Preoperative opioid, sedative, and antidepressant use is associated with increased postoperative hospital costs in colorectal surgery

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Abstract

Background Opioid (OPD), sedative (SDT), and antidepressant (ADM) prescribing has increased dramatically over the last 20 years. This study evaluated preoperative OPD, SDT, and ADM use on hospital costs in patients undergoing colorectal resection at a single institution.

Methods This study was a retrospective record review. The local ACS-NSQIP database was queried for adult patients (age ≥ 18 years) undergoing open/laparoscopic, partial/total colectomy, or proctectomy from January 1, 2013 to December 31, 2016. Individual patient medical records were reviewed to determine preoperative OPD, SDT, and AD use. Hospital cost data from index admission were captured by the hospital cost accounting system and matched to NSQIP query-identified cases. All ACS-NSQIP categorical patient characteristic, operative risk, and outcome variables were compared in medication groups using chi-square tests or Fisher’s exact tests, and continuous variables were compared using Mann–Whitney U tests.

Results A total of 1185 colorectal procedures were performed by 30 different surgeons. Of these, 27.6% patients took OPD, 18.5% SDT, and 27.8% ADM preoperatively. Patients taking OPD, SDT, and ADM were found to have increased mean total hospital costs (MTHC) compared to non-users (30.8 vs 23.6 for OPD, 31.6 vs 24.4 for SDT, and 30.7 vs 23.8 for ADM). OPD and SDT use were identified as independent risk factors for increased MTHC on multivariable analysis.

Conclusion Preoperative OPD and SDT use can be used to predict increased MTHC in patients undergoing colorectal resections.

Keywords Opioids · Prescription drug use · Colorectal surgery · Healthcare costs · ACS-NSQIP

Opioid, sedative, and antidepressant prescribing has increased dramatically over the last 20 years, and their use is now considered at the category of an epidemic. The use of opioids alone has seen an increase of 500% over that time-frame, and sedative medications have seen a nearly 50% increase, particularly in older patients [1]. Roughly one in eight Americans takes an antidepressant and antidepressant prescribing has seen an increase of over 65% [2]. The Centers for Disease Control and Prevention now considers prescription drug use as one of the top five health challenges in the United States [3–5].

Healthcare costs have seen a similar increase. High-risk opioid users have increased overall healthcare costs by placing a nearly $29 billion additional burden on healthcare [6–8]. Preoperative opioid use is prevalent in 25% of patients presenting for non-cardiac surgery and has recently been shown to increase hospital costs, as well as postoperative...
costs, in patients undergoing elective general surgery procedures [9, 10].

The cost of surgery and postoperative admission is taking on a larger focus. Numerous methods have been proposed and protocols developed in attempts to reduce healthcare costs. Statistical-based systems, including the Revised Cardiac Risk Index and American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) Surgical Risk Calculator, have been used for predicting risk [11–13]. However, the effect of preoperative use of opioids, sedatives, and antidepressants has not been examined in colorectal surgery. We hypothesize the use of these medications is an important predictor in increased surgical admission costs. The objective of this study is to evaluate the impact of preoperative opioid, sedative, and antidepressant use on hospital costs in patients undergoing colorectal resection at a single institution.

Methods

Study population

This study was a single-institution retrospective record review. The study received approval from the University of Kentucky, Office of Research Integrity Institutional Review Board, with exemption from patient consent and met the guidelines of the responsible government agency. The local University of Kentucky ACS-NSQIP database was queried for adult patients (age ≥ 18 years) undergoing open or laparoscopic, partial or total, colectomy or proctectomy at the University of Kentucky from January 1, 2013 to December 31, 2016. Patients admitted after trauma, who were under 18 years of age, and who had a major surgical procedure within 30 days prior to the index surgery were excluded. The NSQIP database has been used extensively in literature, is peer regulated by surgeons, and allows for a common interpretation of risk factors and 30-day outcome measurements across studies [14].

Data obtained from the NSQIP database included patient characteristics (gender, age, race, American Society of Anesthesiology [ASA] classification, body mass index [BMI], functional status, smoking status, and medical comorbidities including congestive heart failure [CHF], chronic obstructive pulmonary disease [COPD], diabetes, renal failure, ascites, and hypertension), preoperative laboratory values (white blood cells, sodium, BUN, creatinine, albumin, hematocrit, platelets, INR, alkaline phosphatase, and bilirubin levels), and surgical variables (emergency status, operative indication, procedure type, wound classification, ostomy creation, and operative duration).

