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Statewide Utilization of Multimodal Analgesia and Length of Stay After Colectomy

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Abstract

Background: Both enhanced recovery and anesthesia literature recommend multimodal perioperative analgesia to hasten recovery, prevent adverse events, and reduce opioid use after surgery. However, adherence to, and outcomes of, these recommendations are unknown. We sought to characterize use of multimodal analgesia and its association with length of stay after colectomy.

Materials and Methods: Within a statewide, 72-hospital collaborative quality initiative, we evaluated postoperative analgesia regimens among adult patients undergoing elective colectomy between 2012 and 2015. We used logistic regression to identify factors associated with the use of multimodal analgesia, and performed multivariable linear regression to evaluate its association with postoperative length of stay (LOS).

Results: Among 7265 patients who underwent elective colectomy in the study period, 4660 (64.1%) received multimodal analgesia, 2405 (33.1%) received opioids alone, and 200 (2.8%) received one non-opioid pain medication alone. Multimodal analgesia was independently associated with shorter postoperative LOS, compared with opioids alone (5.60 days [95% CI 5.38 – 5.81] versus 5.96 days [5.68–6.24], p=0.016)

Conclusions: Multimodal analgesia is associated with shorter LOS, yet one third of patients statewide received opioids alone after colectomy. As surgeons increasingly focus on our role in the opioid crisis, particularly in post-discharge opioid prescribing, we must also focus on inpatient

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Author Contributions:

All three authors (ADR, JVV, SER) participated in the study conception and design, analysis and interpretation of data, drafting and revision of the manuscript, and provided final approval. ADR acquired the data.

DISCLOSURE

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postoperative pain management to limit opioid exposure. At the hospital level, this may have the added benefit of decreasing LOS and hastening recovery.

Keywords

multimodal analgesia; length of stay; colectomy; enhanced recovery; analgesia; opioid

INTRODUCTION

Surgeons and hospitals have faced increasing pressure to decrease length of stay (LOS) after surgery, both for the benefit of patients and their recovery, and also to improve hospital throughput and efficiency in the setting of prospective payment for hospitalization. A variety of measures have been employed to reduce LOS in alimentary tract surgery, including enhanced recovery protocols (ERP),[1–3] limiting intravenous fluids,[4,5] and alvimopan.[6,7] Multimodal analgesia is a key piece of enhanced recovery protocols and may improve mobility, prevent opioid-induced ileus, and hasten the transition to oral regimens.[8] Multimodal analgesia regimens using nonsteroidal anti-inflammatory drugs (NSAIDS), acetaminophen, epidurals, and nerve blocks can decrease opioid consumption while preserving pain control.[9–14] Perioperative pain control guidelines recommend limiting opioids[15] and have encouraged multimodal analgesia for years,[16] but there is even greater interest in multimodal regimens as new evidence arises implicating perioperative opioids in new, persistent opioid use.[17–19]

Improving pain control using multimodal analgesia may accelerate post-operative recovery and shorten hospital stay, but real-world use of multimodal analgesia and its effect on hospital stay is understudied. A Cochrane review of randomized controlled trials (RCTs) comparing epidural analgesia versus intravenous opioids found no difference in LOS,[20] while a meta-analysis of ERP RCTs found shorter LOS, with 5 of the 6 studies using epidural analgesia and avoiding systemic morphine use.[21] However, in real-world practice, as opposed to RCTs, adherence to ERP and multimodal analgesia recommendations is often imperfect.[3,22] Even highly focused programs attain only a 76% compliance rate with the ERP.[23] It is unknown how commonly surgeons provide multimodal analgesia, and whether it achieves the goal of shorter postoperative length of stay.

In order to evaluate use and outcomes of multimodal analgesia, we evaluated colorectal resections performed within a statewide surgical quality collaborative collecting specific pain management data and validated clinical parameters in the perioperative period. We chose to focus on colectomy because it is a common major operation, performed in a wide variety of hospitals, and has been included in many of the earliest ERP protocols, both within our state and more broadly.[24] Therefore, we sought to characterize the post-operative medication regimen and the rates of multimodal analgesia use. We also aimed to identify whether there is an effect of multimodal analgesia use on length of stay after surgery for patients undergoing elective colectomy. We hypothesized that multimodal analgesia would be associated with shorter LOS.

