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# Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period

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**IMPORTANCE** Chronic opioid use imposes a substantial burden in terms of morbidity and economic costs. Whether opioid-naive patients undergoing surgery are at increased risk for chronic opioid use is unknown, as are the potential risk factors for chronic opioid use following surgery.

**OBJECTIVE** To characterize the risk of chronic opioid use among opioid-naive patients following 1 of 11 surgical procedures compared with nonsurgical patients.

**DESIGN, SETTING, AND PARTICIPANTS** Retrospective analysis of administrative health claims to determine the association between chronic opioid use and surgery among privately insured patients between January 1, 2001, and December 31, 2013. The data concluded 11 surgical procedures (total knee arthroplasty [TKA], total hip arthroplasty, laparoscopic cholecystectomy, open cholecystectomy, laparoscopic appendectomy, open appendectomy, cesarean delivery, functional endoscopic sinus surgery [FESS], cataract surgery, transurethral prostate resection [TURP], and simple mastectomy). Multivariable logistic regression analysis was performed to control for possible confounders, including sex, age, preoperative history of depression, psychosis, drug or alcohol abuse, and preoperatice use of benzodiazepines, antipsychotics, and antidepressants.

**EXPOSURES** One of the 11 study surgical procedures.

**MAIN OUTCOMES AND MEASURES** Chronic opioid use, defined as having filled 10 or more prescriptions or more than 120 days' supply of an opioid in the first year after surgery, excluding the first 90 postoperative days. For nonsurgical patients, chronic opioid use was defined as having filled 10 or more prescriptions or more than 120 days' supply following a randomly assigned "surgery date."

**RESULTS** The study included 641 941 opioid-naive surgical patients (16[illegible] [SD] age, 44.0 [12.8] years), and 18 011 137 opioid-naive nonsurgical patien[illegible] mean [SD] age, 42.4 [12.6] years). Among the surgical patients, the inc[illegible] opioid in the first preoperative year ranged from 0.119% for Cesarean delivery (95% CI, 0.104%-0.134%) to 1.41% for TKA (95% CI, 1.29%-1.53%) The baseline incidence of chronic opioid use among the nonsurgical patients was 0.136% (95% CI, 0.134%-0.137%). Except for cataract surgery, laparoscopic appendectomy, FESS, and TURP, all of the surgical procedures were associated with an increased risk of chronic opioid use, with odds ratios ranging from 1.28 (95% CI, 1.12-1.46) for cesarean delivery to 5.10 (95% CI, 4.67-5.58) for TKA. Male sex, age older than 50 years, and preoperative history of drug abuse, alcohol abuse, depression, benzodiazepine use, or antidepressant use were associated with chronic opioid use among surgical patients.

**CONCLUSIONS AND RELEVANCE** In opioid-naive patients, many surgical procedures are associated with an increased risk of chronic opioid use in the postoperative period. A certain subset of patients (eg, men, elderly patients) may be particularly vulnerable.

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In the United States, chronic opioid use continues to impose a substantial burden in terms of morbidity and economic costs.[1] Opioid sales have increased sharply over the past decade,[2] particularly in the setting of noncancer pain,[3,4] with a concomitant increase in opioid-related overdoses and deaths.[2,5] In an effort to reduce chronic opioid use, researchers have identified potential risk factors, such as substance use disorders.[6-8]

Several studies have also suggested that surgery is a risk factor for chronic opioid use.[9-11] For example, 1 study estimated a 3% incidence of prolonged opioid use following major elective surgery,[10] while the incidence of chronic neuropathic pain following total knee arthroplasty has been estimated to be as high as 12.7% at 6 months.[12] Most of these studies examined prolonged opioid use in the setting of surgical procedures performed in patients with existing opioid use and surgical procedures that are expected to result in substantial postoperative pain. By contrast, the incidence and risk factors for chronic opioid use among opioid-naive patients undergoing less painful procedures are not as well understood.