Individual patient medical records were reviewed to determine the preoperative use of specific opioids, sedatives, and antidepressants based on the medication reconciliation (which was finalized and confirmed by direct communication with the patient’s pharmacy as well as a pharmacist to patient interview). Preoperative use was defined as a medication listed on the Medication Reconciliation Document on admission by the patient and discussed with a member of pharmacy staff. Hospital cost data from the index admission were captured by the hospital cost accounting system (Allscripts EPSi Version 7.5 FP2, Chicago, IL; Allscripts Healthcare, LLC, Chesterfield, MO) and matched to the cases identified by the NSQIP query. Total hospital costs included operating room services and supplies to include holding room, operating room, post-anesthesia care, as well as ward accommodations, intensive care, pharmacy, diagnostics, ancillary treatments such as physical therapy, and blood. Total hospital costs included both direct (supplies, nursing, and equipment) and indirect costs (administration, facility, and other overhead), but did not include professional fees.

Outcome measures included costs related to normal accommodations, supplies, operating room, pharmacy, diagnostics, intensive care, and ancillary therapies. These costs were aggregated to give us Total Hospital Cost. All patient characteristics, surgical characteristics, and outcomes recorded were strictly defined by the ACS-NSQIP 2017 Participant Use Data File [15]. There were no patients who had missing outcomes data or were lost to follow-up as only complete 30-day follow-up data was recorded into our local NSQIP database.

Statistical analysis

All ACS-NSQIP categorical patient characteristic, operative risk, and outcome variables were compared in medication groups using chi-square tests or Fisher’s exact tests, and continuous variables were compared using Mann–Whitney U tests. A p value of ≤ 0.05 was considered the threshold for statistical significance in the bivariate calculations.

ACS-NSQIP patient and operative risk factors were considered in a backward multivariable logistic regression of total costs (p for entry ≤ 0.05, for exit ≥ 0.10). Medication use variables were then added into the model in the presence of the independent risk factors.

Results

A total of 1185 colorectal procedures were performed at a single site by 30 different surgeons with volumes ranging from 1 to 497 cases. The mean age was 55.8 ± 15.5 years and median age was 57. Six-hundred two (50.8%) were female, 134 (11.3%) minority race, and 59 (0.5%) were of known
Hispanic ethnicity. Seven-hundred ninety-three (66.9%) were elective procedures, and 22.5% were emergent.

**Patient preoperative characteristics predictive of hospital cost**

The mean total hospital cost (MTHC) for the cohort, measured in $1000s, was 25.7 ± 30.5. MTHC was 19.8 for elective cases which increased for non-elective, non-emergent (32.0), and emergent (40.4). Transfer status was also significantly associated with MTHC as patients admitted from home had lower cost than those from outside hospitals, emergency departments, and nursing homes. MTHC increased with increasing ASA class. Functional status, pulmonary status, preoperative inflammatory response, and other significant medical comorbidities were associated with increased MTHC as listed in Table 1.

Patient characteristics that did not vary with MTHC included sex, race or ethnicity, current smoking status, ascites, chronic use of steroids, recent weight loss greater than 10%, and BMI.

Preoperative laboratory values associated with MTHC were assessed. Uremia, hyponatremia and hypernatremia, elevated creatinine, hypoalbuminemia, leukocytosis and leukopenia, anemia, and thrombocytopenia were associated with increased MTHC. Thrombocytosis was associated with decreased MTHC. The mean total hospital costs associated with abnormal laboratory values are listed in Table 2.

After backwards multiple regression, independent patient predictors of cost in order of predictive strength were ASA class, preoperative inflammatory response, functional status, existing open wound, hypoalbuminemia, disseminated cancer, leukocytosis, leukopenia, bleeding disorders, and dyspnea.

