ANESTHESIOLOGY

Surgeon Variation in Perioperative Opioid Prescribing and Medium- or Long-term Opioid Utilization after Total Knee Arthroplasty: A Cross-sectional Analysis

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EDITOR'S PERSPECTIVE

What We Already Know about This Topic

- National efforts to rationalize postoperative opioid prescribing are widespread
- It remains unclear whether early perioperative surgeon prescribing behaviors are associated with long-term opioid utilization

What This Article Tells Us That Is New

- Among 604,093 Medicare beneficiaries undergoing total knee arthroplasty between 2011 and 2016, patients receiving treatment from surgeons in the top quartile of opioid prescribing ("high-intensity") received 36.1 oral morphine milliequivalent per day in the first week after surgery, while the remaining patients received only 17.3 oral morphine milliequivalent per day
- Receiving treatment from a high-intensity opioid-prescribing surgeon was associated with slightly higher opioid utilization between postoperative days 8 and 90 (+2.4 [11.4 *vs.* 9.0] oral morphine milliequivalent per day) and slightly lower opioid utilization between postoperative days 91 and 365 (–1.0 [2.8 *vs.* 3.8] oral morphine milliequivalent per day)
- These differences were clinically small although statistically significant
- Among Medicare beneficiaries undergoing total knee arthroplasty, variations in surgeon early postoperative prescribing is not associated with meaningful differences in medium- or long-term postoperative opioid utilization

ABSTRACT

Background: Whether a particular surgeon's opioid prescribing behavior is associated with prolonged postoperative opioid use is unknown. This study tested the hypothesis that the patients of surgeons with a higher propensity to prescribe opioids are more likely to utilize opioids long-term postoperatively.

Methods: The study identified 612,378 Medicare fee-for-service patients undergoing total knee arthroplasty between January 1, 2011, and December 31, 2016. "High-intensity" surgeons were defined as those whose patients were, on average, in the upper quartile of opioid utilization in the immediate perioperative period (preoperative day 7 to postoperative day 7). The study then estimated whether patients of high-intensity surgeons had higher opioid utilization in the midterm (postoperative days 8 to 90) and long-term (postoperative days 91 to 365), utilizing an instrumental variable approach to minimize confounding from unobservable factors.

Results: In the final sample of 604,093 patients, the average age was 74 yr (SD 5), and there were 413,121 (68.4%) females. A total of 180,926 patients (30%) were treated by high-intensity surgeons. On average, patients receiving treatment from a high-intensity surgeon received 36.1 (SD 35.0) oral morphine equivalent (morphine milligram equivalents) per day during the immediate perioperative period compared to 17.3 morphine milligram equivalents (SD 23.1) per day for all other patients (+18.9 morphine milligram equivalents per day difference; 95% CI, 18.7 to 19.0; $P < 0.001$). After adjusting for confounders, receiving treatment from a high-intensity surgeon was associated with higher opioid utilization in the midterm opioid postoperative period (+2.4 morphine milligram equivalents per day difference; 95% CI, 1.7 to 3.2; $P < 0.001$ [11.4 morphine milligram equivalents per day *vs.* 9.0]) and lower opioid utilization in the long-term postoperative period (–1.0 morphine milligram equivalents per day difference; 95% CI, –1.4 to –0.6; $P < 0.001$ [2.8 morphine milligram equivalents per day *vs.* 3.8]). While statistically significant, these differences are clinically small.

Conclusions: Among Medicare fee-for-service patients undergoing total knee arthroplasty, surgeon-level variation in opioid utilization in the immediate perioperative period was associated with statistically significant but clinically insignificant differences in opioid utilization in the medium- and long-term postoperative periods.

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Perioperative use may play a role in the United States opioid epidemic, with numerous studies demonstrating that surgery places patients at elevated for long-term persistent opioid use.[1–4] In the United States, the patient's surgeon will typically write prescriptions for any outpatient opioids associated with the surgery, although other physicians, such as the patient's primary care physician and emergency room physicians, may write additional prescriptions for emergency or longer-term opioid prescriptions.

This article is featured in "This Month in Anesthesiology," page A1. This article is accompanied by an editorial on p. 131. This article has a related Infographic on p. A17. Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are available in both the HTML and PDF versions of this article. Links to the digital files are provided in the HTML text of this article on the Journal's Web site (www.anesthesiology.org). This article has an audio podcast. This article has a visual abstract available in the online version.

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While anesthesiologists typically do not write prescriptions for outpatient opioids, they can play an important role by utilizing techniques (*i.e.*, nerve blocks) aimed at reducing opioid use[5] and by working with surgeons to reduce opioid prescribing.

The extent to which a particular surgeon's prescribing behavior is associated with an increased risk of chronic opioid use after surgery has not been fully explored. Two studies[6,7] have shown that emergency room patients treated by high-intensity opioid prescribers had 10 to 30% higher rates of long-term opioid use after their emergency room visit, but to date, there have been no studies examining whether the same risks hold for perioperative patients. A large retrospective study found that increased duration of postoperative opioid use was a significant risk factor for subsequent opioid misuse,[8] with an additional week of postoperative opioid use resulting in a 20% relative increase of opioid misuse, dependence, or overdose. However, this study did not examine other outcomes such as actual opioid utilization, and it also did not examine the association between a given surgeon's behavior and opioid-related outcomes.

Given this suggestive evidence that higher opioid use shortly after surgery may be associated with higher long-term postoperative opioid use, a reasonable hypothesis that has not been fully examined is the extent to which patients who are taken care of by surgeons with a higher propensity for opioid prescribing are more likely to use opioids longer postoperatively. Understanding the extent to which surgeon-level prescribing behaviors are associated with longer-term postoperative opioid utilization has important implications for clinical practice. For example, if patients treated by surgeons who are more likely to prescribe opioids are indeed at higher risk for prolonged postoperative opioid use, this would provide additional support for clinical guidelines and laws aimed at standardizing the quantity of opioids that can be prescribed after surgery.

In this study, we utilized administrative claims data for Medicare fee-for-service patients to characterize variation in perioperative opioid utilization among orthopedic surgeons for patients undergoing total knee arthroplasty. We then tested the hypothesis that patients who received care from "high-intensity" surgeons, defined as surgeons whose patients were in the upper quartile of opioid utilization in the immediate perioperative period (7 days before surgery to 7 days after surgery), were more likely to utilize opioids in the medium (8 to 90 days after surgery) and long-term (91 to 365 days after surgery) postoperative periods compared to patients who did not receive treatment from high-intensity surgeons.

