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New Persistent Opioid Use After Minor and Major Surgery in U.S. Adults

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Abstract

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Author Contributions

All authors meet the ICJME definition for authorship. CMB, JW, JG, ME, AB, SK, and BN all made substantial contributions to the conception and design of the work, as well as the interpretation of the data. SM and PL were involved in the acquisition and analysis of the data. All authors were involved in the drafting of the manuscript and approved the final version submitted. All authors to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Declaration of Interest:

Dr. Brummett reports a patent for Peripheral Perineural Dexmedetomidine licensed to University of Michigan and is a consultant with Tonix. Dr. Brummett receives research funding from Neuros Medical Inc. (Willoughby Hills, Ohio). Grants include: NIH; NIAMS RO1 AR060392; NIDA 1R01 DA038261–01A1; University of Michigan School Dean's Office- Michigan Genomics Initiative. Dr. Waljee receives research funding from the Agency for Healthcare Research and Quality (K08 1K08HS023313–01), the American College of Surgeons, and the American Foundation for Surgery of the Hand; serves as an unpaid consultant for 3M Health Information systems. Drs. Brummett, Waljee and Englesbe receive funding from the Michigan Department of Health and Human Services. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Michigan Department of Health and Human Services. There are otherwise no disclosures.

Transparency Declaration

Corresponding author Chad M. Brummett, MD affirms that the manuscript is an honest, accurate, and transparent account of the study being reported. No important aspects of the study have been omitted. Drs. Brummett and Moser had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Importance—Despite increased focus on reducing opioid prescribing for chronic pain, little is known regarding the incidence and risk factors for persistent opioid use after surgery.

Objective—To determine the incidence of new persistent opioid use after surgery after minor and major surgeries.

Design—Using a nationwide insurance claims dataset from 2013–2014, we identified U.S. adults age 18 to 64 years old without opioid use in the year prior to surgery (no opioid fills from 12 months to one month prior to surgery).

Participants—For patients filling a perioperative opioid prescription, we calculated the incidence of persistent opioid use >90 days among opioid naïve patients after both minor surgery (varicose vein removal, laparoscopic appendectomy, hemorrhoidectomy, laparoscopic cholecystectomy, transurethral prostate surgeries, thyroidectomy, parathyroidectomy, and carpal tunnel) and major surgery (bariatric surgery, colectomy, incisional hernia repair, reflux surgery, and hysterectomy). We then assessed for patient-level predictors of persistent opioid use.

Main Outcome and Measures—The primary outcome was defined *a priori* prior to data extraction. The primary outcome was new persistent opioid use, which was defined as an opioid fill between 90–180 days.

Results—36,177 patients met the inclusion criteria (minor surgery=29,068; major surgery=7,109 patients). The rates of new persistent opioid use were similar between the two groups of minor and major surgery, ranging from 5.9–6.5%. By comparison, the incidence in the non-operative control cohort was only 0.4%. Risk factors independently associated with new persistent opioid use included preoperative tobacco use (adjusted odds ratio [aOR] 1.35 [95% confidence interval 1.21–1.49]), alcohol and substance abuse disorders (aOR 1.34 [1.05–1.72]), mood disorders (aOR 1.15 [1.01–1.30]), anxiety (aOR 1.25 [1.10–1.42]), and preoperative pain disorders (back pain 1.57 [1.42–1.75]), neck pain 1.22 [1.07–1.39], arthritis 1.56 [1.40–1.73], centralized pain 1.39 [1.26–1.54]).

Conclusion and Relevance—New persistent opioid use after surgery is common and not significantly different between minor and major surgeries but related to behavioral and pain disorders. This suggests its use is not due to surgical pain but addressable patient-level predictors. New persistent opioid use represents a common, but previously underappreciated, surgical complication that warrants increased awareness.

Introduction

Millions of Americans undergo surgery each year, with expenditures exceeding $500 billion and accounting for approximately 40% of national healthcare spending.[1–6] Although recent Centers for Disease Control (CDC) guidelines address opioid prescribing with respect to chronic pain, little attention is directed toward perioperative outpatient opioid prescribing.[7–9] Currently, postoperative opioid prescribing varies widely and frequently in excess,[10–12] even following minor surgery. More broadly, nearly 530 individuals die each week in the United States due to opioid overdose, demanding comprehensive solutions for this public health crisis.[13–16]

Many patients receive their first exposure to opioids following surgery, but the incidence of new persistent opioid use after surgical care is not well defined. Specifically, the impact of surgical case mix and other preoperative risk factors remain unclear. In a population-based study of insured individuals in the United States, we examined the incidence of new persistent opioid use and associated risk factors across both minor and major surgery. We hypothesized that the incidence of new persistent opioid use would be common and similar between the groups undergoing minor and major surgery, thereby suggesting that persistent opioid use may be less associated with post-surgical pain than addressable patient-level factors.

Methods

Data Sources and Patient Cohort

The Clinformatics™ Data Mart captures administrative health claims across the United States for members of a large national managed care company affiliated with OptumInsight (Eden Prairie, MN). We examined claims from January 1, 2012 to June 30, 2015 among adults ages 18 to 64 to capture surgical procedures performed between 2013 and 2014 to account for the 12-month preoperative and 6-month postoperative study period. We included only individuals with continuous medical and prescription drug coverage to evaluate the complete health care experience. We excluded patients ages 18 and younger, as well as patients older than 64 years due to incomplete capture of Medicare Part D prescriptions claims data. The study was deemed exempt from review by the University of Michigan Institutional Review Board.

