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Evaluation of a Tiered Opioid Prescribing Guideline for Inpatient Colorectal Operations

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EVALUATION OF A TIERED OPIOID PRESCRIBING GUIDELINE FOR INPATIENT COLORECTAL OPERATIONS

A Master's Thesis Presented

By

DAVID CLINTON MEYER

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The signatures of the Master's Thesis Committee signify completion and approval as the style and content of the Thesis

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Abstract:

Background:

In light of the opioid epidemic, reducing excess prescription quantities while tailoring to patient need is key. We previously created an opioid prescribing guideline using retrospective institutional data to satisfy the majority of patients' opioid needs following inpatient colorectal surgery.

Objective:

This study sought to prospectively validate an institutional prescribing guideline based on previously-defined opioid consumption patterns following inpatient colorectal operations.

Methods:

We carried out a cohort study comparing opioid prescribing and consumption patterns before (7/18 – 1/19) and after (9/19 – 2/20) adoption of a tiered opioid prescribing guideline for inpatient elective colorectal operations (colectomies, proctectomies, and ostomy reversals) at a single tertiary care medical center. Opioid use was quantified as Equianalgesic 5mg Oxycodone Pills (EOP), and patients were grouped in three tiers based on opioid consumption in the 24-hours prior to discharge: Tier 1 (0 EOP), Tier 2 (0.1-3 EOP), and Tier 3 (>3 EOP). Our guideline recommended maximum prescriptions of 0 EOP for Tier 1, 12 EOP for Tier 2, and 30 EOP for Tier 3.

Results:

The study included 100 patients before and 101 after guideline adoption. Demographic and operative variables were similar before and after guideline adoption. Guideline adherence was 85%. Overall, there was a 41% reduction in mean prescription quantity and 53% reduction in excess pills per prescription with no change in opioid consumption or refill rates.

Conclusion:

Adoption of a tiered opioid prescribing guideline significantly reduced opioid prescription quantity with no change in consumption or refill rates. Standardization of discharge prescriptions based on patient consumption in the 24 hours prior to discharge may be an important step towards minimizing excess prescribing.

Key Words:

Pain management; Colorectal Surgery; Post-operative pain; Opioid; Narcotic

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All materials (Figures, Tables, etc.) in this thesis represent original work.

List of Abbreviations:

EOP: Equi-analgesic 5-milligram oxycodone pills
EMR: Electronic medical record
AUC: Area Under the Curve
IV: Intravenous

Preface:

Other works that will not be presented as part of this thesis

Manuscripts:

1. Sarani B, Paspulati RM, Hambley J, Efron D, Martinez J, Perez A, Bowles-Cintron R, Yi F, Hill S, **Meyer D**, Maykel J, Attala S, Kochman M, Steel S, Turnbull RB. A Multidisciplinary Approach to Diagnosis and Management of Bowel Obstruction. Curr Probl Surg. 2018 Oct; 55(10):394-438.
2. Hill SS, Chung SK, **Meyer DC**, Crawford AS, Sturrock PR, Harnsberger CR, Davids JS, Maykel JA, Alavi K. Impact of pre-operative care for rectal adenocarcinoma on pathologic specimen quality and post-operative morbidity: a NSQIP analysis. J Am Coll Surg. 2020 Jan; 230(1):17-25.
3. **Meyer DC**, Hill SS, McDade JA, Harnsberger CR, Davids JS, Sturrock PR, Maykel JA, Alavi K. "Opioid consumption patterns after anorectal operations: development of an institutional prescribing guideline." *Dis Colon Rectum (In press)*

Podium Presentations:

1. **Meyer DC,** Resnick AJ, Hill SS, Crawford AS, Sturrock PR, Harnsberger CR, Davids JS, Maykel JA, Alavi K. (2019) "Stop over-prescribing opioids following colorectal surgery: more than half of patients don't take them" Podium presentation at: American College of Surgeons Clinical Congress; 2019 Oct 27-31; San Francisco, CA.
2. **Meyer DC,** Resnick AJ, Harnsberger CR, Davids JS, Maykel JA, Alavi K, Sturrock PR. (2019) "Prolonged Foley catheterization with pre-removal cystogram after surgical repair of colovesical fistula: Are we being too vigilant?" Podium presented at: New England Society of Colon and Rectal Surgeons; 2019 May 18-19; Bretton Woods, NH.

3. **Meyer DC,** Harnsberger CR, Davids JS, Sturrock PR, Alavi K, Maykel JA. (2019) "Endoscopic Formalin Instillation for Radiation-Induced Hemorrhagic Colitis" Podium presented at: New England Society of Colon and Rectal Surgeons; 2019 May 18-19; Bretton Woods, NH.
4. Hill SS, Chung SK, **Meyer DC**, Crawford AS, Sturrock PR, Harnsberger CR, Davids JS, Maykel JA, Alavi K. "Impact of a complete pre-operative work-up for rectal adenocarcinoma on pathologic quality and post-operative morbidity: a NSQIP analysis." Podium presented at: American College of Surgeons Clinical Congress; 2019 Oct 27-31; San Francisco, CA.
5. **Meyer DC**, Hill SS, Resnick AJ, Purkayastha A, Davids JS, Sturrock PR, Maykel JA, Alavi K. "Prospective evaluation of a standardized opioid prescribing guideline for anorectal operations." Podium presented at: American Society of Colon and Rectal Surgeons; 2020 June 6-10; Boston, MA.
6. **Meyer DC**, Hill SS, Monahan PF, Resnik AJ, Davids JS, Maykel JA, Sturrock PR, Alavi K. "Urinary catheter management after colovesical fistula repair: a survey of US board certified colorectal surgeons." Podium presented at: American Society of Colon and Rectal Surgeons; 2020 June 6-10; Boston, MA.

Abstract and Poster Presentations:

1. **Meyer DC,** Wyman AS, Alavi K, LaFemina J, Davids JS. (2018) "General Surgery Resident Attitudes Toward Surgical Simulation." Poster presented at: Massachusetts Chapter of the American College of Surgeons; 2018 Dec 1; Boston, MA.
2. **Meyer DC,** Purkayastha A, Hill SS, Crawford AS, Harnsberger CR, Sturrock PR, Davids JS, Maykel JA, Alavi K. (2019) "Opioid consumption after anorectal surgery: Are we

over-prescribing?" Poster presented at: American Society of Colon and Rectal Surgeons; 2019 June 6-10; Cleveland, OH.

