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Association of new opioid continuation with surgical specialty and type in the United States

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A B S T R A C T

Background: The consequences of opioids—including post-surgical prescriptions—remain a critical public health issue. We sought to determine how procedure type and subspecialty group influence new opioid use after procedures.
Methods: We analyzed 2011–2015 IBM MarketScan Research Databases to identify opioid-naïve adults prescribed opioids for single surgical procedures. We defined new opioid continuation (primary outcome) a priori as receipt of prescription opioids between 90 and 180 days after the procedure.
Results: Among 912,882 individuals, new opioid continuation was higher for non-operating room compared to operating room procedures (13.1% versus 9.2%; aOR 1.61; 95% CI 1.59–1.64) and higher for subspecialties including colorectal surgery (aOR 1.35; 95% CI 1.26–1.43) and cardiovascular surgery (aOR 1.30; 95% CI 1.12–1.50) compared to urology as a referent. New opioid continuation was also associated with perioperative opioid prescription dosage, days' supply, preoperative receipt, and multiple prescriptions.
Conclusions: Opioids prescriptions associated with non-operating room surgical exposures appear to confer higher risk regarding conversion to new long-term opioid use.

Introduction

Millions of individuals undergo surgical procedures every year in the United States, and many more still undergo invasive inpatient procedures.[1] After surgery, patients often receive postoperative opioid prescriptions, even after minor procedures, at amounts well in excess to those needed to adequately control pain.[2–5] While there have been modest reductions in opioid prescribing in the United States since 2010, prescribing levels remain far higher than prior to the opioid epidemic, and long-term opioid use remains a major public health concern. More than 47,000 Americans died from opioids in 2017, including at least 17,000 from prescription opioids, continuing the most serious drug epidemic in the history of the United States.[6]

While there is increasing recognition that prescription opioids have been overused in the surgical setting,[7–9] they continue to be overprescribed, contributing to the potential for diversion[3,10,11] as well as the inadvertent conversion of opioid-naïve patients into longer-term users of opioid analgesics. Prior studies suggest that between 3% and 10% of all patients who receive a postoperative opioid prescription transition to some type of long-term opioid use.[5,12–16]

Despite the insights from these studies, they leave several questions unanswered. In particular, few systematic studies have been conducted that examine variation in the persistence of opioid use across different surgical procedures and subspecialties. We quantified the incidence of new persistent use of opioids after surgical procedures by type of procedure and examined differences by subspecialty group. We hypothesized that the incidence of new

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persisting opioid use after surgical procedures would not differ between procedures performed in the operating room versus those not performed in the operating room, and would differ among surgical subspecialty groups.

Materials and methods

Data sources and patient cohort

This study was exempted from review by a Johns Hopkins Institutional Review Board. The IBM MarketScan® Research Databases contains individual-level, de-identified, healthcare claims information across the continuum of care from large employers and health plans across the United States that provide private healthcare coverage for employees, their spouses, and dependents. We examined claims from January 1, 2010, to December 31, 2015, among adults aged 18–64 years to capture data on procedures performed between January 1, 2011, and December 31, 2014.

We selected individuals who underwent procedures using a preassigned procedure group classification, which in turn is based on *International Statistical Classification of Diseases and Related Health Problems (ICD-9)* diagnoses. MarketScan classifies procedures into mutually exclusive categories labelled as major (i.e., performed under general anesthesia and/or in an operating or special 'treatment' room; not performed in a physician's office or at patient's bedside), minor, or other procedures by processing in a standardized manner raw data provided by individual insurance plans. For this analysis, we used the preassigned MarketScan service categories to define two types of procedures: (1) "operating room (OR) procedures" were those prespecified as "major" procedures or occurring in the operating room, and (2) "non-OR procedures" were procedures prespecified as "minor", "other", or not occurring in the operating room (eTable 1, Supplementary Material). For each invasive procedure claim, we identified the surgical subspecialty using the provider type associated with the claim. We then restricted our cohort to individuals who had only one type of procedure category on a given day, rather than multiple procedures. Thus, an individual carpal tunnel release alone would be included, but an individual undergoing this as well as laparoscopic cholecystectomy would be excluded from the analysis. Based on the date of the procedure, individuals had to fill at least one opioid prescription in the perioperative period, which we defined as the period from 30 days before to 2 weeks after the procedure.

Similar to several prior studies using claims to define an opioid naïve cohort, we excluded individuals who filled one or more opioid prescriptions from 12 months to 31 days (i.e., 11 months) prior to the procedure (eFig. 1, Supplementary Material).[5,12,13] We also excluded individuals who had more than one procedure in the perioperative period, those without continuous or complete claims coverage in the 12 months before and after the procedure, and those who only filled non-analgesic opioid prescriptions.

For a comparison group of individuals not exposed to procedures, we identified a random 10% sample of patients aged 18 to 64 who did not undergo a surgical procedure in the study period. We included only individuals who did not fill an opioid prescription during an 11-month period of time and who had 24 continuous months of claims, similar to the preoperative exclusion criteria. We then assigned a random procedure date to these 619,845 individuals, which was used to determine outcomes.

