

Preoperative Opioid Use is Independently Associated With Increased Costs and Worse Outcomes After Major Abdominal Surgery

David C. Cron, BS,* Michael J. Englesbe, MD,* Christian J. Bolton, BS,† Melvin T. Joseph, BS,†
Kristen L. Carrier, BS,‡ Stephanie E. Moser, PhD,† Jennifer F. Waljee, MD, MPH, MS,§ Paul E. Hilliard, MD,†
Sachin Kheterpal, MD, MBA,† and Chad M. Brummett, MD†

Objective: To explore the clinical and financial implications of preoperative opioid use in major abdominal surgery.

Background: Opioids are increasingly used to manage chronic pain, and chronic opioid users are challenging to care for perioperatively. Given the epidemic of opioid-related morbidity and mortality, it is critical to understand how preoperative opioid use impacts surgical outcomes.

Methods: This was an analysis of nonemergent, abdominopelvic surgeries from 2008 to 2014 from a single center within the Michigan Surgical Quality Collaborative clinical registry database. Preoperative opioid use (binary exposure variable) was retrospectively queried from the home medication list of the preoperative evaluation. Our primary outcome was 90-day total hospital costs. Secondary outcomes included hospital length of stay, 30-day major complication rates, discharge destination, and 30-day hospital readmission rates. Analyses were risk-adjusted for case complexity and patient-specific risk factors such as demographics, insurance, smoking, comorbidities, and concurrent medication use.

Results: In all, 2413 patients met the inclusion criteria. Among them, 502 patients (21%) used opioids preoperatively. After covariate adjustment, opioid users (compared with those who were opioid-naïve) had 9.2% higher costs [95% confidence interval (CI) 2.8%–15.6%; adjusted means \$26,604 vs \$24,263; $P = 0.005$], 12.4% longer length of stay (95% CI 2.3%–23.5%; adjusted means 5.9 vs 5.2 days; $P = 0.015$), more complications (odds ratio 1.36; 95% CI 1.04–1.78; adjusted rates 20% vs 16%; $P = 0.023$), more readmissions (odds ratio 1.57; 95% CI 1.08–2.29; adjusted rates 10% vs 6%; $P = 0.018$), and no difference in discharge destination ($P = 0.11$).

Conclusions: Opioid use is common before abdominopelvic surgery, and is independently associated with increased postoperative healthcare utilization

and morbidity. Preoperative opioids represent a potentially modifiable risk factor and a novel target to improve quality and value of surgical care.

Keywords: complications, costs, discharge, healthcare utilization, length of stay, morbidity, narcotic, opioid, preoperative opioid, readmissions

(*Ann Surg* 2017;265:695–701)

The increasing rate of opioid consumption and misuse in the United States has reached epidemic status in the past 2 decades.^{1,2} Nine million Americans report using opioids for medical reasons, and hydrocodone is among the most prescribed drugs in the United States, with over 130 million prescriptions filled in 2009.³ Despite the rapid increase in use for chronic pain, data do not support efficacy of long-term use.^{4,5} Opioids have many adverse side effects including constipation, bladder dysfunction, respiratory depression, and central nervous system depression.⁶ Chronic opioid use has been linked to poor health outcomes, including opioid dependence, hyperalgesia, and even increased all-cause mortality.^{4,5,7} Surgical patients are commonly prescribed opioid analgesics for management of postoperative pain, but there are many patients who take opioids to manage chronic pain before surgery. The implications of preoperative opioid use on surgical outcomes are unclear.

Opioid users represent a potentially high-risk surgical population and may require tailored perioperative care. Preoperative opioid use has been studied in the orthopedic population and is linked to postoperative hyperalgesia, decreased quality of life, and decreased physical function in this population.^{8–10} The prevalence and clinical impact of this problem in the general surgery population remain unclear. Given the impact of pain control and gastrointestinal function on hospital stay, it is intuitive that opioid users may have increased hospital length of stay (LOS) and may incur more costs. These patients may also be at higher risk for surgical complications. Opioid use represents a potentially modifiable risk factor and thus provides a unique target for surgical quality improvement.

In this study, we explored the clinical and financial implications of preoperative opioid use in a large cohort of major abdominal surgery patients at a single institution. We hypothesized that preoperative opioid use would be associated with increased hospital costs (primary outcome) in patients undergoing abdominal surgery, even after risk adjustment for relevant clinical covariates. Further, we hypothesized that preoperative opioid users would have a higher incidence of postoperative adverse events, including prolonged hospital LOS, major complications, nonhome discharge, and hospital readmission.

METHODS

Study Population

This study was approved by the University of Michigan Institutional Review Board (Ann Arbor, MI). This was a

From the *Department of Surgery, University of Michigan Medical School, Ann Arbor, MI; †Department of Anesthesiology; University of Michigan Medical School, Ann Arbor, MI; ‡University of Michigan College of Pharmacy, Ann Arbor, MI; and §Section of Plastic Surgery, University of Michigan Medical School, Ann Arbor, MI.

