Research Article

Long-Term Trends in Postoperative Opioid Prescribing, 1994 to 2014

Abstract

Introduction: Opioids are routinely prescribed to manage acute postoperative pain, but changes in postoperative opioid prescribing associated with the marketing of long-acting opioids such as OxyContin have not been described in the surgical cohort.

Methods: Using a large commercial claims data set, we studied postoperative opioid prescribing after selected common surgical procedures between 1994 and 2014. For each procedure and year, we calculated the mean postoperative morphine milligram equivalents (MME) filled on the index prescription and assessed the proportion of patients who filled a high-dose prescription (≥350 MME). We reported changes in postoperative opioid prescribing over time and identified predictors of filling a high-dose postoperative opioid prescription.

Results: We identified 1,321,264 adult patients undergoing selected common surgical procedures between 1994 and 2014, of whom 80.3% filled a postoperative opioid prescription. One in five surgery patients filled a high-dose postoperative opioid prescription. Between 1994 and 2014, the mean MME filled increased by 145%, 84%, and 85% for lumbar laminectomy/laminotomy, total knee arthroplasty, and total hip arthroplasty, respectively. The procedures most likely to be associated with a high-dose opioid fill were all orthopaedic procedures (AOR 5.20 to 7.55, \( P < 0.001 \) for all). Patients whose postoperative opioid prescription included a long-acting formulation had the highest odds of filling a prescription that exceeded 350 MME (AOR 32.01, 95% CI, 30.23–33.90).

Discussion: After the US introduction of long-acting opioids such as OxyContin, postoperative opioid prescribing in commercially insured patients increased in parallel with broader US opioid-prescribing trends, most notably among patients undergoing orthopaedic surgical procedures. The increase in the mean annual MME filled starting in the late 1990s was driven in part by the higher proportion of long-acting opioid formulations on the index postoperative opioid prescription filled by orthopaedic surgery patients.
Prescriptions for opioids have increased 10-fold since 1990, and the United States has the highest rate of prescription opioid use per capita in the world, accounting for 80% of the world’s opioid consumption.1,2 Increased opioid prescriptions were accompanied by an increase in the incidence of opioid abuse, addiction, and overdose.3,4 Although prescribing volume peaked in 2010, opioid use continues to be a major public health concern in the United States.4,5 Physicians routinely prescribe opioids to patients to manage acute postoperative pain. There are an estimated 100 million operations done per year in the United States, with approximately 60% of those done in an ambulatory setting.6 Ninety-nine percent of patients who are hospitalized after undergoing a surgical procedure receive opioids,7 and 80% to 90% of patients undergoing outpatient surgery are sent home with an opioid prescription.8,9 Both the proportion of patients receiving an opioid prescription and the total amount prescribed after low-risk outpatient surgery have increased since 2004.8 However, little is known about longer term patterns of postoperative opioid prescribing. In particular, opioid-prescribing changes associated with the approval and aggressive marketing of long-acting opioids such as OxyContin starting in the mid-1990s and the implementation of the Joint Commission’s new hospital pain management standards in the early 2000s have not been described in the surgical cohort.10,11 The destigmatization of opioid use and the widespread recognition of pain as a “fifth vital sign” that followed are credited with increasing physician acceptance of opioid prescribing in the United States during that time.12

We hypothesized that the total amount of opioids prescribed after surgery increased over time in parallel to the broader contextual changes in opioid prescribing in the United States. Using claims and prescribing data from a cohort of commercially insured patients, we studied postoperative opioid-prescribing patterns after selected common surgical procedures from 1994 to 2014. For each procedure type and year, we calculated the mean oral morphine milligram equivalents (MME) filled after surgery. We reported changes in overall patterns of postoperative opioid prescribing during the 21-year study period and identified predictors of filling a high-dose postoperative opioid prescription.

Methods

Study Oversight and Data Source
We studied a cohort of commercially insured enrollees from the OptumLabs...
Data Warehouse, a longitudinal, real-world data asset with more than 200 million deidentified lives across claims and clinical information. The claims data set includes inpatient and outpatient claims as well as pharmacy claims dating from 1993 to the present. Because we used deidentified administrative data, this study did not require institutional review board approval or waiver.