Outcomes

A priori, we defined our primary outcome, new persistent opioid use after procedures, as receipt of an opioid prescription between 90 and 180 days after the procedure. This time period builds on the International Association for the Study of Pain definition of chronic post-surgical pain, which recognizes pain continuing outside the normal timeframe for healing as pain persisting for more than 3 months after a procedure.[16] Secondary outcomes included new long-term opioid use at 6-month and 12-month intervals, defined as having $\geq$66% of days covered or $\geq$2 prescriptions filled in the last two months of the interval. We converted opioid prescriptions to morphine milligram equivalents (MMEs) using standard conversion factors,[17] and calculated opioid prescription characteristics for four variables: (1) prescription before procedures, defined as an opioid prescription fill within 30 days before the procedure, given past work suggesting this increases the odds of continued opioid use after surgery[5]; (2) total perioperative MMEs, defined as the total amount of opioid prescriptions filled 30 days before to 14 days after the procedure; (3) days' supply in the perioperative period, defined as the number of days covered with an opioid prescription; and (4) number of opioid prescriptions filled in the perioperative period.

Patient factors

We included demographic, occupational, and clinical covariates for individuals, including age at time of procedure, region, salary, and union status. Pre-procedure clinical characteristics included use of tobacco products (*ICD-9* code 305.1, V15.82), cancer diagnosis (*ICD-9* codes 140–239), Charlson Comorbidity Index,[18] mental health disorders based on the Agency for Health Research and Quality (AHRQ) Clinical Classification System, and, similar to past studies,[5] pain diagnoses categories for back, neck, arthritis, and other types of pain. We based all pre-procedure diagnoses on *ICD-9* codes existing in the 12 months prior to the procedure.

Statistical analysis

We calculated descriptive statistics for baseline covariates for the cohort and by type of surgical procedure using chi-squared or Wilcoxon rank-sum tests for categorical or continuous data, respectively. We analyzed the primary outcome of new opioid continuation using a multivariable logistic regression model to determine the difference among type of procedure and subspecialty group while controlling for baseline covariates, including demographics (age, gender, year, region), occupational characteristics (employee status, wage type, union status), and clinical covariates (tobacco use, cancer diagnosis, CCI, mental health disorders, and pain diagnoses). The model also included the four perioperative opioid prescription characteristics. Subspecialty groups with a combined number of individuals less than 100 were excluded from the model given low sample size. We also examined differences in the incidence of new opioid use by the four perioperative opioid prescription characteristics using exact 95% confidence intervals. In post-hoc analyses, we examined the amount of opioids prescribed at baseline by surgical subspecialty and type of procedure, the interaction of surgical subspecialty with procedure type, and major vs. minor operating room surgical procedures based on previously defined ICD-9 codes,[5] which included all procedures with AHRQ clinical classification procedure descriptions that matched ICD-9 codes. We analyzed data using SAS 9.4 and Stata 15.2 and considered P-values less than 0.05 to be statistically significant.

Results

We examined 912,882 opioid-naïve patients who underwent only one type of surgical procedure and filled at least one opioid prescription (Fig. 1). A total of 665,957 (73.0%) individuals

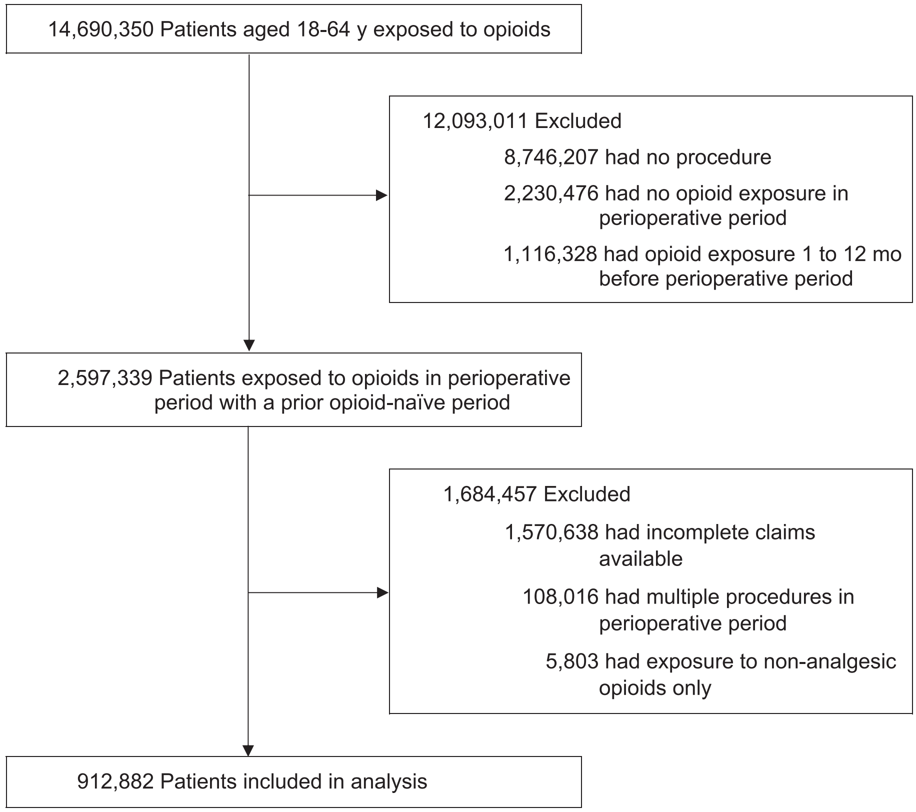

Fig. 1. Study flow diagram.
Source: IBM MarketScan Databases 2010–2015.

underwent OR procedures and 246,925 (27.0%) individuals underwent non-OR procedures. Most individuals were female (515,782 [56.5%]) and employed full time (601,084 [65.8%]), with mean (SD) age of 44.5 (12.2) years (Table 1). The three most common subspecialty groups associated with procedures included orthopedic surgery (373,228 [40.9%]), general surgery (211,913 [23.2%]), and obstetrics/gynecology (162,241 [17.8%]).

