**Online Supplement for “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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**Technical Appendix**

In our main analysis, we implemented an instrumental variables (IV) approach using two stage least square regression. As a first step, we estimated the following multivariable linear regression of our key independent variable (high vs. low intensity prescriber) on the instrumental variable and other covariates:

 $High\_{ijt}=time\_{t}+state\_{j}+αX\_{i}+τdistance\_{ij^{'}t}+ε\_{ijt}$ (1)

In equation (1), $i$, $j$ and $t$ represent the given patient, performing surgeon and the year of surgery, respectively. $time\_{t}$ is a vector of year effects, $state\_{j}$ is a vector of state fixed effects, $X\_{i}$ is a vector of patient characteristics including age, gender, race, Medicare-Medicaid dual eligibility, opioid naïve status, and the comorbidities listed in **Table 1**, and $ε\_{ijt}$ is the error term. $High\_{ijt}$ is the binary, independent variable with value 1 indicating a patient was treated by a “high-intensity” surgeon and 0 otherwise. $distance\_{ij^{'}t}$ is the instrument that measures the distance between patient $i$ and the nearest high-intensity surgeon $j^{'}$. The goal of the first-stage regression is to estimate the extent to which changes in distance to the nearest “high-intensity” surgeon affected the probability of a patient receiving care from a “high-intensity” surgeon. Based on regression results of equation (1), we calculated the predicted probability of patient being treated by a “high-intensity” surgeon—$\tilde{High}\_{ijt}$, given the distance to the nearest “high-intensity” surgeon and other covariates. The predicted probability $\tilde{High}\_{ijt}$ was then included in the following estimation equation:

 $ Outcome\_{ijt}=time\_{t}+state\_{j}+αX\_{i}+β\tilde{High}\_{ijt}+ε\_{ijt}$ (2)

Similar to equation (1), $i$ indicates the given patient, $j$ indexes the performing surgeon, and $t$ represents the year of surgery. The aforementioned $\tilde{High}\_{ijt}$ is the key independent variable of equation (2); other covariates $time\_{t}$, $state\_{j}$ and $X\_{i}$ , and the error term $ε\_{ijt}$ are retained from equation (1). $Outcome\_{ijt}$ is the outcome of interest in this study, including primary outcomes—mid-term (postoperative days 8-90) and long-term (postoperative days 91-365) opioid use. Given that the primary outcomes of our study are continuous variables, we fit multivariable linear regression. $β$—the coefficient of $\tilde{High}\_{ijt}$ is the expected difference in opioid use between patients who received care from high-intensity surgeons compared to those who did not. We selected a linear probability model instead of logistic or probit regression, because the former is more computationally efficient in a circumstance of numerous discrete variables (in this study, the independent variable and most covariates are indicators). In addition, the statistical model outlined in equation (2) includes state and year fixed effects and unlike logit models that may occur the “incidental parameters problem”, the linear probability model does not lead to biased estimation. Furthermore, the use of a linear probability model is a generally accepted method for an instrumental variables approach when the instrumented variable (in this case, whether the patient was treated by a “high-intensity” surgeon) is a discrete one.1 To address the possible issues such as heteroscedasticity or correlations within a given hospital, we clustered standard errors at the hospital level for all models we mentioned above.

The main results of the first stage regression—coefficient $τ$ for instrumental variable $distance\_{ij^{'}t}$ in equation (1) are shown as below (**Supplemental Digital Content, Table1**). The first stage regressions for outcomes of interest were the same, and the coefficient -0.004 with a p-value<0.001 indicates a patient was less likely to receive care from a “high-intensity” surgeon if the distance from that patient’s zip code residence to the nearest “high-intensity” surgeon increased. We also include the F-statistic to test the association between our instrument and whether the patient actually received care from a “high-intensity” surgeon. A failure to reject the null hypothesis for the F-statistic would indicate a weak correlation between the two aforementioned variables, which may lead to a biased estimation in the instrumental variables approach. The F-statistic in our study was 3665.47, which is significantly larger than the critical values for all the tests for a weak correlation (e.g. Stock-Yogo weak F-test and Cragg-Donald Wald F-statistics). Accordingly, we can reject the null hypothesis and conclude that the instrument (distance to the nearest high-intensity surgeon) and whether the patient received care from a “high-intensity” surgeon have a strong correlation.

