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Perioperative opioid prescriptions associated with stress incontinence and pelvic organ prolapse surgery

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Abstract

Background: There is an opioid epidemic in the United States with a contributing factor being opioids prescribed for post-operative pain following surgery.

Objectives: Among women who underwent stress incontinence and pelvic organ prolapse surgeries, our primary objective was to determine the proportion of women who filled perioperative opioid prescriptions and to compare factors associated with these opioid prescriptions. We also sought to assess the risk of prolonged opioid use through one year after SUI and POP surgery.

Study Design: Using a population-based cohort of commercially insured individuals in the 2005–2015 IBM Marketscan® databases, we identified opioid naïve women ≥ 18 years who underwent SUI and/or POP procedures based on CPT codes. We defined the perioperative period as the window beginning 30 days before surgery extending until 7 days after surgery. Any filled opioid prescription in this window was considered a perioperative prescription. For our primary outcome, we report the proportion of opioid naïve women who filled a perioperative opioid

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prescription and report the median quantity dispensed in the perioperative period. We also assessed demographic and perioperative factors associated with perioperative opioid prescription fills. Prior studies defined prolonged use as the proportion who fill an opioid prescription between 90 – 180 days after surgery. We report this estimate, as well as continuous opioid use, defined as the proportion of women with ongoing monthly opioid prescriptions filled through one-year after SUI and/or POP surgery.

Results: Among the 217,460 opioid naïve women who underwent urogynecologic surgery, 61,025 (28.1%) had a POP and SUI surgery, 85,575 (39.4%) had SUI without POP surgery and 70,860 (32.6%) had POP without SUI surgery. Overall, 167,354 (77.0%) filled a perioperative opioid prescription, and the median quantity was 30 pills (interquartile range 20, 30). In a multivariate regression model, younger age, POP surgery with or without SUI, abdominal route, hysterectomy and mesh use remained significantly associated with opioid prescriptions filled. Among those with a filled perioperative opioid prescription, the risk of prolonged use, defined as an opioid fill between 90 – 180 days, was 7.5% (95% CI 7.3%,7.6%). However, the risk of prolonged use, defined as continuous use with at least one monthly opioid prescription filled after surgery was significantly lower with the following rates: 1.2% (1.13%, 1.24%), 0.32%(0.29%, 0.35%), 0.06%(0.05%, 0.08%) and 0.04%(0.02%,0.05%) at 60, 90, 180 and 360 days after surgery, respectively.

Conclusions: Among privately insured, opioid naïve women undergoing SUI and/or POP surgery, 77% of women filled an opioid prescription with a median of 30 opioid pills prescribed. For prolonged use, 7.5% (95% CI 7.3,7.6) filled an opioid within 90–180 days after surgery but the rates of continuously filled opioid prescriptions are significantly lower at 0.06% (95% CI 0.05,0.08) at 180 days and 0.04% (95%CI 0.02,0.05) at 1 year after surgery.

Condensation:

Among opioid naïve women undergoing stress incontinence and prolapse surgery, 79% filled an opioid prescription but the rate of prolonged use was low.

Keywords

Opioids; prolapse; stress incontinence; surgery

Introduction:

There is an opioid epidemic in the United States with 130 Americans dying every day from an opioid overdose[1]. Overdose deaths involving prescription opioids were 5 times higher in 2017 than in 1999[1]; one contributing factor to this epidemic is prolonged opioid use after surgery. Approximately 3% of previously opioid naïve patients continue to use opioids more than 90 days after major elective surgery[2].

Trends in excessive opioid prescribing have been found in the gynecologic literature, with patients being prescribed two to three times the amount of opioids actually used after surgery[3, 4]. An area that deserves particular attention is women undergoing urogynecologic procedures. Pelvic floor disorders are extremely common with 20% of women undergoing surgery for stress urinary incontinence (SUI) and/or pelvic organ prolapse (POP) surgery by

age 80[5]. Only a few studies have evaluated the number of opioids prescribed after SUI and POP surgery, and they indicate trends toward overprescribing[6, 7]. Swenson et al. assessed 50 women and discovered they used one-third of the narcotics prescribed after minimally invasive urogynecologic surgery[6]. Solouki evaluated 143 patients undergoing urogynecology surgery and found that 82% of patients were prescribed opioids. Of those, 54% reported using less than half of the opioids prescribed[7]. At this time, population-based data regarding perioperative and long-term opioid use after SUI and POP surgery are extremely limited.