While opioids were more commonly prescribed before procedures to those undergoing non-OR rather than OR procedures (46.2% versus 26.9%, $p < 0.001$), individuals undergoing OR procedures received higher total doses of opioids (median 225 MME [30 pills of oxycodone 5 mg] versus 150 MME [20 pills of oxycodone 5 mg], $p < 0.001$; eFig. 2), longer days' supply (5 days versus 4 days, $p < 0.001$), and multiple prescriptions more often (21.1% versus 14.8%, $p < 0.001$).

New persistent opioid use by type of procedure and subspecialty group

Persistent opioid use was more common for non-OR compared to OR surgical procedures (Fig. 2). For example, among those undergoing OR procedures, 60,918 (9.2%) individuals filled an opioid prescription 90–180 days after the procedure, compared to 32,241 (13.1%) individuals who filled an opioid prescription after undergoing non-OR procedures (adjusted odds ratio [aOR], 1.61; 95% CI, 1.59–1.64). In contrast, 11,796 (2.0%) individuals in the non-procedural control group filled an opioid prescription 90–180 days after the randomly assigned procedure date. The incidence of prolonged opioid use also varied among subspecialty groups, with greater odds for subspecialty groups including colorectal surgery (aOR 1.35, 95% CI, 1.26–1.43), cardiovascular surgery (aOR 1.30; 95% CI, 1.12–1.50), and thoracic surgery (aOR 1.26; 95% CI, 1.11–1.42), compared to urology (Table 2, eTable 2).

Risk factors for new persistent opioid use

Several opioid prescription characteristics were associated with higher risks of new persistent opioid use after procedures (Fig. 3). Obtaining an opioid prescription before the procedure, compared to obtaining one on or after the day of the procedure, increased the odds of new persistent opioid use (aOR 1.02; 95% CI 1.00–1.04). Compared to the bottom 75th percentile, prescriptions with a total opioid amount in the top 25th percentile (i.e., ≥375 MMEs [50 pills of oxycodone 5 mg]) in the perioperative period had higher odds of new persistent opioid use after procedures (aOR 1.05; 95% CI, 1.03–1.07). Every additional days' supply of opioids in the perioperative period also conferred a greater chance of new persistent opioid use after procedures. (aOR 1.05; 95% CI, 1.05–1.05). Compared to filling one prescription, filling two or more opioid prescriptions also increased the odds of new persistent opioid use (aOR 1.40; 95% CI, 1.37–1.43).

Clinical characteristics that increased risk of new persistent opioid use after procedures included tobacco use (aOR 1.25; 95% CI 1.22–1.29), all pain diagnoses, and several mental health disorders including anxiety (aOR 1.15; 95% CI 1.13–1.18), mood (aOR 1.27; 95% CI, 1.24–1.30), and substance use (aOR 1.40; 95% CI 1.30–1.52) (Table 2). New persistent opioid use varied by demographic and occupational characteristics, with older age, female sex, hourly wage type, and union membership increasing the odds of opioid use after procedures.

Table 1
Baseline characteristics.