Funding: DCC received funding for this work from the 2015 AOA Carolyn L. Kuckein Student Research Fellowship and the Blue Cross Blue Shield of Michigan Foundation Student Research Award.

This work was presented in abstract form at the 2016 Academic Surgical Congress, Jacksonville, FL, February 2016.

Disclosures: MJE is co-founder and equity stakeholder in Prehab Technologies LLC and Prenovo LLC. CMB receives research funding from Neuros Medical Inc. (Willoughby Hills, OH) and is a consultant for Tonix Pharmaceuticals (New York, NY).

DCC and CMB 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.

The authors report no conflicts of interest.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's Web site (www.annalsofsurgery.com).

Reprints: Chad M. Brummett, MD, Burlington Building, 325 E Eisenhower Pkwy, Ste 100, Ann Arbor, MI 48108. E-mail: cbrummet@med.umich.edu.

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0003-4932/16/26504-0695

DOI: 10.1097/SLA.0000000000001901

retrospective review of prospectively collected clinical registry data from a single academic center. The study cohort included patients contained in the Michigan Surgical Quality Collaborative (MSQC) database who underwent nonemergent, inpatient, abdominopelvic surgery at the University of Michigan between 2008 and 2014.^{11,12} The MSQC dataset includes prospectively collected clinical data including demographics, description of operation, patient comorbidities, intraoperative course, and postoperative morbidity and mortality. Data are collected and audited by MSQC trained nurse reviewers using standardized data definitions.^{11,12} These data are routinely assessed for accuracy and inter-rater reliability by the coordinating center.

Patients who were admitted 2 or more days before surgery were excluded, as this group of patients has an inherently more complicated and costly perioperative encounter compared with patients presenting from home for an elective surgery. Further, patients admitted before the operation are likely to receive opioids in the hospital for acute pain, and these patients therefore represent a different group of opioid users than those using opioid medications at home for chronic pain. Patients admitted 1 day preoperatively were included in the study, because many of these patients are intentionally admitted 1 day before a scheduled but urgent operation. Of this group, we performed a thorough chart review to identify patients who were opioid-naïve on admission, but received opioids acutely in the hospital before surgery, and these patients were excluded from the analysis. Patients using buprenorphine preoperatively were excluded from the study, because this medication is most often used to treat opioid dependence, and these patients represent a unique and complex population. Exclusion criteria were defined a priori before any analyses, because the primary interest of the study was the impact of preoperative chronic opioid exposure on postoperative cost and outcomes.

Exposure: Preoperative Opioid Use

Opioid users were retrospectively identified by querying the preoperative anesthesia history and physical examination note in the electronic medical record. This examination is performed by an anesthesiologist on the day of the operation and includes the patient's home medication list. Given the importance of opioid use to perioperative pain management, opioid-naïve status is assumed to be accurate. All charts of those patients reporting preoperative opioid use were individually manually reviewed to verify opioid use at the time of surgery and to exclude opioids administered acutely at the study institution before surgery. For analysis, the exposure variable was a binary variable indicating any preoperative opioid use. Patients not using opioids at the time of surgery were termed opioid-naïve. Further granularity such as dose or duration of home use was not reliably available in the electronic medical record, and we were therefore unable to assess for a dose response with this analysis.

Outcome: Healthcare Utilization

The primary outcome of this study was 90-day total hospital costs. Using the institution's internal cost-accounting database, we obtained inpatient and outpatient financial data for procedural costs and facility fees for each patient. Total hospital costs included direct, indirect, variable, and fixed costs. Professional fees were not included. Financial data were collected from 3 days preoperatively to 90 days postoperatively, and were limited to costs incurred within the study institution's healthcare system. Financial data were adjusted for inflation relative to the 2014 consumer price index. Our institution's cost-accounting database uses Allscripts EPSi (Allscripts Healthcare Solutions, Inc., Chicago, IL)—an integrated multifaceted financial, clinical, and operational decision support system designed to provide informed analytics for cost accounting. Costs

involved in providing patient care are calculated based on direct costs from departmental expenses, overhead costs of operating the hospital, and time and motion studies for labor costs.

Additional outcomes related to healthcare utilization included LOS, discharge destination, and 30-day hospital readmission. The following discharge destinations were considered “nonhome discharge” for this analysis: skilled nursing facility, rehabilitation facility, and home with nursing care.

Outcome: Morbidity

We also assessed 30-day major complication rates. Major complications are recorded by the MSQC and include: surgical site infection (superficial, deep, and organ space), deep venous thrombosis, acute renal failure, postoperative bleeding requiring transfusion, stroke, unplanned intubation, fascial dehiscence, prolonged mechanical ventilation longer than 48 hours, myocardial infarction, pneumonia, pulmonary embolism, sepsis, vascular graft loss, and renal insufficiency. A composite, binary variable of postoperative morbidity indicating incidence of 1 or more complication was used for the main multivariate morbidity analysis. This method is commonly used by quality collaboratives and researchers for studying surgical morbidity.^{13,14} The individual complications were then analyzed separately without risk adjustment for descriptive purposes.