Therefore, the objective of this study was to use a population-based database to evaluate the proportion of women filling perioperative opioid prescriptions and to assess factors associated with these opioid prescriptions following SUI and POP surgery. We also sought to assess the risk of prolonged opioid use through one year after SUI and POP surgery.

Materials and Methods:

This is a retrospective study using a population-based cohort of commercially insured employees, their spouses and dependents in the 2005 to 2015 MarketScan® Commercial Claims and Encounters database and Medicare Supplemental and Coordination of Benefits databases (copyright © 2015 IBM Watson Health. All rights reserved)[8, 9]. These data include inpatient, outpatient, and pharmaceutical claims which allow for evaluation of dates of service, diagnosis and procedure codes, and all reimbursed outpatient prescription medications. These de-identified data have been found to be both valid and reliable. This study was determined to be exempt from further review by the Institutional Review Board at the University of North Carolina at Chapel Hill as only de-identified data were available.

We included women 18 years and older who underwent SUI and/or POP surgery based on current procedural terminology (CPT) codes (Supplementary Table). Patients were required to have a minimum of 180 days of prior continuous enrollment in Marketscan. In addition, they were required to have a least one prescription fill during this time period, indicating use of a prescription coverage benefit. Patients were followed for up to one-year post-operatively and were censored at occurrence of surgery during follow-up period[10], discontinuation of insurance coverage, reaching December 31, 2015 (the last date of available data), or reaching 1-year after surgery.

We assessed prescription claims for drugs including the following opioids: codeine, dextropropoxyphene, hydrocodone, hydromorphone, oxycodone, pentazocine, tramadol, fentanyl, meperidine, morphine, oxymorphone, pethidine, and tapentadol. Of note, the medications are listed according to the active opioid pharmaceutical ingredients. We excluded women with chronic opioid use, which we defined as an opioid prescription filled between 180 to 30 days prior to SUI and/or POP surgery (Figure 1). We were interested in women who were opioid naïve thus women who had ≥ 2 opioid prescriptions filled in the 30-days prior to surgery were also excluded. We acknowledge that some women may receive a prescription at the time of their preoperative visit; thus, we allowed for one opioid prescription within 30-days prior to surgery. The rationale for only allowing one opioid prescription is that two or more opioid prescriptions suggests potential chronic use for nonsurgical related pain.

We defined the perioperative period as the window beginning 30 days before surgery extending until 7 days after surgery. Any filled opioid prescription in this window was considered a perioperative prescription. We used National Drug Code on the prescription claims data to identify the exact opioid prescribed. The data also include information on the number of units dispensed and length in days the prescription was written for (days' supply). We report the proportion of women who received a perioperative opioid prescription and the median quantity dispensed and days' supply in the perioperative period by generic opioid ingredient. We also calculated median morphine milligram equivalents (MME).

For our primary outcome, we used absolute standardized mean difference (ASMD) to compare baseline demographics, health comorbidities, and perioperative data including SUI and POP surgery, POP surgery without SUI surgery, SUI surgery without POP surgery, route of surgery, concurrent hysterectomy, and mesh use between those with and without a perioperative opioid prescriptions filled. The absolute SMD has been shown to be a reliable measure in settings with large sample sizes, with differences in ASMD less than 0.10 considered negligible[11,12]. We also used log-binomial regression adjusting for age, year, region, type of surgery, route of surgery, concurrent hysterectomy and mesh use, and report multivariate adjusted risk ratios and 95% confidence intervals for predictors of perioperative opioid prescriptions.