Characteristic	No. (%)			*P* value
	Overall	Operating room procedures	Non-operating room procedures	
	n = 912882	n = 665957	n = 246925	
Age, y				<0.001
18-29	124161 (13.6)	87642 (13.2)	36519 (14.8)	
30-39	174629 (19.1)	117768 (17.7)	56861 (23.0)	
40-49	244375 (26.8)	185818 (27.9)	58557 (23.7)	
50-59	278047 (30.5)	207995 (31.2)	70052 (28.4)	
60-64	91670 (10.0)	66734 (10.0)	24936 (10.1)	
Female	515782 (56.5)	379614 (57.0)	136168 (55.1)	<0.001
Year				<0.001
2011	269056 (29.5)	193460 (29.0)	75596 (30.6)	
2012	222773 (24.4)	161447 (24.2)	61326 (24.8)	
2013	220321 (24.1)	162548 (24.4)	57773 (23.4)	
2014	200732 (22.0)	148502 (22.3)	52230 (21.2)	
Region				<0.001
New England	38354 (4.2)	28229 (4.2)	10125 (4.1)	
Middle Atlantic	114075 (12.5)	81837 (12.3)	32238 (13.1)	
East North Central	174226 (19.1)	129302 (19.4)	44924 (18.2)	
West North Central	49826 (5.5)	37486 (5.6)	12340 (5.0)	
South Atlantic	203672 (22.3)	144646 (21.7)	59026 (23.9)	
East South Central	79055 (8.7)	57130 (8.6)	21925 (8.9)	
West South Central	105537 (11.6)	78178 (11.7)	27359 (11.1)	
Mountain	51742 (5.7)	39462 (5.9)	12280 (5.0)	
Pacific	80891 (8.9)	58660 (8.8)	22231 (9.0)	
Unknown	15504 (1.7)	11027 (1.7)	4477 (1.8)	
Employee Status				<0.001
Active Full Time	601084 (65.8)	438588 (65.9)	162496 (65.8)	
Active Part Time/Seasonal	10984 (1.2)	7959 (1.2)	3025 (1.2)	
Early Retiree	61560 (6.7)	45544 (6.8)	16016 (6.5)	
Medicare Eligible Retiree	5681 (0.6)	4068 (0.6)	1613 (0.7)	
Retiree (status unknown)	4524 (0.5)	3028 (0.5)	1496 (0.6)	
COBRA Continuee	1375 (0.2)	1038 (0.2)	337 (0.1)	
Long Term Disability	1369 (0.1)	1003 (0.2)	366 (0.1)	
Surviving Spouse/Depend.	1697 (0.2)	1201 (0.2)	496 (0.2)	
Other/Unknown	224608 (24.6)	163528 (24.6)	61080 (24.7)	
Wage type				<0.001
Salary	242248 (26.5)	179148 (26.9)	63100 (25.6)	
Hourly	210672 (23.1)	153442 (23.0)	57230 (23.2)	
Unknown	459962 (50.4)	333367 (50.1)	126595 (51.3)	
Union status				<0.001
Nonunion	380456 (41.7)	279177 (41.9)	101279 (41.0)	
Union	127152 (13.9)	92695 (13.9)	34457 (14.0)	
Unknown	405274 (44.4)	294085 (44.2)	111189 (45.0)	
Tobacco use	40335 (4.4)	29055 (4.4)	11280 (4.6)	<0.001
Cancer diagnosis	239623 (26.2)	180879 (27.2)	58744 (23.8)	<0.001
Charlson Comorbidity Index, mean (SD)	0.5 (1.1)	0.5 (1.1)	0.4 (1.0)	<0.001
Mental health disorder				
Adjustment	24874 (2.7)	17847 (2.7)	7027 (2.8)	<0.001
Anxiety	67444 (7.4)	48233 (7.2)	19211 (7.8)	<0.001
Attention deficit	15281 (1.7)	10808 (1.6)	4473 (1.8)	<0.001
Impulse control	431 (<0.1)	296 (<1)	135 (0.1)	0.046
Mood	78146 (8.6)	55815 (8.4)	22331 (9.0)	<0.001
Personality	1016 (0.1)	707 (0.1)	309 (0.1)	0.016
Schizophrenia	2041 (0.2)	1408 (0.2)	633 (0.3)	<0.001
Alcohol	6673 (0.7)	4477 (0.7)	2196 (0.9)	<0.001
Substance	4706 (0.5)	2941 (0.4)	1765 (0.7)	<0.001
Suicide and self-harm	1254 (0.1)	833 (0.1)	421 (0.2)	<0.001
Miscellaneous	14981 (1.6)	10833 (1.6)	4148 (1.7)	0.076
Pain diagnosis				
Back	183480 (20.1)	134271 (20.2)	49209 (19.9)	0.013
Neck	89286 (9.8)	64784 (9.7)	24502 (9.9)	0.005
Arthritis	500739 (54.9)	380879 (57.2)	119860 (48.5)	<0.001
Other	206895 (22.7)	153211 (23.0)	53684 (21.7)	<0.001
Opioid prescription characteristics				
Prescription before procedure	292837 (32.1)	178831 (26.9)	114006 (46.2)	
Total MME in perioperative period, median (IQR)	225.0 (150.0, 375.0)	225.0 (150.0, 400.0)	150.0 (100.0, 250.0)	<0.001
Days' supply in perioperative period, median (IQR)	5.0 (3.0, 7.0)	5.0 (3.0, 7.0)	4.0 (3.0, 6.0)	<0.001
More than one prescription	177057 (19.4)	140596 (21.1)	36461 (14.8)	<0.001
Provider type				<0.001
Orthopedic Surgery	373228 (40.9)	274127 (41.2)	99101 (40.1)	
General Surgery	211913 (23.2)	175633 (26.4)	36280 (14.7)	
Obstetrics & Gynecology	162241 (17.8)	121662 (18.3)	40579 (16.4)	

(*continued on next page*)

Table 1 (*continued*)

Characteristic	No. (%)			*P* value
	Overall	Operating room procedures	Non-operating room procedures	
	n = 912882	n = 665957	n = 246925	
Urology	94843 (10.4)	39942 (6.0)	54901 (22.2)	
Plastic/Maxillofacial Surgery	36898 (4.0)	27369 (4.1)	9529 (3.9)	
Colorectal Surgery	11673 (1.3)	9176 (1.4)	2497 (1.0)	
Neurological Surgery	9820 (1.1)	8780 (1.3)	1040 (0.4)	
Vascular Surgery	4260 (0.5)	3230 (0.5)	1030 (0.4)	
Thoracic Surgery	2336 (0.3)	1844 (0.3)	492 (0.2)	
Abdominal Surgery	2048 (0.2)	1453 (0.2)	595 (0.2)	
Cardiovascular Surgery	1791 (0.2)	1329 (0.2)	462 (0.2)	
Pediatric Surgery	628 (0.1)	445 (0.1)	183 (0.1)	
Surgical Critical Care	453 (<0.1)	392 (0.1)	61 (<0.1)	
Cardiothoracic Surgery	423 (<0.1)	328 (<0.1)	95 (<0.1)	
Head and Neck Surgery	231 (<0.1)	167 (<0.1)	64 (<0.1)	
Trauma Surgery	64 (<0.1)	56 (<0.1)	8 (<0.1)	
Transplant Surgery	28 (<0.1)	23 (<0.1)	5 (<0.1)	
Dermatologic Surgery	4 (<0.1)	1 (<0.1)	3 (<0.1)	

New persistent opioid use after procedures at 6 and 12 months

New long-term opioid use at 6 and 12 months after procedures, defined as ≥66% of days covered or ≥2 prescriptions filled in the last two months of the interval, appeared to be higher for non-OR compared to OR procedures and for certain subspecialty groups at both intervals (eTable 3 and eTable 4, Supplementary Material). Among those undergoing OR procedures, 10,791 (1.6%) individuals experienced new long-term opioid use at 6 months, compared to 7179 (2.9%) individuals who did so after undergoing non-OR procedures (aOR 2.06; 95% CI, 1.99–2.13). Similarly, at 12 months 11,232 (1.7%) individuals undergoing OR procedures experienced new long-term opioid use, compared to 6577 (2.7%) who did so after undergoing non-OR procedures (aOR 1.78; 95% CI, 1.72–1.84).