MATERIALS AND METHODS:

We performed a retrospective cohort study using clinical registry data from the Michigan Surgical Quality Collaborative (MSQC), a large, statewide surgical registry that includes every major surgical hospital in the state, with a focus on sampling for colectomy. Data is manually abstracted from electronic and paper records by trained nurses and the registry is audited regularly for validity. Collected data include patient characteristics, perioperative processes of care, and postoperative clinical outcomes. The current study was performed with University of Michigan IRB approval HUM00090549.

Patients and procedures

We included patients age 18 and older, undergoing elective colectomy (CPT 44140, 44141, 44143, 44144–47, 44160, 44204–08) between July 2012 and October 2015. After October 2015, data abstraction of pain regimen was no longer mandatory in MSQC. Patients were excluded from the sample if there was missing data for all pain medication variables (n=13). Patients with missing data were excluded from the regression (hospital bed size and teaching status, n=49; insurance status, n=40; totaling 1.3% of the cohort).

Measures

Pain medications captured in the registry included intravenous and oral opioids, acetaminophen, non-steroidal anti-inflammatories (NSAIDs), epidural analgesia, and local analgesia, all identified for the first 24 hours post-operatively.

The primary outcome variable was length of stay. In order to reduce the influence of outliers, but still maintain the effect of prolonged length of stay, we winsorized LOS to 30 days, which assigned a value of 30 days to any LOS beyond 30 days. The primary predictor was receiving multimodal analgesia, defined as a dichotomous variable (0 = opioid alone, 1 = multimodal analgesia: one or more non-opioid medications ± opioid) ordered in the first 24 hours postoperatively. A minority of the study population received a single-agent non-opioid pain regimen (epidural, acetaminophen, NSAID, or local anesthesia). As the patients comprising the single-agent non-opioid cohort were primarily laparoscopic operations and more likely to be treated in smaller hospitals, they were not comparable to the other two cohorts. Accordingly, multimodal analgesia was used for the full analysis and all three pain regimens (multimodal analgesia, opioid alone, and single-agent non-opioid) were used in sensitivity analyses.

Statistical Analyses

We performed bivariate analyses to identify factors associated with pain regimen and length of stay. To evaluate receipt of multimodal analgesia, we used bivariate factors with p value ≤0.1 and *a priori* clinically defined factors (post-operative complications, comorbid conditions, hospital teaching status, patient insurance, surgical approach) in a multivariable logistic regression to identify factors independently associated with receipt of multimodal analgesia. To evaluate LOS, again informed by the results of bivariate analyses, we included covariates with p value ≤0.1 in a multivariable linear regression to identify an association between pain regimen (opioids alone versus multimodal analgesia) and LOS. For LOS

analyses, we also evaluated other models, including Poisson and negative binomial regression, as well as a linear multilevel model with random hospital and surgeon effects. These models identified the same statistically significant predictors and similar effect sizes. For ease of understanding and interpreting the data, we used multivariable linear regression for the primary analysis and we used robust standard errors to correct for cluster effects at the hospital level. In both multimodal analgesia and LOS analyses, we controlled for patient age, race/ethnicity, American Society of Anesthesiologists (ASA) class, postoperative complications, surgical approach (open versus minimally invasive), hospital bed size, hospital teaching status, and patient insurance status. We did not include any *a priori* defined interaction terms in the primary analysis. There was no evidence for multicollinearity using the variance inflation factor. As a secondary analysis, we evaluated a variety of interaction terms, representing specific combinations of medications present in at least 1% of patients (to allow for reliable effect estimation), in a multivariable linear regression.

All statistical tests were two-sided and a p value of <0.05 was used as significance threshold. All analyses were conducted using Stata 15.1, StataCorp, College Station, TX.

RESULTS

Patient Characteristics

The cohort of 7265 patients had a mean age of 62.5 (SD 13.8) years and a range of 18 to 89 years. Over half of the cohort was female and the vast majority (84.6%) was white. When separated by pain regimen, the three groups had statistically significant differences by age, race, comorbidities, surgical approach (open vs. laparoscopic), insurance status, and hospital characteristics (Table 1).