We used administrative health claims data to examine the incidence of chronic opioid use within the first postsurgical year among opioid-naive patients. We identified opioid-naive patients undergoing 1 of 11 common procedures, including several procedures not thought to produce long-term pain (eg, functional endoscopic sinus surgery [FESS]). We then estimated the increased risk for chronic opioid use in the year following surgery by comparing these patients with a reference group of nonsurgical patients. In addition, we tested for several possible risk factors for chronic opioid use among surgical patients, including age, sex, history of alcohol or drug abuse, history of depression, and preoperative use of benzodiazepines, antipsychotics, and antidepressants.

### Key Points

**Question** Are opioid-naive patients undergoing surgery at increased risk for chronic opioid use?

**Findings** This analysis of administrative health claims of 641 941 opioid-naive surgical patients and 18 011 137 opioid-naive nonsurgical patients found that surgery was associated with an increased risk of chronic opioid use among surgical patients.

**Meaning** Opioid-naive patients undergoing surgery are at an increased risk for subsequent chronic opioid use, suggesting that opioid use should be monitored closely in the postoperative period.

## Methods

### Data

We obtained a sample of administrative health claims provided by MarketScan (Truven Health Analytics). MarketScan provides person-level data on utilization and expenditures for the care of people enrolled in private insurance plans through a participating employer, health plan, or government organization. For more recent years, the database contains information on the care of over 35 million beneficiaries; for earlier years, claims from fewer patients are available. The data are frequently used in analyses of health care utilization and spending.[13-16] Our data include all claims between January 1, 2001, and December 31, 2013. Because this study used deidentified administrative health claims data, neither institutional review board approval nor patient written informed consent was required.

The inpatient and outpatient data claims data provide information from specific encounters, including diagnosis codes (*International Classification of Diseases, Ninth Revision* [*ICD-9*]), procedure codes (Current Procedural Terminology [CPT]), and date the service was provided. For the pharmacy claims data, the information includes fill date, quantity supplied, and number of days supplied. The data also provide the National Drug Code, which can be linked to Red Book data (Truven Health Analytics) to obtain the generic name and dose of the prescribed drug.

### Sample

We constructed a sample consisting of patients who underwent 1 of 11 surgical procedures during the sample period: total knee arthroplasty (TKA), total hip arthroplasty (THA), laparoscopic cholecystectomy, open cholecystectomy, laparoscopic appendectomy, open appendectomy, cesarean delivery, FESS, cataract surgery, transurethral prostate resection (TURP), or simple mastectomy. We chose these procedures because they are commonly performed. In addition, with the exception of TKA and THA, these procedures are not indicated to relieve pain and are not thought to place patients at risk for long-term pain. We identified patients who underwent these procedures by identifying inpatient or outpatient claims with a CPT code for the given procedure (eTable 1 in the Supplement). We restricted our analysis to patients aged 18 to 64 years who were continuously enrolled for a period of at least 3 calendar years, encompassing the year before the procedure and the year after. For example, for patients who received their procedure in 2003, we required that the patient be continuously enrolled for at least the time period January 1, 2002, through December 31, 2004. In addition, we excluded patients who underwent 2 or more of the 11 studied surgical procedures. Using data from pharmacy claims, we further restricted our analysis to opioid-naive patients, defined as patients who did not fill a prescription for an opioid in the 12 months prior to their procedure. A flowchart outlining the construction of the sample is provided in the eFigure in the Supplement.

### Outcome Variables

Using pharmacy claims data, we isolated prescriptions for fentanyl (patch or oral form), hydrocodone, hydromorphone (oral form), methadone, morphine, oxymorphone, and oxycodone and excluded prescriptions containing hydrocodone in cough/cold formulation. In addition, we excluded analgesic preparations containing codeine, such as acetaminophen/codeine combinations. Our outcome of interest was chronic opioid use within the first postsurgical year. Previous studies using administrative claims data have defined chronic opioid use as having filled 10 or more prescriptions or more than 120





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days' supply within a 1-year period.[11] Since some opioid use is likely expected in the immediate postoperative period, we slightly modified this definition to having filled 10 or more prescriptions or more than 120 days' supply within the first year after surgery, excluding the first 90 postoperative days (ie, we measure only postoperative days 91-365).