New persistent use among operating room procedures

In post-hoc analyses, the incidence of new persistent use was similar among different types of procedures performed in the operating room setting (eFig. 3, eTable 5).

Discussion

In this cohort of patients without opioid use in the year before their procedure, patients undergoing non-operating room procedures experienced 60% greater odds of new opioid continuation compared to those undergoing procedures in the operating room, a finding consistent across most all surgical specialties and also when examining of 6- and 12-month opioid use outcomes. Rates of new opioid use persisting between 3 and 6 months after a procedure showed more than two-fold variation, ranging from 6.6% to 13.6% based on the surgical specialty associated with the procedure. Thus, new persistent opioid use, recently recognized as one of the most common complications occurring after surgery, appears to be even more prevalent for patients undergoing procedures outside of the operating room and for certain surgical specialties. Our findings are important because of how commonly surgical procedures are performed in the United States, as well as the increased morbidity and mortality that is associated with new persistent opioid use.

This comparison of operating room versus non-operating room surgical procedures, which is a particular strength of this analysis, adds new insight to findings from past studies. Work by Clarke et al. revealed 3% of opioid-naïve patients transition to opioid use at 90 days after undergoing major surgery,[12] while Alam et al. found 7% of patients fill an opioid prescription at one year after undergoing minor surgery.[13] Subsequent examination of new opioid use by procedure type, which focused exclusively on procedures occurring in the operating room, suggested little difference between major and minor types of surgeries. For example, Brummet et al. reported similar odds of new persistent opioid use when comparing eight minor to five major procedures, all of which took place in the operating room, after adjusting for various possible confounders. Our results confirm this finding for operating room procedures.[5] Differences in data sources and definitions of opioid use after surgery have implications on available confounders, type of procedures, and sample size included in each analysis, and may account for variations in each work.

Persistent use appears higher for surgical procedures occurring outside of the operating room

The higher incidence of new persistent opioid use for non-operating room procedures compared to those in the operating room appears consistent across most surgical subspecialties. The difference is most dramatic in cardiothoracic surgery, orthopedic surgery, and pediatric surgery, with the incidence of new opioid use after non-operating room procedures approaching 20% for cardiothoracic surgery and 17% for orthopedic surgery. Possible explanations exist for the observation that new persistent opioid use is more likely after non-operating room procedures compared to those performed in the operating room. If non-operating room procedures result in less pain for patients than those in the operating room, prescription opioids may be needed at lower amounts. However, patients may continue prescription opioids after non-operating room procedures for reasons other than pain. For example, opioids may be taken to facilitate sleep, in response to mood changes, or other non-pain reasons. Alternatively, procedures performed in the operating room may permit patients to receive more opioid sparing techniques such as regional anesthesia or non-opioid pharmacological pain treatment, both of which may result in lower incidence of new persistent opioid use. Additionally, surgical subspecialties differ in regards to comorbidities of patient populations who undergo surgery, which may account for variation in opioid prescribing associated with surgery. Differences in the oversight of prescribers for outpatient versus inpatient settings may result in differences in access to and monitoring of opioids.[19] Because acute pain may transition to chronic pain after the procedure, understanding the biological underpinnings of this transition stands as one of the main approaches to enhancing pain management under the NIH Helping to End Addiction (HEAL)

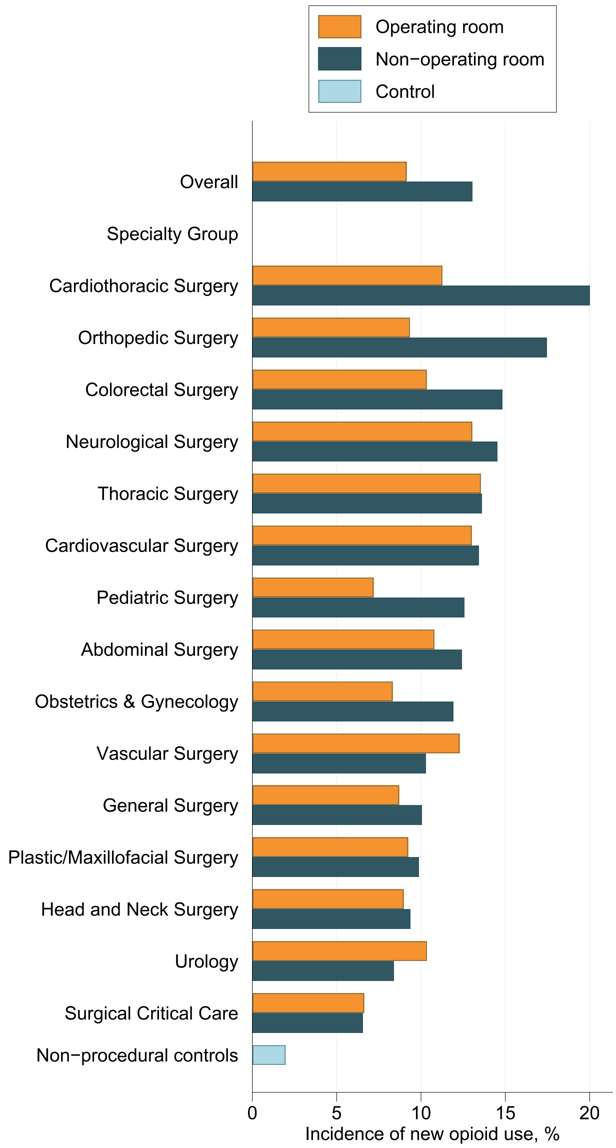

Fig. 2. Incidence of new opioid use for operating room versus non-operating room procedures and by subspecialty group.
Incidence of new opioid use by procedure type and for various specialty groups, ranked by new opioid use after minor surgery. New opioid use was defined as filling one or more prescriptions between 3 months and 6 months after procedure. Specialty groups with less than 100 patients (n = 3; trauma, transplant, and dermatologic surgery) were excluded. Operating room (OR) procedures included those specified as "major" or occurring in the operating room. Non-operating room procedures included those specified as "minor," "other," or not occurring in the operating room.