**Supplemental Digital Content, Table 1**. Association between Distance to the Nearest “High-Intensity” Surgeon and Probability of Receiving Care from “High-Intensity” Surgeon

(Instrumental Variable Approach First-stage Regression Results)

|  |  |
| --- | --- |
|  | Receive care from “high-intensity” surgeon |
| Distance to the nearest “high-intensity” surgeon  | -0.004(-0.005,-0.003)p<0.001 |
| F-statistic | 3665.47 |

**Notes:** The table shows the results of the first stage regression using two stage least squares. The dependent variable of first stage regression (which is also the key independent variable of interest in our study) is whether a patient received care from a “high-intensity” surgeon, and the independent variable (instrument) is the distance from patient’s residence to the nearest “high-intensity” surgeon. The regression coefficient of our instrument is shown above, together with 95% confidence interval and p-value. Coefficients for other covariates in equation (1), such as patient characteristics, comorbidities, year and state fixed effects, were not shown here.

A crucial assumption of the instrumental variables approach is that our instrument (distance to the nearest “high intensity” surgeon) is unlikely to be correlated with any unobservable factors that might predispose to higher postoperative opioid utilization. While this cannot be tested directly, as an indirect way of assessing this issue, we examined the extent to which distance is correlated with *observable* factors that predispose to higher postoperative utilization, reasoning that if distance is uncorrelated with observable factors, then this would provide some reassurance that it is not associated with unobservable factors. To implement this test, we first performed a linear regression in which the dependent variable was average daily MME utilization during the long-term postoperative period (postoperative days 91-365) and the independent variables were the patient characteristics listed in Table 1. The results of this regression were then used to calculate each patient’s predicted opioid utilization during postoperative days 91-365. We then performed a regression in which the dependent variable was the patient’s predicted opioid utilization during postoperative days 91-365 and the independent variable was the distance to the nearest “high-intensity” surgeon. The results of the regression are shown below (**Supplemental Digital Content, Table 2)**.

**Supplemental Digital Content, Table 2**. Association between the Predicted Long-term Opioid Utilization and Distance to the Nearest “High-Intensity” Surgeon

|  |  |  |  |
| --- | --- | --- | --- |
|  | Coefficient | 95% Confidence Interval | p-value |
| **Model 1.** Outcome: Opioid utilization during postoperative days 91-365 |
| Age group (reference: 65-69 year) |  |  |  |
|  70-74 year | -0.68 | (-0.74, -0.62) | <0.001 |
|  75-79 year | -1.14 | (-1.20, -1.08) | <0.001 |
|  80-84 year | -1.54 | (-1.62, -1.46) | <0.001 |
|  >=85 year | -1.84 | (-1.95, -1.74) | <0.001 |
| Female | 0.07 | (0.03, 0.12) | 0.003 |
| Race (reference: White) |  |  |  |
|  Black | 0.23 | (0.12, 0.34) | <0.001 |
|  Other | -1.33 | (-1.42, -1.24) | <0.001 |
| Medicare-Medicaid dual eligibility | 2.64 | (2.56, 2.71) | <0.001 |
| Opioid Naïve | -3.98 | (-4.02, -3.93) | <0.001 |
| Elixhauser comorbidities |  |  |  |
|  Congestive heart failure | 0.70 | (0.62, 0.79) | <0.001 |
|  Valvular disease | -0.15 | (-0.21, -0.08) | <0.001 |
|  Pulmonary circulation disorders | 0.56 | (0.43, 0.68) | <0.001 |
|  Peripheral vascular disease  | 0.36 | (0.29, 0.43) | <0.001 |
|  Hypertension  | 0.47 | (0.42, 0.53) | <0.001 |
|  Paralysis | 0.07 | (-0.21, 0.36) | 0.605 |
|  Other neurological disorders | 0.92 | (0.84, 1.00) | <0.001 |
|  Chronic pulmonary disease | 1.04 | (0.99, 1.10) | <0.001 |
|  Diabetes without chronic complications | 0.09 | (0.04, 0.15) | 0.001 |
|  Diabetes with chronic complications | 0.35 | (0.26, 0.43) | <0.001 |
|  Hypothyroidism  | 0.13 | (0.08, 0.18) | <0.001 |
|  Renal failure | 0.34 | (0.27, 0.41) | <0.001 |
|  Liver disease | 0.28 | (0.13, 0.43) | <0.001 |
|  Chronic peptic ulcer  | 0.73 | (0.40, 1.07) | <0.001 |
|  HIV and AIDS | 2.05 | (0.91, 3.19) | <0.001 |
|  Rheumatoid arthritis/collagen vascular diseases | 2.31 | (2.24, 2.39) | <0.001 |
|  Coagulation deficiency | -0.09 | (-0.20, 0.01) | 0.084 |
|  Obesity | -0.02 | (-0.07, 0.03) | 0.426 |
|  Weight loss | 0.94 | (0.79, 1.09) | <0.001 |
|  Fluid and electrolyte disorders | 0.18 | (0.12, 0.24) | <0.001 |
|  Blood loss anemia | 0.13 | (-0.02, 0.28) | 0.099 |
|  Deficiency anemias | 0.35 | (0.30, 0.41) | <0.001 |
|  Alcohol abuse | -0.28 | (-0.50, -0.07) | 0.009 |
|  Drug abuse | 12.81 | (12.57, 13.05) | <0.001 |
|  Psychoses | 0.58 | (0.46, 0.70) | <0.001 |
|  Depression | 1.59 | (1.54, 1.65) | <0.001 |
| **Model 2.** Outcome: Predicted opioid utilization during postoperative days 91-365  |
|  Distance to the nearest “high-intensity” surgeon | .0022 | [0.0018, 0.0026] | <0.001 |