Study Cohort
Using Current Procedural Terminology (CPT) and International Classification of Diseases, Ninth Revision (ICD-9) diagnosis and procedure codes, we identified patients aged 18 years and older who underwent selected common surgical procedures between 1994 and 2014 and had at least 365 days of continuous enrollment before and 30 days of continuous enrollment after the date of surgery. These procedures were selected because they are common and because procedure-specific CPT and ICD-9 codes were available throughout the 21-year study period. Table S1 in the Online Supplement, http://links.lww.com/JG9/A60, lists the CPT/ICD-9 codes used to define our cohort. Patients with claims for two related procedures on the same day (eg, laparoscopic versus open cholecystectomy) were categorized with the more invasive procedure (ie, open cholecystectomy). Patients who underwent unrelated procedures from our list on the same day were excluded. We also excluded anyone with a hospital length of stay (LOS) over 14 days to account for unanticipated complications that could alter a patient’s postoperative pain management needs. We extracted additional variables including pre-existing comorbidities, previous prescriptions, and surgery location for our analysis.

Predictor Variables
We tested the association between postoperative dose prescribed and patient, procedural, and geographic factors, as well as the year the surgery was done. Patient variables included patient demographics such as age, sex, and race; Deyo-Charlson Comorbidity Index; having pre-existing diagnoses associated with opioid use (chronic pain, anxiety, depression, psychosis, post-traumatic stress disorder, alcohol use, tobacco use, or substance abuse) or a current cancer diagnosis (Table S2, http://links.lww.com/JG9/A60); and previous pharmacy claims for medications including opioids, benzodiazepines, muscle relaxants, antidepressants, or antipsychotics. Diagnoses were considered if they were coded within 12 months of the date of surgery. To avoid overlap with the initial postoperative opioid prescription, all preoperative prescription claims (including all preoperative opioid prescriptions) were assessed starting from 12 months up to 30 days before the date of surgery. Procedure-related variables included procedure type, place of service, and hospital LOS for inpatient procedures. Outpatient procedures were designated as having a LOS of zero days.

Outcome Variable
For each patient, we identified pharmacy claims for the index postoperative opioid prescription fill. Surgeons frequently provide opioid prescriptions to their patients ahead of scheduled surgery. Therefore, we defined the index postoperative opioid prescription fill as the first opioid prescription filled during a 14-day window comprising the 7 days before and after the date of surgery (outpatient procedures) or the date of discharge (inpatient procedures). Using Centers for Disease Control and Prevention (CDC) conversion factors (Table S3, http://links.lww.com/JG9/A60), we converted each unique opioid, dosage, and duration on the index prescription to its oral morphine equivalent dose in milligrams (MME). If patients filled more than one opioid on the date of the index prescription fill, the MME for each opioid was summed to calculate a total MME for the index prescription.

There are currently no nationally accepted guidelines for postoperative opioid prescribing. In this context, some investigators have used 200 MME as a threshold for excessive postoperative opioid prescribing. Other existing state and institutional guidelines recommend prescribing a maximum of 150 to 315 MME (~20 to 42 tablets of oxycodone 5 mg) for most procedures included in our study. Given these guidelines, we adopted a total prescription dosage of ≥350 as a conservative definition of a high-dose postoperative opioid prescription fill.

Statistical Analysis
We evaluated prescriptions filled from 1994 to 2014. For each procedure and year, we calculated the mean and median postoperative MME filled. To account for the effect of the approval and marketing of long-acting opioids on opioid prescribing, we identified the proportion of patients whose index postoperative opioid prescription included a long-acting formulation and the proportion who had filled any preoperative prescription for long-acting opioids. We depicted changes in opioid selection over time. We used multiple logistic regression to assess the association of patient, surgery and geographic factors, year of surgery, and inclusion of long-acting opioids with the receipt of ≥350 MME on the index prescription. Wald chi-square tests were used to determine the statistical significance of these predictors.
Table 1

Baseline Characteristics for Patients Undergoing Selected Surgeries, 1994 to 2014