Initiative.[20] Biomarkers collected at the time of surgery have the potential to advance knowledge about opioid use with pharmacogenetics and other precision medicine insights to help personalize pain treatment after surgery.[21]

Persistent use may be related to surgical subspecialty

These findings also underscore the impact of surgical specialty in rates of new persisting opioid use after procedures, as the odds of new persistent opioid use was highest among colorectal surgery, cardiovascular surgery, and thoracic surgery. The association of surgical specialty with opioid continuation may reflect a number of factors not measured in this investigation. Variation in patient characteristics that mediate new persistent opioid use represent the most likely explanation. While this analysis controlled for comorbid psychiatric, pain, and substance use diagnoses, other important patient characteristics such as education level and expectations about surgical recovery, pain, and pain management likely influence opioid use despite not being present in claims data. Cultural and historical factors about pain and pain management unique to surgeons within each specialty may influence rates of prescribing for both opioid and non-opioid analgesic products. Unique characteristics for procedures performed by a given specialty may result in different types of pain and opioid prescribing as well. While changes in surgical site pain intensity have not correlated with new persistent opioid use, the ability to use non-opioid techniques such as regional, epidural, or spinal anesthesia differs based on the type of procedure.[22]

While these trends raise concern that new persistent opioid use after procedures may escalate in the future, this analysis identifies some areas of optimism. Prescribing opioids using evidence-based guidelines represents one key approach to mitigating overprescription. The CDC Guidelines for Prescribing Opioids in 2016 highlighted best practices for those treating individuals with chronic pain, but the role of opioid prescribing in the perioperative period was not addressed.[23] Prescribing guidelines based on consensus and surgical outcomes have recommended amounts for opioids prescribed to opioid-naïve patients after procedures, and achieved some reductions in overprescribing without compromising post-operative pain relief.[9,24,25] Despite the focus on surgical prescribing, guidelines often fail to address surgical procedures taking place outside of the operating room. While the invasiveness of non-operating room procedures is generally lower than surgical procedures in the operating room, patients appear to be at higher risk for new persistent opioid use after non-operating room procedures. Opioid utilization for non-operating room procedures has not been specifically addressed by recent surgical guidelines, and professional organization as well as investigators should scrutinize opioid and non-opioid prescribing practices associated with non-operating room procedures. Perioperative opioid prescription characteristics, four of which were examined in this work, influence the probability of new persistent opioid use and new long-term opioid use after procedures, and represent areas of focus for guidelines and potential measures of quality prescribing for surgical patients. First, obtaining more than one opioid prescription increased the risk of new persistent opioid use the most among the four prescription characteristics. Second, every additional days supply of opioid in the perioperative period increased the odds of new persistent opioid use by 5%, which aligns with prior studies of surgical and general patient populations.[26,27] Finally, receipt of an opioid prescription before procedures and the total amount of opioids above the 75th percentile also increased the likelihood of opioid continuation. In another area of optimism, the likelihood of new persistent opioid use decreased in a stepwise manner for every additional year after 2011. The steady decline, with patients having 0.83 odds of new persistent opioid use after procedures in 2014 compared to 2011, suggests surgical opioid prescribing practices may be changing for the better as increasing awareness of the broader opioid epidemic continues.

Limitations

While this study has several strengths, we must acknowledge the presence of additional limitations important to the interpretation of these findings. First, while the analysis of claims data permits examination of a large number of patients, data elements for important individual characteristics such as education, income level, and race were not available. Also, this study included patients undergoing procedures until 2014, and may not reflect more recent

Table 2
Multivariable logistic regression model of new opioid use after procedures.