Given the large number of patients in our sample, there is a statistically significant association between predicted opioid utilization during postoperative days 91-365 and distance to the nearest “high-intensity” surgeon. However, the magnitude of this effect is very small. In our sample, distance to the nearest “high-intensity” surgeon ranges from 0 to 557 miles. Therefore, the results from imply a 1.2 MME difference across the range of distances in out sample, which is a clinically insignificant difference.

The results of our second-stage regressions are displayed below (**Supplemental Digital Content, Table 3)**. We list the coefficients along with 95% confidence intervals for all regressors (except for state and year fixed effects). The instrumented independent variable of interest, “*high-intensity surgeon*,” was obtained based on the predicted probability of being treated by a “high-intensity” surgeon in equation (1). The coefficients of “*high-intensity surgeon”* for primary outcomes (columns 2 and 3) suggest that patients treated by high-intensity surgeons were associated with, on average, 2.4 more morphine milligram equivalents (MME) per day in postoperative 8-90 days (p<0.001) and 1 less MME per day in postoperative 91-365 days (p<0.001).

**References**

1. Angrist JD, Pischke J-S. Mostly Harmless Econometrics: An Empiricist’s Companion. Princeton, NJ: Princeton University Press; 2009.

**Supplemental Digital Content, Table 3**. Model Results of Second-stage Regressions Using Instrumental Variable Approach