Materials and Methods

Data

Our data consisted of healthcare claims for Medicare fee-for-service patients submitted between January 1, 2010, and December 31, 2017. These data include demographic information (*i.e.*, race and sex) and information about the utilization of medical services, such as diagnosis codes (International Classification of Diseases, Ninth or Tenth Revision) and procedure codes (Current Procedural Terminology). The data also contain information about drug utilization, including drug name, fill date, quantity dispensed, and number of days supplied.[9] This study follows the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines and received approval from the Institutional Review Board at Stanford University, which also issued a waiver of consent. A data analysis and statistical plan was agreed to and recorded in the investigators' files before the data were analyzed.

Sample

We identified Medicare patients ages 65 and older who underwent total knee arthroplasty between January 1, 2011, and December 31, 2016, by searching for claims submitted by an orthopedic surgeon with a Current Procedural Terminology code of 27447. Using this search, a study sample was created consisting of patients who were continuously enrolled for the time period spanning 1 yr before and 1 yr after the surgery date and for whom the surgeon's claim could be matched to a corresponding hospital claim that (1) had an appropriate International Classification of Diseases, Ninth or Tenth Revision procedure code and (2) had an admission-to-discharge time range covering the surgery date.

From this initial sample of 732,919 patients, we then applied the following exclusion criteria. First, patients treated by orthopedic surgeons who performed fewer than 25 total knee arthroplasties during the study period were excluded (n = 58,467). Second, we excluded patients in the top 1% of opioid utilization, measured in oral morphine milligram equivalent (see the Outcomes section for further details of the construction of this measure) to avoid extreme outliers and potential data errors (n = 15,645). Third, we excluded patients with a cancer diagnosis (n = 46,429), resulting in a sample of 604,093 patients who were treated by 7,141 surgeons. This full sample was used to classify surgeons as high or low intensity based on their patients' opioid utilization in the immediate postoperative period (7 days before to 7 days after surgery) using the methods described below. From this full sample, 8,285 patients were missing a zip code of

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residence and therefore were excluded from the remaining statistical analyses. A flowchart of sample construction is provided in the supplement (Supplemental Digital Content, fig. 1, http://links.lww.com/ALN/C856). Since our study included all observations meeting the inclusion and exclusion criteria, no statistical power calculation was conducted before the study.

Outcomes

Primary outcomes consisted of opioid utilization during the midterm postoperative period (postoperative days 8 to 90) and the long-term postoperative period (postoperative days 91 to 365) measured in oral morphine equivalent (morphine milligram equivalents). Prescriptions for fentanyl (patch or oral), hydrocodone, hydromorphone (oral), methadone, morphine, oxycodone, tramadol, and oxymorphone were identified during the study period. Prescriptions containing hydrocodone in cough/cold formulation and analgesic preparations containing codeine were excluded. For each prescription, morphine milligram equivalents were calculated by multiplying an opioid-specific conversion factor by the drug dose and quantity supplied.[10] The total morphine milligram equivalents during the relevant periods were calculated and then divided by the number of days in each period (275 days for long-term postoperative period and 83 days for midterm postoperative period) to obtain the average daily morphine milligram equivalents during the period.

Exposure

The primary exposure of interest was whether a total knee arthroplasty was performed by a high-intensity or non–high-intensity surgeon, based on opioid prescriptions filled in the immediate perioperative period (7 days before to 7 days after surgery). We chose this time window because most patients who fill their initial postoperative opioid prescription do so during this time, including some patients who fill postoperative prescriptions before the day of surgery.[4]

Since opioid utilization may be based on observable patient characteristics (*e.g.*, age and comorbidities), we first used a regression analysis to identify the extent to which a given surgeon's patients were more likely to utilize opioids in the immediate perioperative period after adjusting for patient factors. To do so, we performed a patient-level multivariable linear regression in which the dependent variable was average daily opioid utilization (in morphine milligram equivalents) during the immediate perioperative period and the independent variables were patient characteristics (age, sex, race, Medicare–Medicaid dual eligibility, and the medical comorbidities described below), year fixed effects, and a fixed effect for each surgeon. In this regression, the surgeon fixed effect can be interpreted as the extent to which a given surgeon's patients deviate from the overall average opioid utilization in the immediate perioperative period, after adjusting for patient factors. For example, a fixed effect of 5 would mean that even after adjusting for observable patient factors, a given surgeon's patients tended, on average, to utilize 5 morphine milligram equivalents per day more than average during the immediate perioperative period.

We *a priori* categorized surgeons into quartiles based on the surgeon fixed effects and defined those in the upper quartile as high-intensity opioid surgeons and the remaining group as non–high-intensity. It is important to highlight that our exposure is not based on the actual morphine milligram equivalents a patient utilized during the immediate perioperative period; rather, the exposure is essentially based on the *average* morphine milligram equivalents utilized across a given surgeon's patient population, after adjusting for potential variables that could influence opioid utilization (*i.e.*, medical comorbidities).

Other Covariates

Our analysis adjusted for several potential confounders including the following demographic factors: age, sex, race or ethnic group, and Medicare–Medicaid dual eligibility. We also defined a dichotomous opioid-naïve group based on whether a patient filled an opioid prescription in the 12 months before surgery. In addition, we identified the presence of Elixhauser comorbidities.[11]

Statistical Analyses

We first compared patient demographics, Elixhauser comorbidities, and primary outcomes between patients treated by surgeons who were high-intensity *versus* non–high-intensity surgeons. We calculated means and standard deviations for both groups, and two-sample, unpaired tailed *t* tests for continuous variables (*e.g.*, age) and chi-square tests for discrete variables (*e.g.*, comorbidities) were used to assess statistical differences between the groups.

A simple comparison of outcomes between patients who received care from high-intensity *versus* non–high-intensity opioid surgeons may be confounded if high-intensity surgeons are more likely to treat patients who are at higher risk for higher opioid utilization during the mid- and long-term postoperative periods. To address this issue, we adjusted for a robust set of potential confounders, including patient demographics (age, race, sex, Medicare–Medicaid dual enrollment), comorbidities (set of indicator variables for comorbidities comprising the Elixhauser index; shown in table 1), opioid naïve (yes or no), and year and state fixed effects. Standard errors were clustered at the hospital level.