**Operative characteristics predictive of hospital cost**

Open colectomy procedures (CPT code beginning with 4414- and 4415-) had increased MTHC, while laparoscopic colectomy procedures (CPT code beginning with 4420- and 4421-) had decreased MTHC. A full listing of operative procedures and costs are listed in Table 3. Increasing operative duration was also predictive of increased MTHC. Clean/contaminated wounds had lower MTHC (20.9) than contaminated (26.2) and dirty/infected wounds (30.0) as did wound closure techniques. Fully closed wounds had MTHC of 23.4, while MTHC increased with closure of only deep layers (42.5) and no closure (75.9). Preoperative transfusion within 72 h was predictive of increased MTHC.

With independent preoperative risk factors fixed in the model, independent operative predictors of cost were procedure group (first four digits of CPT code), duration of operation, wound closure technique, and transfusion requirement.

**Hospital costs by drug class**

Three-hundred twenty-seven (27.6%) patients took opioids (OPD), 219 (18.5%) took sedatives (SDT), and 329 (27.8%) took antidepressants (ADM) preoperatively. All classes of medications studied were associated with increased MTHC (30.8 vs 23.6 for OPD, 31.6 vs 24.4 for SDT, and 30.7 vs 23.8 for ADM).

Patients taking OPD were found to have increased costs compared to non-users for all sub-costs in the analysis. Mean accommodation costs and supply costs were each $970 more than non-users. ICU costs were $2,130 more for OPD users. OPD users had a mean increase of $1,310 in pharmacy costs compared to non-users. A complete listing of cost differences per category can be seen in Table 4. When adjusted for independent preoperative and operative risks for increased cost on multivariate analysis, patients taking OPD had a cost increase of $1,173 (regression coefficient 1.07, 95% confidence interval (CI) 1.01–1.14, \( p = 0.030 \)).

Similar to OPD users, patients taking SDT were associated with increased mean cost of various subcategories. SDT users saw a mean increase of $2,740 in ICU costs and $1,380 in pharmacy costs. Complete listing of cost differences per category can be seen in Table 4. When controlled for significant variables on multivariate analysis, patients taking SDT had a mean cost increase of $1,843 (regression coefficient 1.11, 95% CI 1.03–1.19, \( p = 0.004 \)).

Antidepressant use followed a comparable trend as OPD and SDT use. Mean bed cost was $1,010 higher than non-users. ICU costs were $2,030 higher on average and pharmacy costs were increased by $1,630. Complete listing of cost differences per category can be found in Table 4. On multivariate analysis, ADM users had a mean increase of $838 (regression coefficient 1.05, 95% CI 0.99–1.12, \( p = 0.102 \)).

An interaction term between the drug use classes in the multivariable regression was not a significant predictor of MTHC.