| Patient characteristics | All Patients 1994-2014, N = 1,321,264 | % |
|-------------------------|----------------------------------------|---|
| Age in years (SD)       | 48.4 (12.9)                            |   |
| Sex                     |                                        |   |
| Male                    | 542,423                                | 41.1 |
| Female                  | 778,841                                | 58.9 |
| Race                    |                                        |   |
| White                   | 994,180                                | 75.2 |
| Black                   | 86,679                                 | 6.6 |
| Asian                   | 22,394                                 | 1.7 |
| Hispanic                | 91,217                                 | 6.9 |
| Unknown                 | 126,794                                | 9.6 |
| Geographic region       |                                        |   |
| South                   | 594,124                                | 45.0 |
| West                    | 178,110                                | 13.5 |
| Midwest                 | 438,675                                | 33.2 |
| Northeast               | 110,355                                | 8.4 |
| Deyo-Charlson Comorbidity Index |                       |   |
| 0-1                     | 1,130,752                               | 85.6 |
| 2                       | 117,167                                | 8.9 |
| 3+                      | 73,345                                 | 5.6 |
| Active cancer diagnosis | 14,518                                 | 1.1 |
| Predisposing factors    |                                        |   |
| Post-traumatic stress disorder | 4,694                                 | 0.4 |
| Anxiety                 | 101,287                                | 7.7 |
| Depression              | 143,673                                | 10.9 |
| Psychosis               | 5,038                                  | 0.4 |
| Chronic pain            | 16,249                                 | 1.2 |
| Substance abuse         | 10,054                                 | 0.8 |
| Tobacco use             | 102,207                                | 7.7 |
| Alcohol use             | 13,285                                 | 1.0 |
| Prescriptions in previous 12 mo |                               |   |
| Any opioid              | 466,767                                | 35.3 |
| Long-acting opioids     | 22,877                                 | 1.7 |
| Benzodiazepines         | 176,109                                | 13.3 |
| Muscle relaxants        | 152,208                                | 11.5 |
| Antidepressants         | 276,431                                | 20.9 |
| Antipsychotics          | 6,706                                  | 0.5 |
| Surgical characteristics |                                        |   |
| Procedure type          |                                        |   |
| Arthroscopic knee meniscectomy | 242,605                               | 18.4 |
| Laparoscopic cholecystectomy | 222,762                               | 16.9 |
| Open hysterectomy       | 106,716                                | 8.1 |
| Open inguinal hernia repair | 101,756                               | 7.7 |

ACL = anterior cruciate ligament, LA = long-acting, LOS = length of stay, MME = oral morphine milligram equivalents, SA = short-acting

*Percentages represent proportion of all opioids prescribed.
Table 1 (continued)
Baseline Characteristics for Patients Undergoing Selected Surgeries, 1994 to 2014  

| Procedure                                      | All Patients 1994-2014, N = 1,321,264 | %   |
|------------------------------------------------|--------------------------------------|-----|
| Carpal tunnel release                          | 83,499                               | 6.3 |
| Breast lumpectomy                              | 73,967                               | 5.6 |
| Laparoscopic appendectomy                       | 69,773                               | 5.3 |
| Total knee arthroplasty                        | 68,333                               | 5.2 |
| Lumbar laminectomy/laminotomy                  | 55,175                               | 4.2 |
| Total hip arthroplasty                         | 46,094                               | 3.5 |
| Lap-assisted vaginal hysterectomy               | 41,705                               | 3.2 |
| Vaginal hysterectomy                           | 38,051                               | 2.9 |
| Open rotator cuff repair                       | 34,610                               | 2.6 |
| Open partial colectomy                         | 33,600                               | 2.5 |
| Laparoscopic inguinal hernia repair            | 29,615                               | 2.2 |
| Arthroscopic ACL repair                        | 25,968                               | 2.0 |
| Open appendectomy                              | 18,646                               | 1.4 |
| Simple mastectomy                              | 16,232                               | 1.2 |
| Open cholecystectomy                           | 12,157                               | 0.9 |

Surgery location
- Hospital outpatient department: 612,675 (46.4%)
- Inpatient hospital: 493,900 (37.4%)
- Ambulatory surgery center: 207,922 (15.7%)
- Office: 3,776 (0.3%)
- Unknown: 2,991 (0.2%)

LOS in days
- 0: 854,627 (64.7%)
- 1: 78,862 (6.0%)
- 2: 137,068 (10.4%)
- 3+: 250,707 (19.0%)

Year of surgery
- 1994: 8,149 (0.6%)
- 1995: 9,336 (0.7%)
- 1996: 11,094 (0.8%)
- 1997: 13,894 (1.1%)
- 1998: 20,177 (1.5%)
- 1999: 29,511 (2.2%)
- 2000: 37,265 (2.8%)
- 2001: 40,660 (3.1%)
- 2002: 69,661 (5.3%)
- 2003: 84,413 (6.4%)
- 2004: 88,696 (6.7%)
- 2005: 88,027 (6.7%)
- 2006: 101,000 (7.6%)
- 2007: 100,491 (7.6%)
- 2008: 104,517 (7.9%)
- 2009: 99,772 (7.6%)

ACL = anterior cruciate ligament, LA = long-acting, LOS = length of stay, MME = oral morphine milligram equivalents, SA = short-acting
*Percentages represent proportion of all opioids prescribed.
Sensitivity Analysis

As a sensitivity analysis, we repeated our analyses in opioid-naive patients (patients without an opioid prescription fill starting from 12 months to 30 days before surgery).