For our secondary outcome, we used two definitions of prolonged opioid use. First, we defined prolonged opioid use as *any* prescription filled between 90–180 days after surgery, not requiring any fills in prior months (no continuous use requirement) as this has been the definition commonly used in the existing literature[13, 14]. In this analysis, we evaluated women who had at least 180 days of follow-up enrollment in the data source. This definition of *any* opioid fill allows for comparisons with prior research in this area[13, 15] In addition, we examined the proportion of women who filled at least one prescription in continuous monthly intervals. Among women with complete follow-up at each time point, we reported the proportion with continuous monthly fills through one-year following SUI and/or POP surgery.

Results:

From 2005–2015, 217,460 opioid naïve women underwent SUI and/or POP surgery. Of those 61,025 (28.1%) underwent POP and SUI surgery, 85,575 (39.4%) underwent SUI surgery without POP surgery, and 70,860 (32.6%) had POP without SUI surgery. For our primary outcome, 167,354 (77.0%) of opioid naïve patients filled a perioperative opioid prescription, while 50,106 (23.0%) did not (Table 1).

Patients who filled an opioid prescription were more likely to be younger (53±11.8 filled vs 58±13.6 not filled, ASMD 0.40). The most common route of surgery was vaginal, and this was associated with less opioid prescriptions filled (84.1% filled v 88.7% not filled, ASMD 0.14). Women who underwent concurrent hysterectomy were more likely to fill an opioid at the time of their surgery (37.9% filled v 25.0% not filled, ASMD 0.26). Not having mesh placed at the time of SUI and/or POP surgery was associated with less opioid prescriptions filled (26.6% filled v 37.5% not filled, ASMD 0.24). Those who had both SUI and POP

were associated with more opioid prescription filled (29.3 filled v 24.0% not filled, ASMD 0.12). Those with who willed an opioid prescription were more likely to reside in the South (45.5% filled vs 37.9% not filled, ASMD 0.16), and less likely to reside in the Northeast (9.2% filled vs 15.8 not filled, ASMD 0.20%) when compared to those that did not fill an opioid prescription. Healthier women, based on Charlson Comorbidity Index scores, were also more likely to have an opioid prescription filled (0.2±0.68 filled vs 0.3±0.86 not filled, ASMD 0.11). In a multivariate model that controlled for age, year, region, route of surgery, type of surgery and mesh use, younger age, Northeast region, POP surgery with or without SUI, abdominal route, hysterectomy and mesh use remained significantly associated with opioid prescriptions filled (Table 2)

For perioperative opioids associated with SUI and/or POP surgery, a median quantity of 30 pills were prescribed (IQR 20,30) with a median days' supply of 4 days (IQR 3,5) and median dosage in MME of 200 (IQR 150,270) (Table 3). When evaluating the results by year, day's supply, quantity dispense and MME appear relatively stable over time. Hydrocodone was the most common opioid prescribed in the perioperative period (45.6%), followed by oxycodone (34.9%) and dextropropoxyphene (9.0%).

For our secondary outcome of prolonged use, our first definition included patients with any prescription filled between 90–180 days. Among the 124,667 patients with a perioperative opioid prescription who had at least 180 days of follow-up, 7.5% (95% CI 7.3,7.6) had an opioid prescription 90–180 days post-surgery. The second definition of prolonged opioid use, which was defined as one prescription in continuous monthly intervals during follow-up. Using this definition, the rate of prolonged use for the SUI and/or POP surgery group was much lower at 1.18% (95%CI 1.13,1.24) at 60 days, 0.32% (95%CI 0.29,0.35) at 90 days, 0.06% (95%CI 0.05,0.08) at 180 days and 0.04% (95%CI 0.02,0.05) at 1 year (Table 4).

Comment:

Principal Findings

We found that most women undergoing surgery for SUI and POP surgery had a perioperative opioid prescription filled but the rate of prolonged opioid use was low.

