Original Article

Temporal trends and patterns in initial opioid prescriptions after hospital discharge following colectomy in England over ten years

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ABSTRACT

Background

This retrospective cohort study investigated the changes in the proportion of people receiving initial opioid prescriptions after hospital discharge following colectomy, and describes trends and patterns in prescription characteristics.

Methods

Patients undergoing colectomy in England between 2010-2019 were included using electronic health record data from linked primary (Clinical Practice Research Datalink Aurum) and secondary (Hospital Episode Statistics) care. The proportion of patients having an initial opioid prescription issued in primary care within 90 days of hospital discharge was calculated. Prescription characteristics of opioid type and formulation were described.

Results

Of the 95,155 individuals undergoing colectomy, 15,503 (16.3%) received opioid prescriptions. There was a downward trend in the proportion of patients with no prior opioid exposure (opioid naïve) who had a post-discharge opioid prescription ($p<0.001$), from 11.4% in 2010 to 6.7% in 2019 (-41.3%, $p<0.001$). Whereas the proportions remained stable for those prescribed opioids prior to surgery, from 57.5% in 2010 to 58.3% in 2019 ($p=0.637$). Codeine represented 44.5% of all prescriptions and prescribing increased by 14.5% between 2010 and 2019. Prescriptions for morphine and oxycodone rose significantly by 76.6% and 31.0% respectively, while tramadol prescribing dropped by 48.0%. The most commonly prescribed opioid formulations were immediate-release (83.9%), followed by modified-release (5.8%) and transdermal (3.2%). There was a modest decrease in the

prescribing of immediate-release formulations from 86.0% in 2010 to 82.0% in 2019 ($p<0.001$)

Conclusion

There was a changing pattern of opioid prescribing following colectomy, with a decrease in the proportion of opioid naïve patients prescribed post-discharge opioids.

INTRODUCTION

While opioid analgesics are often necessary for the management of acute postoperative pain, appropriate prescribing practices are crucial to avoid harm.[1-3] Postoperative opioid prescribing may lead to persistent postoperative opioid use (PPOU)[4, 5], with dependence differing by opioid type and likeability.[6, 7] Our previous work demonstrated that 2.5% of opioid naïve patients who underwent colectomy in England developed PPOU, increasing to 40.4% in those with current opioid exposure.[8] Although definitions of PPOU vary,[9, 10] in North America the incidence of PPOU can range from 0.6% to 12% in opioid-naïve patients following abdominopelvic surgery and can be higher in those with previous opioid exposure.[9]

Differences in healthcare systems might have an impact on opioid prescribing practices. The UK has a publicly funded National Health Service (NHS), which provides free healthcare to all residents, including subsidised prescriptions,[11] mainly guided by national policies and drug formularies. In comparison, the US has a private healthcare system linked predominantly to insurance coverage. The variation in patterns of postoperative opioid use can also be linked to the promotion of certain opioids over others, leading to differences in the opioid selection, duration and quantity prescribed to each patient, and between countries.[12-14] For instance, the rate of filled opioid prescriptions in the US and Canada in the first week after discharge was seven times higher than in Sweden.[4] Although the frequency of filled prescriptions was similar between Canada and the US, patients in US hospitals received greater quantities of opioids.[4] Additionally, from 1994 to 2014, 80% of patients undergoing surgery, including colectomy, in the US received post-discharge opioid prescriptions.[5]

Opioid-related adverse events, which are related to potency, formulation and dose, can be reduced by avoiding long-acting and transdermal formulations.[2, 15, 16] Opioids should only be prescribed as immediate-release formulations for management of postoperative pain.[2, 15] Nevertheless, a recent UK study revealed that 10% of previously opioid-naïve patients were discharged with long-acting formulations.[17]Additionally, in the US, patients who were prescribed long-acting opioid formulations following surgical discharge were more likely to obtain prescriptions with higher doses compared with short-acting formulations. Prescriptions with long-acting formulations resulted in a total oral morphine equivalent amount exceeding 350 mg.[5]

While evidence suggests a recent decline in postoperative opioid prescriptions in the US,[18, 19] it is unclear whether a similar trend exists in England. In addition, a comprehensive understanding of the specific opioids and formulations prescribed after surgical discharge and their variation over the years remains unexplored. This study aimed to investigate the changes in the proportion of people receiving initial opioid prescriptions after hospital discharge following colectomy, as well as describe trends and patterns in prescription characteristics, particularly temporal changes in analgesics, including potency and formulation choices.

METHODS

This retrospective cohort study was approved by the Independent Scientific Advisory Committee approval board (Protocol 21_000668) and followed the Reporting of Studies Conducted using Observational Routinely Collected Health Data Statement for Pharmacoepidemiology (RECORD-PE) guidelines.[20]

A repeated cross-sectional analysis was used to describe temporal trends of patients undergoing colectomy and prescribed opioids within 90 days of hospital discharge following surgery,[8] split by year-by-year data to describe trends and changes from 2010 to 2019. The 90-day duration was chosen to ensure that the prescribed opioid was associated with a surgical procedure, considering that the tissue healing process can take up to three months.[21] Moreover, this 90-day period aligns with the timeline used for the definition of chronic pain, which typically requires pain persistence at this stage to be considered chronic.[22]

Anonymised patient records were obtained from two previously validated[23] linked databases: primary Clinical Practice Research Datalink (CPRD) Aurum[24] and linked secondary care Hospital Episode Statistics (HES)[25] data as previously described.[8] The HES database contains details of all admissions to National Health Service (NHS) hospitals in England. Surgery records are coded within the database using the Office of Population Censuses and Surveys (OPCS 4) Classification of Surgical Operations and Procedures (https://www.datadictionary.nhs.uk/supporting_information/opcs_classification_of_interventions_and_procedures.html). Other medical diagnoses are coded within HES using International Classification of Diseases 10th revision (ICD-10) codes (https://icd.who.int/browse10/2019/en). CPRD Aurum contains routinely collected data

from general practitioner (GP) practices. In the UK, 98% of the population is registered with a GP, the gatekeeper of care in the NHS. Data provided by CPRD Aurum captures diagnoses, prescriptions, tests and referrals for 7 million active patients. Links to Office for National Statistics data helped obtain the date of death.

Patients ≥18 years of age, who underwent colectomy between 1 January 2010 and 31 December 2019 were identified from HES using OPCS codes for colectomy procedures (Table S1). The validity and reliability of codes to identify colectomy have been confirmed previously.[23] Patients were excluded if they did not have at least 12 months CPRD Aurum data before their date of surgery, to ensure complete preoperative opioid exposure data.

Patients issued opioid prescriptions were identified based on the presence of a prescription for an opioid within 90 days of hospital discharge after surgery. Opioid prescription records were identified using opioid product codes[8] (Table S2) and extracted from the CPRD Aurum database then prepared for analysis using an adapted version of the DrugPrep algorithm which allows for identifying prescription errors, duplicate records, and dealing with missing data (Table S3).[26] Excluded opioids included higher-strength buprenorphine sublingual tablets (2, 4 and 8 mg), and methadone because they are primarily prescribed for opioid dependence in the UK. Injectable formulations were also excluded as these are typically administered by healthcare professionals rather than self-administered.[8]

The primary outcome was the proportion of patients having initial opioid prescription issued from general practice within 90 days of hospital discharge following colectomy. For this outcome, the method described previously[8] was employed to stratify the population based on opioid exposure before colectomy into three groups (opioid-naïve, currently exposed, and previously exposed). This stratification enabled description of the impact of previous

opioid exposure on postoperative opioid use and determine if there were any differences in outcome between groups. Patients were categorised as opioid-naïve if they did not receive an opioid prescription in the year leading up to their surgical admission. Those who received an opioid prescription within the six months prior to their admission date were considered "currently exposed", while those who received an opioid prescription within 7 to 12 months prior to admission were classified as "previously exposed", forming two separate preoperative groups with no overlap.[8, 27]

Several secondary outcomes were investigated. First, the potency of opioids in the initial prescription: classes of opioids were divided into weak opioids (codeine, dihydrocodeine, meptazinol, pentazocine, tramadol) and strong opioids (morphine, oxycodone, fentanyl, buprenorphine, hydromorphone, pethidine, naloxone/oxycodone, cyclizine/dipipanone, hydromorphone, tapentadol), or combination of both.[28] Tramadol can be classed as a strong[29] or weak opioid,[28] and to allow comparison with other UK studies[30, 31] it was classified as a weak opioid.

Second, the opioid prescribed was determined as defined as the drug class (buprenorphine, codeine, dihydrocodeine, fentanyl, morphine, oxycodone, tramadol, and other opioids). "Other opioids" represent opioids that were not commonly prescribed and combined in one category during drug preparation. Third, opioid formulations were categorised into (immediate-release only, modified-release only, both immediate- and modified-release, transdermal only, and others). Fourth, the amount of opioid in each prescription was described as Oral Morphine Equivalent (OMEQ) dose in mg/day. OMEQ dose was used to convert the doses of different opioids into a standard unit based on their analgesic potency to provide more easily comparable data across a range of opioid medicines. It warrants

consideration as a standard prescribing measure[32] and calculated by multiplying the daily dose of opioids in each prescription by the equivalent analgesic ratio as specified by the US Centers for Disease Control and Prevention[33] (Table S4). For those on a combination of opioids, OMEQ dose was calculated for each drug and combined to provide an overall OMEQ dose in mg/day for each patient, and was categorised into dose ranks: ≤24, 25-49, 50-99, 100-249 and ≥250 mg/day.

Patient characteristics, including sex and age at the time of admission, ethnicity and comorbidities were ascertained. Ethnic groups were classified as White, Asian, Black and others. The Charlson Comorbidity Index was used to group patients, based on the number of comorbidities, into categories of 0, 1, and ≥2. Admission type was categorised as emergency or elective according to the recorded admission classification for the surgical procedure. The patients' level of deprivation was determined using 2015 Index of Multiple Deprivation (IMD) scores,[34] categorised into quintiles ranging from 1 (most deprived) to 5 (least deprived). The surgical technique was categorised as either open or minimally invasive. Minimally invasive surgery included laparoscopic or robotic techniques and was identified using procedural codes (Y50.8, Y57.1, Y75.2, Y75.3). Patients were recorded as having benign disease if the ICD-10 discharge codes for their hospital admission indicated diverticular disease or inflammatory bowel disease. A diagnosis of cancer was confirmed if patients had a recorded diagnosis of colorectal cancer.

Data management and analyses were performed using Stata® version 17 (StataCorp, College Station, TX, USA). Characteristics of the colectomy population over time are presented as proportions for each year. For the primary outcome of the annual proportion of people

receiving an opioid prescription, the analysis was stratified based on opioid exposure prior to colectomy. This was calculated as a percentage for each year:

$$\frac{Number\ of\ individuals\ receiving\ at\ least\ one\ opioid\ prescription\ within\ 90\ days\ of\ discharge\ in\ the\ year \times 100}{Number\ of\ individuals\ who\ had\ colectomy\ that\ year}$$

Trend analysis over the years was performed using the Cochran Armitage test. Absolute and percentage changes between 2010 and 2019 were calculated and tested using unadjusted logistic regression.

For secondary outcomes, characteristics of patients having opioid prescriptions within 90 days of discharge are presented as proportions for each year. Descriptive statistics were used to describe the outcome measures as frequencies, proportions (percentage).

The yearly proportion of prescriptions containing an opioid formulation was calculated:

$$\frac{Number\ of\ prescriptions\ in\ each\ opioid\ drug\ formulation\ category}{Total\ number\ of\ prescriptions\ for\ opioids\ within\ first\ 90\ days\ of\ discharge\ in\ that\ year}$$

The proportion of people who were dispensed an OMEQ dose in each category was calculated and the proportion of people prescribed an opioid in each category was calculated by dividing the number of people based on their daily OMEQ dose by the total number of people with repeated opioid prescriptions following surgery for that year. Utilisation measures were stratified based on opioid exposure before surgery into naïve, currently, and previously exposed.

RESULTS

In total, 95 155 individuals had a colectomy during the study period (Figure 1). The surgical approach shifted toward open colectomy being less frequent than minimally invasive procedures. There was an increase in the number of opioid-naïve patients from 79.1% in 2010 to 86.9% in 2019 (percentage change 9.86%, p<0.005), whereas there was a fall in the currently opioid-exposed group (percentage change -40.5%, p<0.001), (Table S5).

Of the 15 503 (16.3%) individuals who received opioid prescriptions from primary care after hospital discharge following colectomy, the ratio of opioid-naïve to currently exposed individuals and elective to emergency admission remained relatively stable over the study period. However, the proportions of individuals having two or more comorbidities, benign disease, and minimally invasive procedures increased over the study period (Table 1).

Overall, the percentage of patients issued an opioid prescription within 90 days of hospital discharge decreased by 37.3% between 2010 and 2019 (p<0.001). The opioid-naïve group mainly drove this downward trend, with the proportion of people prescribed any opioid decreasing from 11.4% in 2010 to 6.7% in 2019, (percentage change -41.3%, p<0.001). Whereas, for the currently exposed group, the percentage of individuals prescribed opioids remained stable, from 57.5% in 2010 to 58.3% in 2019 (percentage change +1.3%, p=0.697) (Figure 2).

For trends in opioid prescriptions by opioid potency, weak opioids were the most commonly prescribed category during the study period (75.5%), followed by strong opioids (19.9%), with the remainder (4.6%) prescribed a combination of weak and strong opioids. Notably, there was a downward trend in weak opioid prescribing prevalence over the years, with a decline from 82.3% in 2010 to 69.7% in 2019 (percentage change -15.3%, p<0.001). This

decline remained statistically significant for all three strata of previous opioid exposure ($p<0.001$), and for both open and minimally invasive surgeries ($p<0.001$) (Figure 3 and Table S6).