To address the possibility of residual confounding—namely that unobservable patient factors may be correlated with both the likelihood of receiving surgery from a high-intensity *versus* non–high-intensity surgeon and higher opioid utilization during the mid- and long-term postoperative periods—we also conducted an instrumental variable analysis. This approach identifies the causal association

Table 1. Characteristics of the Study Population

Characteristics	Patients Treated by High-intensity Opioid-prescribing Surgeons (N = 180,926)*	Patients Treated by Non–high-intensity Opioid-prescribing Surgeons (N = 423,167)*	*P* Value	Standardized Difference
Age, mean (SD), yr	74 (6)	74 (6)	< 0.001	0.053
Age category, n (%)			< 0.001	0.054
65 to 69 yr	25.7	24.3		
70 to 74 yr	32.8	31.8		
75 to 79 yr	23.7	24.2		
80 to 84 yr	12.5	13.8		
≥ 85 yr	5.3	5.9		
Female, n (%)	122,110 (67.5%)	291,011 (68.8%)	< 0.001	0.027
Race, n (%)			< 0.001	0.021
Non-Hispanic white	160,019 (88.4%)	372,884 (88.1%)		
Black	8,424 (4.7%)	18,940 (4.5%)		
Other	12,483 (6.9%)	31,343 (7.4%)		
Medicare–Medicaid dual eligibility, n (%)	16,749 (9.3%)	48,681 (11.5%)	< 0.001	0.074
Opioid naïve, n (%)†	76,308 (42.2%)	185,045 (43.7%)	< 0.001	0.031
Number of Elixhauser comorbidities (SD)	3.4 (2.1)	3.4 (2.1)	< 0.001	0.044
Selected Elixhauser comorbidities, n (%)				
Congestive heart failure	12,592 (7.0%)	32,394 (7.7%)	< 0.001	0.027
Peripheral vascular disease	18,828 (10.4%)	48,869 (11.6%)	< 0.001	0.037
Hypertension	149,332 (82.5%)	357,930 (84.6%)	< 0.001	0.055
Chronic pulmonary disease	33,650 (18.6%)	82,626 (19.5%)	< 0.001	0.024
Diabetes without chronic complications	47,836 (26.4%)	121,583 (28.7%)	< 0.001	0.051
Diabetes with chronic complications	15,252 (8.4%)	38,613 (9.1%)	< 0.001	0.025
Renal failure	19,490 (10.8%)	45,463 (10.7%)	0.740	0.001
Liver disease	3,797 (2.1%)	8,730 (2.1%)	0.373	0.003
Obesity	53,865 (29.8%)	121,652 (28.8%)	< 0.001	0.023
Alcohol abuse	2,022 (1.1%)	4,454 (1.1%)	0.025	0.006
Drug abuse	1,611 (0.9%)	3,350 (0.8%)	< 0.001	0.011
Psychoses	6,299 (3.5%)	14,771 (3.5%)	0.861	< 0.001
Depression	33,244 (18.4%)	74,564 (17.6%)	< 0.001	0.020
Valvular disease	24,501 (13.5%)	60,005 (14.2%)	< 0.001	0.018
Pulmonary circulation disorders	5,611 (3.1%)	14,224 (3.4%)	< 0.001	0.015
Paralysis	1,041 (0.6%)	2,520 (0.6%)	0.349	0.003
Other neurologic disorders	15,095 (8.3%)	36,280 (8.6%)	0.003	0.009
Hypothyroidism	49,027 (27.1%)	112,120 (26.5%)	0.315	0.014
Chronic peptic ulcer disease	741 (0.4%)	1,749 (0.4%)	0.896	< 0.001

(*Continued*)

Table 1. (Continued)

Characteristics	Patients Treated by High-intensity Opioid-prescribing Surgeons (N = 180,926)*	Patients Treated by Non–high-intensity Opioid-prescribing Surgeons (N = 423,167)*	*P* Value	Standardized Difference
HIV and AIDS	65 (0.0004%)	151 (0.0004%)	0.964	< 0.001
Rheumatoid arthritis/collagen vascular diseases	16,246 (9.0%)	38,353 (9.1%)	0.297	0.003
Coagulation deficiency	8,123 (4.5%)	19,957 (4.7%)	< 0.001	0.011
Weight loss	3,473 (1.9%)	8,961 (2.1%)	< 0.001	0.014
Fluid and electrolyte disorders	29,092 (16.1%)	69,893 (16.5%)	< 0.001	0.012
Blood loss anemia	3,232 (1.8%)	9,486 (2.2%)	< 0.001	0.032
Deficiency anemias	41,149 (22.7%)	102,447 (24.2%)	< 0.001	0.035
Opioid utilization, morphine milligram equivalents per day, mean (SD)				
Preoperative opioid utilization (8 to 365 days before surgery)	4.2 (11.2)	3.7 (10.2)	< 0.001	0.046
Midterm postoperative opioid utilization (8 to 90 days after surgery)	10.8 (14.3)	9.2 (12.3)	< 0.001	0.119
Long-term postoperative opioid utilization (91 to 365 days after surgery)	3.7 (9.7)	3.4 (9.0)	< 0.001	0.040

*High-intensity surgeons were defined as the top quartile of surgeon fixed effects based on multivariate regressions on opioid utilization within a window of 7 days before and 7 days after the surgery date. Non—-high-intensity surgeons were those in the bottom, second, and third quartile of surgeon fixed effects. †"Opioid naïve" is defined as no opioid utilization in the 12 months before surgery.

between a treatment and an outcome through the use of an instrument, which is any variable that (1) influences the independent variable of interest (in this case, whether the patient received care from a high-intensity surgeon) but (2) is otherwise independent of the outcomes of interest. In effect, the instrument is used to quasirandomize patients to treatment and control arms of a study (in this case, whether a patient received care from a high-intensity *vs.* non–high-intensity surgeon). Following previous studies,[12–14] we used distance to the nearest high-intensity surgeon as an instrument. This approach mirrors several other studies that have used distance as an instrumental variable.[15,16] For example, one study[17] used distance to the nearest hospital with regional anesthesia capabilities to examine the association between regional anesthesia and outcomes after hip fracture. The underlying assumption of this approach is that distance to a high-intensity surgeon is unlikely to be correlated with a patient's risk for higher opioid utilization during the mid- and long-term postoperative periods.