3. **Meyer DC**, Resnick AJ, Hill SS, Harnsberger CR, Davids JS, Alavi K, Maykel JA, Sturrock PR. (2019) "Prolonged foley catheterization with pre-removal cystogram after surgical repair of colovesical fistula: are we being too vigilant?" Poster presented at: American Society of Colon and Rectal Surgeons; 2019 Jun 6-10; Cleveland, OH.
4. Hill SS, Dore FJ, Em ST, McLoughlin RJ, **Meyer DC**, Sturrock PR, Harnsberger CR, Maykel JA, Alavi K, Davids JS. "Characterization of Twitter Use Among Departments of Surgery with ACGME General Surgery Residency Programs." Poster presented at: American College of Surgeons Clinical Congress; 2019 Oct 27-31; San Francisco, CA.
5. Hill SS, Foiles Sifuentes AM, **Meyer DC**, Crawford AS, Hahn SJ, Sturrock PR, Davids JS, Maykel JA, Alavi K. The Effect of Race, Ethnicity, and Population Density on Disparities in Timing to Definitive Surgery in Rectal Cancer. Poster presented at: American Society of Colon and Rectal Surgeons; 2020 June 6-10; Boston, MA.
6. Hill SS, Hahn SJ, **Meyer DC**, Harnsberger CR, Sturrock PR, Davids JS, Alavi K, Maykel JA. Transanal minimally invasive surgery (TAMIS) is an effective approach for patients with anastomotic failure requiring redo proctectomy. Poster presented at: American Society of Colon and Rectal Surgeons; 2020 June 6-10; Boston, MA.
7. **Meyer DC**, Monahan PF, Hill SS, Sturrock PR, Maykel JA, Alavi K, Davids JS. Analysis of Procedure Cancellations in an Academic Colorectal Practice. Poster presented at: American Society of Colon and Rectal Surgeons; 2020 June 6-10; Boston, MA.

Chapter I: Introduction

Opioid History and Pharmacology

Opiate alkaloids have been used by humans for thousands of years to treat pain.[1] Harvested from the resin of the opium poppy (*Papaver somniferum*), these molecules have been commercially extracted to produce morphine since the 1820s.[2] The first synthetic opioids were generated around 100 years ago.[2] While the term "opiate" generally refers to alkaloids derived from the opium poppy, such as morphine and codeine, the term "opioid" refers to all compounds that bind to the opioid family of receptors including semi-synthetic opiates such as heroin and oxycodone, and synthetic opioids such as methadone and fentanyl.[3] The term "narcotic" is a legal definition referring to opioids as well as other non-opioid drugs.[3]

Although several types of opioid receptors exist, all opioids achieve their primary analgesic effects by binding to the μ-opioid receptor.[1] Mu-opioid receptors are located in the central and peripheral nervous system.[1] Activation of μ-opioid receptors suppresses key components of the pain pathway, but also suppress respiratory centers in the brainstem, motility in the GI tract, and activate nausea in the chemoreceptor trigger zone of the brainstem.[2] Opioids have other adverse effects including development of hyperalgesia, tolerance, and addiction which are exacerbated with repeated or prolonged exposure. Despite considerable investment into alternative pathways to treat pain, opioids remain the most frequently used medication to treat severe pain and one of the most commonly prescribed medications in the U.S.[2]

Opioid Prescribing in the United States

Opioid prescriptions and overdose deaths in the U.S. have risen dramatically over the past three decades.[4, 5] The number of opioid overdose deaths have quadrupled from 2000 to 2015 and

prescription rates hit a peak of 81.3 prescriptions per 100 residents in 2012.[4, 5] Since that time both prescriptions and overdoses related to this drug have been declining, yet our society remains in the midst of an opioid epidemic.[6]

Opioid medications have a high potential for abuse, diversion, and dependence.[7-10] According to the 2018 National Survey on Drug Use and Health, 4% of adults in the U.S. reported misuse of opioids in the past year.[11] Among the respondents, over half obtained opioid medications through diversion from a friend or family member, approximately 2 in every 5 individuals misused pills from a legitimate prescription, while only 7% reported obtaining the medications from a drug dealer.[11] Excess pills stored in homes are an important source of diversion through sale or theft.[8, 9, 12]

Surgeons play an important role in combating the opioid epidemic since it is well established that U.S. surgeons overprescribe opioids for post-operative pain.[12] A 2017 systematic review of surgical opioid prescribing found that 42-71% of prescribed pills went unused.[10] Overprescribing after surgery not only increases the potential for diversion, but can contribute to misuse and dependence. The quantity of pills prescribed after surgery is strongly associated with the rate of misuse.[9] Additionally, the risk of opioid naïve surgical patients developing long-term opioid use is highly correlated with the quantity of the initial opioid prescription.[13] In opioid naïve surgical patients, the rate of persistent opioid use after one year is between 6-8%.[14, 15] A reduction in excess prescribing after surgery may help combat opioid diversion and dependence.

Current Prescribing Guidelines

A key challenge to improving post-surgical opioid prescribing on the national scale has been a lack of consensus on appropriate prescribing targets for individuals or populations. Most

prescribing guidelines fail to delineate specific prescription quantities. [16-18] The Centers for Disease Control recommend not exceeding a 7-day supply after surgery but does not specify dosages or methods to determine what quantity constitutes a 7-day supply.[16] Massachusetts guidelines state that dosing should be the minimum dosage necessary and the duration should be as short as possible.[17] Guidelines from pain and anesthesia societies, such as the American Pain Society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists are similarly vague and lack specific prescription quantities.[18] The Michigan Opioid Prescribing Engagement Network is the only state-sponsored group to provide procedure-specific prescription guidelines for opioids and recommends the following for colorectal operations: 0-10 pills after laparoscopic colectomies and 0-15 pills after open colectomies or ostomy reversals.[19] While these recommendations are likely adequate for most patients who undergo these surgeries, they do not account for the variable needs of individual patients, in particular, those patients who have high requirements for pain medication at the time of discharge.

Studies that have examined the association between pre-discharge opioid requirements with consumption after discharge have provided an alternative approach to post-surgical opioid prescribing.[20, 21] In a study of inpatient general surgery procedures, Hill et al.[20] suggest a prescribing algorithm for inpatient general surgery operations that ties discharge prescribing to the quantity of opioids consumed in the 24-hours prior to discharge; prospective evaluation of this algorithm remains needed. However, since this algorithm was based on a surgical population that included bariatric, foregut, pancreatectomy, and ventral hernia operations, it may not be applicable to colorectal surgery population. A tiered opioid prescribing guideline based on a similar concept

has been proposed and validated for gynecologic operations.[21] There have been no similar studies performed in the colorectal surgery population.