Pain regimens

Overall, 6778 patients (93.3%) received an opioid for post-operative pain control, with 2405 (33.1%) of patients receiving opioids alone. Intravenous opioids were the most commonly ordered pain medication (6565 patients, 90.4%), followed by oral opioids (3168, 43.6%), acetaminophen (2711, 37.3%), NSAIDs (2560, 35.3%), epidural analgesia (1406, 19.4%) and local anesthetic (100, 1.4%). Two hundred patients (2.8%) received one class of non-opioid medication alone; of those, 173 (86.5%) received epidural analgesia, 14 (7.0%) an NSAID, 12 (6.0%) acetaminophen, and 1 (0.5%) local anesthetic only (Table 1).

Unadjusted associations to lower rates of receiving multimodal analgesia included oldest patient group (65–84 years), diabetes, hypertension, peripheral vascular disease, ASA class 3 and 4, Medicare insurance, Black race, academic hospital, and >500 beds. In bivariate analysis, readmission rates were similar among the three groups of pain regimens (Table 1). After multivariable adjustment, several characteristics were associated with the receipt of multimodal analgesia. Patients aged 65 – 84 were less likely compared to those in younger age groups (OR 0.82, 95% CI 0.69–0.96, p=0.02), while Black patients were less likely compared to those of other races (OR 0.61 95% CI 0.51–0.73, p<0.001). Patients with ASA class 3–4 (OR 0.88, 95% CI 0.77–1.0, p=0.04) also had a lower likelihood of receiving

multimodal analgesia (Table 2). Repeating the analysis adding the 200 patients who received a single-agent non-opioid pain regimen resulted in negligible changes to the effect sizes.

Length of Stay

In the overall sample, prior to winsorization, LOS ranged from 1 to 69 days with mean 5.77 days (SD 4.27). After winsorizing LOS to 30 days, mean LOS was 5.74 days (SD 4.03 days). Unadjusted LOS was 5.52 days (SD 3.91) days for multimodal analgesia, versus 6.12 days (SD 4.23) for opioid alone, and 6.53 (SD 3.99) days for single-agent, non-opioid analgesia. After controlling for patient and hospital factors (Table 3), receipt of multimodal analgesia was associated with a 0.36-day shorter length of stay than opioid alone (5.60 days [95% CI 5.38 – 5.81] versus 5.96 days [5.68–6.24], p=0.016) (Figure 1).

Next, we evaluated whether particular pain medication classes or combinations thereof had a greater effect on LOS. After including pain medication classes individually as dichotomous variables, we found that NSAIDs were associated with a decrease in LOS of 0.62 days ($p<0.001$) and oral opioids a decrease of 0.90 days ($p<0.001$), whereas both epidural/spinal analgesia and intravenous opioids were associated with an increase in LOS (0.88 days and 0.73 days, respectively, both $p<0.001$). There was no association between acetaminophen and LOS. When evaluating for specific combinations of pain medications through interaction terms, among combinations present in at least 1% of patients, there were no statistically significant effects attributable to any specific combinations.

DISCUSSION

Almost all patients received an opioid after elective colectomy and a third received opioids alone in this statewide cohort. Postoperative pain control guidelines have recommended multimodal approaches for many years,[15] so this finding suggests that there is substantial opportunity for improvement in perioperative analgesia regimens in Michigan hospitals. Older patients and those with higher ASA classification were less likely to receive multimodal analgesia, perhaps due to comorbid conditions limiting candidacy for acetaminophen or NSAIDs. Black patients also had lower likelihood of receiving multimodal medication, which could be a provider-level factor in practice patterns and practice site, reflection of other health status, or unequal treatment.[25]

We also found that multimodal analgesia was associated with decreased length of stay. While this difference was small—approximately one third of a day—it may represent the independent influence of these pain regimens, that, combined with other ERP elements and aggregated over many patients, can improve patient throughput and resource utilization in hospitals. It is likely that improved pain management from these regimens contributes to the LOS-shortening effects of ERPs.[20,26,27] A meta-analysis analyzing pain control regimens in colorectal surgery with ERP did not find an effect on LOS, however the included studies were primarily head-to-head pain modality RCTs of epidurals, IV lidocaine, wound infusions, and local blocks, which were used only in a minority of cases in our study.[28] Rather, real-life regimens of non-opioid medications in combination with opioids may provide effective pain control, reduce overall opioid consumption with the potential to reduce ileus, while allowing patients to ambulate and move towards discharge.