To implement our instrumental variable approach, we first calculated the distance between the patient and the nearest high-intensity surgeon based on (1) the zip code of the patient's residence and (2) the zip codes for all the hospitals utilized by high-intensity surgeons. We then implemented our instrumental variable approach using a multivariable two-stage least-squares linear probability model. The regression model included adjustments for potential confounders (*e.g.*, patient sex, clinical comorbidities) previously described and used the distance to the nearest high-intensity surgeon as an instrument for whether the patient received care from a high-intensity surgeon. Further details of our instrumental variable approach, such as the methods used to verify the validity of the approach, are provided in the technical appendix found in the Supplemental Digital Content (http://links.lww.com/ALN/C856). All statistical analyses were performed using Stata 14.0 (Stata Corporation, USA).

Subgroup Analyses

We conducted a preplanned subgroup analysis on patients who were predicted to be at high-risk for higher opioid utilization during the long-term postoperative period. To define this population, we performed a multivariable linear regression in which the dependent variable was opioid utilization in the long-term postoperative period, and the independent variables were the patient characteristics (*e.g.*, demographics and comorbidities) shown in table 1. The results of this model were used to obtain the predicted opioid utilization in the long-term postoperative period for each patient, and high-risk patients were defined as those in the upper quartile of predicted utilization during this period. The instrumental variable approach used for the main analysis was then repeated on this subgroup.

Table 2. Subgroup Analysis of Opioid Utilization in the Year after Surgery among Patients at High Predicted Risk of Long-term Opioid Utilization

	Unadjusted Morphine Milligram Equivalents (95% CI)				Morphine Milligram Equivalents (Instrumental Variable Analysis) (95% CI)			
Outcomes	**High-intensity Surgeons (a)**	**Non–high-intensity Surgeons (b)**	**Difference (a – b)**	***P* Value**	**High-intensity Surgeons (c)**	**Non–high-intensity Surgeons (d)**	**Difference (c – d)**	***P* Value**
Midterm opioid utilization (8 to 90 days after surgery)	16.8 (16.5 to 17.1)	14.3 (14.1 to 14.5)	2.5	< 0.001	17.6 (16.6 to 18.6)	13.9 (13.5 to 14.1)	3.7	< 0.001
Long-term opioid utilization (91 to 365 days after surgery)	8.6 (8.4 to 8.8)	7.8 (7.6 to 7.9)	0.8	< 0.001	7.3 (6.5 to 8.1)	8.3 (7.9 to 8.6)	–1	0.080

The predicted risk of opioid utilization in the year after surgery was estimated from a multivariable linear regression of long-term opioid utilization as a function of patient demographics and comorbidities. Based on this regression, patients who were in the top quartile of predicted long-term opioid utilization were defined as being at higher risk for opioid use. Regression analyses of the relationship between surgeons' intensity of perioperative opioid utilization and mid- or long-term utilization were then performed in this subgroup of patients with high predicted risk of opioid utilization in the year after surgery. An instrumental variable analysis was then used to estimate the association between high-intensity prescribing and mid- and long-term opioid utilization. The results of this analysis are presented in the columns labeled "Morphine Milligram Equivalents (Instrumental Variable Analysis)." 95% CI intervals are shown in parentheses and were calculated using standard errors that are adjusted for clustering at the hospital level.

Sensitivity Analyses

We performed several preplanned sensitivity analyses to examine the robustness of our results. First, we replicated the main analyses by focusing on the comparison between patients treated by high-intensity surgeons or low-intensity surgeons (upper quartile *vs.* lower quartile of surgeon fixed effects) by excluding patients in the middle two quartiles. Second, we considered an alternative outcome—incidence of chronic opioid utilization, defined as (1) having filled 10 or more prescriptions or (2) having more than 120 days' supply during the postoperative days 91 to 365 within the first postsurgical year.

Several *post hoc* sensitivity analyses were performed as a result of the manuscript review process. First, in our baseline analysis, high-intensity surgeons were defined as those in the upper quartile based on the surgeon fixed effects previously described; we performed two sensitivity analyses in which high-intensity surgeons were defined as the top 5th and the top 10th percentile of surgeons based on these surgeon fixed effects. Second, the immediate perioperative period was defined as preoperative day 7 to postoperative day 7 in our baseline analysis; we performed a sensitivity analysis in which this period was redefined as postoperative days 0 through 7. Third, we performed a sensitivity analysis in which we adjusted for whether the patient lived in a rural or urban area, using rural–urban commuting area codes[18] to define rural or urban areas, based on the patient's zip code. Fourth, we performed a sensitivity analysis in which we excluded both (1) patients who received a bilateral total knee arthroplasty and (2) patients who received a second total knee arthroplasty within 365 days of their initial surgery. Fifth, we performed a weighted regression in which the weights were the number of patients treated by each surgeon. Sixth, we performed an analysis where we adjusted for additional measures of preoperative opioid utilization (number of prescriptions, number of days supplied, and average daily morphine milligram equivalents during preoperative days 8 to 365). Seventh, we performed an analysis where we adjusted for the use of nerve blockade. The use of a nerve blockade was identified by searching for claims that were: (1) submitted on the same date as the total knee arthroplasty itself and (2) corresponded to the use of a central or peripheral nerve block.[19]

Results

The study sample included 604,093 Medicare fee-for-service beneficiaries, with an average age of 74 yr (SD 6); there were 413,121 (68.4%) females. A total of 180,926 patients (30%) were treated by high-intensity surgeons, and 423,167 patients (70%) were treated by non–high-intensity surgeons. The number of patients treated by high-intensity surgeons is slightly larger than 23% of the total sample because these surgeons tended to see more patients on average (230 patients per surgeon) compared to surgeons who were not high-intensity (167 patients per surgeon, difference 63 patients per surgeon; 95% CI, 62 to 64; $P < 0.001$ for the difference). Compared to their counterparts, patients treated by a high-intensity surgeon were slightly less likely to be female (67.5% *vs.* 68.8%; $P < 0.001$) and to be dually eligible for Medicare and Medicaid (9.3% *vs.* 11.5%; $P < 0.001$; table 1). Patients treated by high-intensity surgeons were also slightly younger (74.0 *vs.* 74.3 yr; $P < 0.001$) and more likely to be non-Hispanic white (88.4% *vs.* 88.1%; $P < 0.001$). They also had slightly fewer comorbidities (Elixhauser index 3.3 *vs.* 3.4; $P < 0.001$) and slightly higher opioid utilization in the year before surgery (4.2 *vs.* 3.7 morphine milligram equivalents per day; $P < 0.001$). However, while statistically significant, the standardized mean difference between the two groups for most variables was less than 0.1, which generally indicates a difference of small magnitude.[20] Exceptions included opioid utilization in the perioperative period (standardized difference, 0.63) and during postoperative days 8 to 90 (standardized difference, 0.12).