Statistical Analysis

Descriptive statistics were computed for the study cohort. Clinical characteristics were compared between opioid users and those who were opioid-naïve using standardized differences (difference in mean or proportion divided by pooled standard deviation). Continuous variables were compared using Student *t* test or Wilcoxon rank-sum test, as appropriate. Categorical variables were compared using Fisher exact test. Multivariate regression was performed to estimate the effect of opioid use on outcome after risk-adjustment. Hospital costs were log-transformed due to skew, and linear regression was performed. Robust standard errors were calculated to account for violation of the heteroscedasticity assumption. To compute adjusted mean costs, the output of the model (log-costs) was back-transformed, and Duan smearing estimator was applied as a correction for this back-transformation, to produce a more accurate estimate of the adjusted mean costs.^{15,16} For LOS, zero-truncated negative binomial regression with robust standard errors was used. This type of model is used for count data such as LOS and is robust to overdispersion.¹⁷ Logistic regression was used for the binary outcomes of complications, nonhome discharge, and readmission. Logistic regression model calibration was confirmed using Hosmer-Lemeshow goodness-of-fit tests.

For risk adjustment, the following variables were included as covariates in all models: age (continuous variable), sex, non-white race, insurance class (Blue Cross Blue Shield of Michigan, other commercial, Medicare, Medicaid, and charity care), work-relative value units (a well-established measure of case complexity¹⁸; continuous variable), open approach, body mass index (BMI; continuous variable), partially or fully dependent functional status, American Society of Anesthesiologists physical status classification score (ASA class score; coded as scores ≥ 3), smoking, Elixhauser comorbidity index (continuous variable), chronic steroid use, and serum albumin (continuous variable). These factors are collected by the MSQC because they are clinically known to be predictive of surgical morbidity and mortality, and these factors have been shown to be predictive of surgical costs.¹⁸ We also included a variable for time; this was a binary variable relative to July 2012, which roughly divided the cohort into half. For missing values of albumin (9% missing), mean replacement was used. No other covariates had missing values.

Two-sided significance tests with a significance level of $P \leq 0.05$ were used. All analyses were conducted using Stata v13.0 (College Station, TX).

RESULTS

Study Cohort

A total of 2413 patients met inclusion criteria and had complete cost, LOS, and morbidity data. We arrived at this number as follows: 3107 patients in the MSQC database underwent non-emergent, inpatient abdominal surgery at the University of Michigan Health System during the study period. Reasons for exclusion included admitted 2 or more days before surgery ($n = 646$), acute inpatient opioid administration in patients who were previously opioid-naïve ($n = 40$), buprenorphine use ($n = 4$), and missing data ($n = 4$). Our final study cohort therefore included 2413 patients. Case mix included the following: 5% appendectomy (2% among opioid users vs 5% among those who were opioid-naïve), 11% cholecystectomy (10% among opioid users vs 12% among those who were opioid-naïve), 11% hernia repair (11% among opioid users vs 11% among those who were opioid-naïve), 16% colectomy (16% among opioid users vs 16% among those who were opioid-naïve), 9% other bowel operations (14% among opioid users vs 8% among those who were opioid-naïve), 5% liver (5% among opioid users vs 5% among those who were opioid-naïve), 9% pancreas (12% among opioid users vs 8% among those who were opioid-naïve), 3% rectal (4% among opioid users vs 3% among those who were opioid-naïve), 10% vascular (11% among opioid users vs 9% among those who were opioid-naïve), 12% gynecologic (8% among opioid users vs 13% among those who were opioid-naïve), and 8% other abdominal operations (7% among opioid users vs 9% among those who were opioid-naïve).

Prevalence and Characteristics of Preoperative Opioid Use

The overall prevalence of preoperative opioid use was 21% (502 patients). Preoperative opioid use was highest (30%) in patients undergoing noncolectomy bowel operations and was lowest (9%) in patients undergoing appendectomy. Hydrocodone was the most

commonly used drug preoperatively (55% of opioid users). Table 1 describes the differences between preoperative opioid users and those who were opioid-naïve.

Opioid Use Was Associated With Increased Costs

The total 90-day costs in the study cohort were skewed right with an overall median of \$19,236 [interquartile range (IQR) \$21,782]. As shown in Table 2, median unadjusted costs were \$6683 higher in opioid users compared with opioid-naïve (95% confidence interval [CI] \$4544 to \$8820; $P < 0.001$). In multivariate linear regression analysis, preoperative opioid use was associated with a 9.2% increase in mean costs after covariate adjustment (95% CI 2.8%–15.6% increase; $P = 0.005$). Coefficients for all covariates in the multivariate model are shown in the Supplemental Table (<http://links.lww.com/SLA/B61>). The R^2 for this model was 0.42. As shown in Fig. 1A, mean adjusted costs were \$2341 higher in opioid users compared with opioid-naïve ($P = 0.005$).