Characteristic	Adjusted Odds Ratio	95% Confidence Interval	*P* Value
Operating room (0) vs. Non-operating room (1) procedures	1.61	1.59–1.64	<0.001
Subspecialty group			
Urology	1	Ref.	
Orthopedic Surgery	1.13	1.10–1.16	<0.001
Obstetrics & Gynecology	1.18	1.14–1.22	<0.001
General Surgery	1.05	1.02–1.08	<0.001
Plastic/Maxillofacial Surgery	1.07	1.03–1.12	<0.001
Colorectal Surgery	1.35	1.26–1.43	<0.001
Neurological Surgery	0.93	0.87–0.99	0.02
Vascular Surgery	1.21	1.10–1.33	<0.001
Abdominal Surgery	1.09	0.95–1.26	0.24
Cardiovascular Surgery	1.30	1.12–1.50	<0.001
Thoracic Surgery	1.26	1.11–1.42	<0.001
Pediatric Surgery	1.09	0.82–1.44	0.56
Cardiothoracic Surgery	1.17	0.87–1.57	0.29
Head and Neck Surgery	0.98	0.62–1.55	0.92
Surgical Critical Care	0.81	0.55–1.17	0.26
Age, y			
18-29	1	Ref.	
30-39	1.06	1.03–1.09	<0.001
40-49	1.18	1.15–1.21	<0.001
50-59	1.34	1.31–1.38	<0.001
60-64	1.39	1.35–1.43	<0.001
Female	1.15	1.13–1.17	<0.001
Year			
2011	1	Ref.	
2012	0.96	0.94–0.98	<0.001
2013	0.90	0.89–0.92	<0.001
2014	0.83	0.81–0.85	<0.001
Employee Status			
Active Full Time	1	Ref.	
Active Part Time/Seasonal	0.87	0.81–0.93	<0.001
Early Retiree	0.95	0.92–0.98	<0.001
Medicare Eligible Retiree	0.97	0.89–1.05	0.41
Retiree (status unknown)	0.96	0.87–1.05	0.36
COBRA Continuee	1.10	0.94–1.30	0.24
Long Term Disability	1.22	1.05–1.41	0.01
Surviving Spouse/Depend.	0.89	0.77–1.03	0.13
Other/Unknown	1.02	1.00–1.04	0.11
Region			
New England	1	Ref.	
Middle Atlantic	0.99	0.95–1.04	0.68
East North Central	1.28	1.22–1.33	<0.001
West North Central	1.24	1.18–1.30	<0.001
South Atlantic	1.31	1.26–1.36	<0.001
East South Central	1.51	1.45–1.58	<0.001
West South Central	1.46	1.40–1.52	<0.001
Mountain	1.34	1.27–1.40	<0.001
Pacific	1.20	1.15–1.26	<0.001
Unknown	1.54	1.44–1.64	<0.001
Wage type			
Salary	1	Ref.	
Hourly	1.19	1.16–1.21	<0.001
Unknown	1.06	1.04–1.09	<0.001
Union status			
Nonunion	1	Ref.	
Union	1.06	1.03–1.08	<0.001
Unknown	0.97	0.95–0.99	<0.001
Tobacco use	1.25	1.22–1.29	<0.001
Cancer diagnosis	1.01	0.99–1.02	0.54
Charlson Comorbidity Index	1.16	1.15–1.17	<0.001
Mental health disorder			
Adjustment	1.02	0.98–1.07	0.24
Anxiety	1.15	1.13–1.18	<0.001
Attention deficit	1.11	1.05–1.17	<0.001
Impulse control	1.19	0.90–1.57	0.23
Mood	1.27	1.24–1.30	<0.001
Personality	1.02	0.86–1.22	0.81
Schizophrenia	1.05	0.92–1.18	0.47
Alcohol	1.22	1.13–1.30	<0.001
Substance	1.40	1.30–1.52	<0.001
Suicide and self-harm	0.98	0.83–1.14	0.76
Miscellaneous	1.13	1.08–1.19	<0.001
Pain diagnosis			

Table 2 (*continued*)

Characteristic	Adjusted Odds Ratio	95% Confidence Interval	*P* Value
Back	1.18	1.16–1.20	<0.001
Neck	1.07	1.05–1.10	<0.001
Arthritis	1.20	1.18–1.22	<0.001
Other	1.20	1.18–1.22	<0.001
Opioid prescription characteristics			
Total MME in perioperative period ≥75th percentile (i.e., ≥375 MMEs or 50 pills of oxycodone 5 mg)	1.05	1.03–1.07	<0.001
Days' supply in perioperative period	1.05	1.05–1.05	<0.001
More than one prescription	1.40	1.37–1.43	<0.001
Prescription before procedure	1.02	1.00–1.04	0.01