### Risk Factors for Chronic Opioid Use

Based on biological plausibility and the existing literature,[10,17] we examined the use of benzodiazepines, antidepressants, and antipsychotics in the year prior to surgery as potential risk factors for chronic opioid use, by extracting all relevant prescriptions from our pharmaceutical claims data; patients were classified as users of these medications if they filled at least 1 prescription in the year prior to surgery. A full list of the drugs for each class is provided in eTable 2 in the Supplement. In addition, in light of the findings reported in previous literature,[6-8] we also examined whether age, sex, and a history of depression, alcohol abuse, or drug abuse served as risk factors for chronic opioid use. Age and sex were obtained directly from MarketScan. For depression, alcohol abuse, and drug abuse, we used *ICD-9* codes to identify patients with these diagnoses and the first year they received the diagnosis. Patients were considered to have a preoperative history of depression, alcohol abuse, or drug abuse if they had at least 2 claims with the relevant *ICD-9* code prior to the year of their surgery. A list of the *ICD-9* codes we used can be found in eTable 3 in the Supplement.

### Other Covariates

The *ICD-9* diagnosis codes were also used to control for comorbidities including diabetes mellitus, congestive heart failure, peripheral vascular disease, and hypertension. Similar to the criteria used for depression, alcohol abuse, and drug abuse, patients were considered to have a history for the given comorbidity if they filed at least 1 claim prior to the year of their surgery. A full list of the comorbidities we considered is provided in **Table 1**, and the *ICD-9* codes used to identify these comorbidities is provided in the eTable 3 in the Supplement. In addition, we also controlled for a patient's baseline use of health services by obtaining the number of claims that were submitted in the inpatient, outpatient, and pharmacy settings prior to surgery.

### Reference Sample

To calculate the baseline incidence of chronic opioid use, we also created a reference sample of nonsurgical patients. We created this reference sample to measure the degree to which, at the population level, patients typically transition into chronic opioid use for nonsurgical reasons (eg, low back pain). Estimating this baseline incidence allowed us to estimate the increased risk in chronic opioid use associated with surgery.

To construct our reference sample, we began by identifying patients aged 18 to 64 years who did not undergo any of the 11 surgical procedures. We then restricted our analysis to patients who were continuously enrolled for at least 3 calendar years. For each of these patients, we randomly assigned a false "surgery date" during their second year of enrollment. Similar to our surgical patients, we isolated all prescriptions in the 1-year period before the surgery date and restricted our analysis to persons who did not fill any prescriptions for an opioid during that 1-year period. We then measured chronic opioid use in the 1-year period following the surgery date using the same methods used for our surgical patients. Remaining covariates (eg, age, comorbidities) were also obtained using the same methods.

### Statistical Analyses

Since the distribution of many of our covariates differs between our reference sample and our sample of surgical patients (Table 1), a simple comparison of rates of chronic opioid use was likely to be confounded. Therefore, we used a multivariable logistic regression to examine the correlation between surgery and chronic opioid use. We performed a separate logistic regression for each procedure, where the sample in each regression consisted of the patients who underwent the given procedure as well as our reference sample. The dependent variable in this regression was an indicator variable set at 1 if the patient met the criteria for chronic opioid use and 0 otherwise. The independent variable of interest was an indicator variable for receiving the given type of surgery. Coefficients for the surgery indicator variables captured the change in the likelihood of chronic opioid use associated with each surgery relative to nonsurgical patients. We included controls for the preoperative use of benzodiazepines, antipsychotic medications, and antidepressants by generating indicator variables of 1 if a patient filled at least 1 prescription for the given class in the preoperative year and 0 otherwise. We also included controls for an extensive set of comorbidities, as listed in Table 1. Finally, we included controls for age, sex, the year of surgery, and the number of claims submitted in the inpatient, outpatient, and pharmacy settings prior to surgery.