Length of Stay Was Longer in Opioid Users

Hospital LOS in the study cohort was skewed right with an overall median of 4 (IQR 5). As shown in Table 2, median unadjusted LOS was 2 days longer in opioid users compared with those who were opioid-naïve (95% CI 1.5–2.5 days; $P < 0.001$). In multivariate negative binomial regression analysis, preoperative opioid use was associated with a 12.4% increase in mean LOS after covariate adjustment (95% CI 2.3%–23.5% increase; $P = 0.015$). Coefficients for all covariates in the multivariate model are shown in the Supplemental Table (<http://links.lww.com/SLA/B61>). As shown in Fig. 1B, mean adjusted LOS was 0.7 days longer in opioid users compared with those who were opioid-naïve ($P = 0.015$).

Morbidity Was Higher in Opioid Users

The overall 30-day complication rate in the study cohort was 17% (409 patients). As shown in Table 2, the unadjusted complication rate was 1.7-fold higher in opioid users compared with those who were opioid-naïve (absolute difference: 11.0%; 95% CI 6.9%–15.2%; $P < 0.001$). In multivariate logistic regression analysis, preoperative opioid use was significantly associated with increased

TABLE 1. Patient Clinical Characteristics by Preoperative Opioid Use

	Opioid-naïve	Opioid Users	Standardized Difference	P
Total N	79.2% (1911)	20.8% (502)		
Age	56.9 ± 16.1	55.7 ± 14.1	−0.08	0.10
Male	43.7% (835)	42.8% (215)	−0.02	0.76
Non-white race	14.7% (281)	14.1% (71)	−0.02	0.78
Insurance class				
Commercial (Blue Cross Blue Shield of Michigan)	43.5% (832)	36.1% (181)	−0.15	0.003
Commercial (other)	18.8% (360)	21.5% (108)	0.07	0.19
Medicare	33.3% (636)	34.5% (173)	0.03	0.63
Medicaid	4.0% (76)	7.6% (38)	0.15	0.001
Charity care	0.4% (7)	0.4% (2)	0	1.00
Work relative value units	23.6 ± 11.6	26.2 ± 13.0	0.21	<0.001
Open approach	64.9% (1241)	78.7% (395)	0.31	<0.001
Body mass index	29.1 ± 6.9	29.8 ± 10.8	0.08	0.18
Dependent functional status	0.4% (7)	1.2% (6)	0.09	0.036
ASA class ≥3	49.2% (941)	68.1% (342)	0.39	<0.001
Smoker	13.8% (264)	29.7% (149)	0.39	<0.001
Elixhauser score	2.0 ± 2.0	2.6 ± 2.0	0.30	<0.001
Chronic steroid use	5.4% (103)	12.2% (61)	0.24	<0.001
Albumin	4.3 ± 0.4	4.2 ± 0.5	−0.22	<0.001

Numbers represent % (N) and mean ± standard deviation. Standardized difference (for opioid users compared with opioid-naïve patients) = difference in mean or proportion divided by standard deviation. Univariate P values are shown.

TABLE 2. Univariate Comparison of Hospital Costs and Healthcare Utilization by Preoperative Opioid Use

	Opioid-naïve	Opioid Users	Difference (95% CI)	P
Total hospital costs	\$17,950 (\$20,064)	\$24,633 (\$25,828)	\$6683 (\$4544–\$8820)	<0.001
Length of stay	4 (5)	6 (5)	2 (1.5–2.5)	<0.001
30-day major complication rate	14.7% (280)	25.7% (129)	11.0% (6.9%–15.2%)	<0.001
Nonhome discharge destination	10.3% (195)	17.2% (85)	6.9% (3.3%–10.5%)	<0.001
30-day hospital readmission	6.1% (109)	10.7% (51)	4.6% (1.6%–7.5%)	0.001

Numbers are unadjusted and represent median (interquartile range) or % (N). Differences (with 95% confidence interval) are given for opioid users compared with opioid-naïve patients.

complications after covariate adjustment [adjusted odds ratio (OR) 1.36; 95% CI 1.04–1.78; $P = 0.02$]. Coefficients for all covariates in the multivariate model are shown in the Supplemental Table (<http://links.lww.com/SLA/B61>). The area under the receiver-operating characteristic curve (AUROC) for this model was 0.76. As shown in Fig. 1C, the adjusted complication rate was 1.3-fold higher in opioid users compared with those who were opioid-naïve ($P = 0.02$).

Table 3 shows unadjusted rates of specific complications by preoperative opioid use. Opioid users had higher rates of surgical site infection ($P < 0.001$), sepsis ($P = 0.004$), postoperative unplanned intubation ($P = 0.04$), postoperative myocardial infarction ($P = 0.04$), and postoperative transfusion ($P = 0.001$).