We selected 13 common elective surgical procedures, and categorized these into minor and major groups based on prior literature. Minor surgical procedures included varicose vein removal, laparoscopic cholecystectomy, laparoscopic appendectomy, hemorrhoidectomy, thyroidectomy, transurethral prostate surgeries, and parathyroidectomy. Major surgical procedures included ventral incisional hernia repair, colectomy, reflux surgery, bariatric surgery, and hysterectomy. We identified patients undergoing surgery using Current Procedural Terminology (CPT) or International Statistical Classification of Diseases and Related Health Problems (ICD9_ procedure codes (Supplemental Table 1).

We sought to determine new persistent opioid use after surgery, and included only patients who filled an opioid prescription fill either in the month prior to surgery or within two weeks after discharge. Comparable to previous studies of opioid naïve surgical populations,[7,8] patients who had filled one or more prescriptions for opioids 12 months to 31 days prior to their surgical procedure were excluded from the analysis (Figure 1). To account for prescriptions provided preoperatively for postoperative pain control, patients filling opioids in the 30 days prior to surgery were included, and prescriptions filled in this time was included as a covariate in the analyses. Lastly, we excluded patients who underwent additional surgical procedures during the study period using subsequent procedural codes for anesthesia in the 6-month postoperative period.

As a comparison cohort of patients who did not undergo surgery, we identified a random 10% sample patients ages 18 to 64 years of age who did not undergo surgery in the study

period We included only patients in the nonoperative group who did not fill an opioid prescription during a 12 month period and did not have any codes for surgical procedures or anesthesia during this period. These patients were then given a random date of surgery. No patients had an opioid fill in the year prior to their fictitious surgery date nor did they have any anesthesia codes in the 6 months following their fictitious surgery date.

Outcomes

Our primary outcome was new persistent opioid use, defined as an opioid fill between 90–180 days among those patients who filled opioid prescriptions perioperatively (Figure 1), and was defined *a priori* prior to data extraction.[8] This definition of new persistent opioid use represents a time in which normal surgical recovery would be expected for the surgeries selected and is more conservative than the three-month definition of chronic post-surgical pain by the International Association for the Study of Pain.[ϕ] The total amount of opioid prescribed during the surgical window of 30 days prior to surgery to 14 days post-discharge, including the dose of the medication and amount dispensed, were converted to oral morphine equivalents (OMEs).[ϒ]

Patient factors

We included sociodemographic and clinical covariates, including region of residence, and comorbid conditions using both a Charlson Comorbidity Index score and an indicator of current or previous tobacco use (ICD9 305.1; V15.82). In addition, the Clinical Classification System (CCS) from the Agency of Healthcare Research and Quality (AHRQ) were used to create indicators for mental health diagnoses. The subcategories of the mental health diagnoses CCS were collapsed as mood disorders (adjustment, anxiety, and mood disorders), suicidality (suicide and intentional self-inflicted injury), disruptive behavior disorders (attention deficit, conduct, and disruptive behavior disorders; impulse control disorders), personality disorders, schizophrenia and other psychotic disorders, substance use disorders (alcohol and other substance-related disorders), and miscellaneous disorders (Supplemental Table 2). In addition, preoperative pain diagnoses were obtained using ICD9 codes and categorized as back pain, neck pain, arthritis pain, and other pain disorders. The inclusion for preoperative medical comorbidities, pain diagnoses and mental health classifications were restricted to the one-year preoperative study period.

Statistical analysis

All analyses were conducted using Stata version 13.1. Descriptive statistics were calculated for demographic variables and comorbidities for each surgical type. Univariate differences between surgical types were assessed with t-tests or chi-square tests. Further, univariate differences between those with persistent opioid use and those without persistent opioid use within each surgical type were assessed with t-tests and chi-square tests. A multi-level, multivariate logistic regression model with Census geographic region included as a random

[ϕ]International Association for the Study of Pain; New Criteria on Postsurgical and Posttraumatic pain, last accessed January 19, 2017; http://www.iasppain.org/PublicationsNews/NewsDetail.aspx?ItemNumber=5134&navItemNumber=643

[ϒ]CDC opioid conversion table; https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf; last accessed January 24, 2017

intercept was estimated to examine differences in persistent opioid use between surgical types controlling for patient characteristics, including age, sex, race, education, history of tobacco use, mental health disorders, Charlson comorbidity index, pain disorders, and opioid prescription OME within surgical time frame.

Results

A total of 55,359 of the patients met the inclusion criteria of at least 11 months without an opioid prescription prior to the 30 days preceding a qualifying surgical procedure (Figure 2). After exclusion of patients receiving an additional anesthetic during the 180-day postoperative study period, inpatient stays >30 days, and no opioid prescriptions during the perioperative period, the final study cohort consisted of 36,177 patients. There were 29,068 patients in the minor surgery category and 7,109 patients in the major surgery category.

Descriptive data are displayed in Table 1. There were no differences between the groups with respect to opioid prescriptions in the 30 days prior to surgery. The median total dose of all opioid prescriptions during the 30 days prior to surgery to 14 days post-discharge was 225 mg oral morphine equivalents (OME) for both groups, which equates to 45 tablets of 5 mg hydrocodone or 30 tablets of 5 mg oxycodone.