Development of a Tiered Opioid Prescribing Guideline for Colorectal Operations

In order to reduce variability and excess prescribing after colorectal operations, the Division of Colon and Rectal Surgery at the University of Massachusetts Medical School sought to develop a simple opioid prescribing guideline that would couple discharge prescriptions to opioid consumption in the day prior to discharge for patients undergoing major elective inpatient colorectal operations. To develop this guideline, we analyzed the opioid consumption patterns of 100 patients undergoing inpatient colorectal operations (colectomies, proctectomies, and ostomy reversals) between July 2018 and January 2019 performed by five board certified colorectal surgeons at our single academic institution (*unpublished data)*. We found wide variability and excessive prescribing, with over 60% percent of prescribed pills left over and one-half of patients taking no pills after discharge.

Based on these findings, we developed a prescribing guideline designed to satisfy the needs for the majority of patients. To facilitate standardized dosing language, all opioid dosages opioid dosages were converted to Equianalgesic 5-mg Oxycodone Pills (EOP). The prescribing guideline had three tiers based on opioid consumption in the 24-hours prior to discharge: Tier 1 (0 EOP), Tier 2 (0.1–3 EOP), and Tier 3 (3.1 EOP or greater). The cut-point for each tier was determined *post hoc* to maximize equal distribution between tiers. The prescribing recommendation for Tier 1 was set at 0 EOP since less than 25% of patients in Tier 1 consumed any additional opioid pills as an outpatient. For Tier 2 and Tier 3, the prescribing recommendation was set at the 85th percentile of opioid consumption based on similar

methodology published by Hill et al.[20] Our final guideline recommended a maximum discharge prescription for each tier: 0 EOP for Tier 1, 12 EOP for Tier 2, and 30 EOP for Tier 3 (Figure 1). By applying the prescription recommendations to the historical dataset, we calculated that the proposed guideline could reduce prescribed pills by as much as 45% and excess pills by as much as 73%. The guideline was adopted at our institution in August 2019.

Specific Aims:

The primary aim of this prospective study was to examine changes in opioid prescribing and consumption patterns after implementation of a tiered opioid prescribing guideline for inpatient colorectal operations at a single academic medical center. We secondarily sought to determine the rate of guideline adherence among prescribers.

Chapter II: Methods

Adoption of the Prescribing Guideline

In August 2019, we presented the main findings from our guideline development to the surgical residents during time set aside for weekly resident education. We also provided education on the new prescribing guidelines to the physician assistants involved with inpatient management of patients who were undergoing colorectal surgery. The guidelines were distributed on laminated reference cards to all residents and physician assistants and a poster detailing the guidelines was posted in the resident work area. Data collection was started in September 2019, one-month after guideline adoption to allow a transition period for full implementation and adoption of the guidelines. A monthly email summarizing the prescribing guideline was distributed to all members of the colorectal surgery service for the duration of the study, coinciding with scheduled resident turnover.

Study Population

The study population was determined using the inclusion and exclusion criteria that had been used in our previous guideline development study. After guideline adoption, all adult patients who underwent major elective colorectal operations at a single academic medical center performed by four board-certified colorectal surgeons between September 2019 and February 2020 were eligible. Major colorectal operations included in the study were partial colectomy, proctectomy, total abdominal colectomy, total proctocolectomy, ileostomy takedown, and colostomy takedown. Patients were excluded from the present study if they had a hospital stay less than 48 hours, were taking opioid medication within 30 days prior to surgery, or if opioid consumption data were not documented in the first post-operative clinic note. Patients were also excluded if they were

discharged to an inpatient facility (inpatient rehabilitation center, skilled nursing facility, or long-term acute care hospital) because many of these facilities have staff physicians who prescribe patient medications during their facility stay and thus these patients are not provided with an opioid prescription at hospital discharge. All patients received standard of care during their hospitalization. A printed after-visit summary is provided to patients at the time of discharge, which was reviewed by the discharging nurse and provides instructions to expect pain for 2 to 3 weeks after surgery and to alternate using over-the-counter Tylenol and ibuprofen for pain, reserving opioid medications for breakthrough pain.

Data Collection

Data collection was performed using the same methodology that had been utilized in our previous guideline development study. For each patient, the electronic medical record (EMR) was reviewed and selected sociodemographic and clinical characteristics were extracted including patient demographic characteristics, medical history, prior opioid use, alcohol and drug use, and currently prescribed medications. Prior opioid prescriptions were reviewed in the EMR and opioid exposure status was determined for each patient in the following: opioid naïve defined as no documented opioid prescription within 1 year prior to surgery, opioid exposed defined as documented opioid prescription within 1 year, but greater than 30 days prior to the operation.

Operative procedure characteristics were collected from the EMR including procedure type, surgical approach, and operative time. Operative approach was categorized as laparoscopic, robotic, or open. Post-operative variables extracted were length of stay and 30-day complications. Post-operative complication data were collected for occurrences of ileus, urinary tract infection, urinary retention, surgical site infection, deep venous thrombosis, pneumonia, chronic obstructive

pulmonary disease exacerbation, congestive heart failure exacerbation, myocardial infarction, unplanned intensive care unit admission, delirium, anastomotic leak, reoperation, and unplanned readmission occurring within a 30-day postoperative period; a composite any-complication variable was created for purposes of analysis.

Post-operative opioid data collected were: 24-hour prior-to-discharge opioid consumption, prescription quantity (opioid and non-opioid pain medications), quantity of opioid pills consumed prior to the first post-operative appointment, pain in clinic (on a scale of 0 to 10), and opioid refills within 30 days of hospital discharge. Guideline adherence was defined as a prescription that less than or equal to the maximum recommended prescription quantity for each tier. The six-month study after guideline adoption was *a priori* divided into two-month prescribing periods (months 1-2, 3-4, and 5-6) to evaluate potential differences in medication adherence and practice adoption over time. The opioid prescriber was categorized as either off-service resident, surgical resident, fellow, physician assistant, or surgeon. For cases in which no opioid prescriptions were given, the medical provider who signed the discharge paperwork was recorded as the prescriber. Quantity of opioid pills consumed was self-reported by the patient at the time of their first post-operative visit and recorded by the clinic provider. To reduce reporting bias, a waiver of consent was obtained from Institutional Review Board at the University of Massachusetts Medical School and patients were not made aware of the study protocol.