Opioid Use and Discharge Destination

The overall prevalence of nonhome discharge in the study cohort was 12% (280 patients). As shown in Table 2, the unadjusted prevalence of nonhome discharge was 1.7-fold higher in opioid users compared with those who were opioid-naïve (absolute difference: 6.9%; 95% CI 3.3%–10.5%; $P < 0.001$). In multivariate logistic regression analysis, preoperative opioid use was not significantly associated with increased prevalence of nonhome discharge after covariate adjustment (adjusted OR 1.33; 95% CI 0.94–1.88; $P = 0.11$). Coefficients for all covariates in the multivariate model are shown in the Supplemental Table (<http://links.lww.com/SLA/B61>). The AUROC for this model was 0.87. As shown in Fig. 1C, the

adjusted prevalence of nonhome discharge was 1.2-fold higher in opioid users compared with those who were opioid-naïve, though not statistically significant ($P = 0.11$).

Opioid Users Had Higher Readmission Rates

The overall 30-day readmission rate in the study cohort was 7% (160 patients). As shown in Table 2, the unadjusted readmission rate was 1.8-fold higher in opioid users compared with those who were opioid-naïve (absolute difference: 4.6%; 95% CI 1.6%–7.5%; $P = 0.001$). In multivariate logistic regression analysis, preoperative opioid use was significantly associated with increased readmission after covariate adjustment (adjusted OR 1.57; 95% CI 1.08–2.29; $P = 0.018$). Coefficients for all covariates in the multivariate model are shown in the Supplemental Table (<http://links.lww.com/SLA/B61>). The AUROC for this model was 0.71. As shown in Fig. 1C, the adjusted readmission rate was 1.5-fold higher in opioid users compared with those who were opioid-naïve ($P = 0.018$).

DISCUSSION

Preoperative Opioid Use Is Common and Independently Associated With Increased Costs and Worse Outcomes

In this large sample from a single institution, opioid use was common, with 21% of patients using opioids before abdominal

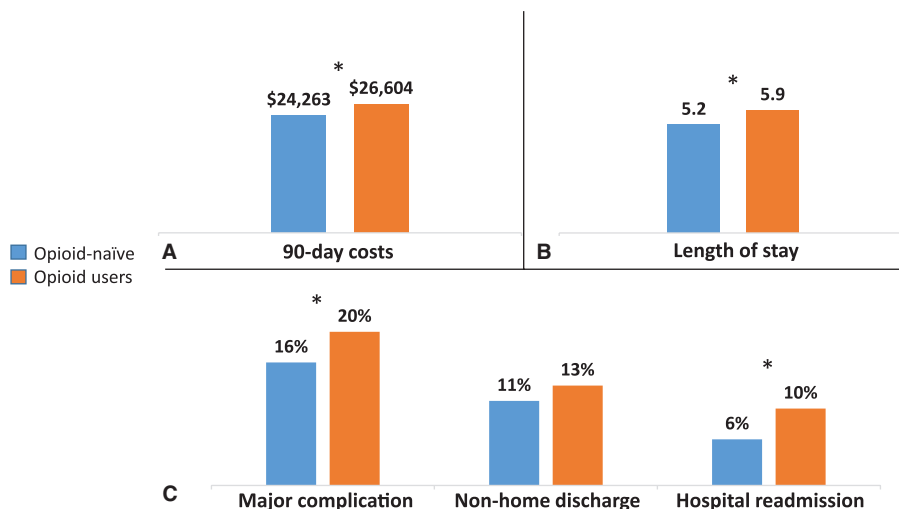


FIGURE 1. A, Mean adjusted 90-day costs by preoperative opioid use. B, Mean adjusted length of stay by preoperative opioid use. C, Adjusted rates of major complication, nonhome discharge, and hospital readmission by preoperative opioid use. All outcomes are risk-adjusted for case complexity and patient-specific risk factors (age, sex, race, insurance type, smoking, medical comorbidities, chronic steroid use, and serum albumin). The symbol “*” indicates a significant difference ($P \leq 0.05$). The P value for nonhome discharge was $P = 0.11$.

TABLE 3. Complication Rates by Preoperative Opioid Use

Complication	Opioid-naïve	Opioid Users	P
Infectious			
Surgical site infection: any	8.3% (159)	14.9% (75)	<0.001
Surgical site infection: superficial	5.8% (110)	10.4% (52)	0.001
Surgical site infection: deep	0.8% (15)	1.4% (7)	0.19
Surgical site infection: organ space	2.2% (41)	3.4% (17)	0.14
Pneumonia	0.9% (17)	2.0% (10)	0.053
Sepsis	1.6% (30)	3.8% (19)	0.004
Severe sepsis	1.2% (23)	1.4% (7)	0.66
<i>Clostridium difficile</i>	0.6% (11)	0.6% (3)	1
Respiratory			
Intraoperative unplanned intubation	0% (0)	0.2% (1)	0.21
Postoperative unplanned intubation	1.3% (24)	2.6% (13)	0.040
Pulmonary embolism	0.5% (9)	0.8% (4)	0.49
Cardiovascular			
Cardiac arrhythmia	0.4% (7)	0.8% (4)	0.26
Postoperative myocardial infarction	0.3% (5)	1.0% (5)	0.038
Postoperative cardiac arrest	0.2% (4)	0.2% (1)	1
Stroke	0.2% (3)	0.2% (1)	1
Deep venous thrombosis	0.6% (12)	0.8% (4)	0.76
Postoperative transfusion	3.5% (66)	7.2% (36)	0.001
Renal			
Acute renal failure	0.7% (14)	1.4% (7)	0.18