Pain control is a key element of perioperative care and the trend toward referring to pain as "the fifth vital sign" particularly increased attention to analgesia over the last decade.[29,30] However, with the ongoing opioid crisis, there is growing awareness of surgical procedures as inciting episodes for new, persistent opioid use.[31] In addition, unused prescriptions' potential for diversion and misuse have increased scrutiny on pain management during the surgical episode.[32] Prescriptions after discharge are the primary focus of this scrutiny,[33] though calls for reform include setting patient expectations before surgery and during the hospitalization, as well as leveraging the expertise of the multidisciplinary team.[17,34] We demonstrate that surgeons still are not providing optimal multimodal pain management, and perhaps that we rely too heavily on opioids during the inpatient stay. Increasing multimodal pain management during hospitalization may contribute to limiting post-discharge opioid use.

This study has several limitations. First, using robust registry data we were able to identify pain medication ordered in the first 24 hours after surgery for a large cohort of patients undergoing elective colectomy, but this does not necessarily reflect administration of these medications nor is actual opioid consumption captured. In addition, some of the opioid-only patients may have had non-opioid analgesics ordered beyond the first 24 hours. However, orders are indicative of surgeon practice and reflect pain management options available to patients. Additionally, the registry data did not capture discharge with an opioid prescription, which is a clinically-relevant outcome of inpatient pain regimen. Second, during the study time period, data on transversus abdominis plane (TAP) blocks, gabapentin, and ketamine use were not collected, though use of those modalities is increasingly referenced in guidelines and reviews.[15,19,35] A third limitation is confounding by indication – there may be factors associated with the decision to order multimodal analgesia for a patient that are also associated with factors influencing length of stay. For example, some providers may preferentially use ERPs, which may promote both multimodal analgesia and early discharge, whereas a provider treating older patients or patients in ASA class 3 or 4 may be reticent to prescribe NSAIDs with impaired renal function and also be slower to discharge such patients.[36] To account for patient factors, we performed multivariable regression using the measured and known variables, however there may be other pain management-related variables that are unmeasured, particularly alternative pain management techniques not captured in the registry: music therapy,[37,38] deep breathing, massage, and relaxation techniques.[39] Fourth, return of bowel function is not captured by the registry and may limit prescribing of oral medications postoperatively. The registry, however, captures intravenous non-opioid medication including acetaminophen and ketorolac. In addition, many enhanced recovery protocols initiate clear liquids within the first postoperative day, prior to return of bowel function. Finally, it may not be that a change in post-operative pain regimens will independently affect length of stay, but rather that multimodal pain therapy is a critical part of a set of interventions that result in faster recovery.

No patient should experience poorly controlled pain, and multimodal analgesia is an easy step for surgeons to take to control pain while helping patients limit opioid exposure and the associated downstream risks. As surgeons increasingly focus on our role in the opioid crisis, particularly in post-discharge opioid prescribing, we must also focus on inpatient pain management to limit opioid exposure. At the hospital level, this may have the added benefit

of decreasing LOS and increasing throughput. Adequately treating pain while limiting opioid consumption should be the end goal. This can be improved through better adherence to guidelines, and through increased education, and accountability in regional quality collaboratives.