Persistent Postoperative Opioid Use Similar Between Major and Minor Surgery Groups

The incidence of new persistent opioid use was similar between the two groups (Figure 1). In the minor surgery 5.9% filled an opioid prescription between 90–180 days versus 6.5% in the major surgery group (OR 1.12, 95% CI 1.01–1.24). By comparison, only 0.4% of the non-surgical comparison group had a fill between 0–90 days of fictitious surgery date and 90–180 days of fictitious surgery date. We did observe a small degree of variation with respect to the incidence of new persistent opioid use across procedures, ranging from 4.5% – 9.9%. After adjustment for all of the preoperative covariates assessed, the small difference between the groups was no longer statistically significant (Table 2; OR 1.04, 95% CI 0.93–1.18, $p = 0.478$). The average number of prescriptions was 1.4 (SD 0.9) with an average of 53 pills (SD 105.3). Of those filling an opioid prescription between 90–180 days after surgery, the average number of opioid prescriptions in the study period was 3.3 (SD 2.0) and an average of 125 pills (SD 200.4).

Risk Factors for New Persistent Opioid Use

In this cohort tobacco use, alcohol and substance abuse disorders, and comorbid conditions increased the risk of new persistent opioid use among opioid naïve patients regardless of surgical procedure (Table 2). In addition, anxiety, depression and other preoperative pain disorders (back pain, neck pain, arthritis, and centralized pain conditions) were independently associated with continued postoperative opioid use. Patients receiving an opioid prescription in the 30 days prior to surgery had almost two times higher odds of persistent opioid use after surgery, even after adjustment for other covariates. While there was a significant association between those patients receiving the most opioid in the perioperative period (300 mg OME or higher) and new persistent use, the effect size was fairly small (adjusted OR 1.14).

In the mixed effects model of the U.S. census regions (Table 2), the West South Central (incidence = 7.02%) and East South Central (incidence = 7.85%) regions were independently associated with higher rates of new persistent opioid use, while the Mid Atlantic region (incidence = 3.78%) was independently associated with a lower incidence of new persistent opioid use.

Discussion

In this study of a large cohort of privately insured patients in the United States, 6% of patients undergoing both minor and major surgery continued to use opioids after 90 days after surgery. Rates of prolonged use were similar between minor and major surgery, and patients with a greater number of comorbidities, including pain conditions, substance abuse, and mental health disorders, were particularly vulnerable to prolonged opioid use (Table 2). Given the declining rates of morbidity and mortality following common, elective surgical procedures, new persistent opioid use represents an important, common, and under-recognized complication of perioperative care.[2,4–6]

Roughly 50 million surgical procedures a year are performed in the United States. As such, our findings suggest that more than 2 million individuals may transition to persistent opioid use following elective surgery each year.[16] These results are aligned with reports published by Clark et al. and Alam et al. describing prolonged postoperative opioid use among a population-based sample of Canadians age 65 years and older.[7,8] Clarke et al.[8] examined opioid use among all patients who filled an opioid prescription within 90 days after surgery, and Alam et al.[7] did not require an opioid prescription after surgery for inclusion. In contrast, we specifically included patients who only filled prescriptions during the immediate perioperative procedure, and excluded patients who received additional anesthesia (and presumably additional procedures) after the index procedure. Our cohort represents the direct transition from postoperative use to persistent use more than three months after surgery among patients who are opioid-naïve. Our results are also comparable to the 5% incidence of new long-term opioids use after the first opioid exposure using data from the Oregon prescription drug monitoring program, which includes non-operative opioid prescriptions.[17]

More recently, Sun et al.[18] described a lower incidence (0.119%−1.41%) following a variety of surgical conditions using a definition of more than 10 opioid fills or more than 120 days supplied between three and 12 months after surgery. While this definition identifies those patients filling large amounts of opioids, it may underestimate the incidence of new persistent opioid use, and captures only the far extreme of opioid consumption. Surgical recovery would be expected well before the 90–180 day outcome time period used in the study, and any opioid use in this time period is considered chronic and inappropriate in a previously opioid-free cohort.

Persistent Use May Not Be Related to Surgical Pain

Our findings also highlight that prolonged opioid use following surgery may not simply be a consequence of poorly controlled pain. The pain experienced after major surgeries would be expected to be greater than for minor surgeries, and we hypothesized that the incidence of

persistent opioid use would be higher among patients undergoing major surgery. However, we observed that new persistent opioid use did not differ between major and minor surgery. Aligned with our previous work, patients likely continue opioids for reasons other than intensity of surgical pain. For example, approximately 4% of total hip and 8% of knee arthroplasty patients who were not taking opioids before surgery continued to use opioids six months after surgery.[9] More interestingly, the change in the surgical knee or hip pain intensity from prior to surgery to 6-months after surgery was unrelated to new persistent opioid use.

Chronic post-surgical pain has received considerable attention in recent years,[19] but the reasons for which patients continue to use opioids after surgery are complex and not simply due to surgical pain. Unfortunately, opioids have been termed “painkillers” despite the fact that their long-term benefit with respect to pain relief has not been demonstrated.[9,20–23] Moreover, because opioids are prescribed medications, patients may overestimate their safety and use opioids intended for post-surgical pain for other symptoms, such as back and neck pain, headaches, osteoarthritis, and insomnia, for which opioids are not effective.[20–22] Previous studies have also demonstrated that psychiatric conditions, such as depression, are associated with chronic opioid use, and patients may continue to use their postoperative opioids to treat emotional pain and affective distress.[24–29] Regional variation was also found with higher rates of new persistent opioid use in the East and West South Central U.S.