Results

Of women undergoing SUI and POP surgery, 77% filled a perioperative opioid prescription. This is a relatively large percentage especially considering that a sizable number of these prescribed opioids go unused[7, 16]. Solouki and colleagues found similar results when evaluating 143 patients undergoing urogynecologic surgery, with 82% being prescribed an opioid[7]. However, this study described an average of 12–17 opioid tablets prescribed, which is lower than our median of 30 tablets prescribed. This difference could be a result of the broad time frame of 2005–2015 and a larger population for our data collection.

Interestingly, although the median number of opioids prescribed was similar over the time period of the study, with 30 pills (IQR 20, 30) in 2005 and 30 pills (IQR 24,40) in 2015. More recently, healthcare institutions have become increasingly aware of opioid over-

prescribing habits and have implemented initiatives, such as enhanced recovery after surgery (ERAS) protocols, in an attempt to reduce about the number of opioids prescribed perioperatively[17, 18]. ERAS protocols are evidence-based interventions designed to standardize perioperative care in order improve recovery after surgery. Implementation of these protocols for pelvic reconstructive surgery have been associated with a decrease in opioid use and other benefits including patient staisfaction[18]. Initiatives such as these may not have been reflected during the time period of our study. Larger studies looking specifically at hysterectomies have also found rates of opioid prescriptions ranging from 82–84%[19, 20]. Our previously published study of persistent opioid use after hysterectomy also found a median number of 30 tablets (IQR 25–40) prescribed at the time of surgery[20]. This further suggests that trends toward over-prescribing are not unique to Urogynecology but span across the entire field.

Although our study centered on perioperative opioid prescriptions filled, prior studies have shown similar findings in regard to risks factors for postoperative pain. We found that concurrent SUI and POP surgery was a risk factor with opioid prescription fill. Previous studies have shown that stress incontinence surgery at the time of prolapse repair to be a risk factor for increased pain[21, 22]. Vaginal route of surgery was associated with less opioid prescriptions filled. This is consistent with findings from Dr. As-Sanie's study on opioid prescribing patterns after benign hysterectomy that showed that vaginal hysterectomy was associated with both less opioids prescribed as well as less reported opioid use following vaginal hysterectomy when compared to laparoscopic and abdominal routes[3]. In contrast to work published by Westermann et al. that concluded that patients reported less pain after robotic sacrocolpopexy when compared to vaginal apical repair using uterosacral ligament suspension[23]. Studies have shown that mesh placement is also associated with increased pain following pelvic reconstructive surgery[24, 25]. Thus, it is not surprising that our study showed mesh placement as a risk factor for opioid prescription fill. Our results showing that younger women were more likely to fill their opioid prescriptions is consistent with previous literature noting higher rates of pain in the acute postoperative period following pelvic reconstructive surgery as well as increased risks of chronic pain following hysterectomies for benign conditions[22, 26, 27].

Our rate of 7.5% for any opioid filled between 90–180 days is similar to prior research. Brummet et al. used nationwide insurance claims from 2013–2014 to assess new persistent opioid use in adults undergoing both major and minor surgeries[13]. They found that in women who underwent a hysterectomy and received an opioid prescription, 6% had persistent use 90–180 days after surgery. Buono and colleagues found a higher rate 15.9% receiving an additional postoperative opioid prescription within 90 days after urogynecologic surgery with the most common indication being chronic pain syndrome[14].

We believe that using the criteria of any opioid filled between 90–180 days after surgery may not adequately reflect patients with persistent opioid use as a result of their surgery. For example, a postoperative patient may suffer a completely unrelated injury 3–6 months after surgery and receive an opioid prescription. Using the definition of any opioid prescription filled in the 90–180 days after surgery, this opioid prescription would meet the definition for prolonged postsurgical opioid use. Thus, we used a potentially more accurate definition of

prolonged use by evaluating continuous monthly fills, thereby capturing ongoing monthly opioid prescription up to one year. Our findings show that continuous monthly fills are quite low with rates of 1.2% at 60 days after surgery and a continued decline to 0.04% at 1 year. Rate of prolonged opioid use varies widely depending on the definition used but we believe that continuous fills may be a more accurate depiction of this issue.