All statistical analyses were done using R version 3.4.3 (The R Foundation).

Results

We identified 1,321,264 patients meeting inclusion criteria, of whom 1,061,104 (80.3%) filled an index postoperative opioid prescription (Table 1). The mean age was 48.4 years (SD 12.9). Patients were predominantly female (58.9%), white (75.2%), and from the South (45.0%). Approximately 35.3% of patients received preoperative opioids, and 1.7% used long-acting opioids preoperatively. The mean and median index postoperative opioid prescription fill was 268.1 and 200 MME, respectively. The mean and median postoperative MME filled each year for each procedure type also increased over time, particularly among patients undergoing orthopaedic procedures (Figure 1, Figures S1 and S2, http://links.lww.com/JG9/A60). Between 1994 and 2014, the mean postoperative MME filled
increased by 145% for lumbar laminectomy/laminotomy, 84% for total knee arthroplasty, and 85% for total hip arthroplasty. All procedures showed a spike in prevalence of long-acting prescription fills in the year 2000 (prevalence ranged from 0.6% for breast lumpectomy to 6.7% for lumbar laminectomy/laminotomy); however, we found that the prescriptions filled by patients undergoing orthopaedic procedures had a sustained increase in the use of long-acting opioids (Figure 3A; Figure S3, http://links.lww.com/JG9/A60). By 2012, 11.1% of patients undergoing total knee arthroplasty, 8.9% undergoing total hip arthroplasty, and 8.6% undergoing lumbar laminectomy/laminotomy filled a long-acting opioid prescription. Preoperative use of long-acting opioids increased substantially during the study period, especially among patients undergoing lumbar laminectomy/laminotomy (Figure 3B; Figure S4, http://links.lww.com/JG9/A60). We found that patients who had previously been opioid-naive were also filling long-acting opioid prescriptions postoperatively (Figure 3C; Figure S5, http://links.lww.com/JG9/A60). Additional longitudinal trends in the opioid-naive cohort were consistent with our main findings (Figures S6 to S8, http://links.lww.com/JG9/A60).

Prescribing of specific opioid medications changed over time (Figure S9, http://links.lww.com/JG9/A60). When looking at all procedures combined, hydrocodone and oxycodone were used in approximately 60% of postoperative opioid prescriptions filled in 1994, compared with 92% in 2014. The proportion of prescription fills that included codeine declined from 19% in 1994 to 3% in 2014. Propoxyphene declined from 21% in 1994 to 0% in 2011 after it was removed from the market in 2010 because of its association with fatal cardiac arrhythmias. After FDA approval in 1995, tramadol use increased to 5% in 2014, while long-acting oxycodone use increased to 2% in 2014. Similar changes in prescribing occurred in the opioid-naive cohort (Figure S10, http://links.lww.com/JG9/A60).

The likelihood of filling a high-dose postoperative opioid prescription was associated with patient-related variables such as younger age, white race, and the presence of predisposing diagnoses such as chronic pain. Adjusted odds ratio (AOR) 1.35,
95% Confidence Interval (CI): 1.31, 1.40), substance abuse (AOR 1.07; 95% CI, 1.02, 1.13), and tobacco use (AOR 1.07; 95% CI, 1.03, 1.09) (Table 2). Prescription drug use in the 12 months before surgery was also associated with a high-dose fill, including antidepressants (AOR 1.11, 95% CI, 1.10, 1.13), muscle relaxants (AOR 1.15, 95% CI, 1.13, 1.16), benzodiazepines (AOR 1.17, 95% CI, 1.15, 1.18), any opioid (AOR 1.27, 95% CI, 1.25, 1.28), and any long-acting opioid (AOR 1.30, 95% CI, 1.26, 1.35).

Patients who were discharged on postoperative day #2 had higher adjusted odds of filling a high-dose postoperative opioid prescription (1.48, 95% CI, 1.44, 1.53), compared with patients with shorter or longer hospitalizations or having ambulatory surgery. Year of surgery from the early 2000s through 2014 was also associated with higher adjusted odds of having a high-dose postoperative prescription fill. The procedures with the highest adjusted odds of patients filling a high-dose postoperative opioid prescription were all orthopaedic procedures: lumbar laminectomy/laminotomy (7.55, 95% CI, 7.37, 7.74), total hip arthroplasty (6.72, 95% CI, 6.54, 6.91), total knee arthroplasty (6.64, 95% CI, 6.47, 6.81), arthroscopic anterior cruciate ligament repair (5.44, 95% CI, 5.27, 5.60), and open rotator cuff repair (5.20, 95% CI, 5.06, 5.35). Patients whose postoperative opioid prescription included a long-acting formulation had the highest adjusted odds of filling a high-dose prescription (AOR 32.01, 95% CI, 30.23, 33.90).