Numbers are unadjusted and represent % (N).

surgery. Healthcare utilization and surgical morbidity were higher in preoperative opioid users compared with opioid-naïve patients, even after risk adjustment. Analyses adjusted for patient and procedural covariates consistently demonstrated the association of opioid use and increased healthcare utilization. Opioid use was significantly associated with a 9% increase in mean costs. This amounted to an average of \$2341 in excess hospital costs attributed to preoperative opioid use (\$26,604 vs \$24,263; Fig. 1A). Opioid users also had 12% longer LOS (5.9 vs 5.2; Fig. 1B), 1.3-fold higher complication rates (20% vs 16%; Fig. 1C), 1.2-fold higher prevalence of nonhome discharge (13% vs 11%, though not statistically significant; Fig. 1C), and 1.5-fold higher readmission rates (10% vs 6%; Fig. 1C) after risk adjustment. The increased morbidity in opioid users was driven largely by infectious complications (surgical site infection and sepsis; Table 3).

Opioids Complicate Pain Control, Impair Gastrointestinal Function, and May Increase Infection Risk

This study is one of the first to investigate the effects of preoperative opioid use in patients undergoing abdominopelvic surgery. Our results suggest that preoperative opioid use is common in this population, with 20% of patients in our sample using opioids preoperatively. For perspective, the prevalence of opioid use in the United States general population has been estimated at 5%.¹⁹ Recent studies in bariatric surgery and kidney transplantation have reported prevalence of preoperative opioid use ranging from 8% to 29%.^{20–22} Given the limitations in our ability to characterize duration of use and reason for opioid use, 20% is likely an overestimate compared with the true prevalence of chronic opioid use preoperatively. Opioid users were sicker than opioid-naïve patients in this sample; these observed differences were expected given the authors' clinical experience with these patients, and such differences have been reported in other studies.^{21–24} The higher costs we observed in opioid users are likely explained in part by their longer LOS, higher rates of postoperative complications, and higher readmission rates. However, even after adjusting for complications in the multivariate models (in secondary

analyses not reported here), opioid use was still significantly associated with costs and LOS. Poor pain control is likely a driver of increased LOS in preoperative opioid users due to opioid tolerance and possibly opioid-induced hyperalgesia. Perioperative pain scores were unavailable for our sample, but our future work will further investigate the relationship between preoperative opioid use, perioperative pain, and healthcare utilization. Another possible driver of increased costs and LOS is impaired gastrointestinal function. Postoperative opioid use—which is higher in preoperative opioid users—is associated with increased rates of ileus, and a recent study of colectomy and cholecystectomy showed increased costs, LOS, and readmission associated with concomitant postoperative opioid use and ileus.²⁵ The increased rate of infectious complications that we observed in opioid users (Table 3) may represent opioid-induced immune suppression. Animal models and clinical studies suggest that opioids have immunosuppressive effects contributing to infection risk.^{26–29} Lastly, knowledge of preoperative opioid use likely impacts processes of perioperative care, which could contribute to increased costs and LOS. However, this point that opioid users may demand additional resource intensive perioperative care further supports our argument that perioperative intervention is needed to optimize care of these patients.

Preoperative Opioid Use Is a Novel Target for Surgical Quality Improvement

This study has potential implications for the quality and value of surgical care. Opioid use represents one of the most important public health challenges in the United States today. In the state of Michigan in particular, hydrocodone is the most prescribed drug, accounting for 32% of all prescriptions written in 2012.³⁰ Rates of opioid use in Michigan are among the highest in the nation. In 2012, the rate of opioid prescriptions in Michigan was 107 prescriptions per 100 people (30% higher than the national average of 82.5 prescriptions per 100 people).³¹ This study addresses the implications of the opioid epidemic on surgical care. Our findings suggest that opioid use is common before major abdominopelvic surgery and represents a novel target for surgical quality improvement. Assuming a

prevalence of 21% as we identified at our institution, we estimate that 80,000 opioid users undergo abdominal surgery annually in Michigan. Assuming \$2300 in excess costs per opioid user, we estimate that the financial impact of preoperative opioid use in this population is \$184 million dollars annually in Michigan alone, even after adjusting for other drivers of increased cost. This back-of-the-envelope math emphasizes the financial implications of opioid use in abdominal surgery.