To examine the effect of our putative risk factors on chronic opioid use, we performed a separate multivariable logistic regression among our sample of surgical patients only. Our baseline analysis considered all surgical patients together; we also performed separate analyses by procedure. In these regressions, the dependent variables were indicator variables set at 1 if the patient met the definition for chronic opioid use in the first postsurgical year and 0 otherwise. For this analysis, our independent variables corresponded to putative risk factors: age (modeled as an indicator variable for persons >50 years), sex, preoperative pharmaceutical use (benzodiazepines, antipsychotics, and antidepressants), and medical history (alcohol abuse, drug abuse, depression, and psychosis). Our analyses also included controls for the full set of comorbidities listed in Table 1. All of our analyses incorporated robust standard errors (SEs) and were performed using Stata software, version 14.0 (StataCorp LP).

### Sensitivity Analysis

Our baseline analyses included a robust set of covariates to control for observable differences between our surgical and nonsurgical sample. We performed a residual confounding analysis[18,19] to investigate the extent to which our results could be explained by other unobservable factors, such as differences in health status between the 2 groups. Specifically, we

Table 1. Sample Summary Characteristics

| Characteristic | Patients[a] Surgical (n = 641 941) | Nonsurgical (n = 18 011 137) | P Value[b] | Hedge g[c] |
|---|---|---|---|---|
| Type of procedure, No. | | | | |
| TKA | 40 672 | NA | NA | NA |
| THA | 22 074 | NA | NA | NA |
| Laparoscopic cholecystectomy | 170 012 | NA | NA | NA |
| Open cholecystectomy | 6263 | NA | NA | NA |
| Laparoscopic appendectomy | 50 899 | NA | NA | NA |
| Open appendectomy | 14 928 | NA | NA | NA |
| Cesarean delivery | 201 662 | NA | NA | NA |
| FESS | 30 848 | NA | NA | NA |
| Cataract surgery | 68 854 | NA | NA | NA |
| TURP | 5568 | NA | NA | NA |
| Simple mastectomy | 30 161 | NA | NA | NA |
| Preoperative pharmaceutical use | | | | |
| Antidepressants | 14.40 (0.0438) | 11.82 (0.0076) | <.001 | NA |
| Antipsychotics | 1.45 (0.0149) | 1.03 (0.0024) | <.001 | NA |
| Benzodiazepines | 9.00 (0.0357) | 6.69 (0.0059) | <.001 | NA |
| Demographics | | | | |
| Age, y | 43.99 (0.0159) | 42.41 (0.0030) | <.001 | 0.125 |
| Male | 26.43 (0.0550) | 49.13 (0.0118) | <.001 | 0.456 |
| Medical comorbidities | | | | |
| Congestive heart failure | 1.42 (0.00148) | 0.45 (0.0158) | <.001 | 0.139 |
| Peripheral vascular disease | 1.87 (0.0169) | 0.53 (0.0017) | <.001 | 0.178 |
| Hypertension | 24.47 (0.0537) | 13.02 (0.0079) | <.001 | 0.337 |
| Medical comorbidities | | | | |
| Chronic obstructive pulmonary disease | 11.91 (0.0404) | 4.46 (0.0049) | <.001 | 0.352 |
| Diabetes mellitus | 9.96 (0.0374) | 4.94 (0.0051) | <.001 | 0.228 |
| Chronic kidney disease | 0.90 (0.0118) | 0.30 (0.0013) | <.001 | 0.106 |
| Cancer | 4.02 (0.0245) | 1.60 (0.0030) | <.001 | 0.189 |
| Cerebrovascular disease | 1.72 (0.0162) | 0.50 (0.0017) | <.001 | 0.166 |
| Dementia | 0.08 (0.0034) | 0.03 (0.0004) | <.001 | 0.026 |
| Myocardial infarction | 0.69 (0.0103) | 0.23 (0.0011) | <.001 | 0.093 |
| Liver disease | 3.31 (0.0224) | 0.96 (0.0023) | <.001 | 0.233 |
| Alcohol abuse | 0.66 (0.0101) | 0.39 (0.0015) | <.001 | 0.043 |
| Drug abuse | 0.39 (0.0078) | 0.25 (0.0012) | <.001 | 0.029 |
| Psychosis | 0.43 (0.0082) | 0.21 (0.0011) | <.001 | 0.046 |
| Depression | 11.74 (0.0402) | 5.37 (0.0053) | <.001 | 0.278 |
| Preoperative health care utilization, total claims | | | | |
| Inpatient | 1.93 (0.0156) | 0.96 (0.0021) | <.001 | 0.113 |
| Outpatient | 48.62 (0.0549) | 20.10 (0.0075) | <.001 | 0.925 |
| Pharmacy | 15.22 (0.0223) | 11.03 (0.0037) | <.001 | 0.284 |