**Discussion**

Preoperative use of OPD, SDT, and ADM has been increasing. Nearly a third of our patients undergoing colorectal surgery used OPD and ADM preoperatively, and over one in five took SDT. Optimizing patients preoperatively is a key surgical principle and has classically focused on modifiable risk factors, such as tobacco use, obesity, and functional status, as well as cardiopulmonary status and nutrition. Only recently has preoperative usage of specific medications been studied as it relates to postoperative outcomes [16, 17]. OPD and SDT have been identified as risk factors for poor surgical outcomes [18,
| Variable                                                                 | n   | Mean total hospital costs $000’s (SD) | p value |
|-------------------------------------------------------------------------|-----|-------------------------------------|---------|
| All patients                                                            | 1185| 25.7 (30.5)                         |         |
| **Presentation**                                                        |     |                                     | <.001   |
| Same-day elective                                                       | 793 | 19.8                                |         |
| Not elective & not emergent                                             | 125 | 32.0                                |         |
| Emergency                                                               | 267 | 40.4                                |         |
| **Transfer status**                                                     |     |                                     | <.001   |
| Not transferred (admitted from home)                                    | 912 | 21.6                                |         |
| Outside emergency department                                            | 164 | 34.6                                |         |
| From acute care hospital inpatient                                     | 80  | 46.3                                |         |
| Nursing home—chronic care—intermediate care                            | 15  | 50.2                                |         |
| Other/Unknown                                                           | 14  | 48.4                                |         |
| **Age quartile, year**                                                 |     |                                     | <.001   |
| ≤ 47                                                                   | 317 | 30.2                                |         |
| 48–57                                                                  | 292 | 35.7                                |         |
| 58–67                                                                  | 307 | 28.7                                |         |
| 68+                                                                    | 269 | 25.9                                |         |
| **ASA physical status classification**                                  |     |                                     | <.001   |
| I–II                                                                   | 373 | 17.5                                |         |
| III                                                                    | 695 | 24.8                                |         |
| IV–V                                                                   | 117 | 57.4                                |         |
| **Diabetes**                                                            |     |                                     | <.001   |
| Non-insulin                                                            | 133 | 27.2                                |         |
| Insulin                                                                | 90  | 34.3                                |         |
| **Preoperative functional status**                                      |     |                                     | <.001   |
| Partially dependent                                                    | 65  | 47.6                                |         |
| Totally dependent                                                      | 17  | 70.3                                |         |
| **Preoperative inflammatory response**                                  |     |                                     | <.001   |
| None                                                                   | 1002| 20.5                                |         |
| SIRS                                                                   | 26  | 29.7                                |         |
| Sepsis                                                                 | 98  | 42.3                                |         |
| Septic shock                                                           | 59  | 74.4                                |         |
| **Dyspnea**                                                            |     |                                     | <.001   |
| No                                                                     | 984 | 26.2                                |         |
| Moderate exertion                                                      | 175 | 26.6                                |         |
| At rest                                                                | 26  | 99.7                                |         |
| Severe COPD                                                            | 119 | 35.9                                | <.001   |
| **Preoperative ventilator**                                            |     |                                     | <.001   |
| CHF                                                                    | 28  | 58.3                                | <.001   |
| Medically treated HTN                                                   | 628 | 29.8                                | <.001   |
| Renal failure                                                          | 7   | 114.8                               | <.001   |
| Dialysis                                                               | 19  | 54.9                                | <.001   |
| Disseminated cancer                                                     | 162 | 27.7                                | .009    |
| Preoperative open wound                                                | 63  | 41.0                                | <.001   |
| Bleeding disorder                                                      | 109 | 45.8                                | <.001   |
| Preoperative transfusion                                               | 18  | 65.8                                | <.001   |

**SIRS** systemic inflammatory response syndrome, **COPD** chronic obstructive pulmonary disease, **CHF** congestive heart failure, **HTN** hypertension
When adjusted for all significant independent preoperative and perioperative risk factors, OPD and SDT significantly increased MTHC. ADM use also showed a trend toward increased MTHC though it did not reach statistical significance. These findings identify preoperative use of OPD and SDT as independent risk factors for increased hospital costs relating to colorectal surgery.

The OPD epidemic has seen a significant increase in prescription and illicit OPD use in Kentucky and surrounding states to levels higher than national averages [20, 21]. OPD has been associated with increased postoperative complications and length of stay in orthopedic and abdominal surgery literature [10, 22, 23]. Patients using OPD have been shown to be at higher risk for pneumonia and respiratory failure. This is due to respiratory depression and is worsened in patients with COPD. OPD has also been associated with factors prolonging length of stay, including postoperative nausea and vomiting, prolonged ileus, and urinary retention. These have also led to increased morbidity and mortality [10, 24, 25]. Our results demonstrate increased cost in effectively all aspects of hospitalization, including costs relating to operating room, supplies, intensive care, pharmacy, diagnostics, and ancillary treatments. After adjusting for known risk factors, preoperative OPD use increased MTHC by nearly $1,200.

Costs related to operating room, intensive care, pharmacy, diagnostics, and ancillary treatments were increased in patients taking SDT preoperatively. As previously stated, SDT has been found to be an independent risk factor for adverse outcomes in non-cardiac surgery [18]. Patients taking these medications also have been found to have increased operative times, increased length of stay, and

### Table 2 Patient preoperative lab values predictive of hospital costs

| Variable                  | n   | Mean total hospital costs $000’s (SD) | p value |
|---------------------------|-----|--------------------------------------|---------|
| All patients              | 1185| 25.7 (30.5)                          |         |
| BUN > 40 mg/dL            | 53  | 62.2                                 | <.001   |
| Sodium < 135 mmol/L       | 70  | 35.3                                 | <.001   |
| Sodium > 145 mmol/L       | 18  | 37.3                                 | <.001   |
| Creatinine > 1.2 mg/dL    | 160 | 43.1                                 | <.001   |
| Albumin < 3.5 g/dL        | 461 | 35.1                                 | <.001   |
| WBC ≤ 4500/mm³            | 78  | 35.1                                 | <.001   |
| WBC > 11,000/mm³          | 241 | 38.5                                 | <.001   |
| HCT < 38%                 | 519 | 30.9                                 | <.001   |
| Platelets < 150,000/mm³   | 94  | 45.7                                 | <.001   |
| Platelets > 400,000/mm³   | 92  | 21.3                                 | <.001   |

