR ICD-9 codes	MVR ICD-10 codes	MVr ICD-9 codes	MVr ICD-10 codes	Other valve ICD-9 codes	Other valve ICD-10 codes
36.10	210093	35.21	02RF07Z	35.12	02QG0ZZ	35.23	02RG07Z	35.25	02RH07Z
36.11	02100A3	35.22	02RF08Z		027G04Z	35.24	02RG08Z	35.26	02RH08Z
36.12	02100J3		02RF0KZ		027G0DZ		02RG0KZ	35.27	02RH0KZ
36.13	02100K3		02RF0JZ		027G0ZZ		02RG0JZ	35.28	02RH0JZ
35.14	02100Z3				02NG0ZZ			35.13	02RJ07Z
36.15	210493				02QG0ZZ			35.14	02RJ08Z
36.16	021009W								02RJ0KZ
36.19	02100AW								02RJ0JZ
	021109W								02QH0ZZ
	02110AW								027H04Z
	021149W								027H0DZ
	021209W								027H0ZZ
	02120AW								02NH0ZZ
	021249W								02QJ0ZZ
	021309W								027J04Z
	02130AW								027J0DZ
	210098								027J0ZZ
	210099								02NJ0ZZ
	021009C								
	02100A8								
	02100A9								
	02100AC								
	02100Z9								
	02100ZC								
	211098								
	211099								
	021109C								
	02110A8								
	02110A9								
	02110AC								
	02110Z8								
	02110Z9								
	02110ZC								
	021209C								
	02120AC								
	02120JC								
	02120ZC								
	021309C								
	02130AC								
	02130JC								
	02130KC								
	02130ZC								

Other valve procedures include pulmonic and tricuspid valve repair and replacement. *CABG*, Coronary artery bypass grafting; *ICD-9*, International Classification of Diseases, Ninth Revision; *ICD-10*, International Classification of Diseases, Tenth Revision; *AVR*, aortic valve replacement; *MVR*, mitral valve replacement; *MVr*, mitral valve repair.

TABLE E2. Marketscan definitions of US regions

Northeast	North Central	South	West
Connecticut	Illinois	District of Columbia	Arizona
Maine	Indiana	Delaware	Colorado
Massachusetts	Michigan	Florida	Idaho
New Hampshire	Ohio	Georgia	Montana
Rhode Island	Wisconsin	Maryland	Nevada
Vermont	Iowa	North Carolina	New Mexico
New Jersey	Kansas	South Carolina	Utah
New York	Minnesota	Virginia	Wyoming
Pennsylvania	Missouri	West Virginia	Alaska
	Nebraska	Alabama	California
	North Dakota	Kentucky	Hawaii
	South Dakota	Mississippi	Oregon
		Tennessee	Washington
		Arkansas	
		Louisiana	
		Oklahoma	
		Texas	

TABLE E3. Multivariable logistic regression of variables associated with new persistent opioid use with perioperative opioids analyzed in quartiles

Variable	Odds ratio	Lower 95% CI	Upper 95% CI	*P* value
Female sex	0.77	0.62	0.95	.016
Annual per capita income	1.00	1.00	1.00	.30
Lives in Southern United States	1.33	1.1	1.61	.004
Charlson Comorbidity Index	1.05	0.97	1.14	.25
Anxiety	1.53	1.18	1.97	.001
Tobacco use	1.32	1.07	1.63	.011
Prior substance abuse	2.17	1.25	3.76	.006
Chronic obstructive pulmonary disease	1.33	1.05	1.69	.017
Chronic kidney disease	1.17	0.83	1.65	.38
Congestive heart failure	1.14	0.93	1.41	.22
Length of stay (d)	1.04	1.01	1.06	.004
Postoperative acute renal failure	1.22	0.88	1.68	.24
Amount of opioids prescribed in perioperative period (MME) by quartile				
Second quartile	18.15	9.81	33.59	<.001
Third quartile	17.50	9.44	32.45	<.001
Fourth (top) quartile	27.97	15.19	51.50	<.001

The first quartile was the reference quartile when the amount of perioperative opioids prescribed was analyzed by quartile. First quartile 0-134 MME, second quartile 135-300 MME, third quartile 301-450 MME, fourth quartile 451+ MME. *CI*, Confidence interval; *MME*, morphine milligram equivalent.

TABLE E4. Review of new persistent opioid use after surgery

First author	Year published	Surgical procedure	No. of patients	Incidence of new persistent opioid use	Risk factors for new persistent opioid use
Brescia[3]	2019	Lung cancer resection	3026	14.00%	Age <64 y, male sex, increased postoperative length of stay, thoracotomy, adjuvant therapy
Bennett[20]	2019	Cosmetic plastic surgery procedures	11,257	6.10%	Increasing Charlson comorbidity index, mood disorder, tobacco use, neck pain, arthritis, other pain disorders
Clarke[6]	2014	Radical prostatectomy, coronary artery bypass, lung resection, colon resection, hysterectomy	39,140	3.10%	Younger age, lower income, diabetes, heart failure, pulmonary disease, any thoracic surgery
Swenson[21]	2018	Hysterectomy	24,331	0.50%	Increasing age, African-American race, gynecological malignancy, depression/ anxiety, preoperative opioid fill
Smith[22]	2018	Bariatric surgery	27,779	6.30%	Preoperative depression, worse psychologic well-being and body image
Saraswathula[4]	2018	Head and neck cancer surgery	1190	18.50%	Postoperative radiation, Charlson comorbidity index
Lee[15]	2017	Patients with cancer undergoing surgery for melanoma, breast, colorectal, lung, esophageal, and hepatobiliary malignancies	68,463	10.40%	Adjuvant chemotherapy
Brummett[2]	2017	Major and minor Surgery	36,177	5.9% (minor surgery) vs 6.5% (major surgery)	Preoperative tobacco use, alcohol/ substance abuse, mood disorders, anxiety, preoperative Pain disorders