Conversion to Equi-analgesic 5mg Oxycodone Pills

Oral opioid dosages were converted to EOP (i.e. 1 EOP = 5 mg oxycodone = 7.5 mg morphine equivalent) based on the opioid conversion factors published by the Centers for Medicare and Medicaid Services.[22] Conversion factors published by University of North Carolina

Health Care Guidelines[23] were used for intravenous (IV) dosages because these were not available from the Centers for Medicare and Medicaid Services.

Sample Size Calculation

Sample size calculation was performed for comparison of two independent means using historical institutional data for mean opioid prescription quantity and the accompanying standard deviation. Application of the proposed prescribing guideline to the historical sample would have reduced the mean prescription quantity by 45%. We assumed an expected guideline adherence of 70% based on data from a prior study of prescription guideline adoption in an academic general surgery practice.[24] Therefore, we based our estimate on a 32% reduction in mean prescription quantity (study mean 12.0 EOP). We performed a sample size calculation for comparing two means, which resulted in a sample size of 57 in each group. Based on our prior guideline development study, we expected 36% of the screened population to be excluded for pre-specified factors, so we anticipated needing to screen a minimum of 89 patients to detect a clinically meaningful difference in mean prescription quantity. We decided on a 6 month period of data collection to ensure that we would meet this minimum number of patients to be studied.

Data Analysis

Univariate analysis was performed comparing data collected after guideline adoption to a historical comparison group collected before guideline adoption. For univariate analysis, Pearson's chi-square and Fisher's Exact tests were used to compare categorical variables, while ANOVA was used to compare continuous variables. Subgroup analysis for guideline adherence was compared between Tiers 1-3, prescriber, and prescribing period using Fisher's Exact test.

Subgroup analysis for opioid prescribing and consumption patterns was performed between Tiers 1-3 using ANOVA and proportion of patients requiring a refill using Fisher's Exact test.

A multivariable logistic regression analysis was performed to model factors independently associated with requiring an opioid refill. For these models, a stepwise multivariable logistic regression was performed starting with the inclusion of all demographic and operative variables until the final model was limited to variables that met a $p < 0.05$ inclusion threshold. Opioid exposure status, procedure category, prescribing tier, length of stay, and ostomy creation were *a priori* determined to be clinically relevant and forced into the stepwise logistic regressions. We calculated area under the curve (AUC) to evaluate model fit. All statistical analyses were performed using STATA software (version 15.1, StataCorp, College Station, TX).

Ethical Considerations:

The study was approved by the Institutional Review Board at the University of Massachusetts Medical School. The study was deemed low risk and a waiver of consent was granted.

Chapter III: Results

Baseline Study Population Characteristics

During the 6-months after guideline adoption, a total of 155 patients underwent major inpatient colorectal operations (partial colectomy, proctectomy, total abdominal colectomy, total proctocolectomy, ileostomy takedown, and colostomy reversal) at our medical center. Of these, 54 patients were excluded: 16 for an emergency procedure, 3 were discharged to an inpatient facility, 16 for recent opioid prescription within 30 days prior to surgery, and 20 for missing follow-up opioid consumption data. Data from 101 patients were analyzed after guideline adoption (Figure 1). This is similar to the historical comparison group in which 157 patients underwent major inpatient colorectal operations at our institution between July 2018 and January 2019 with 57 patients excluded and the data from 100 patients analyzed(Figure 1).

After guideline adoption, the average age of the study population was 64 years and 55% were female (Table 1). The population was predominantly white (89%) and English was the primary language for 91% of patients. The majority (68%) of patients underwent minimally invasive procedures and a diverting ostomy was created in 19% of cases (Table 2). The mean length of stay was 4.5 days with half of all patients discharged in 3 days or less. Most patients (70%) did not require visiting medical services at home after discharge (Table 2).

In comparing the study population after guideline adoption to the historical dataset collected during guideline development, a significantly greater proportion of patients after guideline adoption had a high American Society of Anesthesiologists classification (ASA III or IV) compared to before adoption indicating more severe baseline comorbidities ($p = 0.001$; Table 1). There was also a higher rate of any-readmission within 30-days after guideline adoption (2%

vs 13%; Table 2). All other patient, operative, hospitalization, and post-operative complications characteristics were similar before and after guideline adoption.

Inpatient Medication Use

Receipt of hospital administered non-opioid analgesic medications were not collected in before guideline adoption and, therefore, not available for comparison. After guideline adoption, the pain regimen on post-operative day one consisted of IV opioids (93%), oral acetaminophen (93%), and IV ketorolac (64%) for the majority of patients, while only 8% were taking oral opioids. Other non-opioid analgesic medications administered on the first post-operative day included gabapentin for 22%, transdermal lidocaine patch for 14%, and oral non-steroidal anti-inflammatory medications for 2%. No patients received IV acetaminophen.

Guideline adherence

There was 85% adherence to the discharge opioid prescribing guideline as measured by prescriptions that were less than or equal to the maximum guideline recommendation for each tier (Table 3). Guideline adherence did not differ by prescribing tier, operating surgeon, or prescribing period. There was greater than 90% adherence to the guideline by surgical residents and physician assistants, but there was significantly lower adherence by non-surgical residents rotating on the colorectal surgery service (90% vs 73%, $p = 0.04$; Table 3).

Prescriptions at hospital discharge

After guideline adoption, the mean quantity of opioids prescribed was 10.3 EOP overall, but was significantly different for each prescribing tier: 1.8 EOP for Tier 1, 12.0 EOP for Tier 2

and 25.7 EOP for Tier 3 (Table 4). The mean quantity of opioids prescribed was significantly lower after guideline adoption for Tier 1 (1.8 EOP vs 15.7, $p < 0.001$) and for the total group (10.3 EOP vs 17.5, $p < 0.001$) compared to before guideline adoption but was not significantly different for those in either Tier 2 or Tier 3 (Table 4). Overall, there was a 43% reduction in opioids prescribed (Table 5). Among each prescribing tier, the largest reduction achieved was 89% for patients classified in Tier 1, and a 25% reduction for those in Tier 2; patients in Tier 3 showed an 8% increase in prescription quantity (Table 5).

Opioid Consumption Patterns at First Post-Operative Visit

After guideline adoption, outpatient opioid consumption had an overall mean of 5.2 EOP, but consumption was significantly different between prescribing tier: 0.2 EOP for Tier 1, 5.6 EOP for Tier 2, and 15.1 EOP for Tier 3 ($p < 0.001$; Table 4). Compared to before guideline adoption, opioid consumption in Tier 1 was lower after guideline adoption (0.2 EOP vs 2.5, $p = 0.01$), but was not different for Tier 2, Tier 3, or the overall study population. The proportion of patients requiring a prescription refill for an opioid was 10% after guideline adoption compared to 15% before adoption ($p = 0.27$). The highest refill rate was seen in Tier 3 with 40% requiring a refill before guideline adoption and 28% after guideline adoption. Overall, there was a 52% reduction in excess pills left over with a reduction by 87% in Tier 1, 40% in Tier 2, and a 109% increase in Tier 3.