There was an upward trend in the prescribing prevalence of strong opioids, with a 94.0% increase (13.2% in 2010 to 25.6% in 2019, $p<0.001$). In addition, strong opioid prescribing was more common for currently opioid exposed (64.3%) than for the opioid-naïve (31.9%) and previously exposed groups (3.7%). However, the temporal changes were steeper for the opioid-naïve group, with a 133% increase from 2010 to 2019. Although strong opioid prescribing increased at a similar rate for both open and minimally invasive colectomy (15.0% in 2010 to 31.0% in 2019, $p<0.001$) and (8.1% in 2010 to 18.3% in 2019, $p<0.001$) respectively. Strong opioid prescribing remained lower in the minimally invasive colectomy group than in those having open colectomy (Figure 3 and Table S6).

Codeine was the most commonly prescribed opioid during the study period (44.5%), followed by tramadol (29.9%) and morphine (12.2%). Notably, prescribing of specific opioid medicines changed over time. For the overall population, the prescribing of codeine decreased from 43.5% in 2010 to 40% in 2014 and rose to 50.0% in 2019 ($p<0.001$). When people were stratified either by surgical approach or by opioid exposure before surgery, codeine remained the most commonly prescribed opioid. However, the significantly increased prescribing prevalence was mainly for the opioid-naïve group and minimally invasive surgery (Figure 4 and Table S7).

The proportion of prescriptions for oxycodone and morphine continued to increase. Oxycodone prescribing nearly trebled between 2010 and 2019 for opioid-naïve group and minimally invasive surgery (percentage change: 395% and 471% respectively). On the

contrary, buprenorphine prescribing increased from 2.2% to 4.1% for currently opioid exposed group and from 4.1% to 8.6% for open colectomy. Among all the prescribed opioids, tramadol prescribing decreased significantly, with a steep decline starting in 2014. This decline was evident for all stratified groups.

Overall, immediate-release formulations were the most prescribed formulation over the study period (83.9%), followed by modified-release only (5.8%) and transdermal only (3.1%). Although immediate-release formulations were more prominent, their prevalence decreased from 86.0% in 2010 to 82.0% in 2019 (percentage change -4.7%, $p<0.001$). Transdermal and modified-release formulations were prescribed more for the currently exposed group (76.8% and 69.0% respectively), compared with 20.0% and 27.6% respectively in the opioid-naïve group.

Of the five dose ranks of total OMEQ dose, most people were in the lower dose ranks (43.6% in the 25-49 mg/day group and 30.8% in the 50-99 mg/day group). There was an increasing trend in the percentage of people prescribed opioids in the 25-49 mg/day group from 40.1% to 51.3% ($p<0.001$), with the increase being more predominant for the opioid-naïve and prior exposed groups. On the other hand, a downward trend started in 2013 was seen for doses of 50-99 mg/day (percentage change 34.5%) (Figure 5).

DISCUSSION

There was a notable decrease in patients receiving opioid prescriptions in primary care following discharge after colectomy, particularly among opioid-naïve patients over time. These results are consistent with those of studies from the US that also showed a decline in opioid prescribing after major abdominal and orthopaedic surgeries,[18, 19] despite the differences between post-surgical prescribing practices in the US and the UK. It is essential to note that due to a dearth of studies on post-operative opioid prescribing practices in the UK, direct comparisons with current study findings are limited.

Codeine and tramadol were the most frequently prescribed opioids after colectomy, consistent with findings that codeine and tramadol accounted for approximately 58% and 45% of postoperative prescriptions in Canada and Sweden, respectively, compared with only 7% in the United States.[4] A similar trend was observed in a cross-sectional study that examined the type of opioid initiated for new users in different countries, where a higher proportion of patients were started on codeine and tramadol in the UK, while oxycodone was the most commonly prescribed opioid in the US.[35]

We also found a decrease in prescribing of tramadol after 2014, reaching a similar rate to morphine prescribing by the end of the study period. One possible explanation for this decline is the classification of tramadol as a Schedule 3 controlled substance in the UK in 2014,[36] prompted by safety concerns and potential risks of misuse. This decrease in tramadol prescribing is consistent with a UK study that assessed the impact of reclassification on the use of tramadol for chronic pain.[37] Another observed change over

time was the increase in prescribing of oxycodone and morphine, consistent with trends reported in contemporary prescribing literature from the UK for other indications.[35, 38]

While the data included in this study were obtained before the release of guidelines that advise against using transdermal and long-acting formulations for managing acute pain,[2] the findings are reassuring since immediate-release formulations accounted for most prescribed opioids. However, the unexpected modest decrease in the prescribing of immediate-release formulations in 2019 is noteworthy. It is also worth emphasising that prescribing transdermal formulations was more common among patients with previous opioid exposure, which could be attributed to the continuation of similar formulations after hospital discharge. Nevertheless, increased education and awareness are necessary to discourage the use of long-acting formulations in favour of immediate-release opioids due to their higher risk of misuse, addiction, and difficulty in dose adjustment.

Most patients were prescribed low opioid doses (OMEQ dose in the 25-49 and 59-99 mg/day categories), with an upward trend for patients prescribed OMEQ dose in the 25-49 mg/day category over the years. International guidelines vary in the OMEQ doses that require caution. Canadian guidelines recommend that prescribed OMEQ dose should be limited to <50 mg/day,[39] while US guidelines advise prescribers to avoid increasing the dose to ≥90 mg/day.[33] The UK Faculty of Pain Medicine advises that the potential harms outweigh the benefits when an OMEQ dose of 120 mg/day is exceeded.[40] It is challenging to identify any specific intervention or policy that contributed to the observed trends in prescribing observed in this study. Possible interventions could be the improvement of perioperative pain management approaches and surgical techniques, particularly since there was an

increase in the adoption of minimally invasive surgeries in our cohort. Other contributing factors include the promotion of non-opioid analgesia or opioid-sparing strategies, the availability of patient-provider education and discharge counselling services.[8]

Several clinical implications arise from the findings of this study. First, although the UK guidelines on perioperative opioid prescribing[22, 41] do not provide metrics on the proportion of patients on opioids to indicate best practice, the study findings may indicate a potential decrease in the reliance on opioids for managing acute pain following colectomy in England and could represent a trend towards improved opioid stewardship. Second, the consensus guidelines on preventing opioid-related harm suggest that post-discharge repeat prescriptions for opioids should be avoided, given the potential risks involved.[2, 41] This recommendation becomes particularly relevant as the current analysis showed that some patients still need opioids within 90 days after discharge, which might raise concerns about the possibility of developing chronic post-surgical pain. As opioids are not recommended for managing chronic post-surgical pain[2], requests for additional opioids should prompt a comprehensive patient review by the GP or pain specialists for opioid weaning or assessment for chronic post-surgical pain.[42, 43] Since the data used were collected before the release of these guidelines, future studies should evaluate the impact of guideline implementation on reducing opioid prescribing and opioid-related adverse events for surgical patients.

Third, the study showed that codeine and tramadol were the most commonly prescribed opioids. Despite being classified as weak opioids, being prodrugs both can have different side effect profiles based on individual genetic polymorphisms.[44] The classification of opioids based on potency has been debated[7] as this alone does not protect patients from

potential harm, including dependence and mortality.[45] Notably, while codeine-related deaths in the UK increased by 17-fold from 9 in 1994 to 156 in 2017,[46] the drug is still available over-the-counter. In contrast, the Australian Federal Government reclassified codeine as a prescription-only medicine in 2018, resulting in a subsequent reduction in harms associated with its use.[47, 48] We suggest that the results of the current study can indicate possible opportunities to re-evaluate analgesic selection practices and educate healthcare professionals about the variable effects and side effects profile of different opioids.

This study had some limitations. While it describes trends and patterns in opioid use, it did not assess the specific factors at the patient, provider or system level that influenced them. Accuracy of recorded data is a common concern when using electronic health records. Nevertheless, the databases used in this study have undergone thorough validation and have implemented various measures to ensure data quality and accuracy. Moreover, the opioid prescription data were prepared using a systematic approach with a prescription preparation algorithm. This algorithm addresses missing data, accounts for overlapped prescriptions, and calculates OMEQ dose, allowing for more easily comparable data across different opioid medications since OMEQ dose is considered a standard prescribing measure.

Another shortcoming of electronic health record data is the lack of detailed clinical contexts, such as specific medication-use indications, patient preferences, and clinical decision-making processes. This limitation also applies to analgesics prescribed during hospital stay, which may impact the choice of opioid and prescribed doses. For example, the use of

adjunctive paracetamol or non-steroidal anti-inflammatory drugs immediately after surgery is associated with decreased postoperative opioid requirements and reduced related adverse events.[49] Finally, while using prescription data as a proxy measure of drug consumption is a well-established practice in drug utilisation research,[9] it is essential to acknowledge its limitations. In the current study, the availability of issued opioid prescriptions was used as a surrogate marker to ascertain opioid consumption. However, as information on actual consumption and adherence was lacking, overall utilisation may have been overestimated.

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Data sharing statement

Access to the Clinical Practice Research Datalink and linked data was provided under a licence to the University of Nottingham. Under the terms and agreement of this licence, data cannot be provided for the purposes of sharing.

Declaration of interests

DNL has received an unrestricted educational grant from B. Braun for unrelated work. He has also received speaker's honoraria for unrelated work from Abbott, Nestlé and Corza. No other competing interests declared.