CDC Guidelines Fail to Address Postoperative Prescribing

Despite the sharp focus on the opioid epidemic following the release of the CDC Guidelines for Prescribing Opioids for Chronic Pain,[15,23,30,31] there has been little attention placed on postoperative prescribing. The omission of postoperative prescribing guidelines was appropriate in many ways, as the data presented in the present study are among the first to quantify the very serious scope of the problem and little is known regarding the variation in opioid consumption following surgery. Even with these data, however, the reasons for which patients continue to use their opioids remain unclear. Moreover, this study does not address the millions of patients each year who have excess opioids that often remain stored in an unsecure manner, thereby leading to potential diversion and abuse.[32] While the CDC guidelines and an increased attention on long-term, outpatient management of opioids has and will continue to decrease opioid prescribing,[33] the impact of postoperative use on the opioid overdose epidemic has been less recognized. There are currently no normative data for postoperative opioid prescribing to guide practice, and as such, it has become an issue of convenience and little attention potential morbidity to follow.

Clinical Implications

Although opioids remain an integral part of acute postoperative pain management, the data do not support long-term efficacy. In fact, many experts believe that the risks of opioids far outweigh the potential benefits.[20,22,23] As such, new persistent opioid use after surgery represents a poor long-term outcome and could be termed an adverse event. Given that our cohort is largely comprised of individuals covered by employer-based plans and their dependents, our findings further underscore the importance of prolonged postoperative

opioid use among young individuals during their prime years with respect to career and family demands.

Although we noted some surgeries appeared to have greater issues with persistent opioid use (e.g., colectomy), we believe that new persistent opioid use is inappropriate in most cases. We acknowledge that the interventions may need to be tailored to the condition in some cases, but there are certainly some aspects of patient and provider interventions that are more generalizable.

Limitations

Despite the many strengths of this study, there are some limitations. First, we did not capture actual opioid consumption; however, the repeated opioid prescription fills (with an average of 3.3 fills between 90–180 days) suggest that patients were continuing to use opioids. Despite the fact that the cohort had not filled an opioid prescription in the year prior to their surgeries, it is possible that the postoperative opioid prescriptions were related to another procedure or diagnosis. To mitigate this risk, we eliminated all patients with claims related to additional anesthesia during the postoperative period. As was noted above, the use of claims data does not allow for a granular assessment of other painful conditions and mood disorders (e.g., degree of impairment or symptoms) that may be driving persistent use. Prospective data are needed to better understand the patient-level factors associated with new persistent postoperative opioid use. In addition, our categorization of major versus minor surgical conditions may be subject to critique, but the categories were created *a priori* and with guidance from previous studies on this topic. Reclassifying some of the surgeries (e.g. moving all laparoscopic surgeris to the “minor” surgery category) did not significantly change the results (data not shown). Finally, our cohort was drawn from a large, population-based cohort of insured adults and their dependents, and our findings may not be generalizable to the un-insured, under-insured, and individuals ages 65 and older.

Conclusions

In a cohort of previously opioid naïve patients, approximately 6% continue to use opioids more than three months after their surgery, and as such, prolonged opioid use can be deemed the most common post-surgical complication. New persistent opioid use is not different between minor and major surgery, thereby suggesting that prolonged opioid use is not entirely due to surgical pain.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgements

Declaration of Interest and Acknowledgement of Funding

Dr. Brummett reports a patent for Peripheral Perineural Dexmedetomidine licensed to University of Michigan and is a consultant with Tonix. Dr. Brummett receives research funding from Neuros Medical Inc. (Willoughby Hills, Ohio). Grants include: NIH; NIAMS RO1 AR060392; NIDA 1R01 DA038261–01A1; University of Michigan School Dean’s Office-Michigan Genomics Initiative. Dr. Waljee receives research funding from the Agency for Healthcare Research and Quality (K08 1K08HS023313–01), the American College of Surgeons, and the American

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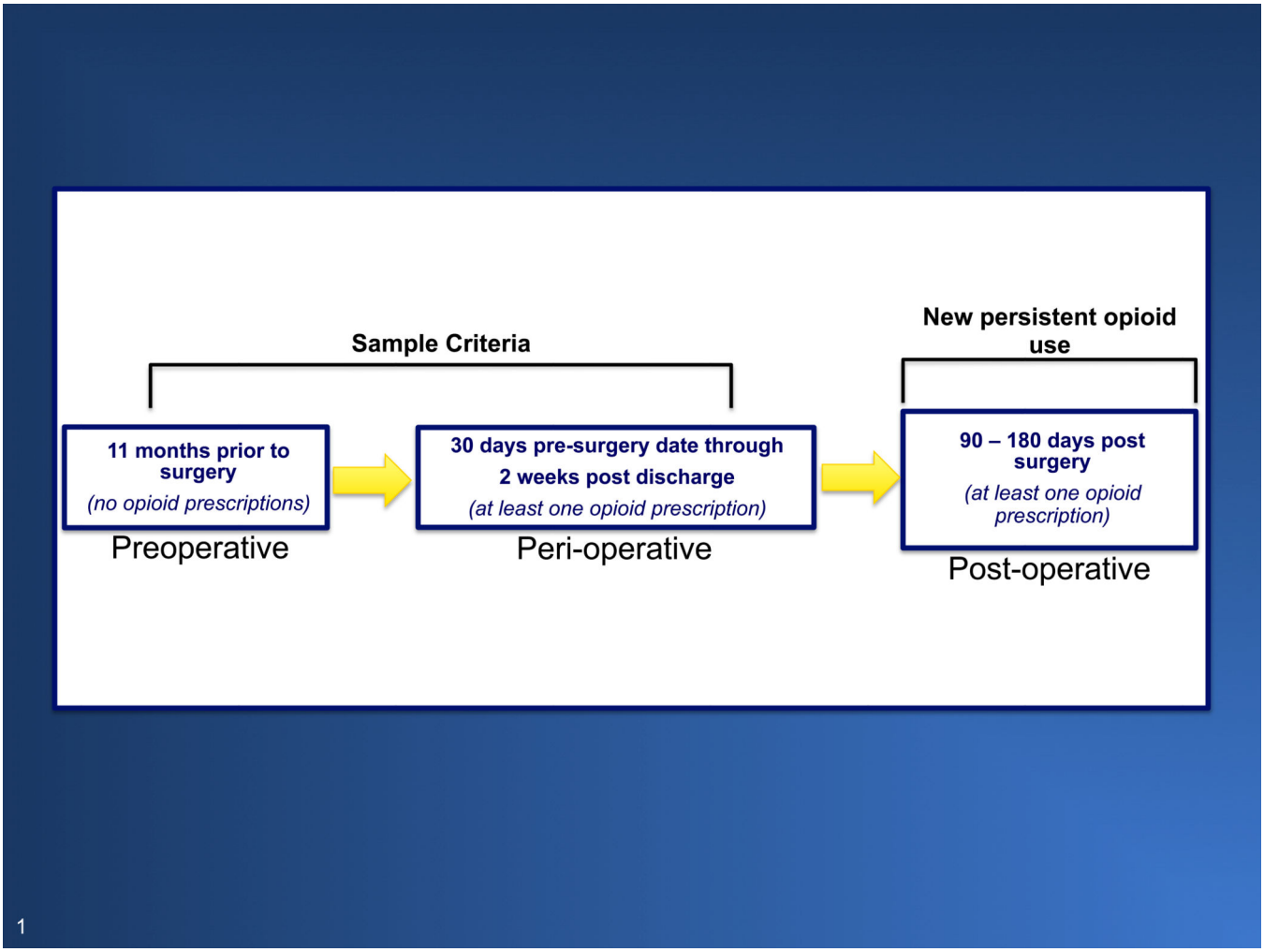