Abbreviations: FESS, functional endoscopic sinus surgery; THA, total hip arthroplasty; TKA, total knee arthroplasty; TURP, transurethral prostate resection.

[a] Table lists summary statistics for study sample of surgical patients and a reference sample of nonsurgical patients. Unless otherwise indicated, data are reported as percentage of patients (standard error).

[b] Determined by *t* test for age and $\chi^2$ test for the remaining variables.

[c] The Hedge g statistic reports the magnitude of the difference (in terms of standard deviations) between the 2 groups.

assumed the presence of an unmeasured, binary confounder that was patient specific and independent of our measured confounders. We assumed that this confounder had a prevalence of 50% among our surgical sample and 0% among the nonsurgical patients. Of note, the assumed difference in prevalence between surgical and nonsurgical patients of this unmeasured confounder is at least an order of magnitude larger than the difference in prevalence for all of the medical comorbidities we examined. Using methods described elsewhere,[19] we then estimated the degree of confounding that would be necessary for this confounder to eliminate the estimated association between surgery and chronic opioid use.

## Results

Table 1 lists summary statistics for the surgical and nonsurgical study patients. Compared with the surgical patients,





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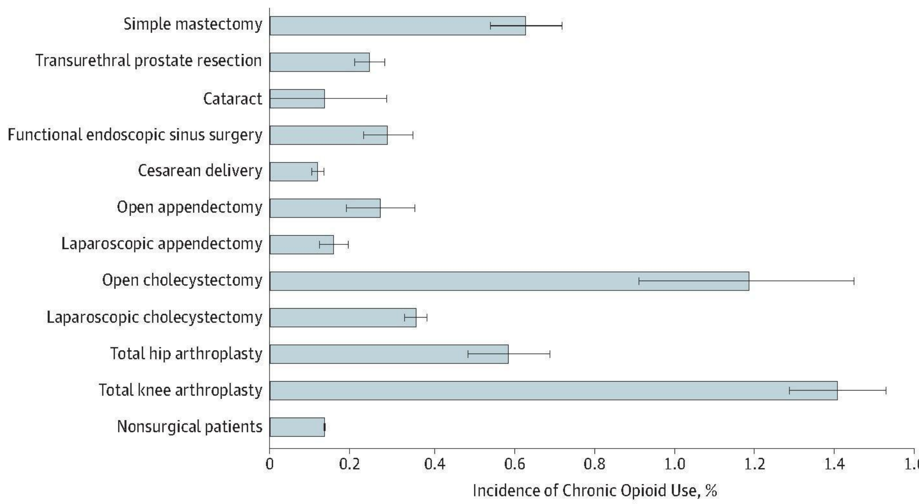
Figure 1. Incidence of Chronic Opioid Use Among Opioid-Naive Surgical and Nonsurgical Patients




Illustrated is the incidence of chronic opioid use within 1 year after surgery for surgical patients and the annual incidence of chronic opioid use among nonsurgical patients. Error bars indicate 95% CIs, which were calculated using robust standard errors.

nonsurgical patients were younger (42.4 vs 44.0 years; $P < .001$) and more likely to be male (49.1% vs 26.4%; $P < .001$). Both findings are consistent with the way our sample was drawn. First, the prevalence of surgery increases with age. Second, for 2 of the surgical procedures we examined—mastectomy and cesarean delivery—the population consisted of only female patients. Nonsurgical patients were also less likely to have used antidepressants (11.8% vs 14.4%; $P < .001$), antipsychotics (1.03% vs 1.45%; $P < .001$), and benzodiazepines (6.69% vs 9.90%; $P < .001$) preoperatively. In addition, the prevalence of each of the comorbidities we examined was lower among nonsurgical patients (Table 1), and overall health care utilization (as measured by the total number of inpatient, outpatient, and pharmacy claims in the preoperative period) was lower among nonsurgical patients (Table 1). Summary statistics broken down by individual procedure are listed in eTable 4 in the Supplement.