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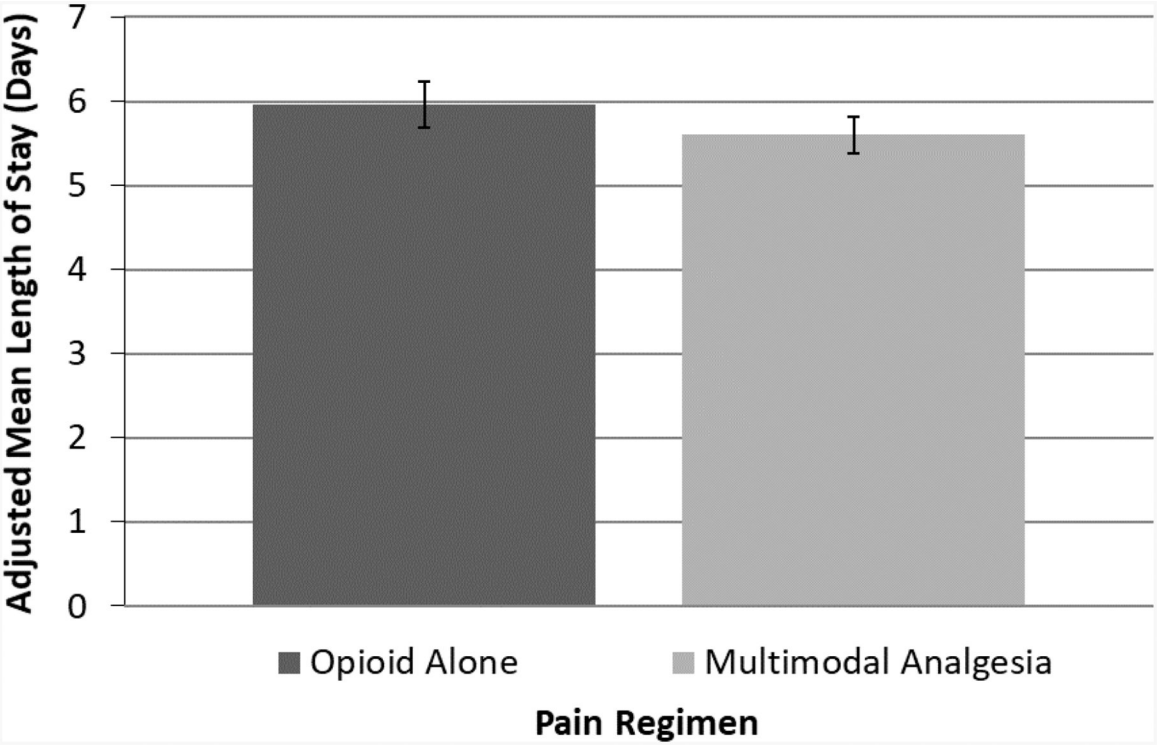

Figure 1:
Adjusted mean length of stay after elective colectomy, by pain regimen. p=0.03

Table 1:

Patient characteristics, by pain regimen.

Characteristics		Opioids Alone N (%)	Multimodal N (%)	Opioid-Free, Single Agent N (%)	p-value
		2405 (33.1)	4660 (64.1)	200 (2.8)	-
Age:	<45	181 (7.5)	519 (11.1)	13 (6.5)	<0.001
	45 to 64	962 (40.0)	2116 (45.4)	90 (45.0)	
	≥ 65	1262 (52.5)	2025 (43.5)	97 (48.5)	
Gender:	Female	1295 (53.9)	2551 (54.7)	117 (58.5)	0.41
Race:	White	1920 (79.8)	4039 (86.7)	183 (91.5)	<0.001
	Black	362 (15.1)	424 (9.1)	10 (5.0)	
	Other	123 (5.1)	195 (4.2)	7 (3.5)	
Obese (BMI >30)		895 (37.4)	1740 (37.5)	75 (37.5)	1.0
ASA Class: 3–4		1396 (58.1)	2358 (50.6)	111 (55.5)	<0.001
Tobacco Use		471 (19.6)	1025 (22.0)	37 (18.5)	0.041
Alcohol Use (>2 drinks/day)		78 (3.2)	152 (3.3)	7 (3.5)	0.98
Diabetes		535 (22.3)	855 (18.4)	31 (15.5)	<0.001
Chronic Obstructive Pulmonary Disease		229 (9.5)	417 (9.0)	18 (9.0)	0.73
Hypertension		1395 (58.0)	2471 (53.0)	112 (56.0)	<0.001
Peripheral Vascular Disease		74 (3.1)	102 (2.2)	8 (4.0)	0.032
Chronic Steroid Use		132 (5.5)	255 (5.5)	6 (3.0)	0.31
Approach:	Open	817 (34.0)	1671 (35.9)	36 (18.0)	<0.001
	Laparoscopic	1588 (66.0)	2989 (64.1)	164 (82.0)	
Procedure:	Partial Colectomy	2326 (96.7)	4468 (96.0)	195 (97.5)	0.37
	Total Colectomy	35 (1.5)	86 (1.9)	3 (1.5)	
	Coloproctectomy	44 (1.8)	106 (2.3)	2 (1.0)	
Insurance:	Medicare	1212 (50.7)	1922 (41.5)	92 (46.0)	<0.001
	Medicaid	83 (3.5)	163 (3.5)	2 (1.0)	
	Private	1029 (43.1)	2299 (49.6)	100 (50.0)	
	Other	66 (2.8)	251 (5.4)	6 (3.0)	
Hospital size >=500 beds		675 (28.3)	1160 (25.1)	54 (27.0)	0.003
	300–499 beds	986 (41.3)	2031 (43.9)	69 (34.5)	
	<300 beds	727 (30.4)	1437 (31.1)	77 (38.5)	
Academic Hospital		616 (25.8)	972 (21.0)	52 (26.0)	<0.001
Postoperative Complication		347 (14.4)	633 (13.6)	27 (13.5)	0.62
Readmission		262 (10.9)	454 (9.7)	20 (10.0)	0.31
Pain Medication:	Intravenous opioid	2389 (99.3)	4176 (89.6)	0	<0.001
	Oral opioid	999 (41.6)	2169 (44.6)	0	<0.001
	Acetaminophen	0	2699 (57.9)	12 (6.0)	<0.001
	Nonsteroidal Anti-inflammatory Drug (NSAID)	0	2546 (54.6)	14 (7.0)	<0.001