After using multivariable regression to adjust for patient characteristics and time trends, there was significant variation in opioid utilization during the immediate perioperative period (7 days before surgery to 7 days after surgery). Figure 1 shows, for each surgeon in our sample, the extent to which their patients on average utilized more (or less) opioid in the immediate perioperative period compared to the median surgeon. For example, the upper quartile of figure 1 was 7 morphine milligram equivalents per day, indicating that after multivariable adjustment, patients for the upper quartile of utilized at least 7 more morphine milligram equivalents per day compared to the median surgeon during the immediate perioperative period. Similarly, the bottom quartile was −5.7, meaning that the patients of the bottom 25% of surgeons utilized 5.7 or less morphine milligram equivalents per day compared to the median surgeon's patients.

On average, patients receiving treatment from a high-intensity surgeon utilized 36.1 morphine milligram equivalents per day during the immediate perioperative period (95% CI, 36 to 36.3) compared to 17.3 morphine milligram equivalents per day for all other patients (95% CI, 17.2 to 17.4; $P < 0.001$ for the difference; fig. 2). However, the difference between these two groups were largely diminished by the midterm postoperative period (postoperative days 8 to 90) and the long-term postoperative period (postoperative days 91 to 365). Unadjusted opioid utilization during the midterm postoperative period was 10.8 morphine milligram equivalents (95% CI, 10.6 to 11.0; $P < 0.001$) for patients treated by high-intensity surgeons and 9.2 morphine milligram equivalents (95% CI, 9.1 to 9.4; $P < 0.001$) for those treated by non–high-intensity surgeons, and unadjusted opioid utilization during the long-term postoperative period was 3.8 morphine milligram equivalents (95% CI, 3.6 to 3.9) for patients treated by high-intensity surgeons compared to 3.4 morphine milligram equivalents (95% CI, 3.3 to 3.5) for patients who were not treated by high-intensity surgeons. In both cases, these differences were statistically significant but small in magnitude.

However, these unadjusted differences may be confounded by underlying differences between high-intensity and non–high-intensity surgeons in the propensity of their patients for postoperative opioid utilization. After using an instrumental variable approach to adjust for potential confounders, patients receiving treatment from a high-intensity surgeon had higher opioid utilization in the midterm postoperative period than patients who did not (fig. 2; adjusted daily morphine milligram equivalents, 11.4 [95%

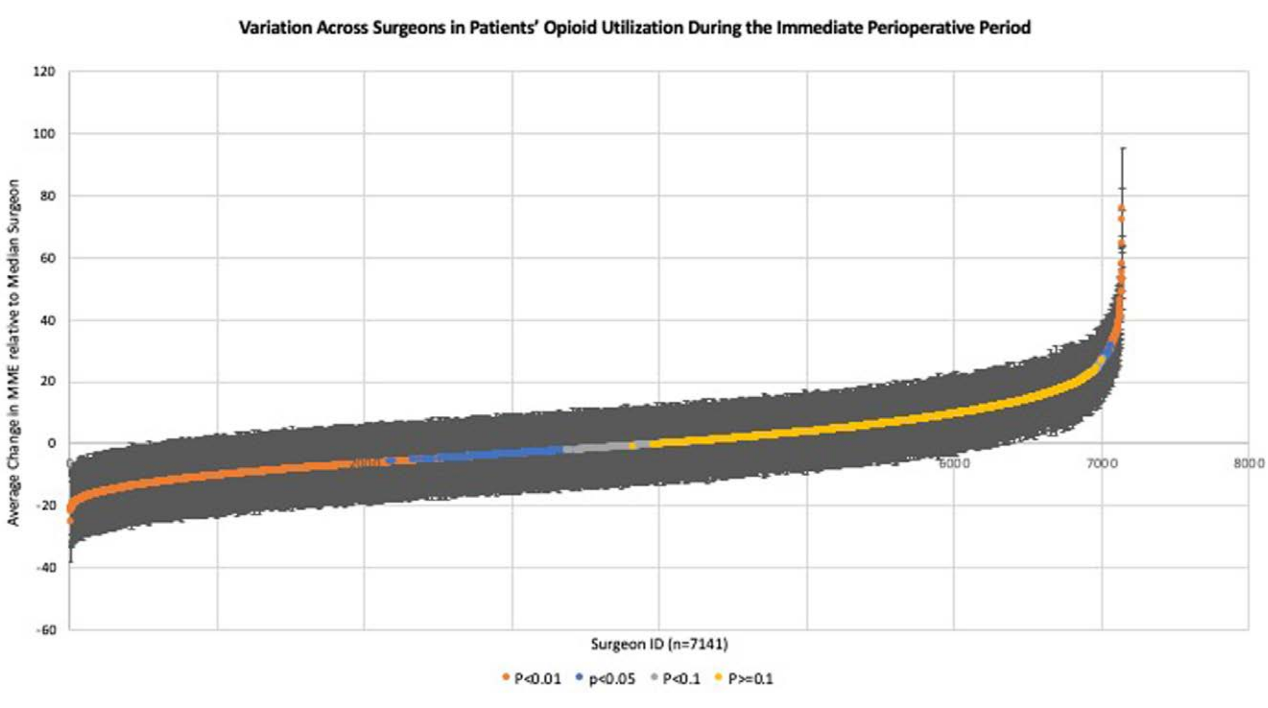

Fig. 1. Variation across surgeons in patients' opioid utilization during the immediate perioperative period. Immediate perioperative period is defined as 7 days before surgery to 7 days after surgery. The overall surgeon fixed effects ranged from −25 to 76 morphine milligram equivalents (median fixed effect was set as 0), with different colors indicating P values at different significance levels relative to the median surgeon: *orange*, $P < 0.01$; *blue*, $P < 0.05$; *gray*, $P < 0.1$; and *yellow*, $P \geq 0.1$.