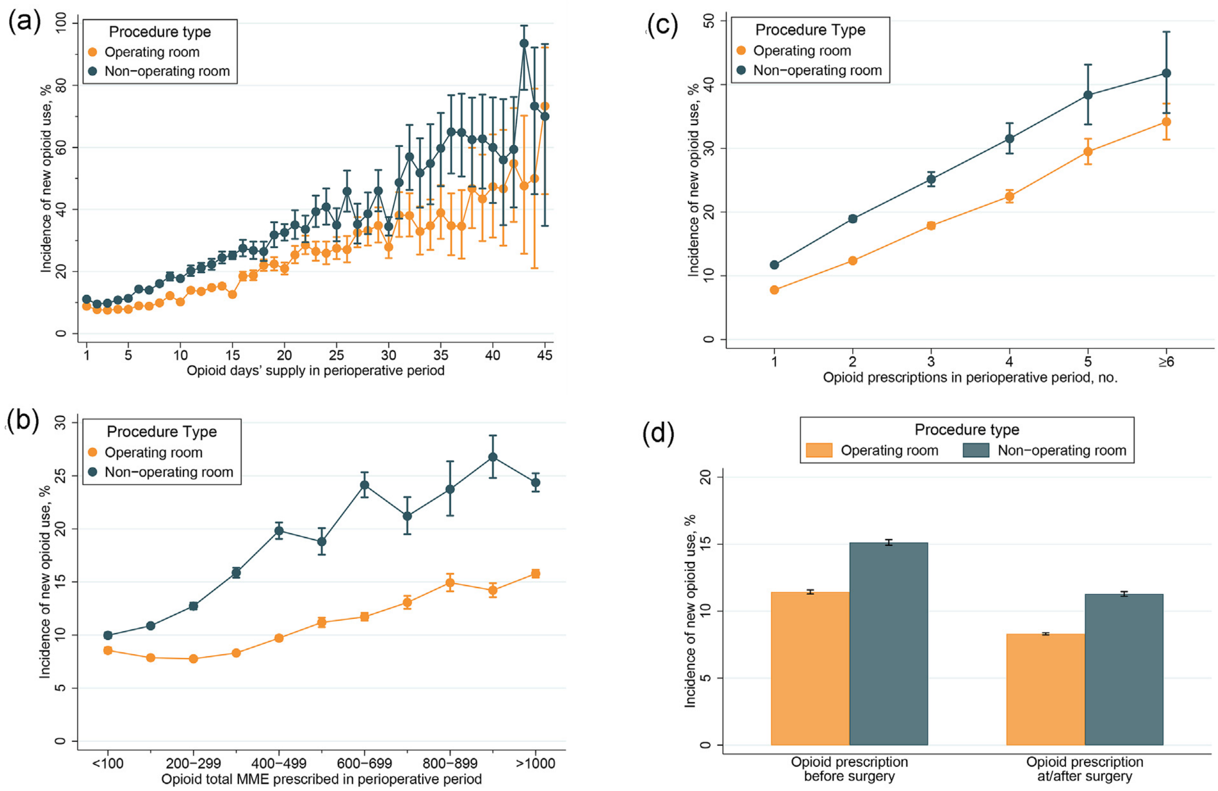

Fig. 3. A Incidence of new opioid use by opioid days' supply in perioperative period.
The dot shows the incidence of new opioid use, with whiskers showing 95% confidence intervals at each day for operating room (OR) and non-OR types of surgical procedures. The trajectory line connects the incidence at each day. Days' supply of opioids calculated as days the patient was covered with an opioid medication in the perioperative period, which ranged from 30 days before to 14 days after the surgical procedure. New opioid use was defined as filling one or more prescriptions between 3 months and 6 months after procedure. Operating room (OR) procedures included those specified as "major" or occurring in the operating room. Non-operating room procedures included those specified as "minor," "other," or not occurring in the operating room.
B. Incidence of new opioid use by number of opioid prescriptions in perioperative period.
The dot shows the incidence of new opioid use, with whiskers showing 95% confidence intervals at each day for operating room (OR) and non-OR types of surgical procedures. The trajectory line connects the incidence at each additional prescription. The number of opioid prescriptions was counted within the perioperative period, which ranged from 30 days before to 14 days after the surgical procedure. New opioid use was defined as filling one or more prescriptions between 3 months and 6 months after procedure. Operating room (OR) procedures included those specified as "major" or occurring in the operating room. Non-operating room procedures included those specified as "minor," "other," or not occurring in the operating room.
C. Incidence of new opioid use by total opioid (MME) prescribed in perioperative period
The dot shows the incidence of new opioid use, with whiskers showing 95% confidence intervals at each day for operating room (OR) and non-OR types of surgical procedures. The trajectory line connects the incidence at each level of total opioids prescribed. The total amount of opioid prescribed was calculated in morphine milligram equivalents (MME) within the perioperative period, which ranged from 30 days before to 14 days after the surgical procedure, in 100 MME increments (13.3 pills of oxycodone 5 mg). New opioid use was defined as filling one or more prescriptions between 3 months and 6 months after procedure. Operating room (OR) procedures included those specified as "major" or occurring in the operating room. Non-operating room procedures included those specified as "minor," "other," or not occurring in the operating room.
D. Incidence of new opioid use by timing of opioid prescription in perioperative period.
The bar shows the incidence of new opioid use, with whiskers showing 95% confidence intervals for operating room (OR) and non-OR types of surgical procedures. The perioperative period ranged from 30 days before to 14 days after the surgical procedure. New opioid use was defined as filling one or more prescriptions between 3 months and 6 months after procedure. Operating room (OR) procedures included those specified as "major" or occurring in the operating room. Non-operating room procedures included those specified as "minor," "other," or not occurring in the operating room.

changes in opioid prescribing after surgical procedures. Second, claims data fails to capture more nuanced measures of actual opioid use, as well as clinical outcomes relevant to the analysis such as pain. For example, the possibility exists for patients to fill prescriptions and not use some or all pills, which may be common after surgery.[4] Because of this, the reliance on use of total opioid prescribed represents a coarse estimate of opioid use and may introduce some imprecision regarding the relationship of opioid exposure to outcomes of interest. In the event an individual fails to use all opioids prescribed, leftover pills may pose a safety risk and raise the possibility of misuse or diversion given that many people who misuse opioids do so with drugs obtained through a legitimate prescription, including surgical prescribing.[3,28] Third, claims data may not fully capture substance use or mental health disorders, given variation in the accuracy of these diagnoses. While claims may be criticized for bias towards those seeking treatment, administrative data generally predict these types of diagnoses.[29] Also, classification of surgical subspecialties from claims data may lead to categories with possible overlap, such as thoracic, cardiovascular, and cardiothoracic surgery. Fourth, the generalizability of the findings to Medicaid and Medicare populations is limited because MarketScan data represent only individuals with private health insurance.

Conclusion

In this cohort of patients without opioid use in the year before their procedure, the rate of new opioid use persisting between 3 and 6 months after a procedure was higher among procedures performed in non-operating room compared to operating room settings. New opioid continuation ranged from 6.6% to 13.6% by surgical subspecialty. Persistent use of opioids after procedures also differed based on surgical subspecialty, suggesting that prolonged opioid use may be due to factors associated with particular surgical specialties.

Conflicts of interest

Dr. Alexander serves as Chair of the US Food and Drug Administration's Peripheral and Central Nervous System Advisory Committee; is a paid advisor to IQVIA; holds equity in Monument Analytics, a consultancy that provides services to the life sciences industry and to plaintiffs in opioid litigation; and is a member of OptumRx's National P&T Committee. These arrangements have been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies.

Dr. Bicket serves on the advisory board of and holds stock options in Axial Healthcare. These arrangements have been reviewed and approved by Johns Hopkins University in accordance with its conflict of interest policies.

Drs. Murimi, Mr. Mansour, and Dr. Wu have no conflicts of interest to declare.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amjsurg.2019.04.010.

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