Characteristics		Opioids Alone N (%)	Multimodal N (%)	Opioid-Free, Single Agent N (%)	p-value
	Epidural	0	1233 (26.5)	173 (86.5)	<0.001
	Local Anesthetic	0	99 (2.1)	1 (0.5)	<0.001

Table 2:

Results of the multivariable logistic regression model to identify associations between patient and clinical characteristics and use of multimodal analgesia.

Use of Multimodal Pain Therapy			
	Multivariable Logistic Regression		
Covariate	**Coefficient**	**95% CI**	**p value**
Complication	1.01	0.84–1.21	0.89
Age - 65–84 years *	0.82	0.69–0.96	0.02
Age - ≤44 years *	1.32	1.10–1.57	0.002
Race (Black/Other v. White)	0.61	0.51–0.73	<0.001
ASA3/4	0.88	0.77–1.00	0.04
Hypertension	1.02	0.88–1.17	0.84
Peripheral Vascular Disease	0.78	0.55–1.10	0.16
Diabetes	1.00	0.89–1.11	0.94
Active smoker	1.06	0.91–1.22	0.45
Teaching hospital	0.80	0.29–2.17	0.67
Minimally invasive approach	1.00	0.80–1.24	0.99
Hospital bedsize <300 **	1.02	0.42–2.49	0.97
Hospital bedsize 300–499 **	1.09	0.44–2.69	0.85
Insurance - Medicaid ***	1.06	0.80–1.40	0.69
Insurance - Private ***	1.19	1.02–1.40	0.03
Insurance - Other ***	2.05	0.77–5.43	0.15
Constant	3.57		

Model was constructed using all covariates from the bivariate analysis with p value <0.1 Number of observations: 6974

Pseudo R^2 = 0.019

* Comparator is Age 45–64

** Comparator is bedsize >=500

*** Comparator is Medicare

Table 3:

Results of the multivariable linear regression model to identify the association between multimodal analgesia and length of stay.

Length of Stay			
	Multivariable Linear Regression		
Covariate	**Coefficient**	**95% CI**	**p value**
Multimodal Pain Therapy	−0.36	−0.65 – −0.07	0.015
Complication	4.30	3.78–4.83	<0.001
Age (continuous)	0.007	−0.004–0.019	0.22
Race (Black/Other v. White)	0.70	0.29–1.11	0.001
ASA3/4	0.83	0.60–1.06	<0.001
Hypertension	−0.013	−0.19–0.16	0.88
Peripheral Vascular Disease	0.55	−0.40–1.50	0.25
Diabetes	−0.14	−0.37–0.088	0.22
Active smoker	0.078	−0.17–0.32	0.54
Teaching hospital	0.12	−0.47–0.71	0.68
Minimally invasive approach	0.56	0.29–0.82	<0.001
Hospital bedsize <300 *	−0.028	−0.66–0.60	0.93
Hospital bedsize 300–499 *	−0.18	−0.76–0.38	0.52
Insurance - Medicaid **	0.19	−0.41–0.79	0.53
Insurance - Private **	−0.53	−0.74– −0.32	<0.001
Insurance - Other **	−0.57	−1.28–0.14	0.11
Constant	4.73		

Model was constructed using all covariates from the bivariate analysis with p value <0.1 Number of observations: 6974

$R^2 = 0.19$

* Comparator is bedsize >=500

** Comparator is Medicare