Clinical Implications

This study illustrates that opioids are routinely prescribed after SUI and POP surgery but the risk of prolonged use in this population is low. While this data is reassuring clinicians should strive find ways to reduce the amount opioids prescribed to our patients. Policy makers should continue to support research identifying alternatives to opioids and promote educational tools to the public to combat opioid addiction in this country.

Research Implications

It will be important to continue developing nonopioid multimodal therapies to decrease the rate and number of opioids prescribed to treat postoperative pain in those having pelvic floor surgery. In addition, questionnaires to indicate what patients are less likely to need opioids would help surgeons individualize postoperative pain management hopefully leading to a decrease in prescribed opioids. More recent population-based studies that include institutions with ERAS protocols will also give a more accurate view of the current state of opioid prescribing habits in the urogynecology population.

Strengths and Limitations

The strengths of this study include the evaluation of a large population-based cohort with over 194,000 women. We used an insurance claims database covering patients across the United States undergoing SUI and/or POP surgery. We assessed opioid naïve women and used two definitions of prolonged opioid use allowing for both comparisons to previous studies as well as introducing continuous use data that may provide more precise information regarding prolonged opioid use after surgery.

Limitations include that the results reflect women with private insurance; thus, these results may not be generalizable to those who are underinsured or uninsured. We also cannot determine the exact indication for opioid prescriptions filled but using the definition of continuous monthly fill allows for a better estimate of prolonged opioid use related to surgery. The claims data does not include information on pain severity prior to or following surgery, which may be an important factor related to receipt of a perioperative opioid prescription and risk of prolonged opioid use. This study was unable to account for opioids purchased directly without insurance or obtained from other sources, therefore, there is a possibility that the rate of prolonged opioid use after surgery is higher.

Conclusions

In conclusion, among opioid naïve women undergoing SUI and/or POP surgery 79% of women filled an opioid prescription with a median of 30 opioid pills prescribed. While it is clear that opioid prescribing has become a routine part of perioperative care, the risk of

prolonged use after surgery is reassuring with continuous monthly opioid fills being extremely low through one year after surgery.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Disclosure statement:

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AJOG at a Glance

Why was this study conducted?

The study was conducted to evaluate the proportion of women filling perioperative opioid prescriptions and to compare factors associated with women who filled perioperative opioid prescriptions to those that did not following pelvic reconstructive surgery

What are the key findings?

Among opioid naïve women undergoing urogynecologic surgery, 77% of women filled an opioid prescription, but the risk of prolonged use was low.

What does this study add to what is already know?

This study evaluates opioid prescriptions filled after urogynecologic surgery using a large population-based cohort and provides data on prolonged opioid use using two definitions.

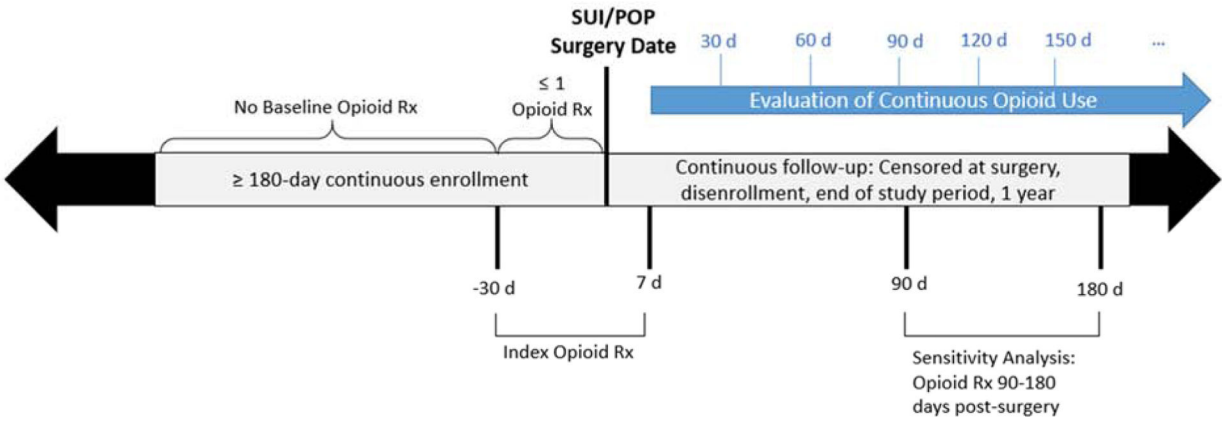

Figure 1.
Study schematic illustrating requirements for cohort entry.