Figure 1: Sample criteria and outcomes.

Patients undergoing the predefined surgeries were included if they met the following criteria: 1) continuous insurance coverage during the 12 months prior to surgery through the 6 months after surgery; 2) no opioid prescriptions during the 11 months prior to surgery; 3) at least on opioid prescription fill during the perioperative period, which was defined as the 30 days prior to surgery to 2 weeks after discharge. The outcome of new persistent opioid use was defined as at least one opioid prescription fill between 90–180 days after surgery.

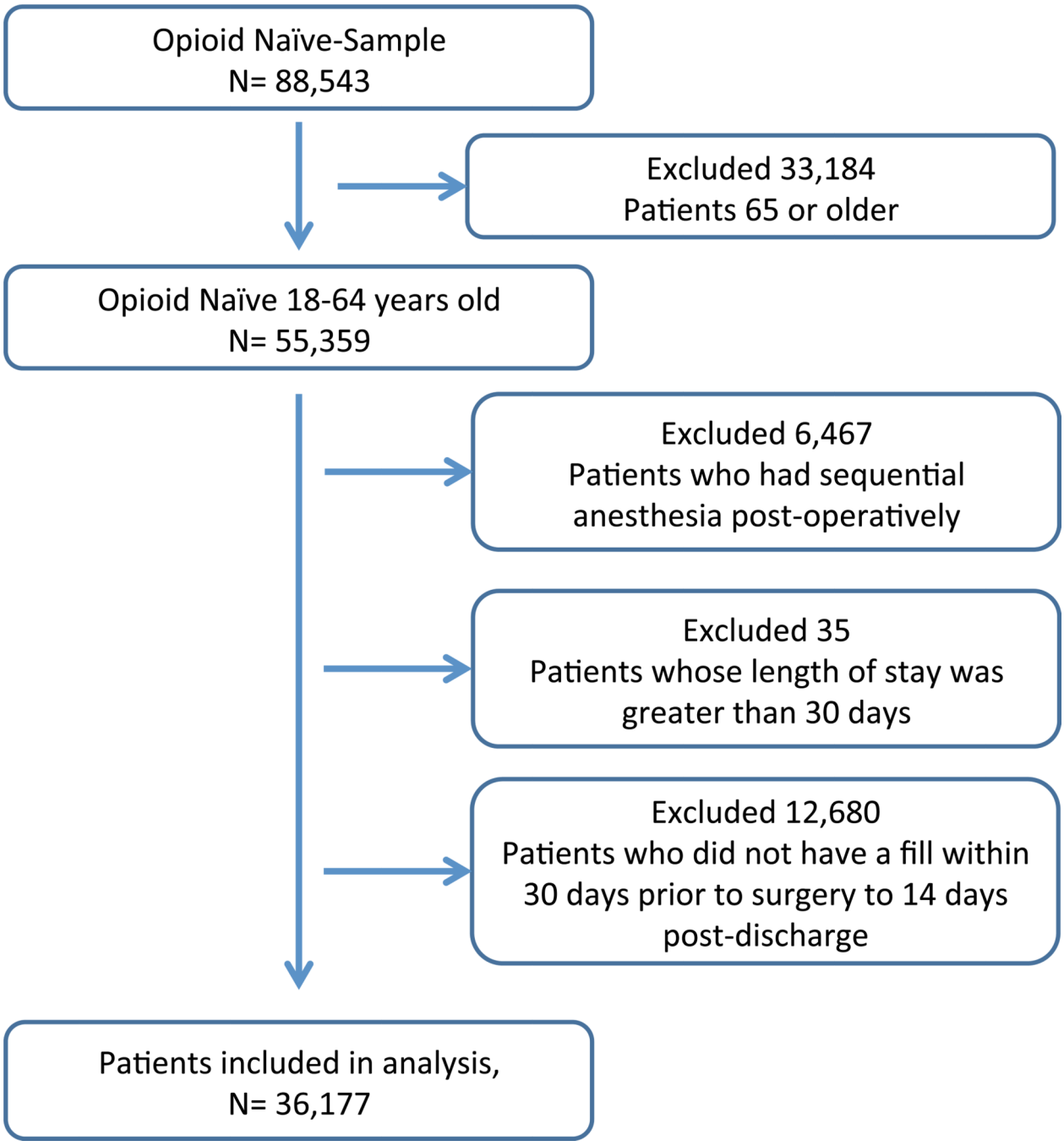

Figure 2:
Flow diagram.