**Figure 1** shows the incidence of chronic opioid use in the first postoperative year, which ranged from 0.119% for cesarean delivery (95% CI, 0.104%-0.134%) to 1.41% for TKA (95% CI, 1.29%-1.53%). By contrast, the baseline incidence of chronic opioid use among nonsurgical patients was 0.136% (95% CI, 0.134%-0.137%). The incidence of chronic opioid use was significantly higher for all of the procedures that we examined ($P < .001$, $\chi^2$ test; eTable 5 in the Supplement) except for cesarean delivery, where the incidence rate was significantly lower ($P = .04$; eTable 5 in the Supplement), and laparoscopic appendectomy, where there was no significant difference ($P = .15$; eTable 5 in the Supplement).

Although Figure 1 suggests that most of the surgical procedures we examined were associated with a higher incidence of chronic opioid use compared with nonsurgical controls, the values shown are unadjusted for differences in the surgical and nonsurgical population detailed in Table 1. To adjust for these differences, we used a multivariable logistic regression to calculate the odds ratios (ORs) for chronic opioid use associated with each procedure, controlling for age, sex, and preoperative use of the medications shown in Table 1. **Figure 2** illustrates these ORs. After adjusting for potential confounders, we found that TKA (OR, 5.10; 95% CI, 4.67-5.58; $P < .001$), open cholecystectomy (OR, 3.60; 95% CI, 2.80-4.62; $P < .001$), THA (OR, 2.52; 95% CI, 2.11-3.01; $P < .001$), simple mastectomy (OR, 2.65; 95% CI, 2.28-3.08; $P < .001$), laparoscopic cholecystectomy (OR, 1.62; 95% CI, 1.49-1.76; $P < .001$), open appendectomy (OR, 1.69; 95% CI, 1.24-2.31; $P = .001$), and cesarean delivery (OR, 1.28; 95% CI, 1.12-1.46; $P < .001$) were associated with a significant increase in the incidence of chronic opioid use. There was no significant association in the cases of TURP (OR, 1.14; 95% CI, 0.73-1.77; $P = .57$), laparoscopic appendectomy (OR, 1.05; 95% CI, 0.84-1.32; $P = .65$), FESS (OR, 1.11; 95% CI, 0.90-1.37; $P = .33$), or cataract surgery (OR, 0.87; 95% CI, 0.74-1.02; $P = .08$).

We considered several putative risk factors for chronic opioid use: age (>50 years), male sex, preoperative medication use (benzodiazepines, antidepressants, or antipsychotics), and comorbidities (depression, psychosis, alcohol abuse, or drug abuse). **Table 2** summarizes our results. Across all surgical patients, male sex (OR, 1.34; 95% CI, 1.22-1.47; $P < .001$), age greater than 50 years (OR, 1.74; 95% CI, 1.56-1.93; $P = .P < .001$), preoperative use of benzodiazepines (OR, 1.82; 95% CI, 1.63-2.04; $P < .001$), preoperative use of antidepressants (OR, 1.65; 95% CI, 1.47-1.84; $P < .001$), depression history (OR, 1.15; 95% CI, 1.02-1.30; $P = .03$), alcohol abuse history (OR, 1.83; 95% CI, 1.35-2.47; $P < .001$), and drug abuse history (OR, 3.15; 95% CI, 2.24-4.40; $P < .001$) were associated an increased risk of chronic opioid use. Separate analyses by procedure are provided in eTable 6 in the Supplement.