Multivariable Models

During our prior guideline development study, there were 17 patients (17%) who consumed more pills than would be prescribed according to the guideline. Using a stepwise

elimination procedure, a history of inflammatory bowel disease was the only variable that was significantly associated with an increased odds of consuming more than the prescription guideline (aOR 7.2, 95% CI 1.6-32.6) after adjustment for prescribing tier, opioid naïve status, procedure type, ostomy creation, length of stay, and prescription quantity. The model AUC was 0.80.

We applied the same stepwise elimination modeling procedure to the study cohort after guideline adoption to determine factors associated with requiring an opioid refill, which is analogous to consuming more than the prescription guideline. We found no independent variables remaining in the model. Among the forced exposure variables, prescribing tier was significantly associated with requiring a prescription refill after adjustment for opioid naïve status, procedure type, ostomy creation, length of stay, and prescription quantity. Patients in Tier 3 had a 75-fold greater odds of requiring a prescription refill (aOR 75.2, 95% CI 2.6 – 2142) compared with those in Tier 1, while Tier 2 was not significantly different (aOR 3.9, 95% CI 0.2- 62.9) from Tier 1 after adjustment for similar potentially confounding variables. The model AUC was 0.87.

Chapter IV: Discussion

We found that a simple, three-tiered, opioid prescribing guideline can dramatically reduce discharge prescription quantities without increasing prescription refills. After guideline adoption, prescription quantities for opioids were reduced by 43% with the greatest reduction achieved for patients in Tier 1. Prescribing variability was also reduced within each prescribing tier. Adherence to the guideline was high among all prescribers with 85% of all prescribers following the prescribing recommendations. By tailoring discharge prescriptions to a patient's opioid usage in the day prior to discharge, surgeons can better align discharge prescription quantity with a patient's outpatient needs, thus limiting the overprescribing of these addictive medications.

Rationale for a tiered prescribing algorithm

We previously found that over 60% of prescribed opioids went unused after major colorectal operations at our institution, which is consistent with the prior literature in the general surgery population.[10, 20] Outpatient opioid consumption varied greatly between individuals, but usage patterns emerged when patients were stratified by prior to discharge opioid requirements. This association between inpatient opioid requirements and outpatient consumption was similar to findings from prior studies of opioid consumption after major inpatient general surgery operations[20] and gynecological operations[21], and confirms findings from our own data prior to guideline adoption. Prescribing guidelines that fail to account for a patient's opioid consumption prior to discharge will lead to excessive prescriptions for some patients and inadequate prescriptions for others. Our guideline takes into consideration prior to discharge opioid consumption by using a tiered prescribing system – no use (Tier 1), low use (Tier 2), high use (Tier 3) – to better align prescription quantity with patients' actual needs.

Impact of guideline adoption on opioid prescribing patterns

After adoption of the tiered guideline, the number of excess pills was reduced by 51%. As expected, reductions in excess pills were different across prescribing tiers. The largest reduction was seen in Tier 1 where excess pills were dramatically reduced by 87%. This could be attributable to the fact that Tier 1 represents a group of patients who were unlikely to require outpatient opioids for pain control; however, prior to guideline adoption, most of these patients still received an average prescription of 16 EOP. By recommending no opioid prescription for patients in Tier 1, we were able to almost completely eliminate excessive prescriptions for one-half of all discharged patients. Similarly, we were able to reduce excess pills among patients in Tier 2 by 40% while simultaneously reducing prescription refills from 16% to 8%. This finding could be attributable to the wide variation and inconsistent quantities prescribed prior to guideline adoption, with a dramatic reduction in variability seen after guideline adoption. Prior studies have shown wide variability in prescribing among the general surgery population including one study that showed wide variability in prescription quantities among patients undergoing similar operations on the same acute care surgery service.[20, 25, 26] Standardized prescription guidelines have been shown to decrease this prescribing variability. For example, adoption of standardized prescribing guideline reduced the standard deviation of prescribed pills after laparoscopic colectomy from 17 to 7, inguinal hernia repair from 16 to 9, and partial mastectomy with sentinel lymph node biopsy from 11 to 2.[24]

We did find an increase in excess pills for patients in Tier 3, but this is not surprising given that the maximum recommended prescription quantity for this group (30 EOP) was greater than mean prescription before guideline adoption (24 EOP). The guideline was designed to meet the

needs for 85% of patients in this group. The recommended prescription for Tier 3 was greater than the historical mean because a substantial proportion of these patients were historically under-prescribed opioids for pain control as evidenced by the 40% historical refill rate for patients in this tier.

The Michigan Opioid Prescribing Engagement Network recommends 0-10 pills after laparoscopic colectomies and 0-15 pills after open colectomies or ostomy reversals.[19] In our study, the mean outpatient consumption for Tier 3 exceeded the Michigan Opioid Prescribing Engagement Network recommendations. Therefore, consideration should be given to providing larger prescriptions for Tier 3 patients than recommended by the Michigan group. Tier 3 only represents a quarter of all surgical patients while Tiers 1 and 2 represent the majority (75%) of patients. The excess pills prescribed to Tier 3 were offset by a much greater reduction in pills for Tiers 1 and 2. The slight increase in prescription recommended for patients in Tier 3 was accompanied by clinically significant reduction in prescription refills from 40% to 28%. In total, these findings show that a tiered guideline based on a patient's opioid requirement at the time of discharge is a pragmatic way to align prescription quantities with the actual needs of the patient.

Guideline adherence

The results of this study benefitted from high guideline adherence. Only 15% of prescriptions were written in excess of the adopted guideline. Our 85% guideline adherence rate is higher than the 68% adherence found in a before and after cohort study of guideline implementation in a general surgery practice using similar adherence measures[24], but lower than the 96% adherence in a randomized controlled trial of guideline adoption after gynecologic operations.[21] Prior to our guideline development there was no standardization for discharge opioid

prescribing at our institution. Guideline adherence may have been particularly effective in our study because once providers were provided with an evidence-based prescribing guideline, there was no substantial barrier to change.

Study Strengths and Limitations

The main strength of this study is its prospective design which allows evaluation changes in opioid prescribing patterns after guideline adoption. Another strength of the study is that patients were blinded to the study design which helped to minimize potential observation bias. The study also included only patients undergoing select inpatient colorectal operations which provided a more homogenous population than previous studies of general surgery operations.