These results argue the potential cost-effectiveness of intervention in this unique patient population. Opioid use is a potentially modifiable risk factor, and major surgery can provide powerful leverage to improve health behavior. Our institution has implemented a preoperative program to optimize high-risk patients for surgery.^{32,33} Using the infrastructure of this prehabilitation program, we plan to counsel patients on the risks of opioids and to attempt to wean opioids preoperatively. We do not know if the latter will be possible, but there are no good data to support the efficacy of long-term opioid use for chronic pain.^{5,34} As such, weaning patients down or off of opioids or replacing opioids with alternative analgesics preoperatively may be possible. Additionally, our current work with preoperative smoking cessation and exercise intervention suggests that the preoperative period is uniquely well-suited for transformational behavioral change.^{32,33} Perioperative care of opioid-tolerant patients is complex, and we aim to use the quality improvement platform of the MSQC to develop best practices for surgical care in this high-risk patient population of opioid users. Lastly, although this study focuses on preoperative opioid use, postoperative opioid use is also an important area of research and policy need. The CDC recently released guidelines for opioid prescribing for chronic pain in the outpatient setting.³⁵ However, guidelines are needed for perioperative pain management for patients both with and without chronic pain.

Limitations and Strengths

This study has limitations. As a single-center study, these findings may not be generalizable across all centers and geographic regions. Opioid use was identified retrospectively from the electronic medical record. As such, we were unable to obtain reliable estimates of dose, schedule, and duration of use. Such granularity requires pharmaceutical claims or prospectively collected data, which were not available for this study. Therefore, we chose to define preoperative opioid use with a binary variable for objectivity. Given these limitations, we took steps to exclude patients who received opioids acutely in the hospital preoperatively. Nevertheless, it is still possible that some opioid users in our study were using opioids over a shorter time period for pain related to their surgical disease. One may argue that the effect of opioid use that we identified is a mere proxy for disease severity; however, this is less likely given that we adjusted for numerous markers of disease severity, functional status, and case complexity. Importantly, it is not possible with most current medical records or claims datasets to truly identify the reason for a patient's opioid use given the prevalence of opioid use in practice; our future work aims to elucidate this through prospective collection of patient-reported opioid histories. Given the detailed methodology for record review, our identification of opioid users was assumed to be accurate. Our outcomes were limited to costs and events that occurred within our own healthcare system. It is possible that complications occurred and were managed outside of our healthcare system. It is also possible that patients were readmitted to hospitals outside of our healthcare system. We were unable to identify these events or capture their associated costs. Further, for patients who were admitted to nursing or rehabilitation facilities outside of our healthcare system, these costs were not captured. Costs and outcomes from outside of

our institution would, however, be expected to be distributed somewhat evenly between opioid users and the opioid-naïve cohort.

Strengths of our data included the clear definitions of covariates and outcome measures, and also the granularity of preoperative risk factors that are prospectively recorded and audited in standardized fashion by the MSQC. We were therefore able to adjust for a number of risk factors that are not recorded in larger administrative databases. Further, postoperative complications are prospectively recorded by the MSQC clinicians with a level of detail unattainable through administrative databases. Data accuracy is ensured by rigorous training of MSQC staff and performance of data audits.

CONCLUSIONS

In summary, opioid use was common before abdominopelvic surgery and was independently associated with increased healthcare utilization and morbidity. Preoperative opioids represent a potentially modifiable risk factor and a novel target for surgical quality improvement. Addressing the perioperative needs of opioid users has potential to improve the quality and value of surgical care.