We performed a residual confounding analysis to estimate the degree of confounding that would need to be present to explain our results. In the case of TKA, we computed that the true OR for chronic opioid use would be statistically indistinguishable from 1 in the presence of an unmeasured binary confounder with (1) a prevalence of 50% in the surgical population, (2) a prevalence of 0% in the nonsurgical





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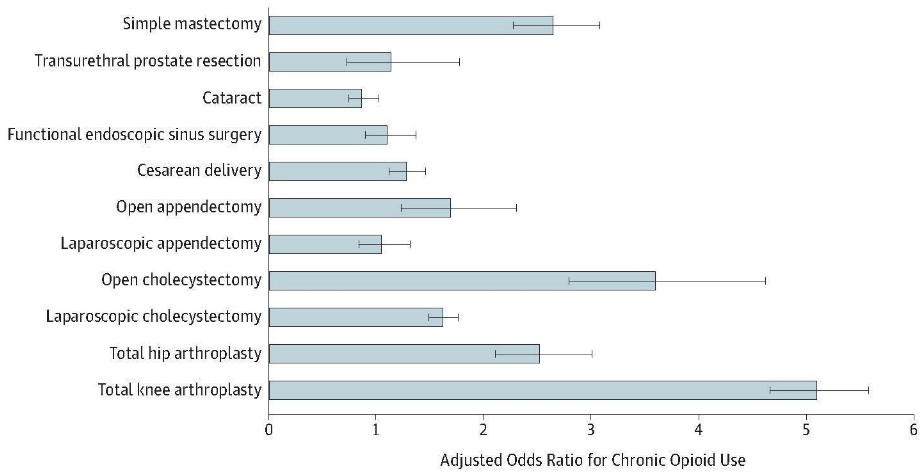
Figure 2. Risk of Chronic Opioid Use Following Surgery




Illustrated are the adjusted odds ratios for chronic opioid use within 1 year after surgery for each study surgical procedure. Error bars indicate 95% CIs, which were calculated using robust standard errors. Our regression model included controls for age, sex, year of surgery, and overall health care utilization. In addition, the model also included controls for preoperative use of benzodiazepines, antidepressants, and antipsychotics, and controls for the medical comorbidities listed in Table 1.

population, and (3) an adjusted OR of 8.34 for chronic opioid use. Assuming the same prevalence, this hypothetical confounder would need to have an OR for chronic opioid use of 3.22 to nullify our findings for THA. For the remaining procedures, the required ORs would need to be at least 1.98 for laparoscopic cholecystectomy, 4.6 for open cholecystectomy, 1.48 for open appendectomy, 1.24 for cesarean delivery, and 3.56 for simple mastectomy.

## Discussion

In this study, we examined the incidence of chronic opioid use following surgery in opioid-naive patients. Compared with a reference group of nonsurgical patients, we found an increased rate of chronic opioid use for patients undergoing TKA, open cholecystectomy, THA, simple mastectomy, laparoscopic cholecystectomy, FESS, open appendectomy, laparoscopic appendectomy, and cesarean delivery. Preoperative use of benzodiazepines and antidepressants was associated with an increased risk of chronic opioid use for most of the procedures, as was a history of drug abuse.

Our analysis extends previous work in several ways. First, previous studies have typically reported rates of opioid use following surgery without considering the baseline incidence of opioid use in the population, making it unclear the degree to which these rates exceed the expected rate of opioid use. In this study, we addressed this issue by comparing the incidence of chronic opioid use among postsurgical patients with the incidence of chronic opioid use among a reference group of nonsurgical patients. Second, in contrast to much of the existing literature, our study focuses on opioid-naive patients. Third, we analyze the role of several potential risk factors—such as drug and alcohol abuse history as well as preoperative benzodiazepine use—that have not been considered in previous work. Finally, some previous studies were performed among Canadian patients[9,10]; we evaluate patients in the United States, where a different set of opioid consumption and prescribing behaviors may exist.[20,21]

We surmise that chronic opioid use following surgery occurs because surgery may unmask an individual's susceptibility toward long-term opioid use. Patients undergoing surgery are clearly at risk for postsurgical pain, a subjective experience that is modulated by many factors, including psychological, behavioral, and medical characteristics. Moreover, acute postoperative pain, when severe, is predictive of the development of chronic pain.[22] Put together, these individual factors may render some patients susceptible to amplification of acute postsurgical pain, thereby increasing their risk for chronic opioid use following surgery.