This study had several limitations. The prescribing guideline was developed and prospectively evaluated at a single academic institution, which may limit its generalizability. The surgical population was predominantly white and English-speaking, which may not reflect the patient demographic characteristics at other institutions. We also may not have captured opioid refills for all patients. To obtain these data, we queried the EMR for refill data, which would capture refills prescribed by any provider within the University of Massachusetts network, but may not capture refills obtained from an outside provider. Finally, we determined the cut-points for our three tiers to maximize equal distribution of patients. Use of alternative cut-points could potentially lead to an even greater reduction in excess pills.

Chapter V: Conclusions

This study shows that adoption of a simple, three-tiered, opioid prescribing guideline based on prior to discharge opioid consumption can dramatically reduce excessive prescribing without increasing prescription refills. By tailoring discharge prescriptions to a patient's opioid usage in the day prior to discharge, surgeons can better align discharge prescription quantity with a patient's outpatient needs. The success at our institution suggests that a similar effort at the state or national level could be successful in markedly reducing excessive prescribing by surgeons on larger scale.

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Tables:

Table 1. Patient Characteristics

Variable	Before Guideline Adoption (N=100)	After Guideline Adoption (N=101)	p-value
Age, mean, yrs (SD)	60 (14)	64 (13)	0.05
Female	55 (55)	55 (55)	0.94
White	90 (90)	90 (89)	0.84
Language			n/a
English	NC	92 (91)	
Spanish	NC	4 (4)	
Other	NC	5 (5)	
Insurance			0.46
Private	62 (63)	54 (54)	
Government †	36 (36)	45 (45)	
None	1 (1)	1 (1)	
ASA			0.001
I or II	70 (70)	48 (48)	
III or IV	30 (30)	53 (52)	
BMI, mean (SD)	27 (7)	29 (6)	0.20
Social History			
Current Smoker	16 (16)	13 (13)	0.53
Moderate/heavy Alcohol Use, (≥4 drinks/week)	15 (15)	16 (16)	0.87
Recreational Drug Use	11 (11)	5 (5)	0.11
Medical History			
Diabetes	12 (12)	18 (18)	0.25
Hypertension	42 (42)	51 (51)	0.23
Psychiatric History ‡	24 (24)	29 (29)	0.45
IBD	16 (16)	15 (15)	0.82
Prior abdominal surgery	60 (60)	65 (64)	0.52
Opioid naïve §	71 (71)	69 (68)	0.68
Current medications:			
Benzodiazepines	20 (20)	13 (13)	0.17
Antidepressants	16 (16)	15 (15)	0.82
Gabapentin or pregabalin	NC	6 (6)	n/a

Data are presented n (%) unless otherwise stated.

NC = not collected, ASA = American Society of Anesthesiologists classification, BMI = Body Mass Index, IBD = Inflammatory Bowel Disease

† Government insurance refers to Medicaid, Medicare, Massachusetts health or Veteran's Administration

‡ Diagnosis of anxiety/depression/bipolar/other

§ Opioid naive determined by no documented prescription within 1 year pre-operatively

Table 2. Operative and hospitalization details

Variable	Before Guideline Adoption (N=100)	After Guideline Adoption (N=101)	p-value
Operative time in minutes, mean (SD)	191 (84)	190 (88)	0.92
Procedure Approach			0.21
Open	23 (23)	27 (27)	
Laparoscopic	74 (74)	66 (65)	
Robotic	3 (3)	8 (8)	
Conversion to open	2 (2)	5 (5)	0.44
Procedure type			0.68
Partial colectomy	75 (75)	65 (65)	
Proctectomy	9 (9)	12 (12)	
Total abdominal colectomy	1 (1)	3 (3)	
Total proctocolectomy	2 (2)	4 (4)	
Ileostomy takedown	10 (10)	13 (13)	
Colostomy takedown	3 (3)	3 (3)	
Splenic flexure taken-down	33 (33)	26 (26)	0.19
Ostomy creation	16 (16)	19 (19)	0.60
Surgical drain placed	19 (19)	29 (29)	0.11
Length of stay			0.83
≤3 days	49 (49)	51 (50)	
>3 days	51 (51)	50 (50)	
Discharge disposition			0.64
Home with no services	74 (74)	71 (70)	
Home with services	26 (26)	30 (30)	
Days from discharge to follow-up, mean (SD)	13 (7)	13 (4)	0.59
Any complication †	19 (19)	28 (28)	0.14
Any readmission‡	2 (2)	13 (13)	0.01

Data are presented n (%) unless otherwise stated.

† Any complication within 30-day post-operative period

‡ Any readmission refers to any hospital admission within 30-days post-operatively regardless of the attributable reason.

Table 3. Guideline adherence

Variable	Guideline Adherence	Guideline Non-adherence	p-value
All Patients	86 (85.1)	15 (14.9)	n/a
Prescribing Tiers			0.44
Tier 1	41 (80.4)	10 (19.6)	
Tier 2	22 (88.0)	3 (12.0)	
Tier 3	23 (92.0)	2 (8.0)	
Operating Surgeon			0.28
A	10 (83.3)	2 (16.7)	
B	23 (79.3)	6 (20.7)	
C	38 (92.7)	3 (7.3)	
D	15 (79.0)	4 (21.1)	
Prescriber			0.04
Non-surgical resident	27 (73.0)	10 (27.0)	
Surgical resident	38 (90.5)	4 (9.5)	
Physician assistant	21 (95.5)	1 (4.6)	
Prescribing Period			0.57
Month 1-2	26 (89.7)	3 (10.3)	
Month 3-4	28 (87.5)	4 (12.5)	
Month 5-6	32 (80.0)	8 (20.0)	

Data are presented n (%)