Table 1:

Demographics associated with perioperative opioid prescriptions filled

Characteristic	Perioperative Opioids N=167,354 (77.0%)	No Perioperative Opioids N=50,106 (23.0%)	ASMD
Age at Index Procedure, mean(SD)	53.0(11.75)	58.1(13.63)	0.40
Age Category			
18–34	7,640 (4.4%)	1,882 (3.6%)	0.04
35–44	35,448 (20.6%)	6,610 (12.8%)	0.21
45–54	55,231 (32.0%)	12,773 (24.7%)	0.16
55–64	48,340 (28.0%)	14,802 (28.6%)	0.01
65+	25,700 (14.9%)	15,654 (30.3%)	0.37
Route			
Abdominal	14,545 (8.7%)	3,184 (6.4%)	0.09
Laparoscopic	12,006 (7.2%)	2,457 (4.9%)	0.10
Vaginal	140,803 (84.1%)	44,465 (88.7%)	0.14
Mesh			
No Mesh	44,440 (26.6%)	18,799 (37.5%)	0.24
Abdominal	7,877 (4.7%)	1,764 (3.5%)	0.06
Laparoscopic	10,927 (6.5%)	2,258 (4.5%)	0.09
Vaginal	104,110 (62.2%)	27,285 (54.5%)	0.16
Concurrent Hysterectomy	61,976 (37.0%)	12,544 (25.0%)	0.26
Type of Surgery			
SUI w/out POP	65,067 (38.9%)	20,508 (40.9%)	0.04
POP w/out SUI	53,297 (31.8%)	17,563 (35.1%)	0.07
SUI and POP	48,990 (29.3%)	12,035 (24.0%)	0.12
Region			
Midwest	45,050 (26.9%)	14,646 (29.2%)	0.05
Northeast	15,327 (9.2%)	7,936 (15.8%)	0.20
South	76,189 (45.5%)	18,996 (37.9%)	0.16
West	29,071 (17.4%)	8,099 (16.2%)	0.03
Unknown	1,717 (1.0%)	429 (0.9%)	0.02
Year			
2005	13,247 (7.9%)	4,742 (9.5%)	0.06
2006	12,673 (7.6%)	4,186 (8.4%)	0.03
2007	13,520 (8.1%)	4,222 (8.4%)	0.01
2008	17,238 (10.3%)	5,296 (10.6%)	0.01
2009	20,009 (12.0%)	5,801 (11.6%)	0.01
2010	19,348 (11.6%)	5,467 (10.9%)	0.02
2011	20,326 (12.1%)	6,004 (12.0%)	0.01
2012	17,676 (10.6%)	5,301 (10.6%)	0.00

Characteristic	Perioperative Opioids N=167,354 (77.0%)	No Perioperative Opioids N=50,106 (23.0%)	ASMD
2013	13,918 (8.3%)	3,906 (7.8%)	0.02
2014	12,623 (7.5%)	3,492 (7.0%)	0.02
2015	6,776 (4.0%)	1,689 (3.4%)	0.04
Charlson Comorbidity	0.2(0.68)	0.3(0.86)	0.11
Index, mean(SD)			
Surgical Details			
Inpatient	52,462 (31.3%)	15,654 (31.2%)	0.00
Length of Service, mean(SD)	0.3(1.91)	0.3(2.47)	0.01
[*]**Baseline Non-Opioid Analgesic**	23,398 (14.0%)	6,416 (12.8%)	0.04