|  |  |
| --- | --- |
|  | Primary Outcomes |
|  | Mid-term opioid utilization(8-90 days after surgery) | Long-term opioid utilization(91-365 days after surgery) |
| “High-Intensity Surgeon” | 2.4 (1.7, 3.2)p<0.001 | -1.0 (-1.4, -0.6)p<0.001 |
| Age group (reference: 65-69 year) |  |  |
|  70-74 year |  -1.7 (-1.8, -1.6) | -0.7 (-0.8, -0.6) |
|  75-79 year |  -3.4 (-3.5, -3.3) | -1.1  (-1.2, -1.1) |
|  80-84 year |  -4.9 (-5.0, -4.8) | -1.5 (-1.6, -1.4) |
|  >=85 year |  -6.2 (-6.4, -6.1) | -1.8  (-1.9, -1.7) |
| Female |  -0.02  (-0.09, 0.06) | 0.1(0.0, 0.1) |
| Race (reference: White) |  |  |
|  Black | 0.3  (0.0, 0.5) | 0.1 (-0.0, 0.3) |
|  Other | -1.5  (-1.8, -1.3) | -1.5 (-1.6, -1.3) |
| Medicare-Medicaid dual eligibility | 1.9 (1.7, 2.1) | 2.6 (2.4, 2.7) |
| Opioid Naïve |  -5.6 (-5.7, -5.6) | -3.9  (-4, -3.8) |
| Elixhauser comorbidities |  |  |
|  Congestive heart failure | 0.3  (0.1, 0.4) | 0.7 (0.5, 0.8) |
|  Valvular disease |  -0.1 (-0.2, 0.005) |  -0.1  (-0.2, -0.0) |
|  Pulmonary circulation disorders | 0.6  (0.4, 0.8) | 0.6  (0.4, 0.7) |
|  Peripheral vascular disease  | 0.2  (0.1, 0.3) | 0.4 (0.3, 0.5) |
|  Hypertension  |  0.1 (-0.1, 0.1) | 0.4(0.4, 0.5) |
|  Paralysis |  -1.4 (-1.9, -1.0) |  0.0  (-0.3, 0.4) |
|  Other neurological disorders | 0.5 (0.3, 0.6) | 0.9(0.8, 1.0) |
|  Chronic pulmonary disease | 1.2 (1.2, 1.3) | 1.0(0.9, 1.1) |
|  Diabetes without chronic complications | 0.3(0.2, 0.4) |  0.1 (-0.0, 0.1) |
|  Diabetes with chronic complications | 0.1 (-0.0, 0.3) | 0.4 (0.3, 0.5) |
|  Hypothyroidism  | 0.2(0.1, 0.2) | 0.10 (0.1, 0.2) |
|  Renal failure | -0.3 (-0.4, -0.2) |  0.3  (0.3, 0.4) |
|  Liver disease | 0.8  (0.5, 1.0) |  0.3  (0.1, 0.5) |
|  Chronic peptic ulcer  | 1.2  (0.6, 1.8) |  0.8  (0.4, 1.3) |
|  HIV and AIDS |  2.3  (-0.1, 4.7) |  1.9  (0.0, 3.8) |
|  Rheumatoid arthritis/collagen vascular diseases | 1.7 (1.5, 1.8) |  2.3  (2.2, 2.4) |
|  Coagulation deficiency | -0.1  (-0.3, 0.1) |  -0.1  (-0.2, 0.0) |
|  Obesity | -0.1  (-0.2, -0.0) | 0.1  (0.0, 0.1) |
|  Weight loss | 0.6  (0.3, 0.9) | 0.9  (0.6, 1.1) |
|  Fluid and electrolyte disorders |  0.1  (0.0, 0.2) |  0.2  (0.1, 0.3) |
|  Blood loss anemia |  0.20  (-0.1, 0.5) |  0.1  (-0.1, 0.3) |
|  Deficiency anemias | 0.3(0.2,0.3) |  0.3  (0.3, 0.4) |
|  Alcohol abuse |  0.3  (-0.1, 0.7) | -0.2(-0.5, 0.1) |
|  Drug abuse | 13.7  (13.9, 14.6) |  12.7 (12.0, 13.4) |
|  Psychoses |  0.2  (0.0, 0.4) |  0.6  (0.4, 0.8) |
|  Depression | 1.8  (1.7, 1.9) |  1.6  (1.5, 1.7) |

**Notes:** The table summarizes the results of the secondary stage regressions using two stage least squares approach. We performed multivariate linear regressions for opioid utilization in the mid-term and long-term postoperative periods (columns 2 and 3), respectively. All models were adjusted for patient’s demographics and comorbidities, with year and state fixed effects.

**Supplemental Digital Content, Figure 1**. Sample Construction Flow Chart

Initial Sample: Patients >=65 years undergoing TKA who were (1) continuously enrolled for three calendar years, encompassing the year prior to and the year after surgery, and (2) have continuous Part D enrollment during the study period. N=732,919

Exclude individuals receiving TKA by surgeons who performed less than 25 cases during the study period. N=58,467

N=674,452

Exclude top 1% of opioid users, measured by oral morphine milligram equivalents (MMEs) used between (1) -7 and +7 days, (2) 8-90 days, or (3) 91-365 days. N=15,645

N=658,807

Exclude patients with cancer diagnosis. N=46,429

N=612,378

Exclude patients with missing geo coordinates (to calculate instrument variables based on zip code). N=8,285

N=604,093

**Supplemental Digital Content, Figure 2.** Odds of Chronic Opioid Utilization, Categorized by the Intensity of Opioid Utilization in the Immediate Perioperative Period by Quartiles

The figure is based on results of sensitivity analysis in which 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 91-365 within the first postsurgical year. A multivariable logistic regression was conducted to investigate the association between the incidence of chronic opioid utilization and a given surgeon’s quartile in terms of average opioid utilization in the immediate perioperative period. We adjusted for a robust set of potential confounders in the model, including patient demographics (age, race, sex, Medicare-Medicaid dual eligibility), Elixhauser comorbidities, opioid utilization in the year prior to surgery (measured in MMEs), and year and state fixed effects.