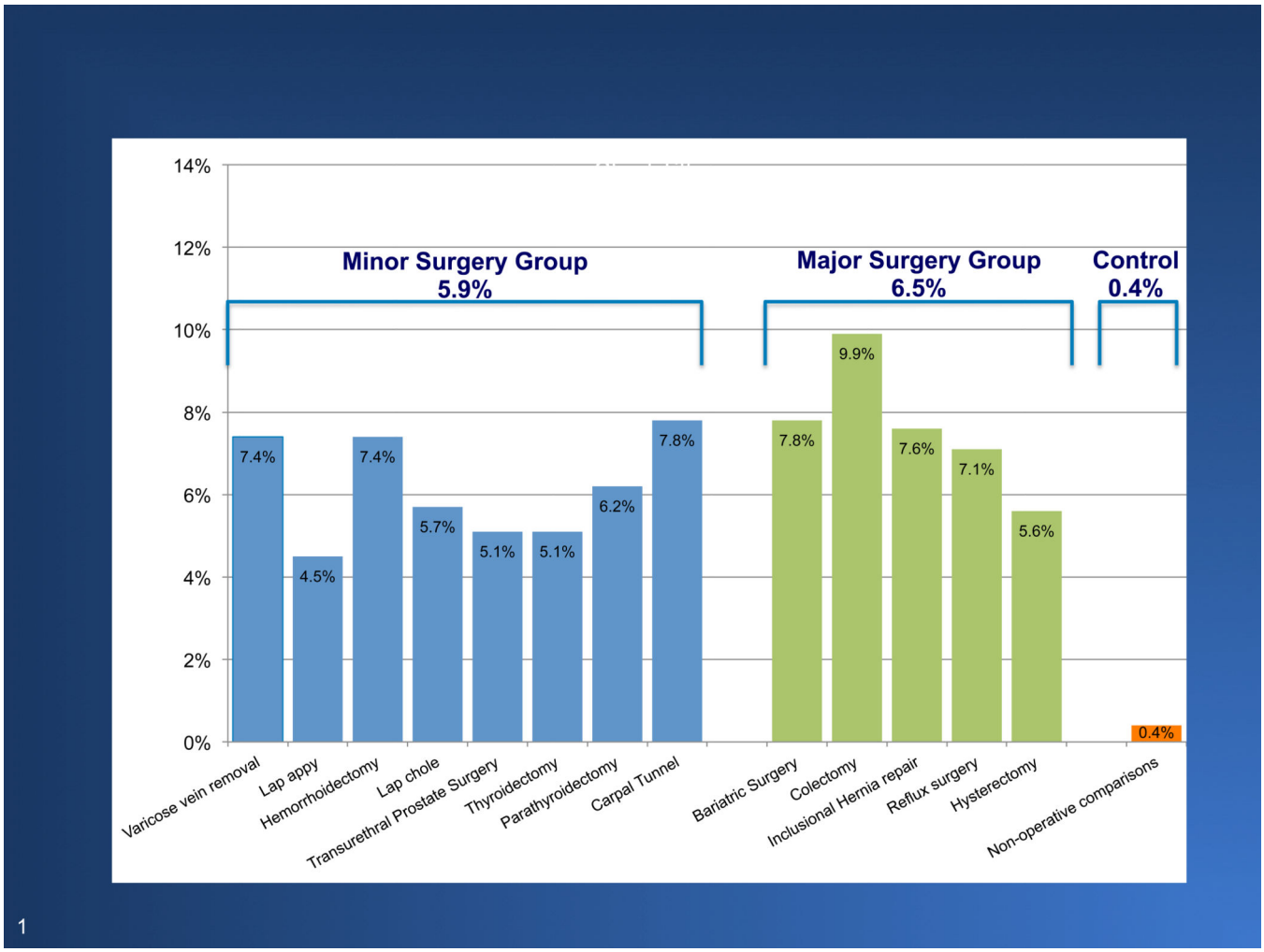

Figure 3: Incidence of new persistent opioid use by surgical condition.

The incidence of new persistent opioid use was similar between the two groups (minor surgery= 5.9% vs. major surgery = 6.5%; OR 1.12, SE 0.06, 95% CI 1.01–1.24). By comparison, the incidence in the nonoperative control group was only 0.4%.

Table 1.

Preoperative patient characteristics and univariate outcomes analyses.