FIGURE LEGENDS

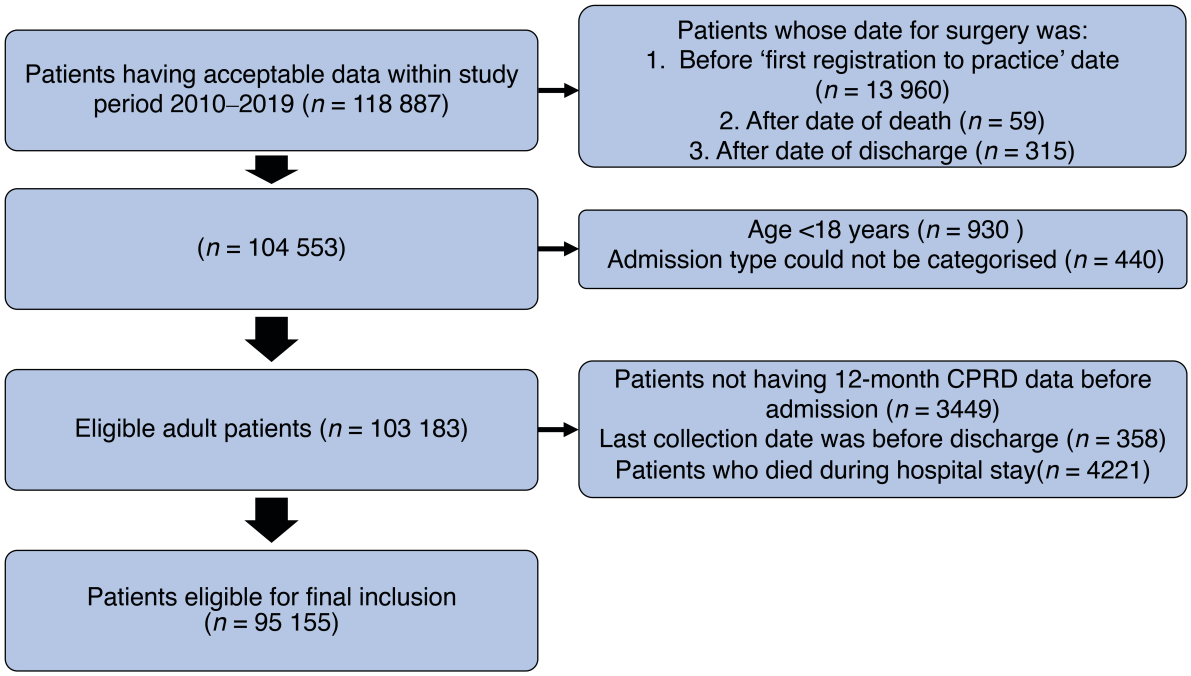

Figure 1: Study flow diagram

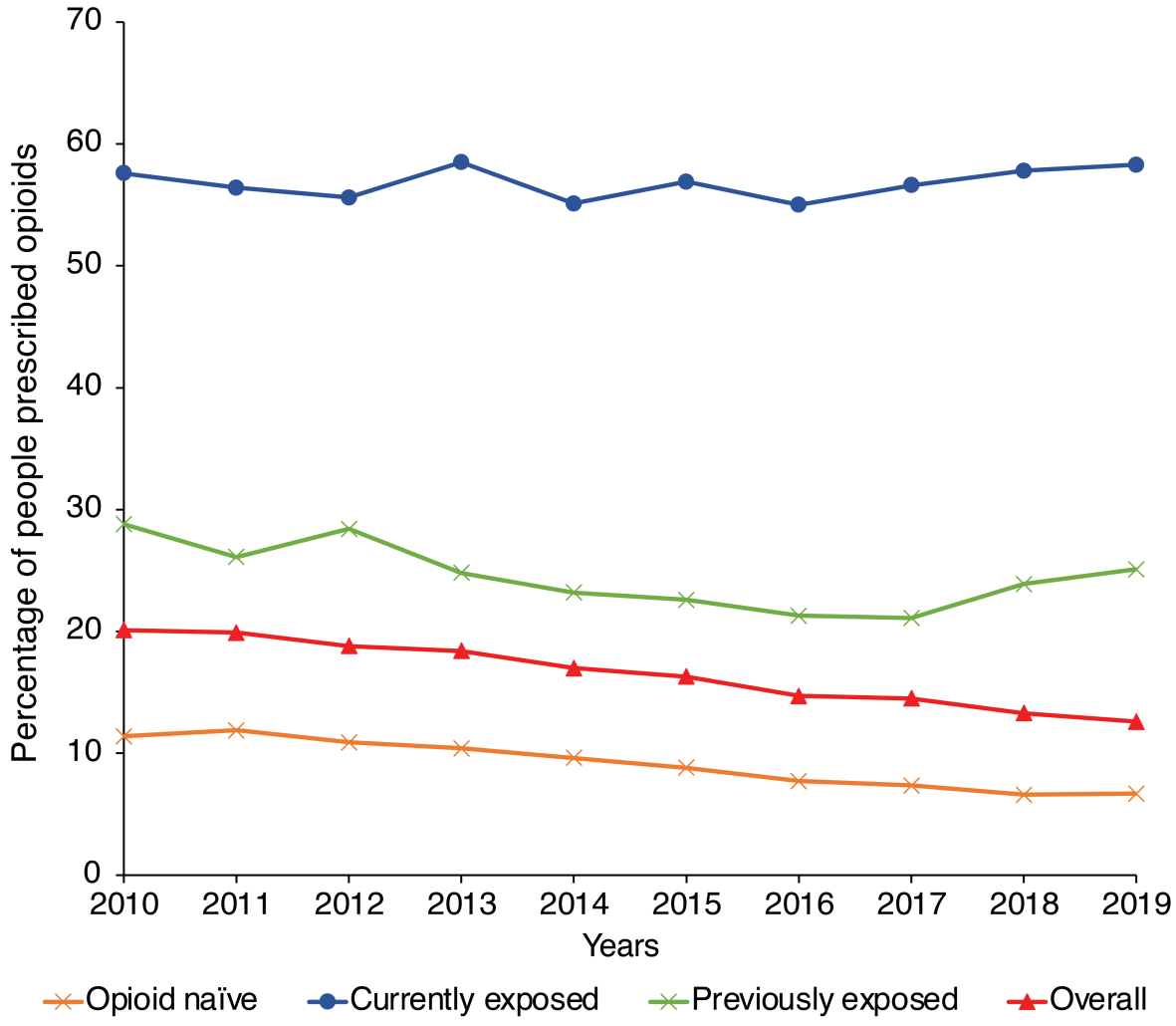

Figure 2: Temporal trend of percentage of patients who received opioid prescriptions after discharge

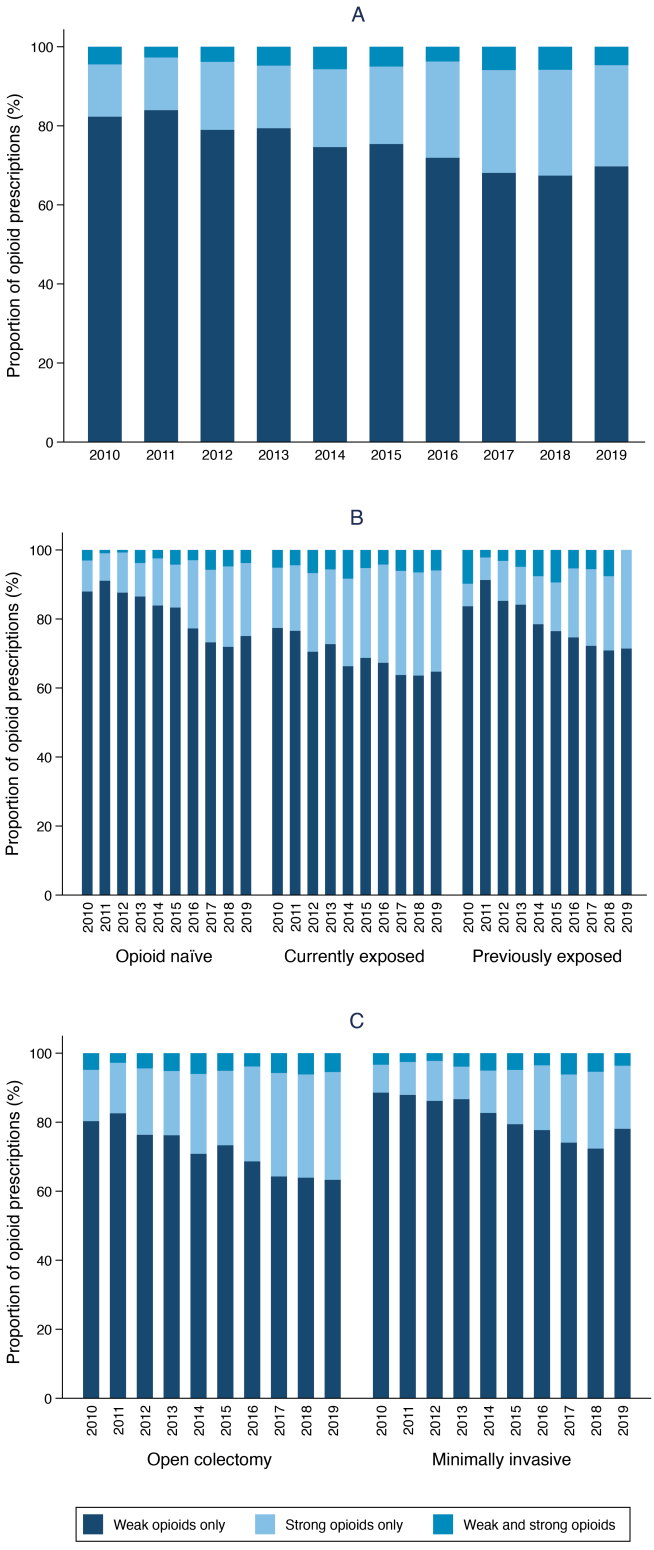

Figure 3: Yearly trend in the potency of opioid prescribed in initial prescription received after discharge, (A) overall cohort, (B) cohort stratified by opioid exposure before colectomy, and (C) cohort stratified by surgical approach

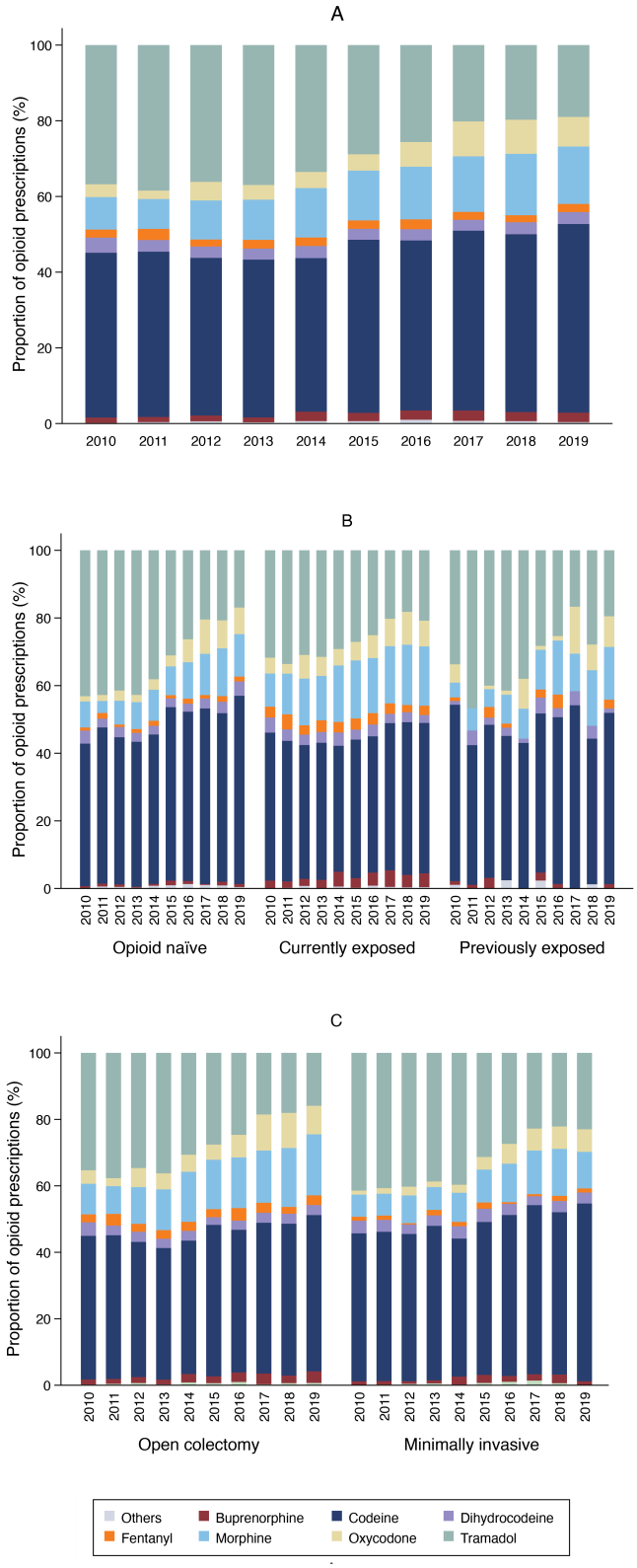

Figure 4: Yearly trend in the type of opioid prescribed in initial prescription received after discharge, (A) overall cohort, (B) cohort stratified by opioid exposure before colectomy, and (C) cohort stratified by surgical approach

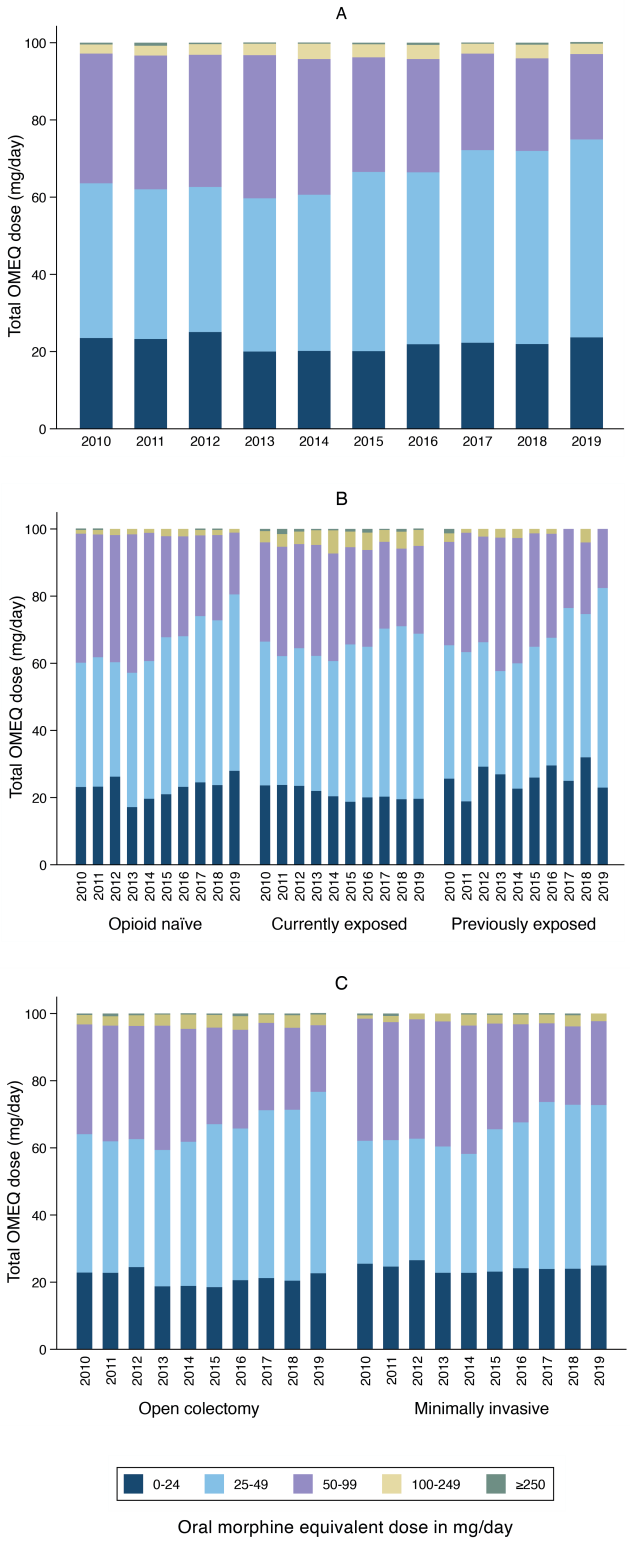

Figure 5: Yearly trend in total oral morphine equivalent doses prescribed in initial prescription received after discharge, (A) overall cohort, (B) cohort stratified by opioid exposure before colectomy, and (C) cohort stratified by surgical approach.