Table 4. Opioid prescription and consumption patterns

Prescribing Tiers	Before Guideline Adoption	After Guideline Adoption	p-value
All patients, n	**100**	**101**	
Prescribed, mean EOP (SD)	17.5 (10.5)	10.3 (11.6)	<0.001
Consumed, mean EOP (SD)	6.7 (10.9)	5.2 (8.5)	0.27
Excess, mean EOP (SD)	10.7 (10.2)	5.1 (7.6)	<0.001
Refills, n (%)	15 (15.0)	10(9.9)	0.27
Tier 1, n	**53**	**51**	
Prescribed, mean EOP (SD)	15.7 (9.0)	1.8 (3.9)	<0.001
Consumed, mean EOP (SD)	2.5 (6.5)	0.2 (0.8)	0.01
Excess, mean EOP (SD)	13.2 (9.5)	1.7 (3.8)	<0.001
Refills, n (%)	2 (3.8)	1 (2.0)	1.00
Tier 2, n	**25**	**25**	
Prescribed, mean EOP (SD)	16.0 (7.7)	12.0 (6.5)	0.06
Consumed, mean EOP (SD)	5.2 (6.2)	5.6 (5.3)	0.81
Excess, mean EOP (SD)	10.8 (11.0)	6.5 (5.7)	0.09
Refills, n (%)	4 (16.0)	2 (8.0)	0.68
Tier 3, n	**22**	**25**	
Prescribed, mean EOP (SD)	23.7 (14.1)	25.7 (9.3)	0.56
Consumed, mean EOP (SD)	18.6 (14.8)	15.1 (10.8)	0.35
Excess, mean EOP (SD)	5.1 (8.8)	10.6 (10.8)	0.06
Refills, n (%)	9 (40.1)	7 (28.0)	0.74

EOP = Equianalgesic 5-mg Oxycodone Pills

Table 5. Relative reduction in opioid prescribing

Prescribing Tiers	Patients (n)	Mean Prescribed Before Guideline Adoption (EOP)	Mean Prescribed After Guideline Adoption (EOP)	Quantity Would Have Been Prescribed	Quantity Actually Prescribed	% Decrease
Tier 1	51	15.7	1.8	801	92	88.5%
Tier 2	25	16.0	12.0	400	300	25.0%
Tier 3	25	23.7	25.7	593	643	-8.4%
Total				**1794**	**1035**	**42.3%**

EOP = Equianalgesic 5-mg Oxycodone Pills

Figures

Figure 1. Discharge prescribing guideline worksheet

Discharge Prescribing Guideline After Inpatient Colorectal Surgery

This opioid prescription guideline is intended for:

- Adults who have undergone major colorectal surgery and at least 48 hours inpatient stay.
- Patients with no pre-existing outpatient opioid prescription.

Step 1: Calculate the quantity of opioid used in the 24-hours prior to discharge

Opioid Medication	Total Quantity	Conversion Factor *	= equivalent (mg) oxycodone
PO Oxycodone	__ mg	x 1	= ___ mg (a)
PO Tramadol	__ mg	x 0.0667	= ___ mg (b)
PO Hydromorphone	__ mg	x 2.667	= ___ mg (c)
IV Fentanyl	__ micrograms	x 0.2	= ___ mg (d)
IV Hydromorphone	__ mg	x 13.333	= ___ mg (e)
IV Morphine	__ mg	x 2	= ___ mg (f)
		(g)	Sum (a-f) = Total (mg) oxycodone equivalent

* Adapted from CMS Opioid Conversion Factors

Step 2: Determine prescribing Tier (g)

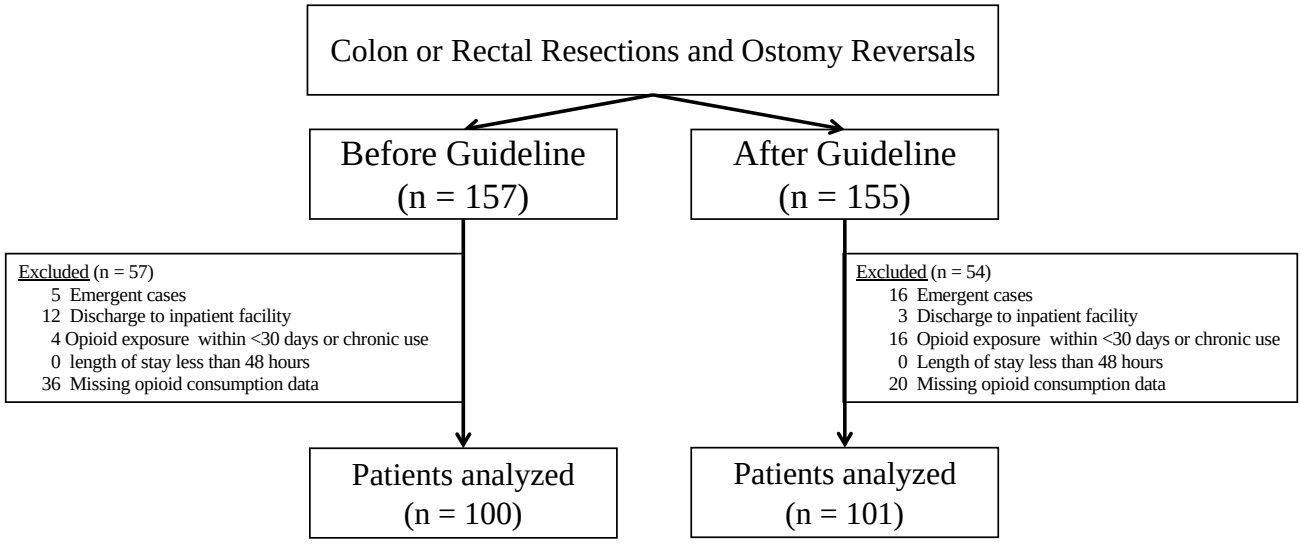
(a) Tier 1 (0mg oxycodone equivalent)
(b) Tier 2 (≤15 mg oxycodone equivalent)
(c) Tier 3 (>15 mg oxycodone equivalent)

Step 3: Prescribe according to prescribing Tier (determined in Step 2).

	Prescribing Tiers		
Choose pain medication	**(a) Tier 1**	**(b) Tier 2**	**(c) Tier 3**
[a] **Oxycodone 5mg pills** (total mg oxycodone)	**0 pills** (0 mg)	**12 pills** (60 mg)	**30 pills** (150 mg)
[b] Hydrocodone 5mg pills (total mg hydrocodone)	0 pills (0 mg)	18 pills (90 mg)	45 pills (225 mg)
Tramadol 50mg pills (total mg tramadol)	0 pills (0 mg)	18 pills (900 mg)	45 pills (2250 mg)
Hydromorphone 2mg pills (total mg hydromorphone)	0 pills (0 mg)	~11 pills (22.5 mg)	~28 pills (56.2 mg)

[a] or equivalent (eg. Percocet)
[b] or equivalent (eg. Norco, Vicodin)

Figure 2. Study Flow Diagram



53 (53%)	Tier 1*	51 (50%)
25 (25%)	Tier 2	25 (25%)
22 (22%)	Tier 3	25 (25%)

* Tiers based on opioid consumption 24-hours prior to discharge

Figure 3. Comparison of equi-analgesic 5-milligram oxycodone pills (EOP) prescribed and consumed according to prescribing tiers.