In a sensitivity analysis limited to opioid-naive patients (Table S4, http://links.lww.com/JG9/A60), procedure type and use of a long-acting formulation in the postoperative prescription remained the strongest predictors for filling a high-dose postoperative opioid prescription (Table S5, http://links.lww.com/JG9/A60).

**Discussion**

In this study of long-term postoperative opioid-prescribing trends in commercially insured patients, we found that changes in the
characteristics of the index postoperative opioid prescription filled by adult patients undergoing common surgical procedures mirrored the broader increase in opioid prescribing in the United States.\textsuperscript{1,2} Postoperative opioid prescription fills increased in both prevalence and total MME prescribed, and—after new long-acting opioids such as OxyContin became widely marketed—in the likelihood that a long-acting formulation was included.

The increase in the prevalence and dose of postoperative opioids is notable because it occurred despite improvements in both surgical technique and perioperative pain management approaches during the same period. The use of minimally invasive approaches, advances in neuraxial and regional anesthetic techniques, and the introduction of enhanced recovery pathways and multimodal analgesic approaches for many of these procedures should have decreased patients’ postoperative pain and the opioid dosage on the index prescription that would have been expected to meet their needs.\textsuperscript{20–23} However, these perioperative advances coincided with the introduction and marketing of OxyContin and other long-acting opioids in the mid-1990s,\textsuperscript{10,24} the simultaneous liberalization of what were considered to be appropriate indications for receiving a new opioid prescription,\textsuperscript{25} and the implementation of the Joint Commission standards for the evaluation and treatment of pain among hospitalized patients in the early 2000s.\textsuperscript{12,26} Others have noted that the increased likelihood of pre-existing opioid tolerance and the
| Predictors of Receiving High-Dose Opioids on Index Postoperative Opioid Prescription | Unadj. OR (95% CI) | Adj. OR (95% CI) | P (Wald test) |
|---|---|---|---|
| **Age (yr)** | | | |
| 18-35 (ref) | — | — | — |
| 35-45 | 1.10 (1.09, 1.12) | 1.01 (0.99, 1.03) | 0.187 |
| 45-55 | 1.34 (1.32, 1.36) | 0.99 (0.98, 1.01) | 0.255 |
| 55-65 | 1.67 (1.65, 1.69) | 0.92 (0.90, 0.93) | <0.001 |
| 65-75 | 1.46 (1.43, 1.49) | 0.67 (0.66, 0.69) | <0.001 |
| 75+ | 0.97 (0.93, 1.00) | 0.38 (0.37, 0.40) | <0.001 |
| **Sex** | | | |
| Male (ref) | — | — | — |
| Female | 0.87 (0.86, 0.88) | 1.00 (0.99, 1.02) | 0.479 |
| **Race** | | | |
| White (ref) | — | — | — |
| Black | 0.90 (0.89, 0.92) | 0.91 (0.90, 0.93) | <0.001 |
| Asian | 0.74 (0.71, 0.77) | 0.87 (0.83, 0.90) | <0.001 |
| Hispanic | 0.79 (0.77, 0.80) | 0.95 (0.93, 0.97) | <0.001 |
| Unknown | 0.78 (0.77, 0.79) | 0.96 (0.94, 0.98) | <0.001 |
| **Geographic region** | | | |
| South (ref) | — | — | — |
| West | 1.05 (1.04, 1.07) | 0.95 (0.94, 0.97) | <0.001 |
| Midwest | 0.96 (0.95, 0.97) | 0.94 (0.93, 0.96) | <0.001 |
| Northeast | 0.71 (0.69, 0.72) | 0.69 (0.68, 0.70) | <0.001 |
| **Deyo-Charlson Comorbidity Index** | | | |
| 0-1 (ref) | — | — | — |
| 2 | 1.04 (1.03, 1.06) | 0.97 (0.96, 0.99) | 0.003 |
| 3+ | 1.12 (1.10, 1.14) | 1.00 (0.98, 1.03) | 0.678 |
| Active cancer diagnosis | 1.01 (0.97, 1.05) | 0.97 (0.92, 1.01) | 0.169 |
| **Predisposing factors** | | | |
| Post-traumatic stress disorder | 1.31 (1.22, 1.40) | 0.96 (0.89, 1.04) | 0.328 |
| Anxiety | 1.20 (1.19, 1.22) | 0.99 (0.97, 1.01) | 0.273 |
| Chronic pain | 3.28 (3.18, 3.38) | 1.35 (1.30, 1.41) | <0.001 |
| Substance abuse | 1.91 (1.84, 2.00) | 1.07 (1.02, 1.13) | 0.008 |
| Tobacco use | 1.30 (1.28, 1.32) | 1.07 (1.05, 1.09) | <0.001 |
| Alcohol use | 1.32 (1.27, 1.38) | 0.97 (0.93, 1.02) | 0.268 |
| **Prescriptions in previous 12 mo** | | | |
| Any opioid | 1.89 (1.87, 1.91) | 1.27 (1.25, 1.28) | <0.001 |
| Long-acting opioids | 4.24 (4.13, 4.35) | 1.30 (1.26, 1.35) | <0.001 |
| Benzodiazepines | 1.53 (1.51, 1.54) | 1.17 (1.15, 1.18) | <0.001 |
| Muscle relaxants | 1.84 (1.82, 1.86) | 1.15 (1.13, 1.16) | <0.001 |
| Antidepressants | 1.38 (1.37, 1.40) | 1.11 (1.10, 1.13) | <0.001 |
| Antipsychotics | 1.72 (1.63, 1.81) | 1.04 (0.98, 1.10) | 0.220 |
| **Procedure type** | | | |
| Laparoscopic cholecystectomy (ref) | — | — | — |
| Lumbar laminectomy/laminotomy | 10.20 (9.98, 10.42) | 7.55 (7.37, 7.74) | <0.001 |