	Overall Group	Minor Surgery Cohort	Persistent opioid use	No persistent opioid use	p-value	Major Surgery Cohort	Persistent opioid use	No persistent opioid use	p-value	(Minor vs. Major p-value)
Demographics										
Age										
18–29	4663 (12.89%)	4436 (15.26%)	258 (5.82%)	4178 (94.18%)		227 (3.19%)	17 (7.49%)	210 (92.51%)		
30–39	7090 (19.6%)	5938 (20.43%)	276 (4.65%)	5662 (95.35%)		1152 (16.20%)	88 (7.64%)	1064 (92.36%)		
40–49	10364 (28.65%)	7389 (25.42%)	392 (5.31%)	6997 (94.69%)	<0.001	2975 (41.85%)	159 (5.34%)	2816 (94.66%)	0.015	<0.001
50–59	10207 (28.21%)	8099 (27.86)	548 (6.77%)	7551 (93.23%)		2108 (29.65%)	151 (7.16%)	1957 (92.84%)		
60–64	3853 (10.65%)	3206 (11.03%)	237 (7.39%)	2969 (92.61%)		647 (9.10%)	50 (7.73%)	597 (92.27%)		
Gender (% female)	23913 (66.10%)	17860 (61.44%)	1101 (64.35%)	16759 (61.26%)	0.011	6053 (85.15%)	385 (82.80%)	5668 (85.31%)	0.141	<0.001
Race										
Caucasian	26091 (72.12%)	21,388 (73.58%)	1268 (74.11%)	20120 (73.55%)		4703 (66.16%)	300 (64.52%)	4403 (66.27%)		
African-American	3268 (9.03%)	2161 (7.43%)	151 (8.83%)	2010 (7.35%)	<0.001	1107 (15.57%)	73 (15.70%)	1034 (15.56%)	0.177	<0.001
Hispanic	4283 (11.84%)	3467 (11.93%)	183 (10.70%)	3284 (12.00%)		816 (11.48%)	57 (12.26%)	759 (11.42%)		
Asian	1076 (2.97%)	865 (2.98%	27 (1.58%)	838 (3.06%)		211 (2.97%)	9 (1.94%)	202 (3.04%)		
Missing/Unknown	1459 (4.03%)	1187 (4.08%)	82 (4.49%)	1105 (4.04%)		272 (3.83%)	26 (5.59%)	246 (3.70%)		
Education										
< 12th Grade	184 (0.51%)	149 (0.51%)	8 (0.47%)	141 (0.52%)		35 (0.49%)	3 (0.65%)	32 (0.48%)		
High School	9781 (27.04%)	7763 (26.71%)	504 (29.46%)	7259 (26.53%)		2018 (28.39%)	147 (31.61%)	1871 (28.16%)		
Some College	19781 (54.68%)	15827 (54.45%)	959 (56.05%)	14868 (54.35%)	<0.001	3954 (55.62%)	254 (54.62%)	3700 (55.69%)	0.171	<0.001
College Degree +	6129 (16.94%)	5097 (17.53%)	223 (13.03%)	4874 (17.82%)		1032 (14.52%)	54 (11.61%)	987 (14.72%)		
Missing/Unknown	302 (0.83%)	232 (0.80)	17 (0.99%)	215 (0.79%)		70 (0.98%)	7 (1.51%)	63 (0.95%)		
Region										
East North Central	6293 (17.40%)	5245 (18.04%)	320 (18.70%)	4925 (18.00%)		1048 (14.74%)	61 (13.12%)	987 (14.86%)		
East South Central	1452 (4.01%)	1206 (4.15%)	94 (5.49%)	1112 (4.06%)		246 (3.46%)	20 (4.30%)	226 (3.40%)		
Middle Atlantic	2196 (6.07%)	1641 (5.65%)	62 (3.62%)	1579 (5.77%)	<0.001	555 (7.81%)	21 (4.52%)	534 (8.04%)	0.053	<0.001

	Overall Group	Minor Surgery Cohort	Persistent opioid use	No persistent opioid use	p-value	Major Surgery Cohort	Persistent opioid use	No persistent opioid use	p-value	(Minor vs. Major p-value)
Mountain	3767 (10.41%)	3101 (10.67%)	175 (10.23%)	2926 (10.70%)		666 (9.37%)	38 (8.17%)	628 (9.45%)		
New England	992 (2.74%)	780 (2.68)	42 (2.45%)	738 (2.70%)		212 (2.98%)	9 (1.94%)	203 (3.06%)		
Pacific	2252 (6.22%)	1721 (5.92%)	67 (3.92%)	1654 (6.05%)		531 (7.47%)	32 (6.88%)	499 (7.51%)		
South Atlantic	8279 (22.88%)	6583 (22.65%)	389 (22.74%)	6194 (22.64%)		1696 (23.86%)	128 (27.53%)	1568 (23.60%)		
West North Central	4724 (13.06%)	3878 (13.34%)	220 (12.86%)	3658 (13.37%)		846 (11.90%)	60 (12.90%)	786 (11.83%)		
West South Central	6198 (17.13%)	4896 (16.84%)	340 (19.87%)	4556 (16.65%)		1302 (18.31%)	95 (20.43%)	1207 (18.17%)		
Missing/Unknown	24 (0.07%)	17 (0.06%)	2 (0.12%)	15 (0.05%)		7 (0.10%)	1 (0.22%)	6 (0.09%)		
Comorbidities										
Charlson Comorbidity Index	0.83 (1.5)	0.75 (1.38)	1.00 (1.58)	0.74 (1.36)	<0.001	1.14	1.96 (2.73)	1.08 (1.80)	<0.001	<0.001
History of tobacco use	8449 (23.35%)	6953 (23.92%)	549 (32.09%)	6404 (23.41%)	<0.001	1496 (21.04%)	128 (27.53%)	1368 (20.59%)	<0.001	<0.001
Mental Health Disorders										
Adjustment disorders	1626 (4.49%)	1061 (3.65%)	68 (3.97%)	993 (3.63%)	0.461	565 (7.95%)	39 (8.39%)	526 (7.92%)	0.717	<0.001
Anxiety disorders	5767 (15.94%)	4487 (15.44%)	376 (21.98%)	4111 (15.03%)	< 0.001	1280 (18.01%)	117 (25.16%)	1163 (17.50%)	< 0.001	<0.001
Mood disorders	5856 (16.19%)	4393 (15.11%)	362 (21.16%)	4031 (14.73%)	<0.001	1463 (20.58%)	130 (27.96%)	1333 (20.06%)	< 0.001	<0.001
Suicide or self-harm	123 (0.34%)	104 (0.36%)	9 (0.53%)	95 (0.35%)	0.230	19 (0.27%)	4 (0.86%)	15 (0.23%)	0.010	0.240
Disruptive disorders	993 (2.74%)	831 (2.86%)	62 (3.62%)	769 (2.81%)	0.050	162 (2.28%)	11 (2.37%)	151 (2.27%)	0.897	0.007
Personality disorders	82 (0.23%)	72 (0.25%)	8 (0.47%)	64 (0.23%)	0.059	10 (0.14%)	0 (0.00%)	10 (0.15%)	0.402	0.089
Psychosis disorders	195 (0.54%)	157 (0.54%)	21 (1.23%)	136 (0.50%)	<0.001	38 (0.53%)	5 (1.08%)	33 (0.50%)	0.098	0.954
Other disorders	1309 (3.62%)	749 (2.58%)	58 (3.39%)	691 (2.53%)	0.029	560 (7.88%)	36 (7.74%)	524 (7.89%)	0.911	<0.001
Alcohol or substance abuse disorders	887 (2.45%)	744 (2.56%)	75 (4.38%)	669 (2.45%)	<0.001	143 (2.01%)	19 (4.09%)	124 (1.87%)	0.001	0.007
Pain disorders										
Arthritis	16781 (46.39%)	13281 (45.69%)	1075 (62.83%)	12206 (44.62%)	<0.001	3500 (49.23%)	291 (62.58%)	3209 (48.30%)	<0.001	<0.001
Back	9047 (25.01%)	7283 (25.06%)	672 (39.28%)	6611 (24.17%)	<0.001	1764 (24.81%)	191 (41.08%)	1573 (23.68%)	<0.001	0.674
Neck	4660 (12.88%)	3841 (13.21%)	361 (21.10%)	3480 (12.72%)	<0.001	819 (11.52%)	95 (20.43%)	724 (10.90%)	<0.001	<0.001
Other Pain Conditions	14546 (40.21%)	10813 (37.20%)	874 (51.08%)	9939 (36.33%)	<0.001	3733 (52.51%)	277 (59.57%)	3456 (52.02%)	0.002	<0.001
Opioid prescription fills										