Supplementary Material

Table S1: HES using OPCS codes for colectomy procedures

Table S2: Opioid products codes

Table S3: Decisions made to prepare opioid prescriptions using DrugPrep algorithm

Table S4: Equianalgesic ratios to calculate Oral Morphine Equivalent dose

Table S5: Yearly characteristics of the colectomy cohort

Table S6: Changes in the potency of opioid prescribed in initial prescription received after discharge

Table S7: Changes in the type of opioid prescribed in initial prescription received after discharge

Table 1: Baseline characteristics of patients having opioid prescriptions within 90 days following colectomy discharge between the years 2010 and 2019

All results are expressed as n (%) except where specifically mentioned

Variable	Years									
	2010	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
Whole colectomy	n=8001	n=8470	n=8850	n=8963	n=9038	n=9614	n=10 009	n=10 286	n=10 794	n=11 130
Issued Initial opioid prescription	n=1607 (100%)	n=1689 (100%)	n=1663 (100%)	n=1653 (100%)	n=1537 (100%)	n=1566 (100%)	n=1466 (100%)	n=1489 (100%)	n=1435 (100%)	n=1398 (100%)
Age, y (mean ± SD)	65.2 ± 14.3	64.9 ± 14.3	64.1 ± 15.3	63.7 ± 15.2	64.5 ± 15.0	63.7 ± 15.2	63.5 ± 15.4	63.4 ± 15.4	63.2 ± 14.8	63.4 ± 15.4
Sex										
Female	850 (52.9)	843 (49.9)	886 (53.3)	892 (53.9)	821 (53.4)	831 (53.1)	808 (55.1)	811 (54.5)	779 (54.3)	773 (55.3)
Male	757 (47.1)	846 (50.1)	777 (46.7)	761 (46.0)	716 (46.6)	735 (46.9)	658 (44.9)	678 (45.5)	656 (45.7)	625 (44.7)
Ethnicity										
White	1530 (95.2)	1600 (94.7)	1563 (93.9)	1560 (94.3)	1437 (93.5)	1452 (92.7)	1355 (92.4)	1370 (92.0)	1328 (92.5)	1258 (90.0)
Black	32 (1.9)	22 (1.3)	21 (1.3)	25 (1.5)	20 (1.3)	33 (2.1)	26 (1.8)	30 (2.01)	32 (2.2)	34 (2.4)
Asian	36 (2.2)	41 (2.4)	47 (2.8)	40 (2.4)	40 (2.6)	37 (2.4)	40 (2.7)	38 (2.6)	32 (2.2)	49 (3.5)
Others	9 (0.56)	26 (1.5)	32 (1.9)	28 (1.7)	40 (2.6)	44 (2.8)	45 (3.1)	51 (3.4)	43 (3.0)	57 (4.1)
Index of Multiple Deprivation (1 most deprived, 5 least deprived)										
1	315 (19.6)	338 (20.0)	316 (19.0)	323 (19.5)	298 (19.4)	324 (20.7)	276 (18.8)	305 (20.5)	305 (21.3)	265 (18.9)
2	335 (20.9)	343 (20.3)	334 (20.1)	349 (21.1)	311 (20.2)	305 (19.5)	295 (20.1)	293 (19.7)	258 (17.9)	270 (19.3)
3	348 (21.7)	325 (19.2)	326 (19.6)	316 (19.1)	318 (20.7)	315 (20.1)	330 (22.5)	289 (19.4)	298 (20.8)	285 (20.4)
4	306 (19.0)	347 (20.5)	324 (19.5)	351 (21.2)	325 (21.2)	291 (18.6)	299 (20.4)	289 (19.4)	282 (19.7)	275 (19.6)
5	301 (18.7)	332 (19.7)	363 (21.8)	314 (19.0)	283 (18.4)	330 (21.1)	263 (17.9)	311 (20.9)	291 (20.3)	303 (21.7)
Missing	2 (0.12)	4 (0.24)	-	-	-	-	3 (0.20)	2 (0.13)	1 (0.07)	-
Charlson Comorbidity Index										
0	261 (16.3)	252 (14.9)	279 (16.8)	282 (17.1)	248 (16.1)	262 (16.7)	220 (15.0)	204 (13.7)	206 (14.3)	198 (14.2)
1	119 (7.4)	120 (7.1)	110 (6.6)	104 (6.3)	99 (6.4)	103 (6.6)	88 (6.0)	114 (7.7)	87 (6.1)	82 (5.9)
≥2	1227 (76.4)	1317 (77.9)	1274 (76.6)	1267 (76.7)	1190 (77.4)	1201 (76.7)	1158 (78.9)	1171 (78.6)	1142 (79.6)	1118 (79.9)
Preoperative opioid exposure										
Opioid naïve	721 (44.9)	804 (47.6)	774 (46.5)	752 (45.5)	707 (46.0)	695 (44.4)	642 (43.8)	632 (42.5)	607 (42.3)	647 (46.3)
Currently exposed	808 (50.3)	795 (47.1)	800 (48.1)	823 (49.8)	755 (49.1)	794 (50.7)	753 (51.4)	789 (52.3)	753 (52.5)	677 (48.4)
Previously exposed	78 (4.9)	90 (5.3)	89 (5.4)	78 (4.7)	75 (4.9)	77 (4.9)	71 (4.8)	68 (4.6)	75 (5.2)	74 (5.3)
Surgical approach										
Open	1211 (75.4)	1259 (74.5)	1196 (71.9)	1140 (68.9)	1032 (67.1)	1026 (65.5)	932 (63.6)	900 (60.4)	831 (57.9)	781 (55.9)
Minimally invasive	396 (24.6)	430 (25.5)	467 (28.1)	513 (31.0)	505 (32.9)	540 (34.5)	534 (36.4)	589 (39.6)	604 (42.1)	617 (44.1)
Cancer diagnosis										
No	680 (42.3)	656 (38.8)	756 (45.5)	734 (44.4)	685 (44.6)	699 (44.6)	657 (44.8)	681 (45.7)	653 (45.5)	662 (47.4)
Yes	927 (57.7)	1,033 (61.2)	907 (54.5)	919 (55.6)	852 (55.4)	867 (55.4)	809 (55.2)	808 (54.3)	782 (54.5)	736 (52.6)
Admission type										
Emergency	453 (28.2)	497 (29.4)	531 (31.9)	526 (31.8)	486 (31.6)	503 (32.1)	464 (31.7)	452 (30.4)	438 (30.5)	468 (33.5)
Elective	1154 (71.8)	1192 (70.6)	1132 (68.1)	1127 (68.2)	1051 (68.4)	1063 (67.9)	1002 (68.4)	1037 (69.6)	997 (69.5)	930 (66.5)

Original Article

Temporal trends and patterns in initial opioid prescriptions after hospital discharge following colectomy in England over ten years

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Supplementary Materials - Index

Supplementary Figures and Tables

Supplementary Materials

Table S1: OPCS and ICD codes used to identify colectomy, inflammatory bowel disease and diverticular disease

Colectomy codes

H04 Total excision of colon and rectum *(Clean-Contaminated)*
H04.1 Panproctocolectomy and ileostomy
Includes: Proctocolectomy not elsewhere classified
H04.2 Panproctocolectomy and anastomosis of ileum to anus and creation of pouch however further qualified
H04.3 Panproctocolectomy and anastomosis of ileum to anus not elsewhere classified
H04.8 Other specified
H04.9 Unspecified

H05 Total excision of colon *(Clean-Contaminated*)
H05.1 Total colectomy and anastomosis of ileum to rectum
H05.2 Total colectomy and ileostomy and creation of rectal fistula however further qualified
H05.3 Total colectomy and ileostomy not elsewhere classified
H05.8 Other specified
H05.9 Unspecified

H06 Extended excision of right hemicolon *(Clean-Contaminated)*
Includes: Excision of right colon and other segment of ileum or colon and surrounding tissue
H06.1 Extended right hemicolectomy and end to end anastomosis
H06.2 Extended right hemicolectomy and anastomosis of ileum to colon
H06.3 Extended right hemicolectomy and anastomosis not elsewhere classified
H06.4 Extended right hemicolectomy and ileostomy however further qualified
H06.5 Extended right hemicolectomy and end to side anastomosis
H06.8 Other specified
H06.9 Unspecified

H07 Other excision of right hemicolon *(Clean-Contaminated*)
Includes: Limited excision of caecum and terminal ileum caecum
H07.1 Right hemicolectomy and end to end anastomosis of ileum to colon
Includes: Ileocaecal resection
H07.2 Right hemicolectomy and side to side anastomosis of ileum to transverse colon
H07.3 Right hemicolectomy and anastomosis not elsewhere classified
H07.4 Right hemicolectomy and ileostomy however further qualified
H07.5 Right hemicolectomy and end to side anastomosis
H07.8 Other specified
H07.9 Unspecified

H08 Excision of transverse colon *(Clean-Contaminated)*
H08.1 Transverse colectomy and end to end anastomosis
H08.2 Transverse colectomy and anastomosis of ileum to colon
H08.3 Transverse colectomy and anastomosis not elsewhere classified

H08.4 Transverse colectomy and ileostomy however further qualified
H08.5 Transverse colectomy and exteriorisation of bowel not elsewhere classified*
H08.6 Transverse colectomy and end to side anastomosis
H08.8 Other specified
H08.9 Unspecified
Note: *Use secondary code for exteriorisation of caecum (H14) or other exteriorisation of colon (H15)*

H09 Excision of left hemicolon (*Clean-Contaminated)*
H09.1 Left hemicolectomy and end to end anastomosis of colon to rectum
H09.2 Left hemicolectomy and end to end anastomosis of colon to colon
H09.3 Left hemicolectomy and anastomosis not elsewhere classified
H09.4 Left hemicolectomy and ileostomy however further qualified
H09.5 Left hemicolectomy and exteriorisation of bowel not elsewhere classified*
H09.6 Left hemicolectomy and end to side anastomosis
H09.8 Other specified
H09.9 Unspecified
Note: *Use secondary code for exteriorisation of caecum (H14) or other exteriorisation of colon (H15)*

H10 Excision of sigmoid colon (*Clean-Contaminated)*
H10.1 Sigmoid colectomy and end to end anastomosis of ileum to rectum
H10.2 Sigmoid colectomy and anastomosis of colon to rectum
H10.3 Sigmoid colectomy and anastomosis not elsewhere classified
H10.4 Sigmoid colectomy and ileostomy however further qualified
H10.5 Sigmoid colectomy and exteriorisation of bowel not elsewhere classified*
H10.6 Sigmoid colectomy and end to side anastomosis
H10.8 Other specified
H10.9 Unspecified
Note: *Use secondary code for exteriorisation of caecum (H14) or other exteriorisation of colon (H15)*

H11 Other excision of colon *(Clean-Contaminated)*
Includes: Excision of colon where segment removed is not stated
H11.1 Colectomy and end to end anastomosis of colon to colon not elsewhere classified SSI H11.2 Colectomy and side to side anastomosis of ileum to colon not elsewhere classified
H11.3 Colectomy and anastomosis not elsewhere classified
H11.4 Colectomy and ileostomy not elsewhere classified
H11.5 Colectomy and exteriorisation of bowel not elsewhere classified*
H11.6 Colectomy and end to side anastomosis NEC
H11.8 Other specified
Please see minimum wound class against each procedure
H11.9 Unspecified
Includes: Colectomy or hemicolectomy not elsewhere classified
Note*: Use secondary code for exteriorisation of caecum (H14) or other exteriorisation of colon (H15)*

H29 Subtotal excision of colon and rectum *(Clean contaminated)*
H29.1 Subtotal excision of colon and rectum and creation of colonic pouch and anastomosis of colon to anus
H29.2 Subtotal excision of colon and rectum and creation of colonic pouch NEC
H29.3 Subtotal excision of colon and creation of colonic pouch and anastomosis of colon to rectum.
H29.4 Subtotal excision of colon and creation of colonic pouch NEC
H29.8 Other specified subtotal excision of colon
H29.9 Unspecified subtotal excision of colon

H33 Excision of rectum *(Clean contaminated)*
Includes: Excision of whole or part of rectum with or without part of sigmoid colon
H33.1 Abdominoperineal excision of rectum and end colostomy
H33.2 Proctectomy and anastomosis of colon to anus
H33.3 Anterior resection of rectum and anastomosis of colon to rectum using staples
Includes: Rectosigmoidectomy and anastomosis of colon to rectum
H33.4 Anterior resection of rectum and anastomosis not elsewhere classified
H33.5 Rectosigmoidectomy and closure of rectal stump and exteriorisation of bowel*
H33.6 Anterior resection of rectum and exteriorisation of bowel*
H33.7 Perineal resection of rectum HFQ
H33.8 Other specified
H33.9 Unspecified
Includes: Rectosigmoidectomy not elsewhere classified
***Note:** Use secondary code for creation of artificial opening into ileum (G74); exteriorisation of caecum (H14) or other exteriorisation of colon (H15*

Inflammatory bowel disease codes

K50, K500, K501, K508, K509, K51, K510, K512, K513, K514, K515, K518, K519, K520, K521, K522,

K523, K528, K529

Diverticular disease codes

K57,K570, K571, K572, K573, K574, K575, K578, K579

Table S2: Opioid products code

ProdCodeId	DMDCode	drugsubstancename	substancestrength	formulation
1.23539E+16	3.45353E+16	Tramadol hydrochloride	75mg	Modified-release tablet
1.23538E+16	3.45363E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.23537E+16	3.45349E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
1.23536E+16	3.45358E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
1.85044E+15	4.61411E+14	Tramadol hydrochloride	400 mg	Modified-release tablet
1.85034E+15	9.29211E+14	Tramadol hydrochloride	300 mg	Modified-release tablet
1.85024E+15	1.42111E+14	Tramadol hydrochloride	200 mg	Modified-release tablet
1.85014E+15	1.39611E+14	Tramadol hydrochloride	150 mg	Modified-release tablet
4.25924E+15	1.19853E+16	Tramadol hydrochloride	50 mg	Modified-release tablet
1.56474E+15	3.15611E+14	Tramadol hydrochloride	200 mg	Modified-release tablet
1.56464E+15	3.62111E+14	Tramadol hydrochloride	150 mg	Modified-release tablet
1.56454E+15	3.06311E+14	Tramadol hydrochloride	100 mg	Modified-release tablet
1.56484E+15	3.14411E+14	Tramadol hydrochloride	50 mg	Soluble tablet

1.56434E+15	2.03811E+14	Tramadol hydrochloride	50 mg	Capsule
1.56154E+15	3.77801E+15	Morphine sulfate	60 mg	Modified-release capsule
1.56144E+15	3.65161E+15	Morphine sulfate	30 mg	Modified-release capsule
1.56134E+15	4.03551E+15	Morphine sulfate	200 mg	Modified-release capsule
1.56114E+15	3.65211E+15	Morphine sulfate	10 mg	Modified-release capsule
1.56124E+15	3.88161E+15	Morphine sulfate	100 mg	Modified-release capsule
1.12435E+16	3.21335E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.12431E+16	3.21385E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.12434E+16	3.21367E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.12433E+16	3.21402E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.12432E+16	3.21353E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
4.41754E+15	1.28716E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
4.41764E+15	1.28712E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
4.41774E+15	1.28698E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
2.74614E+15	7.5011E+13	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Tablet
2.74594E+15	3.14111E+14	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Capsule