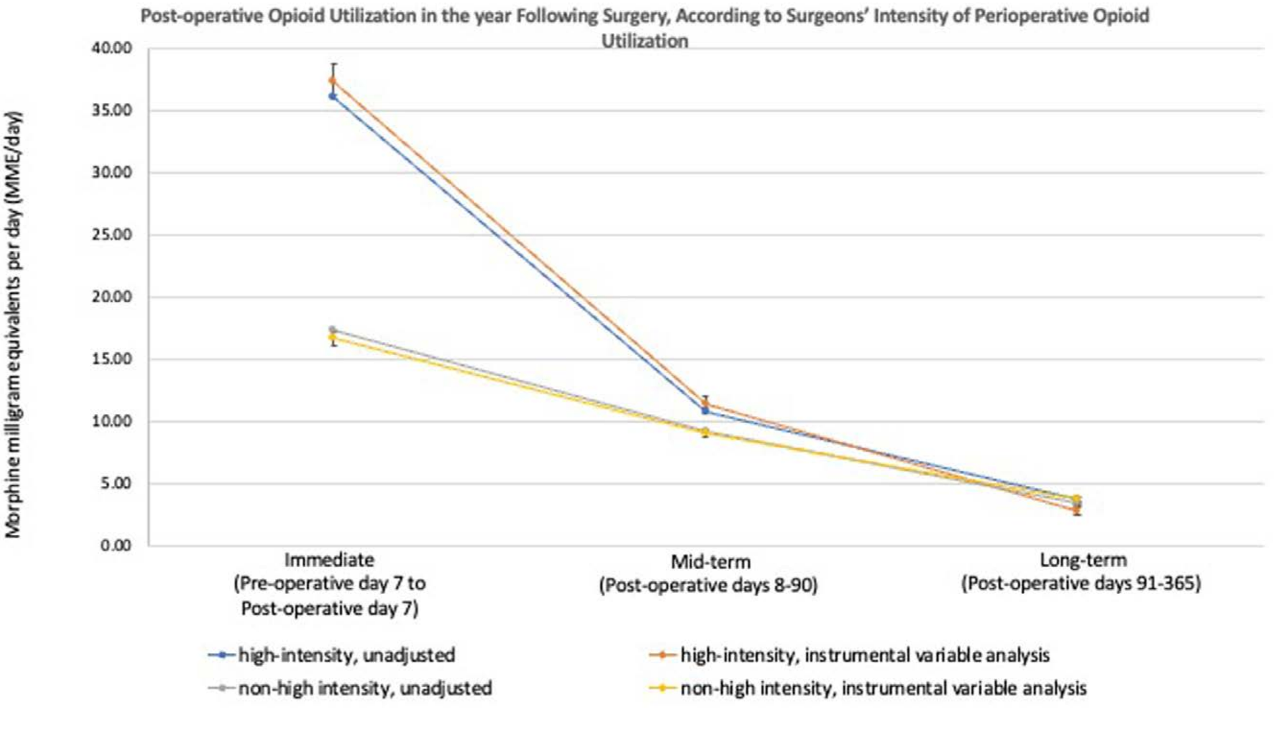

Fig. 2. Association between prescribing intensity in the immediate perioperative period and subsequent utilization in in the mid- and long-term postoperative periods. 95% CI calculated using standard errors that were adjusted for clustering at the hospital level. "Instrumental variable analysis" refers to an analysis that adjusted for all the patient characteristics listed in table 1 and that also used an instrumental variable approach, based on distance to the nearest high-intensity prescriber, to reduce confounding from unobservable patient and physician characteristics.

CI, 10.9 to 12.0] *versus* 9.0 [95% CI, 8.7 to 9.2]; difference in adjusted daily morphine milligram equivalents, 2.4; $P < 0.001$), a difference that was statistically significant but clinically small. Patients who received treatment from a high-intensity surgeon had lower opioid utilization during the long-term postoperative period (adjusted daily morphine milligram equivalents, 2.8 [95% CI, 2.5 to 3.1]) compared to patients treated by non–high-intensity surgeons (adjusted daily morphine milligram equivalents, 3.8 [95% CI, 3.6 to 3.9]). Again, while statistically significant ($P < 0.001$), this difference was clinically small.

In subgroup analysis of patients at high predicted risk for higher opioid utilization during the long-term postoperative period (n = 150,819), there was a statistically significant association receiving treatment from a high-intensity surgeon and opioid utilization during the mid-term postoperative period (table 2; adjusted daily morphine milligram equivalents, 17.6 for high-intensity surgeons [95% CI 16.6 to 18.6] *versus* 13.9 for non–high-intensity surgeons [95% CI 13.5 to 14.1]; difference, 3.7 morphine milligram equivalents; $P < 0.001$). In a test of interactions, the difference between the effect for this subgroup and the effect among non–high-risk patients was statistically significant ($P = 0.008$). However, among high-risk patients, there was no association between receiving treatment from a high-intensity surgeon and opioid utilization in the long-term postoperative period (adjusted daily morphine milligram equivalents, 7.3 [95% CI 6.5 to 8.1] *vs.* 8.3 [95% CI 7.9 to 8.6]; difference in adjusted daily morphine milligram equivalents, –1; $P = 0.08$). There was no statistically significant difference between this estimated effect and the estimated effect for low-risk patients ($P = 0.81$ in a test of interactions).

We performed a sensitivity analysis in which we considered the incidence of chronic opioid utilization as an alternative outcome. Compared with low-intensity surgeons (*i.e.*, the bottom quartile of surgeons), patients treated by surgeons in the second, third, and fourth quartiles had higher odds of filling 10 or more prescriptions or having more than 120 days' opioid supply during the postoperative days 91 to 365 (Supplemental Digital Content, fig. 2, http://links.lww.com/ALN/C856). We observed stepwise higher incidence of chronic opioid utilization with exposure to physicians in each quartile of perioperative opioid utilization. The results of our other sensitivity analyses were qualitatively similar to our main results (table 3). For example, sensitivity analyses that examined alternate thresholds for defining high-intensity surgeons produced results that

Table 3. Association between Surgeon Prescribing Intensity and Postoperative Opioid Utilization: Sensitivity Analyses