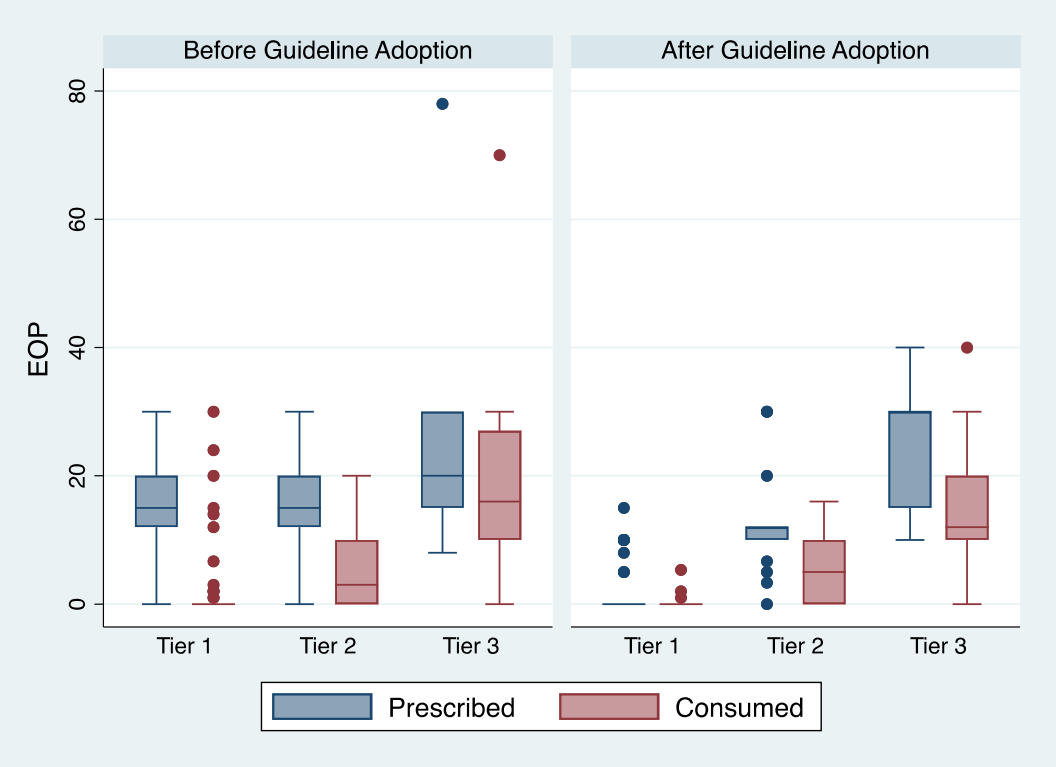


Figure 3. The box-plot shows the distribution of opioid quantities prescribed and consumed for each prescribing tier. The plot on the left shows the distribution for the historical data collected before guideline adoption and the plot on the right show the distribution of data from the present study after guideline adoption. After guideline adoption, prescription quantity was significantly reduced for Tier 1, but not for Tier 2 or 3. There was no change in consumption for any prescribing tier.

APPENDICES

Appendix (i) - Hospital Administered Medications

Phase of Care	Medication	After Guideline Adoption N=101
Post-anesthesia care unit		
	IV ketorolac	43 (43)
	PO Tylenol	45 (45)
	gabapentin	6 (6)
	IV Tylenol	0 (0)
Post-operative day 1		
	IV opioid	94 (93)
	PO Tylenol	94 (93)
	IV ketorolac	65 (64)
	gabapentin	22 (22)
	alvimopan	17 (17)
	TD lidocaine	14 (14)
	PO opioid	8 (8)
	PO NSAID	2 (2)
	epidural	0 (0)
	IV Tylenol	0 (0)

Data are presented as n (%).

IV = intravenous, PO = by mouth, TD = transdermal, NSAID = non-steroidal anti-inflammatory drug

Appendix (ii) – Discharge prescriptions

Prescription	Total N=201	Before Guideline Adoption N=100	After Guideline Adoption N=101	p-value
Non-opioid Prescribed				
Tylenol	174 (87)	83 (83)	91 (90)	0.15
Ibuprofen	52 (26)	16 (16)	36 (36)	0.002
Naproxen	0 (0)	0 (0)	0 (0)	1.00
Gabapentin	0 (0)	0 (0)	0 (0)	1.00
Opioid Prescribed				<0.0001
None	51 (25)	9 (9)	42 (42)	
Oxycodone	137 (68)	84 (84)	53 (53)	
Hydromorphone	3 (1)	1 (1)	2 (2)	
Hydrocodone	1 (0)	1 (1)	0 (0)	
Tramadol	9 (4)	5 (5)	4 (4)	
Combo Pill †	3 (1)	3 (3)	0 (0)	0.12

Data are presented as n (%).

† Combo pill refers to a prescription opioid formulation in combination with non-steroidal anti-inflammatory drug

Appendix (iii). Post-operative Complications

Complication	Total N=201	Before Guideline Adoption N=100	After Guideline Adoption N=101	p-value
Any complication *	47 (23)	19 (19)	28 (28)	0.14
Ileus	22 (11)	13 (13)	9 (9)	0.38
UTI	4 (2)	1 (1)	3 (3)	0.62
Urinary retention	6 (3)	3 (3)	3 (3)	1.00
SSI	10 (5)	4 (4)	6 (6)	0.75
ICU admission	2 (1)	1 (1)	1 (1)	1.00
Reoperation	2 (1)	1 (1)	1 (1)	1.00
Sepsis	1 (0)	1 (1)	0 (0)	0.50
DVT	1 (0)	1 (1)	0 (0)	0.50
Renal failure	1 (0)	0 (0)	1 (1)	1.00
Other	13 (7)	3 (3)	10 (10)	0.08
High ostomy output	2 (1)	0 (0)	2 (2)	0.50
OSI	1 (0)	0 (0)	1 (1)	1.00
Anastomotic leak	1 (0)	1 (1)	0 (0)	0.50
30-day readmission†	15 (7)	2 (2)	13 (13)	0.01

Data are presented as n (%).
UTI = urinary tract infection, SSI = surgical site infection, ICU = intensive care unit, DVT = deep venous thrombosis, OSI = organ space infection
* Any-complication refers to number of patients with a reported complication within 30-days
† Re-admission refers to any hospital admission within 30-days post-operatively regardless of the attributable reason.