1.54954E+15	2.1011E+13	Tramadol hydrochloride	50 mg	Modified-release capsule
1.54944E+15	9.411E+12	Tramadol hydrochloride	200 mg	Modified-release capsule
1.54934E+15	7.11511E+14	Tramadol hydrochloride	150 mg	Modified-release capsule
1.54924E+15	3.31011E+14	Tramadol hydrochloride	100 mg	Modified-release capsule
2.98044E+15	5.19701E+15	Tramadol hydrochloride	50 mg	Orodispersible tablet
1.54804E+15	4.00911E+14	Tramadol hydrochloride	50 mg	Capsule
3.34444E+15	9.53321E+15	Tramadol hydrochloride	400 mg	Modified-release tablet
3.34434E+15	9.53291E+15	Tramadol hydrochloride	300 mg	Modified-release tablet
3.34424E+15	9.53261E+15	Tramadol hydrochloride	200 mg	Modified-release tablet
3.34414E+15	9.53221E+15	Tramadol hydrochloride	150 mg	Modified-release tablet
1.0598E+16	3.00022E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
1.05981E+16	3.0002E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
1.05982E+16	3.00017E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
1.05978E+16	3.0003E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
5.00724E+15	1.53636E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
5.00754E+15	1.53634E+16	Fentanyl	50 microgram/1 hour	Transdermal patch

5.00744E+15	1.53632E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
1.15076E+16	3.25202E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
5.00734E+15	1.53638E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
1.47964E+15	3.60311E+14	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Capsule
1.24286E+16	3.49121E+16	Buprenorphine	70 microgram/1 hour	Transdermal patch
1.24285E+16	3.49119E+16	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
1.24284E+16	3.49117E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
2.73804E+15	3.44931E+15	Buprenorphine	70 microgram/1 hour	Transdermal patch
2.73794E+15	3.44881E+15	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
2.73784E+15	3.44661E+15	Buprenorphine	35 microgram/1 hour	Transdermal patch
4.45954E+15	1.27908E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
4.45944E+15	1.27905E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
4.45934E+15	1.27903E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
4.52304E+15	1.15921E+16	Tramadol hydrochloride	50 mg	Modified-release capsule
4.52334E+15	1.15927E+16	Tramadol hydrochloride	200 mg	Modified-release capsule
4.52324E+15	1.15925E+16	Tramadol hydrochloride	150 mg	Modified-release capsule

4.52314E+15	1.15923E+16	Tramadol hydrochloride	100 mg	Modified-release capsule
1.70204E+15	3.24291E+15	Tramadol hydrochloride	50 mg	Effervescent powder
1.70194E+15	3.25011E+15	Tramadol hydrochloride	100 mg	Effervescent powder
1.45454E+15	4.51511E+14	Tramadol hydrochloride	50 mg	Capsule
2.07814E+15	3.59212E+16	Tramadol hydrochloride	75 mg	Modified-release tablet
1.46574E+15	322633008	Tramadol hydrochloride	50 mg	Soluble tablet
2.98034E+15	5.21281E+15	Tramadol hydrochloride	50 mg	Orodispersible tablet
4.25914E+15	1.20374E+16	Tramadol hydrochloride	50 mg	Modified-release tablet
1.46294E+15	3.59401E+16	Tramadol hydrochloride	50 mg	Modified-release capsule
1.70224E+15	322645004	Tramadol hydrochloride	50 mg	Effervescent powder
1.45424E+15	322623000	Tramadol hydrochloride	50 mg	Capsule
1.85004E+15	3.5921E+16	Tramadol hydrochloride	400 mg	Modified-release tablet
1.84994E+15	3.59209E+16	Tramadol hydrochloride	300 mg	Modified-release tablet
1.46254E+15	3.59208E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.46284E+15	3.59207E+16	Tramadol hydrochloride	200 mg	Modified-release capsule
1.46244E+15	3.59206E+16	Tramadol hydrochloride	150 mg	Modified-release tablet

1.46274E+15	3.59205E+16	Tramadol hydrochloride	150 mg	Modified-release capsule
6.38914E+15	1.92004E+16	Tramadol hydrochloride	100 mg/1 ml	Oral drops
1.46234E+15	3.59203E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
1.46264E+15	3.59202E+16	Tramadol hydrochloride	100 mg	Modified-release capsule
1.70214E+15	322646003	Tramadol hydrochloride	100 mg	Effervescent powder
3.99664E+15	1.1055E+16	Tramadol hydrochloride	300 mg	Modified-release tablet
3.99654E+15	1.10548E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
3.99644E+15	1.10546E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
3.33284E+15	9.50851E+15	Fentanyl	75 microgram/1 hour	Transdermal patch
3.33294E+15	9.50821E+15	Fentanyl	50 microgram/1 hour	Transdermal patch
3.33304E+15	9.50801E+15	Fentanyl	25 microgram/1 hour	Transdermal patch
3.33314E+15	9.50891E+15	Fentanyl	100 microgram/1 hour	Transdermal patch
1.23502E+16	2.16951E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.23501E+16	2.16945E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
1.235E+16	2.16929E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
6.52774E+15	1.99574E+16	Buprenorphine hydrochloride	400 microgram	Sublingual tablet

6.52764E+15	1.99572E+16	Buprenorphine hydrochloride	200 microgram	Sublingual tablet
1.42864E+15	7.62111E+14	Buprenorphine hydrochloride	400 microgram	Sublingual tablet
1.42614E+15	8.67611E+14	Buprenorphine hydrochloride	200 microgram	Sublingual tablet
5.23444E+15	1.58509E+16	Naloxone hydrochloride/ Oxycodone hydrochloride	2.5 mg + 5 mg	Modified-release tablet
5.23454E+15	1.58513E+16	Naloxone hydrochloride/ Oxycodone hydrochloride	20 mg + 40 mg	Modified-release tablet
4.89834E+15	1.4976E+16	Naloxone hydrochloride/ Oxycodone hydrochloride	10 mg + 20 mg	Modified-release tablet
4.89844E+15	1.49757E+16	Naloxone hydrochloride/ Oxycodone hydrochloride	5 mg + 10 mg	Modified-release tablet
6.13214E+15	442341005	Tapentadol hydrochloride	75 mg	Tablet
6.13204E+15	442472008	Tapentadol hydrochloride	50 mg	Tablet
6.13314E+15	1.86722E+16	Tapentadol hydrochloride	50 mg	Modified-release tablet
6.13354E+15	1.86721E+16	Tapentadol hydrochloride	250 mg	Modified-release tablet
9.16014E+15	2.44088E+16	Tapentadol hydrochloride	20 mg/1 ml	Oral solution
6.13344E+15	1.8672E+16	Tapentadol hydrochloride	200 mg	Modified-release tablet
6.13334E+15	1.86719E+16	Tapentadol hydrochloride	150 mg	Modified-release tablet
6.13324E+15	1.86718E+16	Tapentadol hydrochloride	100 mg	Modified-release tablet
1.83554E+15	2.92611E+14	Buprenorphine hydrochloride	400 microgram	Sublingual tablet

1.35254E+15	1.0411E+13	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Effervescent tablet
1.69804E+15	2.47311E+14	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Capsule
1.36384E+15	3.41211E+14	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Tablet
9.29294E+15	6.04311E+14	Codeine phosphate/ Paracetamol	12.8mg + 500 mg	Tablet
1.2187E+16	3.40276E+16	Oxycodone hydrochloride	1 mg/1 ml	Oral solution
9.06154E+15	2.36578E+16	Oxycodone hydrochloride	5 mg	Capsule
9.06174E+15	2.36582E+16	Oxycodone hydrochloride	20 mg	Capsule
1.21871E+16	3.40278E+16	Oxycodone hydrochloride	10 mg/1 ml	Oral solution
9.06164E+15	2.3658E+16	Oxycodone hydrochloride	10 mg	Capsule
1.27664E+15	3.07931E+15	Morphine sulfate	50 mg	Tablet
1.75204E+15	3.45141E+15	Morphine sulfate	20 mg/1 ml	Oral solution
1.27864E+15	3.07731E+15	Morphine sulfate	20 mg	Tablet
1.75254E+15	3.16411E+15	Morphine sulfate	2 mg/1 ml	Oral solution
1.27854E+15	2.89861E+15	Morphine sulfate	10 mg	Tablet
1.17562E+16	3.34807E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.17564E+16	3.34811E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch

1.17563E+16	3.34809E+16	Buprenorphine	10 microgram/1 hour	Transdermal patch
1.26374E+16	3.55433E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.26364E+16	3.55419E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.26373E+16	3.55429E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.26372E+16	3.55427E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.26369E+16	3.55425E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.26367E+16	3.55423E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
1.26365E+16	3.55421E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.16454E+15	6.80111E+14	Dihydrocodeine tartrate/ Paracetamol	20 mg + 500 mg	Tablet
1.15754E+15	4.19911E+14	Dihydrocodeine tartrate/ Paracetamol	30 mg + 500 mg	Tablet
9.17684E+15	2.44679E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
9.80984E+15	2.79933E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
9.17704E+15	2.44669E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
9.17714E+15	2.44677E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
9.80974E+15	2.7993E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
9.17724E+15	2.44674E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet

9.80964E+15	2.79928E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
9.17734E+15	2.44671E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.21951E+16	3.41721E+16	Buprenorphine	70 microgram/1 hour	Transdermal patch
1.2195E+16	3.41723E+16	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
1.21949E+16	3.41725E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
1.17325E+16	3.30387E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.17324E+16	3.30393E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.17323E+16	3.30391E+16	Buprenorphine	15 microgram/1hour	Transdermal patch
1.17322E+16	3.30389E+16	Buprenorphine	10 microgram/1hour	Transdermal patch
1.37513E+16	3.87287E+16	Buprenorphine	5 microgram/1hour	Transdermal patch
1.37515E+16	3.8746E+16	Buprenorphine	20 microgram/ 1hour	Transdermal patch
1.37514E+16	3.87456E+16	Buprenorphine	10 microgram/1hour	Transdermal patch
1.15772E+16	3.26437E+16	Buprenorphine	70 microgram/1hour	Transdermal patch
1.15771E+16	3.26432E+16	Buprenorphine	52.5 microgram/1hour	Transdermal patch
1.15079E+16	3.25762E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
6.52744E+15	1.99566E+16	Buprenorphine hydrochloride	400 microgram	Sublingual tablet

1.37472E+16	3.89564E+16	Pethidine hydrochloride	50 mg	Tablet
1.06564E+15	322612004	Pethidine hydrochloride	50 mg	Tablet
1.33006E+16	1.23034E+16	Pethidine hydrochloride	50 mg	Capsule
1.04464E+15	322600003	Pentazocine hydrochloride	50 mg	Capsule
1.06804E+15	322601004	Pentazocine hydrochloride	25 mg	Tablet
1.04304E+15	4.65611E+15	Dihydrocodeine tartrate/ Paracetamol	7.4 mg + 500mg	Tablet
1.03014E+15	6.55311E+14	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Effervescent tablet
4.43204E+15	7.72811E+14	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Capsule
1.17309E+16	3.30542E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.17308E+16	3.30546E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.17307E+16	3.30544E+16	Buprenorphine	10 microgram/1 hour	Transdermal patch
2.96884E+15	8.41911E+14	Codeine phosphate/ Paracetamol	12.8 mg + 500 mg	Tablet
1.03704E+15	3.87041E+15	Hydromorphone hydrochloride	8 mg	Modified-release capsule
1.03694E+15	3.83851E+15	Hydromorphone hydrochloride	4 mg	Modified-release capsule
1.03674E+15	3.86941E+15	Hydromorphone hydrochloride	2 mg	Modified-release capsule
1.03684E+15	4.00411E+15	Hydromorphone hydrochloride	24 mg	Modified-release capsule

1.03664E+15	4.00141E+15	Hydromorphone hydrochloride	16 mg	Modified-release capsule
1.02924E+15	3.83751E+15	Hydromorphone hydrochloride	2.6 mg	Capsule
1.02914E+15	3.83641E+15	Hydromorphone hydrochloride	1.3 mg	Capsule
6.13384E+15	1.86635E+16	Tapentadol hydrochloride	50 mg	Modified-release tablet
6.13424E+15	1.86652E+16	Tapentadol hydrochloride	250 mg	Modified-release tablet
6.13414E+15	1.86647E+16	Tapentadol hydrochloride	200 mg	Modified-release tablet
6.13404E+15	1.86644E+16	Tapentadol hydrochloride	150 mg	Modified-release tablet
6.13394E+15	1.86641E+16	Tapentadol hydrochloride	100 mg	Modified-release tablet
6.13234E+15	1.86629E+16	Tapentadol hydrochloride	75 mg	Tablet
6.13224E+15	1.86625E+16	Tapentadol hydrochloride	50 mg	Tablet
9.16024E+15	2.41208E+16	Tapentadol hydrochloride	20 mg/1 ml	Oral solution
1.26652E+16	3.58474E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.26651E+16	3.58472E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.2665E+16	3.5846E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.26649E+16	3.5847E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.26648E+16	3.58468E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet

1.26647E+16	3.58466E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.26646E+16	3.58464E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
1.26645E+16	3.58462E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.98844E+15	2.89821E+15	Oxycodone hydrochloride	1 mg/1 ml	Oral solution
1.98804E+15	2.89571E+15	Oxycodone hydrochloride	5 mg	Capsule
1.98824E+15	2.89631E+15	Oxycodone hydrochloride	20 mg	Capsule
1.98834E+15	2.89751E+15	Oxycodone hydrochloride	10 mg/1.000ml	Oral solution
1.98814E+15	2.89601E+15	Oxycodone hydrochloride	10 mg	Capsule
8.04844E+15	2.09694E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
8.04804E+15	2.09686E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
8.04834E+15	2.09692E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
8.04824E+15	2.0969E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
8.04814E+15	2.09688E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.98794E+15	2.89811E+15	Oxycodone hydrochloride	80 mg	Modified-release tablet
6.12564E+15	1.86433E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
2.74854E+15	4.07491E+15	Oxycodone hydrochloride	5 mg	Modified-release tablet