*BUN* blood, urea, nitrogen, *WBC* white blood cell, *HCT* hematocrit

### Table 3 Operative characteristics predictive of hospital costs

| Variable                               | n   | Mean total hospital costs $000’s (SD) | p value |
|----------------------------------------|-----|--------------------------------------|---------|
| All patients                           | 1185| 25.7 (30.5)                          |         |
| Procedure group                        |     |                                      |         |
| Open partial colectomy                 | 405 | 33.6                                 | <.001   |
| Total abdominal colectomy              | 58  | 50.3                                 |         |
| Proctectomy                            | 47  | 22.9                                 |         |
| Lap partial colectomy                  | 425 | 17.7                                 |         |
| Lap total abdominal colectomy          | 75  | 18.3                                 |         |
| Lap proctectomy                        | 76  | 20.6                                 |         |
| Ostomy                                 | 650 | 29.3                                 | <.001   |
| Duration of operation, incision to close, mins. | |                                      |         |
| ≤ 120                                  | 322 | 22.5                                 | <.001   |
| 121–180                                | 409 | 25.3                                 |         |
| 181–240                                | 248 | 27.2                                 |         |
| 241+                                   | 206 | 30.1                                 |         |
| Wound class                            |     |                                      | <.001   |
| Clean/Contaminated                     | 706 | 20.9                                 |         |
| Contaminated                           | 276 | 26.2                                 |         |
| Dirty/Infected                         | 203 | 41.9                                 |         |
| Wound closure                          |     |                                      | <.001   |
| All layers of incision (deep and superficial) fully closed | 1111 | 23.4                     |         |
| Only deep layers closed; superficial left open | 33  | 42.5                                 |         |
| No layers of incision are surgically closed | 41  | 75.9                                 |         |
| Transfused w/in 72 h of incision       | 146 | 56.3                                 | <.001   |
Table 4 Costs in drug use and non-use cohorts; by cost center ($000's)

| Cost center       | All pts. | Opioid | Diff. | Sedative | Diff. | Antidepressant | Diff. |
|-------------------|----------|--------|-------|----------|-------|----------------|-------|
| No. pts.          | 1185     | 828    | 327   | p-value  | 966   | 219            | p-value |
| Mean total costs (SD) | 25.7 (30.5) | 23.6 | 30.8 | <.001   | 24.4 | 31.6 | .002 | 23.8 | 30.7 | .001 |
| Bed costs         | 6.43 (6.01) | 6.14 | 7.11 | .011   | 6.28 | 7.11 | .065 | 6.15 | 7.16 | .010 |
| Med-Surg supply costs | 5.20 (5.39) | 4.91 | 5.88 | .005   | 5.10 | 5.66 | .165 | 5.05 | 5.61 | .109 |
| OR costs          | 4.82 (2.63) | 4.70 | 5.09 | .022   | 4.74 | 5.18 | .023 | 4.79 | 4.91 | .486 |
| ICU costs         | 3.59 (10.4) | 2.95 | 5.08 | .001   | 3.08 | 5.82 | <.001 | 3.03 | 5.06 | .003 |
| Pharmacy costs    | 2.66 (6.43) | 2.27 | 3.58 | .001   | 2.41 | 3.79 | .004 | 2.21 | 3.84 | <.001 |
| Diagnostics costs | 2.06 (3.82) | 1.82 | 2.62 | .001   | 1.95 | 2.57 | .028 | 1.79 | 2.78 | <.001 |
| Ancill. Trx. costs | 0.74 (2.30) | 0.59 | 1.08 | .001   | 0.64 | 1.17 | .002 | 0.62 | 1.06 | .003 |
| Blood costs       | 0.23 (0.97) | 0.20 | 0.32 | .043   | 0.23 | 0.27 | .546 | 0.21 | 0.29 | .235 |

Increased readmissions [26]. This could be attributed to the effects of SDT on respiratory and cognitive functions which have been demonstrated to contribute to poor surgical outcomes [27–29]. Chronic use of SDT has also been shown to increase postoperative delirium, and decrease adequate pain control and overall prolonged surgical recovery [30–33]. Adverse events, such as surgical site infection, lead to a need for further procedures, longer hospital stays, and amplified care requirements. After adjusting for significant independent risk factors, SDT use increased MTHC by over $1,800.