	Midterm Opioid Utilization (Average Daily Morphine Milligram Equivalents, Postoperative Days 8 to 90)				Long-term Opioid Utilization (Average Daily Morphine Milligram Equivalents, Postoperative Days 91 to 365)			
	High Intensity	Non–high Intensity	Difference	*P* Value	High Intensity	Non–high Intensity	Difference	*P* Value
Main analysis	11.4 (10.9, 12.0)	9.0 (8.7, 9.2)	2.4 (1.7, 3.2)	< 0.001	2.8 (2.5, 3.1)	3.8 (3.7, 3.9)	–1.0 (–1.4, –0.6)	< 0.001
High-intensity prescribers defined as top 5% of prescribers	14.9 (12.3, 17.5)	9.3 (9.1, 9.5)	5.6 (2.8, 8.3)	< 0.001	0.7 (–0.5, 2.0)	3.7 (3.6, 3.8)	–2.9 (–4.3, –1.6)	< 0.001
High-intensity prescribers defined as top 10% of prescribers	14.1 (12.6, 15.5)	9.1 (8.9, 9.3)	5.0 (3.4, 6.6)	< 0.001	2.2 (1.5, 2.9)	3.7 (3.6, 3.8)	–1.5 (–23, –0.7)	< 0.001
Immediate perioperative period defined as postoperative days 0 to 7	11.6 (11.0, 12.1)	8.9 (8.7, 9.1)	2.7 (1.9, 3.4)	< 0.001	2.9 (2.6, 3.2)	3.8 (3.6, 3.9)	–0.9 (–1.3, –0.5)	< 0.001
Added adjustment for rural status	11.1 (10.6, 11.6)	9.1 (8.9, 9.3)	2.0 (1.3, 2.7)	< 0.001	3.3 (3.0, 3.6)	3.6 (3.4, 3.7)	–0.3 (–0.7, 0.1)	0.199
Added additional adjustment for preoperative opioid use	11.9 (11.4, 12.4)	8.8 (8.6, 9.0)	3.2 (2.5, 3.8)	< 0.001	3.3 (3.2, 3.5)	3.6 (3.5, 3.6)	–0.2 (–0.5, 0.0)	0.072
Adjusted for use of nerve block	11.3 (10.8, 11.9)	9.0 (8.8, 9.2)	2.3 (1.6, 3.1)	< 0.001	2.8 (2.5, 3.1)	3.8 (3.7, 3.9)	–1.0 (–1.4, –0.6)	< 0.001
Excluded patients with multiple surgeries	11.3 (10.7, 11.8)	8.9 (8.7, 9.1)	2.4 (1.7, 3.1)	< 0.001	2.8 (2.5, 3.1)	3.8 (37, 3.9)	–1.0 (–1.4, –0.5)	< 0.001
Weighted regression	11.1 (10.3, 11.9)	8.7 (8.3, 9.1)	2.4 (1.3, 3.5)	< 0.001	2.6 (2.3, 3.0)	3.5 (3.3, 3.7)	–0.9 (–1.4, –0.3)	0.003
Comparison between patients treated by high-intensity or low-intensity surgeons	11.0 (10.6, 11.3)	8.4 (8.0, 8.8)	2.6 (1.9, 3.2)	< 0.001	3.4 (33, 3.6)	3.6 (3.4, 3.8)	–0.2 (–0.5, 0.2)	0.358

The table presents the results of several sensitivity analyses. The first row presents the results of our main analysis, which examined the association between receiving treatment from a high-intensity surgeon (those whose patients were in the upper quartile in terms of opioid utilization during the immediate perioperative period) and opioid utilization (average daily morphine milligram equivalents) during the midterm (postoperative days 8 to 90) and long-term (postoperative days 91 to 365) postoperative periods. The second and third rows present the results of analyses in which high-intensity was redefined as, respectively, the top 5th and top 10th percentile of opioid utilization during the immediate perioperative period. The fourth row presents the results of an analysis in which the immediate perioperative period was defined as postoperative days 0 to 7. The fifth row presents the results of an analysis that adjusted whether the patient lived in a rural or urban area, and the sixth row presents the results of an analysis that adjusted for additional variables regarding preoperative opioid use, such as average daily morphine milligram equivalents during the preoperative period. The seventh row presents the results of an analysis which adjusted for the use of nerve block during the procedure, and the eighth row presents the results of an analysis that excluded patients with a bilateral total knee arthroplasty or who received a second total knee arthroplasty within 365 days of the first surgery. The ninth row presents the results of an analysis that used a weighted regression approach in which the weights were the number of patients cared for by each surgeon. The last row represents the result of an analysis that focused on patients treated by high-intensity surgeons (those in the upper quartile in terms of opioid utilization during the immediate perioperative period) and low-intensity surgeons (those in the lower quartile) and that excluded the middle two quartiles.

were higher in magnitude than our baseline analyses, but the effects remained clinically small.

Discussion

We examined the association between receiving treatment from high-intensity surgeons (those whose patients were in the upper quartile in terms of opioid utilization in the immediate perioperative period) and subsequent opioid utilization during the midterm and long-term postoperative periods for Medicare fee-for-service patients undergoing total knee arthroplasty. Because patients treated by high-intensity surgeons may be systematically different from those treated by lower-intensity surgeons, we relied on an instrumental variable approach to minimize confounding and selection bias. Across several analyses, we found significantly higher midterm (postoperative 8 to 90 days) prescription opioid utilization among patients who received surgery from high-intensity surgeons compared to patients treated by non–high-intensity surgeons. We also found significantly lower long-term (91 to 365 postoperative days) opioid utilization among patients who received surgery from high-intensity surgeons. However, any large study such as ours is likely to find statistically significant findings that are small in magnitude, and the differences found in this study (less than 3 morphine milligram equivalents per day), which correspond to less than 1 hydrocodone tablet per day, are unlikely to be clinically significant. Indeed, studies examining opioid utilization in chronic pain patients generally define clinically significant reductions in opioid utilization as being at least 8 to 30 morphine milligram equivalents per day.[21–23] As such, the primary finding of our study is that differences in surgeon prescribing behaviors are unlikely to meaningfully impact opioid utilization in the mid- and long-term postoperative periods among patients undergoing total knee arthroplasty.

Several factors could explain the lack of correlation between surgeon prescribing behaviors and long-term postoperative opioid utilization. First, the difference in perioperative opioid utilization for patients seeing high-intensity surgeons—roughly 19 morphine milligram equivalents per day during a 15-day period—may not have been sufficiently large to place patients at risk of higher opioid utilization in the mid- and long-term postoperative periods. Second, to the degree higher opioid utilization improves pain control in the immediate perioperative period, it may reduce the risk of chronic postoperative pain and therefore the transition to chronic opioid utilization.[24] Finally, high-intensity surgeons may also provide more patient education regarding the risks of longer-term opioid utilization.