	Overall Group	Minor Surgery Cohort	Persistent opioid use	No persistent opioid use	p-value	Major Surgery Cohort	Persistent opioid use	No persistent opioid use	p-value	(Minor vs. Major p-value)
Opioid in 30 days prior to surgery	6539 (18.08%)	5222 (17.96%)	435 (25.42%)	4787 (17.50%)	<0.001	1317 (18.53%)	108 (23.23%)	1209 (18.20%)	0.007	0.271
Total opioid dose (OME) of prescriptions within surgical window	225 [150]	225 [150]	225 [187.5]	225 [150]	<0.001	225 [187.5]	300 [262.5]	225 [187.5]	<0.001	<0.001

Data are presented as mean (standard deviation), number (percentage) or median [interquartile range] as appropriate. Univariate analyses were performed within each of the surgical groups, as well as between groups, for the outcome of new persistent opioid use.

Table 2.

Multivariate logistic regression model of new persistent opioid use.

	Odds Ratio	SE	P-value	95% CI	
Minor (0) vs Major Surgery Cohort (1)	1.09	0.07	0.175	0.96	1.23
Age (18–29 is reference group)					
30–39	0.76	0.07	0.002	0.64	0.90
40–49	0.72	0.06	<0.001	0.61	0.84
50–59	0.88	0.07	0.127	0.75	1.04
60–64	0.90	0.09	0.302	0.74	1.10
Female	0.99	0.05	0.904	0.89	1.10
Race (Caucasian is reference group)					
African-American	1.13	0.09	0.120	0.97	1.33
Asian	0.73	0.13	0.083	0.51	1.04
Hispanic	0.98	0.08	0.828	0.84	1.15
Education (College graduate is reference group)					
Some college	1.19	0.09	0.018	1.03	1.38
High school	1.22	0.10	0.014	1.04	1.43
< 12th grade	1.08	0.39	0.839	0.53	2.18
History of tobacco use	1.35	0.07	<0.001	1.21	1.49
Charlson Comorbidity Index	1.10	0.01	<0.001	1.08	1.13
Adjustment disorders	0.86	0.10	0.179	0.68	1.07
Anxiety disorders	1.25	0.08	<0.001	1.10	1.42
Mood disorders	1.15	0.07	0.036	1.01	1.30
Disruptive disorders	1.03	0.14	0.982	0.78	1.34
Other psychiatric disorders	0.85	0.10	0.172	0.67	1.08
Alcohol or substance abuse disorders	1.34	0.17	0.021	1.05	1.72
Other Pain Disorders	1.39	0.07	<0.001	1.26	1.54
Back Pain	1.57	0.09	<0.001	1.42	1.75
Neck Pain	1.22	0.08	0.002	1.07	1.39
Arthritis Pain	1.56	0.08	<0.001	1.40	1.73
Opioid prescription in 30 days prior to surgery	1.93	0.12	<0.001	1.71	2.19
Total opioid dose (OME) of opioids during surgical window 300mg or greater (75% percentile or greater)	1.14	0.06	0.015	1.03	1.27
Random effects parameter	Estimate	SE	95%	CI	
Region- variance	0.03	0.02	0.007	0.10	

OME = oral morphine equivalency.