ADM use has been shown to be associated with increased adverse events, prolonged LOS, and higher morbidity and mortality [34, 35]. Our study showed significantly increased costs relating to bed costs, intensive care, pharmacy, diagnostics, and ancillary therapies. Nonetheless, our multivariate analysis did not demonstrate that preoperative ADM use independently increases MTHC. Also, any combined use of multiple medication classes did not have a synergistic effect on MTHC greater than the risk of each medication class alone.

Prior to this study, the association between preoperative medication use and postoperative hospital costs had not been studied in colorectal surgery literature. It has been reported that preoperative OPD use has increased overall healthcare costs [7]. Reports from spine surgery literature have shown increased costs following cervical and lumbar fusions [36, 37]. Elective abdominal general surgery procedures have also shown increased hospital costs as well as overall postoperative costs [10]. However, no study to date has investigated the relationship between preoperative OPD and SDT use to all-comers in colorectal surgery resections.

Given our results, the preoperative use of OPD and SDT should be considered in the preoperative risk stratification and optimization of colorectal surgery patients. Enhanced Recovery after Surgery (ERAS) is a surgical optimization program that systematically works to decrease surgical complications, LOS, and costs [38–40]. While ERAS has previously primarily focused on perioperative OPD use, our findings indicate that SDT use may also be considered in the prediction of increased perioperative costs. Provider’s knowledge of preoperative use of these medications may allow for expectant management of postoperative complications and reduce costs.

The ACS-NSQIP database allows for comparison with other studies performed through its database, given the precise definition of each outcome variable and homogeneity of the data series within a fixed timeframe. However, there are limitations to this study. We cannot prove causality within a retrospective study despite demonstrating a strong association between SDT and increased MTHC. Also, with the study performed at a single institution, the results may not apply to all centers. There lies the possibility of unmeasured confounders as well, including high-risk comorbid conditions or clinical risk factors among medication users which could influence morbidity and mortality more than the medication itself. Multivariate analysis will adjust for known confounders, but it is impossible to capture all risk factors associated with outcomes and cost. In the same light, preoperative medication users could be higher risk than captured in our bivariate analysis. Under these circumstances, recognition of preoperative medication use can aide in identifying patients with higher risk of increased cost. Two sources of potential bias were identified. First, not all preoperative and operative risk factors were captured in our study. Examples could be patient compliance and socioeconomic status. However, the NSQIP database is one of the most robust clinical datasets available, including blood tests and other granular clinical variables. Additionally, there is unknown treatment bias related to this retrospective review that could alter the outcomes resulting from unknown surgical decision making as it relates to technique, approach, and indications. Our study did include multiple surgeons from different services which partially mitigates selection bias.
Further limitations include the lack of both specific dosage and length of use for each medication preoperatively in our data analysis. This would allow us to stratify users based on these factors and improve generalizability. Unfortunately, we were limited by the capabilities of the medication record, which is currently being improved to allow linkage to a statewide electronic recording system. Lastly, preoperative illicit use of these medications was not captured in our database. With the current state of the OPD epidemic and illicit use of SDT, we may be significantly underestimating the true amount of preoperative SDT use as well as OPD use. These could skew the data analysis and give falsely low results. Certainly, future randomized prospective studies are warranted to further this project and also to identify the impact of medication dose or chronicity on healthcare costs.

**Conclusion**

OPD, SDT, and ADM use is increasingly prevalent and can be used to predict increased total hospital costs in patients undergoing colorectal resections. These increased costs, in combination with previous findings of risk for adverse outcomes, underscore the importance of preoperative evaluation of drug usage for both risk prediction and optimization.

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**Compliance with ethical standards**

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