REFERENCES

1. Boudreau D, Von Korff M, Rutter CM, et al. Trends in long-term opioid therapy for chronic non-cancer pain. *Pharmacoeconomics Drug Saf*. 2009;18:1166–1175.
2. Centers for Disease Control and Prevention. CDC grand rounds: prescription drug overdoses - a U.S. Epidemic. *MMWR Morb Mortal Wkly Rep*. 2012;61:10–13.
3. Herper M. America's most popular drugs [Forbes]. May 11, 2010. Available at: <http://www.forbes.com/2010/05/11/narcotic-painkiller-vicodin-business-healthcare-popular-drugs.html>. Accessed December 26, 2014.
4. Ballantyne JC, Mao J. Opioid therapy for chronic pain. *N Engl J Med*. 2003;349:1943–1953.
5. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a national institutes of health pathways to prevention workshop. *Ann Intern Med*. 2015;162:276–286.
6. Drugs for pain. *Treat Guidelines Med Lett*. 2007;5:23–32.
7. Ekholm O, Kurita GP, Hojsted J, et al. Chronic pain, opioid prescriptions, and mortality in Denmark: a population-based cohort study. *Pain*. 2014;155:2486–2490.
8. Pivec R, Issa K, Naziri Q, et al. Opioid use prior to total hip arthroplasty leads to worse clinical outcomes. *Int Orthop*. 2014;38:1159–1165.
9. Zywił MG, Stroh DA, Lee SY, et al. Chronic opioid use prior to total knee arthroplasty. *J Bone Joint Surg Am*. 2011;93:1988–1993.
10. Lee D, Armaghani S, Archer KR, et al. Preoperative opioid use as a predictor of adverse postoperative self-reported outcomes in patients undergoing spine surgery. *J Bone Joint Surg Am*. 2014;96:e89.
11. Campbell DA Jr, Kubus JJ, Henke PK, et al. The Michigan surgical quality collaborative: a legacy of Shukri Khuri. *Am J Surg*. 2009;198:S49–55.
12. Campbell DA Jr, Englesbe MJ, Kubus JJ, et al. Accelerating the pace of surgical quality improvement: the power of hospital collaboration. *Arch Surg*. 2010;145:985–991.
13. Ghaferi AA, Birkmeyer JD, Dimick JB. Variation in hospital mortality associated with inpatient surgery. *N Engl J Med*. 2009;361:1368–1375.
14. Shih T, Cole AI, Al-Attar PM, et al. Reliability of surgeon-specific reporting of complications after colectomy. *Ann Surg*. 2015;261:920–925.
15. Duan N. Smearing estimate: a nonparametric retransformation method. *J Am Stat Assoc*. 1983;78:605–610.
16. Rosenman M, Madsen K, Hui S, et al. Modeling administrative outcomes in fever and neutropenia: clinical variables significantly influence length of stay and hospital charges. *J Pediatr Hematol Oncol*. 2002;24:263–268.
17. Hilbe JM. Negative binomial regression. In: Hilbe JM, editor. *Modeling Count Data*. Cambridge: Cambridge Univ Press; 2014:126–160.
18. Davenport DL, Henderson WG, Khuri SF, et al. Preoperative risk factors and surgical complexity are more predictive of costs than postoperative complications: a case study using the national surgical quality improvement program (NSQIP) database. *Ann Surg*. 2005;242:463–468.
19. Kelly JP, Cook SF, Kaufman DW, et al. Prevalence and characteristics of opioid use in the US adult population. *Pain*. 2008;138:507–513.

20. Raebel MA, Newcomer SR, Reifler LM, et al. Chronic use of opioid medications before and after bariatric surgery. *JAMA*. 2013;310:1369–1376.
21. Barrantes F, Luan FL, Kommareddi M, et al. A history of chronic opioid usage prior to kidney transplantation may be associated with increased mortality risk. *Kidney Int*. 2013;84:390–396.
22. Lentine KL, Yuan H, Tuttle-Newhall JE, et al. Quantifying prognostic impact of prescription opioid use before kidney transplantation through linked registry and pharmaceutical claims data. *Transplantation*. 2015;99:187–196.
23. Campbell G, Nielsen S, Bruno R, et al. The Pain and Opioids IN Treatment study: characteristics of a cohort using opioids to manage chronic non-cancer pain. *Pain*. 2015;156:231–242.
24. Mellbye A, Karlstad O, Skurtveit S, et al. Co-morbidity in persistent opioid users with chronic non-malignant pain in Norway. *Eur J Pain*. 2014;18:1083–1093.
25. Gan TJ, Robinson SB, Oderda GM, et al. Impact of postsurgical opioid use and ileus on economic outcomes in gastrointestinal surgeries. *Curr Med Res Opin*. 2015;31:677–686.
26. Wang J, Barke RA, Charboneau R, et al. Morphine impairs host innate immune response and increases susceptibility to *Streptococcus pneumoniae* lung infection. *J Immunol*. 2005;174:426–434.
27. Wang J, Barke RA, Charboneau R, et al. Morphine induces defects in early response of alveolar macrophages to *Streptococcus pneumoniae* by modulating TLR9-NF-kappa B signaling. *J Immunol*. 2008;180:3594–3600.
28. Mora AL, Salazar M, Pablo-Caeiro J, et al. Moderate to high use of opioid analgesics are associated with an increased risk of *Clostridium difficile* infection. *Am J Med Sci*. 2012;343:277–280.
29. Oppeltz RF, Holloway TL, Covington CJ, et al. The contribution of opiate analgesics to the development of infectious complications in trauma patients. *Int J Burns Trauma*. 2015;5:56–65.
30. State of Michigan Department of Licensing and Regulatory Affairs. Michigan automated prescription system drug utilization report 2012. http://www.michigan.gov/lara/0,4601,7-154-72600_72603_55478_55484--,00.html. Accessed December 26, 2014.
31. Paulozzi LJ, Mack KA, Hockenberry JM. Variation among states in prescribing of opioid pain relievers and benzodiazepines—United States, 2012. *J Safety Res*. 2014;51:125–129.
32. Friedman J, Lussiez A, Sullivan J, et al. Implications of sarcopenia in major surgery. *Nutr Clin Pract*. 2015;30:175–179.
33. Englesbe MJ, Lussiez AD, Friedman JF, et al. Starting a surgical home. *Ann Surg*. 2015;262:901–903.
34. Deyo RA, Von Korff M, Duhrkoop D. Opioids for low back pain. *BMJ*. 2015;350:g6380.
35. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain: United States, 2016. *MMWR Recomm Rep*. 2016;65:1–49.