ACL = anterior cruciate ligament, LA = long-acting, LOS = length of stay, MME = oral morphine milligram equivalents, OR = odds ratio

*Depression was removed as predictor variable because it was highly colinear with antidepressant use in the previous 12 months.
Table 2 (continued)

Predictors of Receiving High-Dose Opioids on Index Postoperative Opioid Prescription

|                        | Unadj. OR | (95% CI)     | Adj. OR | (95% CI)     | P (Wald test) |
|------------------------|-----------|--------------|---------|--------------|---------------|
| Total hip arthroplasty | 8.07      | (7.89, 8.25) | 6.72    | (6.54, 6.91) | <0.001        |
| Total knee arthroplasty| 7.80      | (7.65, 7.96) | 6.64    | (6.47, 6.81) | <0.001        |
| Arthroscopic ACL repair| 5.61      | (5.45, 5.77) | 5.44    | (5.27, 5.60) | <0.001        |
| Open rotator cuff repair| 5.33     | (5.20, 5.46) | 5.20    | (5.06, 5.35) | <0.001        |
| Simple mastectomy     | 2.00      | (1.92, 2.08) | 1.78    | (1.70, 1.86) | <0.001        |
| Arthroscopic knee meniscectomy | 1.88 | (1.85, 1.91) | 2.10    | (2.06, 2.14) | <0.001        |
| Open cholecystectomy  | 1.81      | (1.73, 1.90) | 1.72    | (1.63, 1.81) | <0.001        |
| Carpal tunnel release | 1.58      | (1.54, 1.62) | 1.67    | (1.63, 1.71) | <0.001        |
| Open partial colectomy| 1.53      | (1.48, 1.58) | 1.50    | (1.45, 1.56) | <0.001        |
| Open hysterectomy     | 1.38      | (1.35, 1.41) | 1.20    | (1.17, 1.23) | <0.001        |
| Breast lumpectomy     | 1.25      | (1.22, 1.28) | 1.50    | (1.46, 1.54) | <0.001        |
| Lap-assisted vaginal hysterectomy | 1.16 | (1.12, 1.20) | 1.02    | (0.99, 1.05) | 0.288         |
| Vaginal hysterectomy  | 1.12      | (1.08, 1.16) | 1.02    | (0.98, 1.05) | 0.301         |
| Open inguinal hernia repair | 1.01 | (0.98, 1.03) | 1.21    | (1.18, 1.24) | <0.001        |
| Open appendectomy     | 0.98      | (0.93, 1.03) | 1.01    | (0.96, 1.06) | 0.835         |
| Laparoscopic inguinal hernia repair | 0.85 | (0.82, 0.89) | 0.96    | (0.92, 1.00) | 0.041         |
| Laparoscopic appendectomy | 0.75     | (0.73, 0.77) | 0.73    | (0.71, 0.75) | <0.001        |