Our study adds to evidence that there is a wide variation in opioid utilization during the immediate perioperative period for total knee arthroplasty, one of the most common surgical procedures among older adults. We additionally quantified the extent of this variation across surgeons and studied its relationship with opioid utilization in the mid- and long-term postoperative periods. Previous studies have also not employed quasiexperimental statistical approaches such as instrumental variable analysis to overcome confounding that may occur because patients who utilize opioids, or larger amounts of opioids, in the immediate perioperative period may systematically differ from patients who do not in ways that are also correlated with longer-term opioid utilization.

Our results have potential policy implications given a growing interest in limiting opioid prescribing after surgery though the use of clinical guidelines and legislation.[25,26] Since variation in opioid utilization during the immediate perioperative period appears to be associated with clinically insignificant effects on opioid utilization in the mid- and long-term postoperative periods, our results suggest that further efforts to implement these policies should consider take into account the possibility that these initiatives may not reduce mid- and long-term opioid utilization and weigh this fact against the potential costs of these policies, such as less well controlled pain.

Our study had several limitations. First, our study was limited to patients undergoing total knee arthroplasty, a procedure that is often indicated for the relief of pain, and the results may be different for other procedures (*i.e.*, appendectomy) for which pain is not an indication. Second, our study was limited to Medicare fee-for-service patients and may not apply to other populations. However, Medicare patients comprise the majority of total knee arthroplasty patients.[27] Moreover, older adults may be particularly susceptible to risks associated with prolonged opioid utilization.[28,29] Third, while surgeons play an important role in opioid prescribing during the immediate perioperative period, we cannot exclude the possibility that some opioid prescribing during the immediate perioperative period is outside of the surgeon's control, which could result in misclassification of surgeons into the high-intensity group. Along these lines, we were only able to observe opioid utilization (*i.e.*, filled prescriptions) as opposed to actual prescribing behaviors or opioid consumption. Fourth, since this is an observational study, our findings should be interpreted as associations rather than causal relationships; however, our approach did utilize instrumental variable approach to minimize confounding from unobservable patient factors. Some of these potential factors include opioids administered during the hospital stay and the use of prescription adjuncts such as nonsteroidal anti-inflammatory drug. Fifth, our sample consisted of patients undergoing surgery from 2011 to 2016, and subsequent to this period, many laws and policies were enacted aimed at limiting opioid prescribing.[30,31]

In conclusion, patients undergoing total knee arthroplasty by high-intensity surgeons—those whose patients were more likely to utilize opioids in the immediate perioperative period—had slightly higher opioid utilization in the subsequent 8 to 90 days after surgery and slightly lower opioid utilization in the subsequent 91 to 365 days after surgery compared to patients who underwent the procedure by surgeons with a lower propensity to prescribe opioids in the perioperative setting. However, while statistically significant, both of these differences were of small clinical significance. Our findings, along with previous work on opioid prescribing after surgery, have implications for the development of clinical practice guidelines in reducing inappropriate opioid prescribing under the framework proposed by a report from the National Academies of Sciences, Engineering, and Medicine.[26] Future research may explore surgeon-level prescribing behaviors across a range of surgeries and quantify thresholds of overuse. Such studies could provide insights into clinical guidelines for pain management strategies associated with surgery.

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Competing Interests

Dr. Sun is on the advisory board of Lucid Lane, LLC (Los Altos, California) and reports receiving consulting fees unrelated to this work from Analysis Group (Boston, Massachusetts). Dr. Jena reports receiving (in the last 36 months) consulting fees unrelated to this work from Bioverativ (Waltham, Massachusetts), Merck/Sharp/Dohme (Kenilworth, New Jersey), Janssen (Titusville, New Jersey), Edwards Life Sciences (Irvine, California), Novartis (East Hanover, New Jersey), Amgen (Thousand Oaks, California), Eisai (Nutley, New Jersey), Otsuka Pharmaceuticals (Princeton, New Jersey), Vertex Pharmaceuticals (Boston, Massachusetts), Celgene (Summit, New Jersey), Sanofi Aventis (Bridgewater, New Jersey), Precision Health Economics and Analysis Group (Boston, Massachusetts). Dr. Jena also reports receiving (in the last 36 months) income unrelated to this work from hosting the podcast Freakonomics, M.D. (Boston, Massachusetts), and from book rights from Doubleday Books (New York, New York). Dr. Jena also reports being retained as an expert witness in lawsuits against opioid manufacturers and distributors. Dr. Mackey reports receiving research funding unrelated to this work from the Redlich Professorship and Rosenkrans Pain Research Endowment Fund at the Stanford University School of Medicine (Palo Alto, California), the Stanford Wu Tsai Neurosciences Institute (Palo Alto, California), the UCSF-Stanford Center of Excellence in Regulatory Science and Innovation (Palo Alto, California), the National Institutes of Health (R61NS118651, R03HD094577, R01DA045027, R01NS109450, R01AT008561, R01DA035484, P01AT00665105; Bethesda, Maryland), and the Patient Centered Outcomes Research Institute (Washington, DC). Dr. Mackey reports travel expenses and/or honoraria unrelated to this work from the Walter Reed National Military Medical Center (Bethesda, Maryland), The Georgetown University School of Medicine (Washington, DC), Harvard University (Cambridge, Massachusetts), the American Academy for Pain Medicine (Orlando, Florida), Washington University (St. Louis, Missouri), the US Food and Drug Administration (Silver Spring, Maryland), the National Institutes of Health (Bethesda, Maryland), the University of Washington (Seattle, Washington), George Washington University (Washington, DC), New York University (New York, New York), Weill Cornell Medical College (New York, New York), and the Canadian Pain Society (Markham, Ontario). Dr. Mackey reports consulting fees unrelated to this work from the American Society of Anesthesiologists (Schaumburg, Illinois), Fain, Anderson, VanDerhoef, Rosendahl, O'Halloran, and Spillane, PLLC (Seattle, Washington), Cox, Wootton, Lerner, Griffin, and Hansen (San Francisco, California), Lewis Brisbois Bisgaard and Smith (Los Angeles, California), Muro and Lampe (Folsom, California), and the Oklahoma Health Sciences Center (Norman, Oklahoma). Dr. Cen declares no competing interests.

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Supplemental Digital Content

Statistical Model Description and Supplemental Results, http://links.lww.com/ALN/C856

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