ASMD= absolute standardized mean difference

ASMDs below 0.10 are considered negligible

[*] Classified by redbook therapeutic class=59. Analgesics/Antipyretics, Nonsteroidal anti-inflammatory medications

Table 2:

Multivariate Regression for associations of perioperative opioid prescription fill

Predictors	Adjusted Risk Ratio	95% CI	
Age Group			
18–34	1.02	1.01	1.03
35–44	1.03	1.02	1.03
45–54 (Referent)	1.00	1.00	1.00
55–64	0.95	0.95	0.96
65+	0.79	0.79	0.80
Year			
2005	0.98	0.97	0.99
2006	0.99	0.98	1.00
2007	0.99	0.98	1.00
2008	0.99	0.99	1.00
2009	1.00	0.99	1.01
2010	1.01	1.00	1.01
2011 (Referent)	1.00	1.00	1.00
2012	1.00	0.99	1.01
2013	1.02	1.01	1.03
2014	1.03	1.02	1.04
2015	1.04	1.03	1.05
Region			
Midwest	1.14	1.13	1.15
Northeast (Referent)	1.00	1.00	1.00
South	1.17	1.16	1.18
West	1.16	1.15	1.17
Unknown	1.18	1.15	1.20
Surgery Type			
SUI without POP (Referent)	1.00	1.00	1.00
POP without SUI	1.04	1.03	1.05
SUI and POP	1.03	1.03	1.04
Route			
Abdominal	1.03	1.03	1.04
Laparoscopic	1.00	0.99	1.00
Vaginal (Referent)	1.00	1.00	1.00
Concurrent Hysterectomy			
Yes	1.08	1.08	1.09
No (Referent)	1.00	1.00	1.00
Mesh			
Yes	1.12	1.11	1.12

Predictors	Adjusted Risk Ratio	95% CI	
No (Referent)	1.00	1.00	1.00

Table 3:

Days and quantities of dispensed opioids

Year	Median (IQR)		
	Days' Supply	Quantity Dispensed	MME
2005	4 (3,5)	30 (20,30)	200 (150,270)
2006	4 (3,5)	30 (20,30)	200 (150,270)
2007	4 (3,5)	30 (20,30)	216 (150,300)
2008	4 (3,5)	30 (20,30)	200 (150,270)
2009	4 (3,5)	30 (20,30)	200 (150,270)
2010	4 (3,5)	30 (20,30)	200 (150,270)
2011	4 (3,5)	30 (20,30)	188 (150,270)
2012	4 (3,5)	30 (20,30)	188 (150,270)
2013	5 (3,5)	30 (24,40)	225 (180,300)
2014	5 (3,5)	30 (24,40)	225 (150,300)
2015	5 (3,6)	30 (24,40)	225 (162,300)
Overall	4 (3,5)	30 (20,30)	200 (150,270)

Table 4:

Rate of continuous and any medication refills post-surgery

Days Post Surgery	Monthly Refills	
	Continuous Fills % (95%CI)	Any Fills % (95%CI)
30	10.12 (9.97, 10.27)	9.81 (76.78, 77.14)
60	1.18 (1.13, 1.24)	3.32 (3.23, 3.41)
90	0.32 (0.29, 0.35)	2.97 (2.89, 3.06)
120	0.15 (0.13, 0.17)	2.95 (2.86, 3.04)
150	0.09 (0.08, 0.11)	3.00 (2.91, 3.09)
180	0.06 (0.05, 0.08)	3.07 (2.97, 3.16)
210	0.05 (0.04, 0.06)	3.11 (3.01, 3.21)
240	0.05 (0.03, 0.06)	3.02 (2.92, 3.12)
270	0.04 (0.03, 0.06)	3.00 (2.89, 3.10)
300	0.04 (0.03, 0.05)	3.19 (3.08, 3.30)
330	0.04 (0.03, 0.05)	3.18 (3.07, 3.29)
360	0.04 (0.02, 0.05)	2.98 (2.87, 3.09)