Surgery location

|                        | Unadj. OR | (95% CI)     | Adj. OR | (95% CI)     | P (Wald test) |
|------------------------|-----------|--------------|---------|--------------|---------------|
| Hospital outpatient department (ref) | —         | —            | —       | —            | —             |
| Inpatient hospital     | 1.82      | (1.80, 1.84) | 0.91    | (0.89, 0.94) | <0.001        |
| Ambulatory surgery center | 1.19    | (1.17, 1.20) | 0.93    | (0.92, 0.94) | <0.001        |
| Office                 | 0.88      | (0.81, 0.97) | 0.82    | (0.75, 0.90) | <0.001        |
| Unknown                | 1.22      | (1.12, 1.34) | 0.90    | (0.81, 0.99) | 0.033         |

LOS

|                        | Unadj. OR | (95% CI)     | Adj. OR | (95% CI)     | P (Wald test) |
|------------------------|-----------|--------------|---------|--------------|---------------|
| 0 (ref)                | —         | —            | —       | —            | —             |
| 1                      | 1.19      | (1.17, 1.21) | 1.23    | (1.20, 1.27) | <0.001        |
| 2                      | 1.61      | (1.59, 1.63) | 1.48    | (1.44, 1.53) | <0.001        |
| 3+                     | 2.08      | (2.06, 2.10) | 1.27    | (1.23, 1.30) | <0.001        |
| Postop prescription included LA opioid | 70.94 | (67.12, 74.99) | 32.01    | (30.23, 33.90) | <0.001 |

Year of surgery

|                        | Unadj. OR | (95% CI)     | Adj. OR | (95% CI)     | P (Wald test) |
|------------------------|-----------|--------------|---------|--------------|---------------|
| 1994 (ref)             | —         | —            | —       | —            | —             |
| 1995                   | 0.98      | (0.90, 1.07) | 0.98    | (0.89, 1.07) | 0.617         |
| 1996                   | 1.04      | (0.96, 1.13) | 1.01    | (0.93, 1.10) | 0.742         |
| 1997                   | 1.07      | (0.99, 1.16) | 1.03    | (0.95, 1.12) | 0.432         |
| 1998                   | 1.06      | (0.99, 1.14) | 1.00    | (0.92, 1.08) | 0.944         |
| 1999                   | 1.14      | (1.07, 1.23) | 1.03    | (0.96, 1.11) | 0.444         |
| 2000                   | 1.23      | (1.15, 1.31) | 1.05    | (0.98, 1.13) | 0.161         |
| 2001                   | 1.34      | (1.26, 1.44) | 1.13    | (1.06, 1.22) | <0.001        |
| 2002                   | 1.25      | (1.17, 1.34) | 1.03    | (0.96, 1.11) | 0.349         |
| 2003                   | 1.33      | (1.24, 1.41) | 1.07    | (1.00, 1.15) | 0.052         |
| 2004                   | 1.33      | (1.25, 1.42) | 1.07    | (1.00, 1.14) | 0.059         |
| 2005                   | 1.39      | (1.30, 1.48) | 1.09    | (1.02, 1.17) | 0.011         |
| 2006                   | 1.54      | (1.45, 1.65) | 1.21    | (1.13, 1.30) | <0.001        |

ACL = anterior cruciate ligament, LA = long-acting, LOS = length of stay, MME = oral morphine milligram equivalents, OR = odds ratio

*Depression was removed as predictor variable because it was highly colinear with antidepressant use in the previous 12 months.
trend toward same-day surgeries and earlier discharge after inpatient surgery also may have contributed to escalating opioid dosages, compared with an earlier epoch when more patients would have been opioid-naive before surgery and would have had longer inpatient stays after surgery.\(^1,12,26\) In addition, pharmaceutical manufacturers may have targeted marketing to certain physicians preferentially based on their specialty.\(^10,20,24,27\)

These broader influences on postoperative opioid prescribing are illustrated by our study results, particularly among patients undergoing orthopaedic surgery. The strongest predictor of receiving a high-dose opioid prescription in our study was whether the prescription included a long-acting opioid, followed closely by whether patients were undergoing one of several common orthopaedic procedures. Our study does not specifically address the factors that may have led to the more frequent reliance on long-acting opioids in orthopaedic surgery patients postoperatively compared with patients undergoing nonorthopaedic procedures. Notably, most of the orthopaedic procedures included in our study are indicated to treat chronic musculoskeletal pain, which makes it more likely that these patients were already receiving opioids preoperatively. This is evidenced by the longitudinal increase in prevalence of long-acting opioids, especially among patients undergoing lumbar laminectomy/laminotomy.