1.98784E+15	2.89721E+15	Oxycodone hydrochloride	40 mg	Modified-release tablet
6.12554E+15	1.86446E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.98774E+15	2.89661E+15	Oxycodone hydrochloride	20 mg	Modified-release tablet
6.12544E+15	1.86451E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
6.12574E+15	1.86417E+16	Oxycodone hydrochloride	120 mg	Modified-release tablet
1.98764E+15	2.89171E+15	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.98254E+15	3.61315E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
6.12524E+15	3.61313E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.98744E+15	3.61312E+16	Oxycodone hydrochloride	1 mg/1 ml	Oral solution
1.37084E+16	3.87524E+16	Oxycodone hydrochloride	5 mg	Tablet
2.74844E+15	3.6131E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.98714E+15	322691007	Oxycodone hydrochloride	5 mg	Capsule
1.98214E+15	3.61309E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
6.12514E+15	3.61307E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.37086E+16	3.87523E+16	Oxycodone hydrochloride	20 mg	Tablet
1.98204E+15	3.61304E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet

1.98734E+15	322693005	Oxycodone hydrochloride	20 mg	Capsule
6.12504E+15	3.61302E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
6.12534E+15	1.86455E+16	Oxycodone hydrochloride	120 mg	Modified-release tablet
1.98754E+15	3.613E+16	Oxycodone hydrochloride	10 mg/1 ml	Oral solution
1.37085E+16	3.87522E+16	Oxycodone hydrochloride	10 mg	Tablet
1.98194E+15	3.61295E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.98724E+15	322692000	Oxycodone hydrochloride	10 mg	Capsule
1.37087E+16	3.84567E+16	Oxycodone hydrochloride	5 mg	Tablet
1.37089E+16	3.84559E+16	Oxycodone hydrochloride	20 mg	Tablet
1.37088E+16	3.84533E+16	Oxycodone hydrochloride	10 mg	Tablet
1.03338E+16	2.96767E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.03337E+16	2.96774E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.03331E+16	2.96503E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.03336E+16	2.96776E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.03335E+16	2.96772E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.03334E+16	2.96783E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet

1.03333E+16	2.96781E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
1.03332E+16	2.96778E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
4.95624E+15	1.53028E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
4.95614E+15	1.53026E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
4.95604E+15	1.53024E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
5.30044E+15	1.60889E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
4.95634E+15	1.5303E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
4.50304E+15	1.35679E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
4.50294E+15	1.35677E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
4.50284E+15	1.35675E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
4.50314E+15	1.35681E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
1.01464E+15	3.60971E+15	Morphine sulfate	6 mg/1 ml	Oral solution
1.01494E+15	3.45351E+15	Morphine sulfate	20 mg/1 ml	Oral solution
1.01444E+15	3.33161E+15	Morphine sulfate	2 mg/1 ml	Oral solution
1.01484E+15	3.16431E+15	Morphine sulfate	2 mg/1 ml	Oral solution
1.01454E+15	3.60841E+15	Morphine sulfate	20 mg/1 ml	Oral solution

8.88474E+15	3.79754E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
8.88464E+15	3.79749E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
8.88454E+15	3.79739E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
8.88444E+15	3.79726E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
8.88434E+15	3.79757E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
1.21857E+16	3.40522E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.21856E+16	3.40513E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.21855E+16	3.40519E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.21853E+16	3.40516E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.23471E+16	1.49836E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.2347E+16	1.49834E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
1.23469E+16	1.49832E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
4.42424E+15	1.29484E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
9.20454E+15	2.45608E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
9.20444E+15	2.45606E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
1.03368E+16	2.45604E+16	Fentanyl	25 microgram/1 hour	Transdermal patch

9.20434E+15	2.45602E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
9.20464E+15	2.4561E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
9.44541E+14	3.88261E+15	Morphine sulfate	90 mg	Modified-release capsule
9.44441E+14	3.77821E+15	Morphine sulfate	60 mg	Modified-release capsule
9.44341E+14	3.65181E+15	Morphine sulfate	30 mg	Modified-release capsule
9.44241E+14	4.38801E+15	Morphine sulfate	200 mg	Modified-release capsule
9.44141E+14	3.88291E+15	Morphine sulfate	150 mg	Modified-release capsule
9.44041E+14	3.88321E+15	Morphine sulfate	120 mg	Modified-release capsule
9.40341E+14	4.08831E+15	Morphine sulfate	60 mg	Modified-release granules
9.40841E+14	4.38001E+15	Morphine sulfate	30 mg	Modified-release granules
9.40741E+14	4.37931E+15	Morphine sulfate	20 mg	Modified-release granules
9.40241E+14	4.08921E+15	Morphine sulfate	200 mg	Modified-release granules
9.40141E+14	4.08861E+15	Morphine sulfate	100 mg	Modified-release granules
9.41241E+14	2.88321E+15	Morphine sulfate	60 mg	Modified-release tablet
9.40441E+14	9.22411E+14	Morphine sulfate	5 mg	Modified-release tablet
9.41141E+14	3.07871E+15	Morphine sulfate	30 mg	Modified-release tablet

9.41341E+14	3.94011E+14	Morphine sulfate	200 mg	Modified-release tablet
9.40041E+14	2.72811E+14	Morphine sulfate	15 mg	Modified-release tablet
9.40941E+14	3.07771E+15	Morphine sulfate	10 mg	Modified-release tablet
9.41041E+14	2.88361E+15	Morphine sulfate	100 mg	Modified-release tablet
4.43424E+15	1.21437E+16	Morphine sulfate	1 mg/1 ml	Oral solution
1.37548E+16	1.23005E+16	Morphine sulfate	100 microgram/1 ml	Oral solution
9.31941E+14	3.63151E+15	Morphine sulfate	6 mg/1 ml	Oral solution
9.33941E+14	322455007	Morphine sulfate	30 mg	Suppository
9.31641E+14	3.61286E+16	Morphine sulfate	20 mg/1 ml	Oral solution
9.34241E+14	322433004	Morphine sulfate	20 mg	Suppository
9.33841E+14	322428003	Morphine sulfate	15 mg	Suppository
9.31741E+14	3.52131E+15	Morphine sulfate	2 mg/1 ml	Oral solution
9.31541E+14	3.61283E+16	Morphine sulfate	2 mg/1 ml	Oral solution
9.34141E+14	322432009	Morphine sulfate	10 mg	Suppository
9.31841E+14	3.63141E+15	Morphine sulfate	20 mg/1 ml	Oral solution
9.34641E+14	322446009	Morphine hydrochloride	15 mg	Suppository

7.85994E+15	1.21407E+16	Morphine hydrochloride	2 mg/1 ml	Oral solution
2.06844E+15	3.61278E+16	Morphine sulfate	90 mg	Modified-release capsule
9.36741E+14	3.61277E+16	Morphine sulfate	60 mg	Modified-release tablet
9.30241E+14	4.11091E+15	Morphine sulfate	60 mg	Modified-release granules
1.92414E+15	3.61276E+16	Morphine sulfate	60 mg	Modified-release capsule
9.30341E+14	3.61275E+16	Morphine sulfate	5 mg	Modified-release tablet
9.38241E+14	322728004	Morphine sulfate	50 mg	Tablet
2.06884E+15	3.61274E+16	Morphine sulfate	50 mg	Modified-release capsule
9.36641E+14	3.61273E+16	Morphine sulfate	30 mg	Modified-release tablet
3.03294E+15	4.38951E+15	Morphine sulfate	30 mg	Modified-release granules
1.92404E+15	3.61272E+16	Morphine sulfate	30 mg	Modified-release capsule
9.39541E+14	322709006	Morphine sulfate	20 mg	Tablet
3.03284E+15	4.38941E+15	Morphine sulfate	20 mg	Modified-release granules
2.06874E+15	3.61271E+16	Morphine sulfate	20 mg	Modified-release capsule
9.33141E+14	3.6127E+16	Morphine sulfate	200 mg	Modified-release tablet
9.30141E+14	4.11081E+15	Morphine sulfate	200 mg	Modified-release granules

1.92434E+15	3.61269E+16	Morphine sulfate	200 mg	Modified-release capsule
9.29941E+14	3.61268E+16	Morphine sulfate	15 mg	Modified-release tablet
2.06864E+15	3.61267E+16	Morphine sulfate	150 mg	Modified-release capsule
2.06854E+15	3.61266E+16	Morphine sulfate	120 mg	Modified-release capsule
9.36441E+14	322708003	Morphine sulfate	10 mg	Tablet
9.29741E+14	3.61265E+16	Morphine sulfate	10 mg	Modified-release tablet
1.92394E+15	3.61264E+16	Morphine sulfate	10 mg	Modified-release capsule
9.36541E+14	3.61262E+16	Morphine sulfate	100 mg	Modified-release tablet
9.30041E+14	4.11071E+15	Morphine sulfate	100 mg	Modified-release granules
1.92424E+15	3.61258E+16	Morphine sulfate	100 mg	Modified-release capsule
1.31187E+16	3.60226E+16	Morphine anhydrous	10 mg/1 ml	Oral drops/ Oral solution
2.91234E+15	4.52721E+15	Morphine sulfate	60 mg	Modified-release tablet
2.91224E+15	4.52681E+15	Morphine sulfate	30 mg	Modified-release tablet
2.91214E+15	4.52591E+15	Morphine sulfate	10 mg	Modified-release tablet
2.91244E+15	4.52791E+15	Morphine sulfate	100 mg	Modified-release tablet
9.30941E+14	4.03501E+15	Morphine sulfate	50 mg	Modified-release capsule

9.30841E+14	3.88171E+15	Morphine sulfate	20 mg	Modified-release capsule
9.30741E+14	3.88221E+15	Morphine sulfate	100 mg	Modified-release capsule
4.38684E+15	1.28824E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
4.38674E+15	1.2882E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
8.96234E+15	2.36823E+16	Fentanyl	37.5 microgram/1 hour	Transdermal patch
4.38704E+15	1.28817E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
4.38664E+15	1.28815E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
4.38694E+15	1.28826E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
8.96441E+14	2.34611E+14	Meptazinol hydrochloride	200 mg	Tablet
8.96341E+14	333936002	Meptazinol hydrochloride	200 mg	Tablet
3.33154E+15	9.52931E+15	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Effervescent tablet
3.33454E+15	9.8711E+13	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Capsule
4.89914E+15	1.49774E+16	Tramadol hydrochloride	50mg	Modified-release capsule
4.89944E+15	1.49768E+16	Tramadol hydrochloride	200 mg	Modified-release capsule
4.89934E+15	1.4977E+16	Tramadol hydrochloride	150 mg	Modified-release capsule
4.89924E+15	1.49772E+16	Tramadol hydrochloride	100 mg	Modified-release capsule

4.02294E+15	1.10857E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
4.02284E+15	1.10853E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
4.02274E+15	1.10849E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
4.02264E+15	1.10845E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
4.02304E+15	1.10859E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
4.82444E+15	1.96244E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
4.82434E+15	1.96246E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
4.82424E+15	1.96248E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
1.15684E+16	2.46375E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.15681E+16	2.46372E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
1.15678E+16	2.46369E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
3.90974E+15	2.04754E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
3.90964E+15	2.04752E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
3.90954E+15	2.0475E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
8.53734E+15	2.26865E+16	Oxycodone hydrochloride	5 mg	Capsule
8.53754E+15	2.26869E+16	Oxycodone hydrochloride	20 mg	Capsule

8.53744E+15	2.26867E+16	Oxycodone hydrochloride	10 mg	Capsule
7.88664E+15	2.09383E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.0492E+16	2.98388E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
7.88624E+15	2.09375E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
7.88654E+15	2.09381E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.04916E+16	2.98386E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
7.88644E+15	2.09379E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.04915E+16	2.98384E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
1.04922E+16	2.98382E+16	Oxycodone hydrochloride	120 mg	Modified-release tablet
7.88634E+15	2.09377E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.18086E+16	3.36302E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.18085E+16	3.363E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.18084E+16	3.3629E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.18083E+16	3.36298E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.18082E+16	3.36296E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.18081E+16	3.36294E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet

1.1808E+16	3.36292E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
4.02864E+15	9.10121E+15	Tramadol hydrochloride	200 mg	Modified-release tablet
4.02854E+15	9.10101E+15	Tramadol hydrochloride	150 mg	Modified-release tablet
4.02834E+15	9.10081E+15	Tramadol hydrochloride	100 mg	Modified-release tablet
1.74124E+15	3.25151E+15	Codeine phosphate/ Paracetamol	60 mg + 1 gram	Effervescent powder
1.62184E+15	3.25371E+15	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Effervescent powder
7.96641E+14	2.32711E+14	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Tablet
3.05754E+15	7.33601E+15	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Effervescent tablet
1.83084E+15	7.37111E+14	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Capsule
6.13794E+15	1.7572E+16	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Tablet
1.2667E+16	3.5859E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.26669E+16	3.58587E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.26668E+16	3.58535E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.26667E+16	3.58579E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.26666E+16	3.58574E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.26665E+16	3.58583E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet

1.26664E+16	3.58578E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
1.26663E+16	3.58576E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
4.42574E+15	3.24635E+16	Fentanyl	40 microgram/1 dose	Transdermal system
1.23467E+16	2.19646E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.23466E+16	2.19644E+16	Tramadol hydrochloride	150 mg	Modified-release tablet
1.23464E+16	2.19642E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
5.30004E+15	1.60341E+16	Fentanyl citrate	50 microgram/1 dose	Spray
5.30024E+15	1.60353E+16	Fentanyl citrate	200 microgram/1 dose	Spray
5.30014E+15	1.60347E+16	Fentanyl citrate	100 microgram/1 dose	Spray
3.22914E+15	3.60452E+16	Codeine phosphate/ Ibuprofen	20 mg + 300 mg	Modified-release tablet
7.38641E+14	3.60577E+16	Hydromorphone hydrochloride	8 mg	Modified-release capsule
7.38541E+14	3.60576E+16	Hydromorphone hydrochloride	4 mg	Modified-release capsule
7.38341E+14	3.60574E+16	Hydromorphone hydrochloride	2 mg	Modified-release capsule
7.38441E+14	3.60573E+16	Hydromorphone hydrochloride	24 mg	Modified-release capsule
7.28741E+14	322667003	Hydromorphone hydrochloride	2.6mg	Capsule
7.38241E+14	3.60572E+16	Hydromorphone hydrochloride	16 mg	Modified-release capsule

7.28641E+14	322665006	Hydromorphone hydrochloride	1.3 mg	Capsule
8.88294E+15	2.34466E+16	Buprenorphine	70 microgram/1.000hour	Transdermal patch
8.88284E+15	2.34464E+16	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
8.88274E+15	2.34462E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
6.24441E+14	3.44691E+15	Codeine phosphate	3 mg/1 ml	Oral solution
1.00457E+16	2.84912E+16	Buprenorphine hydrochloride	400 microgram	Sublingual tablet
6.09341E+14	3.79251E+15	Pentazocine hydrochloride	25 mg	Tablet
2.75354E+15	9.3411E+13	Morphine sulfate	60 mg	Modified-release tablet
2.75344E+15	3.07891E+15	Morphine sulfate	30 mg	Modified-release tablet
4.81724E+15	1.49306E+16	Morphine sulfate	200 mg	Modified-release tablet
2.75334E+15	3.07521E+15	Morphine sulfate	10 mg	Modified-release tablet
2.75364E+15	2.19511E+14	Morphine sulfate	100 mg	Modified-release tablet
5.75241E+14	3.61203E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
5.75141E+14	3.61202E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
1.14692E+16	421136001	Fentanyl	40 microgram/1 dose	Transdermal system
8.96224E+15	2.37077E+16	Fentanyl	37 microgram/1 hour	Transdermal patch

5.75041E+14	3.612E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
3.83934E+15	9.75231E+15	Fentanyl	12 microgram/1 hour	Transdermal patch
5.74941E+14	3.61199E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
4.89314E+15	1.49519E+16	Fentanyl citrate	100 microgram	Sublingual tablet
4.42614E+15	1.2875E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
4.42624E+15	1.28749E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
4.42634E+15	1.28748E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
4.42604E+15	1.28751E+16	Fentanyl	100 microgram/1 hour	Transdermal patch
6.44104E+15	1.94873E+16	Fentanyl	75 microgram/1 hour	Transdermal patch
6.44094E+15	1.94871E+16	Fentanyl	50 microgram/1 hour	Transdermal patch
6.44084E+15	1.94869E+16	Fentanyl	25 microgram/1 hour	Transdermal patch
6.44074E+15	1.94867E+16	Fentanyl	12 microgram/1 hour	Transdermal patch
6.44114E+15	1.94875E+16	Fentanyl	100 microgram/ 1hour	Transdermal patch
1.23472E+16	3.45772E+16	Dihydrocodeine tartrate/ Paracetamol	10 mg + 500 mg	Tablet
7.85914E+15	2.04746E+16	Dihydrocodeine tartrate/ Paracetamol	30 mg + 500 mg	Tablet
7.85904E+15	2.04743E+16	Dihydrocodeine tartrate/ Paracetamol	20 mg + 500 mg	Tablet

3.24824E+15	9.09011E+15	Fentanyl	75 microgram/1 hour	Transdermal patch
3.24814E+15	9.08991E+15	Fentanyl	50 microgram/1 hour	Transdermal patch
3.24804E+15	9.08971E+15	Fentanyl	25 microgram/1 hour	Transdermal patch
3.83944E+15	9.75111E+15	Fentanyl	12 microgram/1 hour	Transdermal patch
3.24834E+15	9.09031E+15	Fentanyl	100 microgram/1 hour	Transdermal patch
4.90541E+14	2.83671E+15	Fentanyl	75 microgram/1 hour	Transdermal patch
4.90441E+14	2.83641E+15	Fentanyl	50 microgram/1 hour	Transdermal patch
4.90341E+14	2.83701E+15	Fentanyl	25 microgram/1 hour	Transdermal patch
4.90241E+14	2.83811E+15	Fentanyl	100 microgram/1 hour	Transdermal patch
1.31188E+16	3.71229E+16	Morphine anhydrous	10 mg/1 ml	Oral drops/ Oral solution
2.18374E+15	8.05511E+14	Tramadol hydrochloride	400 mg	Modified-release tablet
2.18364E+15	1.7411E+13	Tramadol hydrochloride	300 mg	Modified-release tablet
2.18354E+15	1.09211E+14	Tramadol hydrochloride	200 mg	Modified-release tablet
2.18344E+15	8.47811E+14	Tramadol hydrochloride	150 mg	Modified-release tablet
2.07824E+15	4.24611E+14	Tramadol hydrochloride	75 mg	Modified-release tablet
2.07854E+15	2.78411E+14	Tramadol hydrochloride	200 mg	Modified-release tablet

2.07844E+15	9.19611E+14	Tramadol hydrochloride	150 mg	Modified-release tablet
2.07834E+15	2.16911E+14	Tramadol hydrochloride	100 mg	Modified-release tablet
8.83854E+15	2.30473E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
8.83874E+15	2.30208E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
8.83864E+15	2.30206E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
8.83884E+15	2.33668E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
3.17964E+15	322556006	Cyclizine hydrochloride/ Dipipanone hydrochloride	30 mg + 10 mg	Tablet
4.69541E+14	3.91125E+16	Dihydrocodeine tartrate	90 mg	Modified-release tablet
4.68741E+14	3.91124E+16	Dihydrocodeine tartrate	60 mg	Modified-release tablet
4.62841E+14	322553003	Dihydrocodeine tartrate	40 mg	Tablet
4.68541E+14	322539003	Dihydrocodeine tartrate	30 mg	Tablet
4.69441E+14	3.91126E+16	Dihydrocodeine tartrate	120 mg	Modified-release tablet
1.35829E+16	8.45731E+15	Dihydrocodeine tartrate	2 mg/1 ml	Oral suspension
4.42841E+14	3.60986E+16	Dihydrocodeine tartrate	2 mg/1 ml	Oral solution
4.33541E+14	3.03751E+15	Dihydrocodeine tartrate	90 mg	Modified-release tablet
4.33341E+14	3.03711E+15	Dihydrocodeine tartrate	60 mg	Modified-release tablet

4.33441E+14	3.03781E+15	Dihydrocodeine tartrate	120 mg	Modified-release tablet
4.33141E+14	3.03821E+15	Dihydrocodeine tartrate	40 mg	Tablet
3.85144E+15	8.42771E+15	Dihydrocodeine tartrate/ Paracetamol	2 mg/1 ml + 100 mg/1 ml	Oral suspension
5.89124E+15	1.3893E+16	Dihydrocodeine tartrate/ Paracetamol	2 mg/1 ml + 100 mg/1 ml	Oral solution
2.85004E+15	3.80311E+15	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Tablet
6.38654E+15	1.92072E+16	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Effervescent tablet
6.43144E+15	1.91919E+16	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Capsule
3.71341E+14	322504003	Codeine phosphate	60 mg	Tablet
3.71241E+14	322503009	Codeine phosphate	30 mg	Tablet
3.71141E+14	322502004	Codeine phosphate	15 mg	Tablet
3.36741E+14	3.42011E+15	Codeine phosphate/ Ibuprofen	20 mg + 300 mg	Modified-release tablet
3.72941E+14	322307006	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Tablet
1.34975E+16	3.85552E+16	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Effervescent tablet
3.73041E+14	322343000	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Effervescent tablet
2.94841E+14	322344006	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Capsule
4.59064E+15	1.15792E+16	Codeine phosphate/ Paracetamol	8 mg + 500 mg	Tablet

1.23561E+16	3.46253E+16	Codeine phosphate/ Paracetamol	60mg + 1 gram	Tablet
1.34177E+16	3.80639E+16	Codeine phosphate/ Paracetamol	6 mg/1 ml + 100 mg/1 ml	Oral solution
3.70641E+14	322341003	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Tablet
3.26141E+14	322365000	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Effervescent tablet
1.58874E+15	322323006	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Effervescent powder
2.95441E+14	322366004	Codeine phosphate/ Paracetamol	30 mg + 500 mg	Capsule
2.87534E+15	3.80561E+15	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Tablet
6.38644E+15	1.92307E+16	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Effervescent tablet
6.43134E+15	1.92002E+16	Codeine phosphate/ Paracetamol	15 mg + 500 mg	Capsule
5.33454E+15	322379008	Codeine phosphate/ Paracetamol	12.8 mg + 500 mg	Tablet
1.26037E+16	3.55441E+16	Buprenorphine	70 microgram/1 hour	Transdermal patch
1.26036E+16	3.55439E+16	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
1.26035E+16	3.55437E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
1.14898E+16	3.21973E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.09848E+16	3.13222E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.14897E+16	3.21968E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet

1.09851E+16	3.1324E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.09849E+16	3.13235E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
3.34364E+15	9.56531E+15	Buprenorphine	5 microgram/1 hour	Transdermal patch
3.34384E+15	9.56591E+15	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.10772E+16	3.18772E+16	Buprenorphine	15 microgram/1 hour	Transdermal patch
3.34374E+15	9.56561E+15	Buprenorphine	10 microgram/1 hour	Transdermal patch
1.10293E+16	3.12792E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.10295E+16	3.12786E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.21068E+16	3.40274E+16	Buprenorphine	15 microgram/1 hour	Transdermal patch
1.10294E+16	3.12789E+16	Buprenorphine	10 microgram/ 1hour	Transdermal patch
1.24095E+16	3.48388E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.24097E+16	3.48392E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.24096E+16	3.4839E+16	Buprenorphine	10 microgram/1 hour	Transdermal patch
2.73774E+15	3.59139E+16	Buprenorphine	70 microgram/1 hour	Transdermal patch
3.34334E+15	9.56721E+15	Buprenorphine	5 microgram/1 hour	Transdermal patch
2.73764E+15	3.59138E+16	Buprenorphine	52.5microgram/1 hour	Transdermal patch

1.74241E+14	322492007	Buprenorphine hydrochloride	400 microgram	Sublingual tablet
2.73754E+15	3.59137E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
2.92264E+15	3.59136E+16	Buprenorphine hydrochloride	300 microgram/1 ml	Solution for injection
3.34354E+15	9.56731E+15	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.72641E+14	322498006	Buprenorphine hydrochloride	200 microgram	Sublingual tablet
1.1077E+16	3.20384E+16	Buprenorphine	15 microgram/1 hour	Transdermal patch
3.34344E+15	9.56741E+15	Buprenorphine	10 microgram/1 hour	Transdermal patch
1.23257E+16	3.45518E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.2326E+16	3.45522E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.23259E+16	3.4552E+16	Buprenorphine	10 microgram/1 hour	Transdermal patch
1.17808E+16	3.35481E+16	Buprenorphine	70 microgram/1 hour	Transdermal patch
1.17807E+16	3.35464E+16	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
1.17806E+16	3.35466E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch
1.14845E+16	3.24846E+16	Buprenorphine	70 microgram/1 hour	Transdermal patch
1.14844E+16	3.24844E+16	Buprenorphine	52.5 microgram/1 hour	Transdermal patch
1.14843E+16	3.24842E+16	Buprenorphine	35 microgram/1 hour	Transdermal patch

1.26034E+16	3.55443E+16	Buprenorphine	5 microgram/1 hour	Transdermal patch
1.26033E+16	3.55451E+16	Buprenorphine	20 microgram/1 hour	Transdermal patch
1.26032E+16	3.55445E+16	Buprenorphine	10 microgram/1 hour	Transdermal patch
1.3712E+16	3.88113E+16	Tramadol hydrochloride	200 mg	Modified-release tablet
1.2389E+16	3.47334E+16	Tramadol hydrochloride	100 mg	Modified-release tablet
1.06421E+16	3.07217E+16	Oxycodone hydrochloride	80 mg	Modified-release tablet
1.0642E+16	3.07214E+16	Oxycodone hydrochloride	60 mg	Modified-release tablet
1.06414E+16	3.07193E+16	Oxycodone hydrochloride	5 mg	Modified-release tablet
1.06419E+16	3.07208E+16	Oxycodone hydrochloride	40 mg	Modified-release tablet
1.06418E+16	3.07211E+16	Oxycodone hydrochloride	30 mg	Modified-release tablet
1.06417E+16	3.07205E+16	Oxycodone hydrochloride	20 mg	Modified-release tablet
1.06416E+16	3.07201E+16	Oxycodone hydrochloride	15 mg	Modified-release tablet
1.06415E+16	3.07198E+16	Oxycodone hydrochloride	10 mg	Modified-release tablet
1.06314E+15	322604007	Pentazocine lactate	50 mg	Suppository
3.68541E+14	3.65661E+16	Codeine phosphate	5 mg/1 ml	Oral solution
2.64504E+15	3.88964E+16	Codeine phosphate	3 mg/1 ml	Oral solution

Table S3: Decisions made to prepare opioid prescriptions using DrugPrep algorithm