Our results have several clinical implications. First, while we found that surgical patients are at an increased risk for chronic opioid use, the overall risk for chronic opioid use remains low among these patients, at less than 0.5% for most of the procedures that we examined. Thus, our results should not be taken as advocating that patients forgo surgery out of concerns for chronic opioid use. Rather, our results suggest that primary care clinicians and surgeons should monitor opioid use closely in the postsurgical period. Moreover, they indicate that surgical patients, particularly those at higher risk for chronic opioid use, may benefit from techniques to reduce the risk of chronic opioid use, such as multimodal analgesia[23] and regional anesthesia,[23] particularly in light of literature suggesting that these interventions may improve other perioperative outcomes including mortality, complication rates, length of stay, opioid use, and opioid-related adverse events.[24-26] Finally, patients may also benefit from other preoperative and postoperative interventions, such as evidence-based psychobehavioral pain management skills.

Our study should be viewed in the context of its limitations. Our nonsurgical population differed in several ways from our surgical population, and while we controlled for many possible confounders, we cannot exclude the possibility that differences in opioid use between the 2 groups may be due to unobserved confounding. In particular, since pain is often the indication for a given surgery (eg, THA or TKA), one might expect a relatively high baseline incidence of chronic pain (postoperatively) among these patients relative

Table 2. Risk Factors for Chronic Opioid Use Following Surgery[a]

| Risk Factor | Odds Ratio (SE)[a] | P Value |
|---|---|---|
| Demographics | | |
| Male | 1.34 (0.0648) | <.001 |
| Age >50 y | 1.74 (0.0942) | <.001 |
| Preoperative drug use | | |
| Benzodiazepines | 1.82 (0.1049) | <.001 |
| Antidepressants | 1.65 (0.0928) | <.001 |
| Antipsychotics | 1.14 (0.1330) | .28 |
| Medical comorbidities | | |
| Depression | 1.15 (0.0717) | .03 |
| Psychosis | 1.03 (0.2094) | .89 |
| Alcohol abuse | 1.83 (0.2834) | <.001 |
| Drug abuse | 3.15 (0.5385) | <.001 |

[a] Table lists the results of a multivariable logistic regression in which the dependent variable was chronic opioid use and the independent variables were preoperative use of benzodiazepines, antidepressants, or antipsychotics; reported odds ratios are for chronic use associated with each risk factor, with robust standard errors (SEs) reported in parentheses. Not shown are controls for the remaining medical variables listed in Table 1 or controls for year of surgery.

to the general population. However, it is important to note that pain is not the primary indication for all of the procedures we considered. Moreover, even in the cases of TKA and THA, our analysis considered patients whose pain was not sufficient to require opioids prior to their procedure. We were also unable to measure 1 possible confounder, socioeconomic status. We did perform a residual confounding analysis, the results of which suggested that the magnitude of confounding (in terms of the prevalence of a hypothetical confounder among the surgical population and its effect on chronic opioid use) would need to be extremely large to explain our results. Nonetheless, on the whole, more work is needed to establish a definitive causal relationship between surgery and opioid use.

Second, our study was limited to privately insured patients aged 18 to 64 years, and therefore may not generalize to other populations, such as the elderly or those receiving Medicaid. Finally, it is worth noting that our patients were opioid naive in the sense of not having filled an opioid prescription in the 1 year prior to their surgery date; we do not know if they had used any opioid prior to this period or whether they used opioids surreptitiously in the year prior to surgery.

## Conclusions

In sum, our results suggest that opioid-naive patients are at an increased risk for chronic opioid use following surgery, and that patients using antidepressants or benzodiazepines, as well as patients with a history of drug abuse, are at particularly high risk. Whether these results apply to other surgical procedures and patient populations, and whether interventions in the postoperative period can reduce the risk of chronic opioid use, is a subject for further research.

### ARTICLE INFORMATION

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*Study concept and design:* Sun, Baker, Mackey.
*Acquisition, analysis, or interpretation of data:* Sun, Darnall.
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