However, our results among opioid-naive patients showed similar increases in MMEs prescribed over time. Consistent with our findings in the overall cohort, the inclusion of a long-acting formulation and undergoing the same orthopaedic procedures were the strongest predictors of filling a high-dose prescription in the opioid-naive cohort as well. Others have reported on the inclusion of OxyContin in orthopaedic clinical pathways to facilitate earlier hospital discharge, which may be contributing to the greater prescription dosages in these patients.\(^20,27\) These results suggest that postoperative opioid-prescribing practice changes over time were not driven solely by patients’ preoperative opioid use.

The use of OxyContin in the postoperative setting continued despite changes in the labeling of OxyContin in July 2001 that specified it should not be used to treat pain in the immediate postoperative period.\(^28\) Others have shown that the initiation of postoperative opioids in previously opioid-naive patients is associated with increased risk of chronic use,\(^29,30\) and introducing long-acting opioids to opioid-naive patients is associated with increased all-cause mortality.\(^31\) For many patients, surgery is the instigating event for first opioid use; therefore, surgeons have a particular responsibility to avoid the inappropriate use of long-acting opioids.\(^32,33\)

Our study has several limitations. First, there were changes to the OptumLabs data set over the 21-year study period, including changes in number of covered lives and case mix represented. Second, we studied selected surgical procedures in a commercially insured cohort, which may limit the generalizability of our findings to patients undergoing other procedures or who are not commercially insured. Other limitations related to the use of administrative claims data also apply. Third, some of the index prescriptions filled within our designated 14-day prescribing window may have been provided for indications unrelated to surgery. Furthermore, the prescriptions we analyzed only included those that were filled and submitted to insurance. Therefore, the exclusion of written but unfilled opioid prescriptions could have affected

| Year | Unadj. OR (95% CI) | Adj. OR (95% CI) | P (Wald test) |
|------|--------------------|-----------------|--------------|
| 2007 | 1.60 (1.50, 1.71)   | 1.23 (1.15, 1.32) | <0.001 |
| 2008 | 1.73 (1.62, 1.84)   | 1.32 (1.23, 1.41) | <0.001 |
| 2009 | 1.79 (1.68, 1.91)   | 1.34 (1.26, 1.44) | <0.001 |
| 2010 | 1.85 (1.74, 1.98)   | 1.39 (1.30, 1.49) | <0.001 |
| 2011 | 1.62 (1.52, 1.73)   | 1.17 (1.10, 1.26) | <0.001 |
| 2012 | 1.73 (1.62, 1.85)   | 1.25 (1.17, 1.34) | <0.001 |
| 2013 | 1.80 (1.68, 1.92)   | 1.28 (1.19, 1.37) | <0.001 |
| 2014 | 1.90 (1.78, 2.02)   | 1.37 (1.27, 1.46) | <0.001 |

ACL = anterior cruciate ligament, LA = long-acting, LOS = length of stay, MME = oral morphine milligram equivalents, OR = odds ratio

\(^a\) Depression was removed as predictor variable because it was highly collinear with antidepressant use in the previous 12 months.
our results, since patients who fill opioid prescriptions after surgery may differ from patients who receive an opioid prescription but do not fill it. Fourth, the goal of this study was to understand long-term postoperative opioid-prescribing trends reflected by the index postoperative opioid prescription during the years immediately after the introduction of new long-acting opioids such as OxyContin through the peak of the prescription opioid epidemic; postoperative opioid-prescribing practices may have changed since 2014. Finally, our high-dose prescription threshold of 350 MME may not be the optimal threshold for all types of surgical pain, especially for more invasive procedures such as total knee arthroplasty. However, since there are currently no nationally accepted standards for postoperative opioid prescribing in the surgical cohort, our designation of 350 MME as a threshold for high-dose prescribing provides a starting point for further discussion.

In summary, we found that postoperative opioid prescribing in commercially insured patients increased in parallel with broader US opioid-prescribing trends since the mid-1990s, especially among patients undergoing orthopaedic surgical procedures. The increase in the mean annual MME filled starting in the late 1990s was driven in part by the higher proportion of long-acting opioid formulations on the index postoperative opioid prescription filled by orthopaedic surgery patients. Understanding the factors that contribute to high-dose opioid prescribing after surgery is critical to maximizing the benefits of opioid therapy while avoiding opioid-associated adverse events. Surgeons should continue to limit the use of long-acting opioids in the immediate postoperative setting as a way to reduce high-dose prescription fills in patients undergoing orthopaedic surgical procedures.

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