Step	**A.Data cleaning**				
Decision node:	**1** **Clean implausible qty**	**2** **Clean missing qty**	**3** **Clean implausible ndd**	**4** **Clean missing ndd**	**5** **Clean all available duration variables**
Raw data	a. Use implausible value	a. Keep as missing	a. use implausible value	a. keep as missing	a.Do nothing
	b. Set to missing	b.set to individual median	b.set to missing	b.set to individual median	b(6). Set to missing if >6months
	c. Set to individual median	c.set to population median	c. set to imdividual median	C. set to population median	b(12).set to missing if >12 months
	d. set to population median	d.use previous value	d. set to population median	d.use previous value	b(24). Set to missing if >24 months
	e. Use previous value	e.use next value	e. use previous value	e. use next value	c(6). Set to 6 months if >6 months
	f. Use next value		f. use next value		c(12). Set to 12 months if > 12 months
					c. calculated for each prescription by dividing the imputed quantity by numeric daily doses.
Step	**B. Define prescription length**		**C. Handle concurrent &sequential prescriptions**		
Decision node:	**6** **Generate stop dates**	**7** **Clean missing stop dates**	**8** **Handle multiple prescriptions**	**9** **Handle overlapping prescriptions**	**10** **Handle gaps between prescriptions**

a.Start + numdays	a.keep missing	a.do nothing	a.Ignore overlap	a.do nothing :allow gap
b.start+dose_duration	b.set to individual mean	b.use mean ndd & duration	b.Add overlap to end 2nd prescription	b(15)assume continuous us eif gap <15b days
c.start+qty/ndd	c.set to population mean	c.use prescription with smallest ndd		b(30) assume continuous use if gap <30 days
d.(15)use mean if gap<15 days	d.use population mean if individual mean is missing	d.use prescription with largest ndd		b(60)assume continuous us if gap < 60 days
d(30) use mean if gap<30 days		e.use shortest prescription		
d(60) use mean if gap <60 days		f.use longest prescription		
d(90)use mean if gap <90 days		g.sum durations		
d. use mean regardless of gap				

Table S4: Equianalgesic ratios to calculate Oral Morphine Equivalent Doses

Opioid*	Form**	Equianalgesic ratio***
Buprenorphine	Transdermal patch Sublingual tablet	1.8 10
Codeine		0.15
Codeine/ Ibuprofen		0.15
Codeine/ Paracetamol		0.15
Dihydrocodeine		0.25
Dihydrocodeine/Paracetamol		0.25
Fentanyl	Transdermal patch Sublingual tablet Nasal spray	2.4 0.13 0.16
Hydromorphone		4
Meptazinol		0.03
Morphine Sulfate		1
Naloxone/Oxycodone		1.50
Oxycodone		1.50
Pentazocine		0.37
Pethidine		0.10
Tapentadol		0.40
Tramadol		0.20
Cyclizine/Dipipanone		0.5

*Opioid doses are in $mg.day^{-1}$ except for fentanyl transdermal (in $\mu g.h^{-1}$)

**Form refers to an oral preparation unless otherwise stated

***Equianalgesic ratio: the potency of respective opioid/opioid formulations compared with oral morphine.

Table S5: Baseline characteristics of patients undergoing colectomy between the years 2010 and 2019

	Years									
Variable	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**	**2017**	**2018**	**2019**
	N= 8001	**N= 8470**	**N= 8850**	**N= 8963**	**N= 9038**	**N= 9614**	**N= 10 009**	**N= 10 286**	**N= 10 794**	**N= 11 130**
Age, years	66.8	66.9	66.3	65.8	66.3	65.2	65.0	65.0	63.9	63.9
Sex										
Female	3938 (49.2)	4087 (48.3)	4377 (49.5)	4417 (49.3)	4489 (49.7)	4853 (50.5)	5130 (51.3)	5150 (50.1)	5561 (51.5)	5776 (51.9)
Male	4063 (50.8)	4383 (51.8)	4473 (50.5)	4546 (50.7)	4549 (50.3)	4761 (49.5)	4879 (48.8)	5136 (50.1)	5233 (48.5)	5354 (48.1)
Preoperative opioid										
Naïve	6326 (79.1)	6715 (79.3)	7097 (80.2)	7242 (80.8)	7345 (81.3)	7878 (81.9)	8307 (83.0)	8571 (83.3)	9178 (85.1)	9674 (86.9)
Currently	1404 (17.6)	1410 (16.7)	1440 (16.3)	1406 (15.7)	170 (15.2)	1396 (14.5)	1368 (13.7)	1393 (13.5)	1302 (12.1)	1161 (10.4)
Previously	271 (3.4)	345 (4.1)	313 (3.5)	315 (3.5)	323 (3.6)	340 (3.54)	334 (3.3)	322 (3.13)	314 (2.9)	295 (2.7)
Index of Multiple Deprivation										
1	1775 (22.2)	1934 (22.8)	1979 (22.4)	2015 (22.5)	2035 (22.5)	2154 (22.4)	2198 (21.9)	2328 (22.6)	2415 (22.4)	2459 (22.1)
2	1795 (22.4)	1820 (21.8)	1835 (20.7)	1928 (21.5)	1857 (20.6)	2005 (20.9)	2125 (21.2)	2203 (21.4)	2304 (21.4)	2390 (21.5)
3	1677 (20.9)	1719 (20.3)	1842 (20.8)	1768 (19.7)	1810 (20.0)	1957 (20.4)	2063 (20.6)	2064 (20.1)	2099 (19.5)	2270 (20.4)
4	1439 (17.9)	1617 (19.1)	1608 (18.2)	1726 (19.3)	1777 (19.7)	1786 (18.6)	1898 (18.9)	1961 (19.1)	2138 (19.8)	2116 (19.0)

5	1307 (16.3)	1370 (16.2)	1572 (17.8)	1519 (16.9)	1550 (17.2)	1703 (17.7)	1706 (17.0)	1710 (16.6)	1827 (16.9)	1883 (16.9)
Missing	8 (0.10)	10 (0.12)	14 (0.16)	7 (0.08)	9 (0.10)	9 (0.09)	19 (0.19)	20 (0.19)	11 (0.10)	12 (0.11)
Charlson comorbidity index										
0	1968 (24.6)	1859 (21.9)	2090 (23.6)	2249 (25.1)	2178 (24.1)	2433 (25.3)	2412 (24.1)	2361 (22.9)	2588 (23.9)	2591 (23.3)
1	608 (7.6)	649 (7.7)	668 (7.55)	648 (7.2)	639 (7.1)	725 (7.5)	772 (7.7)	791 (7.7)	791 (7.3)	789 (7.1)
≥2	5425 (67.8)	5962 (70.4)	6092 (68.8)	6066 (67.7)	6221 (68.8)	6456 (67.2)	6825 (68.2)	7134 (69.4)	7415 (68.7)	7750 (69.6)
Surgical approach										
Open	5812 (72.6)	5915 (69.8)	5973 (67.5)	5796 (64.7)	5606 (62.0)	5661 (58.9)	5707 (57.0)	5523 (53.7)	5661 (52.5)	5385 (48.4)
Minimally invasive	2189 (27.4)	2555 (30.2)	2877 (32.5)	3167 (35.3)	3432 (37.9)	3953 (41.1)	4302 (42.9)	4763 (46.3)	5133 (47.5)	5745 (51.6)
Cancer diagnosis										
No	3367 (42.1)	3419 (40.4)	3725 (42.1)	3913 (43.7)	3947 (43.7)	4369 (45.4)	4452 (44.5)	4610 (44.8)	4858 (45.0)	5028 (45.2)
Yes	4634 (57.9)	5051 (59.6)	5125 (57.9)	5050 (56.3)	5091 (56.3)	5245 (54.6)	5557 (55.5)	5676 (55.2)	5936 (54.9)	6102 (54.8)
Admission type										
Elective	5735 (71.7)	5948 (70.2)	6229 (70.4)	6185 (69.0)	6340 (70.2)	6715 (69.8)	6963 (69.6)	7348 (71.4)	7609 (70.5)	7977 (71.7)
Emergency	2266 (28.3)	2522 (29.8)	2621 (29.6)	2778 (30.9)	2698 (29.9)	2899 (30.2)	3046 (30.4)	2938 (28.6)	3185 (29.5)	3153 (28.3)

Table S6: Changes in the potency of opioid prescribed in initial prescription received after discharge

			Opioid potency		
			Weak opioids	**Strong opioids**	**Both weak & strong**
Stratified by Opioid exposure before colectomy	**Naïve** **N=6981**	2010 n=721	87.9%	9.0%	3.0%
		2019 n=647	75.1%	20.9%	3.8%
		Percent change, p value	-14.8%, p<0.001	+132.9%, p<0.001	+26.3%, p=0.436
	Currently **N=7747**	2010 n=808	77.4%	17.5%	5.0%
		2019 n=677	64.8%	29.4%	5.9%
		Percent change, p value	-16.3%, p<0.001	+67.9%, p<0.001	+18.4%, p=0.476
	previously **N=775**	2010 n=78	83.7%	6.5%	9.8%
		2019 n=74	71.4%	28.6%	0%
		Percent change, p value	14.7%, p=0.055	+338.7%, p<0.001	-100%, p<0.005
Stratified by surgical approach	**Open** **N=10,308**	2010 n=1326	80.0%	14.9%	4.8%
		2019 n=861	63.0%	30.9%	5.4%
		Percent change, p value	-21.3 %, p<0.001	+106.0%, p<0.001	12.5%, p=0.510
	Laparoscopic	2010 n=420	88.5%	8.1%	3.3%

	N= 5,195	2019 n=662	78.1%	18.3%	3.6%
		Percent change, p value	-11.8%, p<0.001	+125.9%, p<0.001	+9%, p=0.799

N represents total number of patients in this strata, n = number of patients in this stratum in certain year.

Table S7: Changes in the type of opioid prescribed in initial prescription received after discharge

Changes in type of opioid prescribed for the overall cohort

Opioids analgesics		**2010 n=1746**	**2019 n=1523**	**Absolute change**	**Percent change**	**P value**
Weak Opioids	Codeine	43.5%	49.8%	+6.3	+14.5%	**<0.001**
	Dihydrocodeine	4.0%	3.2%	-0.90	-21.5%	**0.043**
	Tramadol	36.8%	18.9%	-17.8	-48.4%	**<0.001**
Strong opioids	Morphine	8.6%	15.2%	+6.6	+76.9%	**<0.001**
	Oxycodone	3.4%	7.8 %	+4.4	+131.1%	**<0.001**
	Buprenorphine	1.4%	2.5%	+ 1.1	+74.8%	**0.041**
	Fentanyl	2.1%	2.2%	+ 0.10	+2.4%	0.920

Changes in type of opioid prescribed stratified by surgical approach

	Surgical approach									
	Open colectomy					Laparoscopic				
Opioid analgesics	**2010 n=1326**	**2019 n=861**	**Absolute change**	**Percent change**	**P value**	**2010 n=420**	**2019 n=662**	**Absolute change**	**Percent change**	**P value**
Codeine	43.2	46.9	+3.8	+8.9%	0.054	44.5	53.5	+9.0	+20.2%	**<0.001**
Dihydrocodeine	4.07	3.02	-1.9	-25.8%	**0.0259**	3.8	3.3	-0.49	-12.9	0.822
Tramadol	35.3	15.9	-19.4	-54.9%	**<0.001**	41.4	22.9	-18.5	-44.5%	0.326
Morphine	9.2	18.3	+9.2	+98.9%	**<0.001**	6.7	11.0	+4.3	+65.3%	**0.007**
Oxycodone	4.1	8.6	+4.5	+110.9%	**<0.001**	1.2	6.8	+5.6	+470.9	**<0.001**
Buprenorphine	1.5	3.5	+1.9	+130.0%	**0.003**	1.2	1.2	+0.02	+1.7 %	0.925
Fentanyl	2.4	2.9	+0.49	+20.3%	0.317	1.2	1.2	+0.02	+1.7 %	**<0.001**

Changes in type of opioid prescribed stratified by opioid exposure before colectomy

Opioid analgesics	Opioid exposure before surgery														
	Naïve n=7382					Currently exposed n=8676					Previously exposed n=828				
	2010 N=756	**2019 N=686**	**Absolute change**	**Percent change**	**P value**	**2010 N=898**	**2019 N=760**	**Absolute change**	**Percent change**	**P value**	**2010 N=92**	**2019 N=77**	**Absolute**	**Percent**	**P value**
Codeine	42.2%	55.7%	+13.5	+31.9%	**<0.001**	43.8%	44.5%	+0.73	+1.6%	0.779	52.1%	50.7%	-1.4	-2.7%	0.552
Dihydrocodeine	3.8%	4.2%	+0.39	+10.1%	0.904	4.5%	2.37%	-2.1	-46.7%	0.019	1.1%	1.3%	+0.21	+19.3%	**0.054**
Tramadol	43.1%	16.9%	-26.2	-60.8%	**<0.001**	31.7%	20.8%	-20.8	-34.4%	<0.001	33.7%	19.5%	-14.2	-42.1%	**0.021**
Morphine	7.7%	12.5%	+4.8	+62.9%	**<0.001**	9.8%	17.5%	+7.7	+78.6%	<0.001	4.4%	15.6%	+11.3	+258.1%	0.057
Oxycodone	1.6%	7.8%	+6.3	+395.3%	**<0.001**	4.7%	7.6%	+2.9	+63.2%	<0.001	5.4%	9.1%	+3.7	+67.4%	0.532
Buprenorphine	0.53%	0.87%	+0.34	+64.1%	0.429	2.2%	4.1%	+1.9	+82.9%	0.032	1.1%	1.3%	+0.21	+19.3%	0.667
Fentanyl	0.93%	1.5%	+0.53	+56.9%	0.275	3.2%	2.8%	-0.47	-14.5%	0.607	1.1%	2.6%	+1.5	+138.1%	0.540

n represents total number of patients in this strata, N = number of patients in this stratum in certain year.