

## National Variation in Opioid Prescription Fills and Long-Term Use in Opioid Naïve Patients after Urological Surgery



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### Abbreviations and Acronyms

LOS = length of stay

OME = oral morphine equivalent

TURBT = transurethral resection of bladder tumor

TURP = transurethral prostate resection

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**Purpose:** Prescription opioid use is increasing, leading to increased addiction and mortality. Postoperative care is often the first exposure to opioids of a patient but little data exist on national prescription patterns in urology. We examined post-discharge opioid fills after urological procedures and the association with long-term use.

**Materials and Methods:** We identified patients in a private national insurance database who underwent 1 of 15 urological procedures between October 1, 2010 and September 30, 2014. Patients with an opioid fill in the preceding 6 months were excluded from study. Claims for opioids from 30 days before the operation until 7 days after discharge characterized an initial prescription. Factors associated with persistent opioid use (an opioid claim 91 to 180 days after the operation) and chronic opioid use (10 or more refills of a 120-day or greater supply in the year after the operation) were analyzed using multivariable logistic regression.

**Results:** Overall 96,580 patients were included in study, of whom 49,391 (51%) filled an initial opioid prescription. Variation in the initial prescribed amount existed within procedures. Persistent use occurred in 6.2% of patients while chronic use occurred in 0.8%. Increased prescription in patients treated with transurethral prostate resection, vasectomy, female sling surgery, cystoscopy and stent insertion were associated with an increased risk of persistent as well as chronic use.

**Conclusions:** National variation in opioid prescribing practice exists after urological operations. Patients who fill larger amounts of opioids after certain major and minor urological procedures are at increased risk for long-term opioid use. This provides evidence for procedure specific prescribing guidelines to minimize risk and promote standardization.

**Key Words:** urologic surgical procedures; narcotics; opioid-related disorders; practice patterns, physicians'; risk

THE United States faces an epidemic of opioid addiction and mortality. Since 2002, prescription opioid use has increased, followed by an increase in deaths.<sup>1,2</sup> In 2015 opioids were involved in more than 33,000 drug related deaths (63%).<sup>3</sup>

Opioids prescribed postoperatively contribute to this crisis. Approximately 6% of previously opioid naïve patients will continue to use opioids 6 months after surgery.<sup>4</sup> Over-prescription is common and a significant contributor to the pool of

medication available for abuse in the community.<sup>5,6</sup> In urology data are limited on national opioid postoperative prescribing patterns. Knowledge of the state of this issue is a critical step to improve safety and develop interventions across the discipline.

We examined variation in post-discharge opioid fills after 15 urological procedures. We also examined factors affecting prolonged opioid use in the year following a procedure. We hypothesized that variation exists in opioid fills and contributes to long-term use.

## MATERIALS AND METHODS

### Cohort Selection

OptumInsight (Optum, UnitedHealth Group, Eden Prairie, Minnesota) is a private administrative database of claims of more than 60 million patients. This population is representative of privately insured Americans in terms of age, gender and race.<sup>7</sup> This study was deemed exempt from review by the University of Pennsylvania Institutional Review Board (IRB No. 832485).

Included in analysis were 310,072 patients with a surgeon billed claim with the CPT code of a common urological procedure between October 1, 2010 and September 30, 2014 (supplementary Appendix 1, <https://www.jurology.com>). Figure 1 shows the creation of an opioid naive cohort. Because cystoscopy and stent insertion are often performed with other procedures, we excluded patients who underwent these procedures and had multiple surgical CPT codes on the same day as the index operation. A reduced cohort excluded patients who underwent procedures in the year following the index operation as defined by anesthesia CPT codes, those who were not prescribed opioids at discharge home and those without an opioid amount recorded or an amount greater than 10,000 OME. Supplementary Appendix 2 (<https://www.jurology.com>) shows codes of exclusions.

### Variables

We identified opioid claims in the year following an operation using the NDC (National Drug Code). Methadone and nontablet formulations were excluded. Other variables included age, gender, race, region, state, education level, poverty status, the Elixhauser comorbidity score,<sup>8</sup> chronic pain or fatigue disorders, mental health disorders and LOS. Race was categorized as Caucasian, African American, Asian, Hispanic and unknown/other. Education level was stratified as less than 12th grade, a high school diploma, some college, a bachelor degree or higher and unknown/missing. Poverty status was defined as greater than 400% of the federal poverty level, less than 400% of the federal poverty level or unknown/missing. The Elixhauser comorbidity score was categorized as zero, 1, 2, or 3 or more. State was determined by the state of the prescribing provider using the NPI (National Provider Identifier) code. Chronic pain or fatigue and mental health disorders were determined by ICD-9 codes from

claims in the year prior to an operation (supplementary Appendix 2, <https://www.jurology.com>).<sup>9–11</sup> For outpatient procedures LOS was recorded as zero.

Opioid type and the number of days supplied were used to calculate the OME, a standardized method of reporting quantities across drug types.<sup>12</sup> The OME was used in 100 unit increments for the regression. Laparoscopic prostatectomy was chosen as the reference procedure as the median oral morphine equivalent was the smallest of the major procedures but larger than the OME of transurethral, scrotal or endoscopic operations.

### Outcomes of Interest

The initial opioid prescription was defined as 1 opioid fill between 30 days before the operation to 7 days after discharge home with post-discharge prescriptions taking priority. For cystoscopy, stent and nephrolithiasis procedures only postoperative prescriptions were included. We excluded prescriptions filled during hospitalization. To describe provider variation we calculated the difference between the initial and the procedure specific median oral morphine equivalent dose in each patient. Persistent opioid use was defined as filling a prescription 91 to 180 days after discharge if an initial prescription was filled.<sup>4</sup> Chronic use was defined as a total of 10 or more refills, or an opioid supply of 120 days or greater in the year following discharge if an initial prescription was filled.<sup>13</sup>

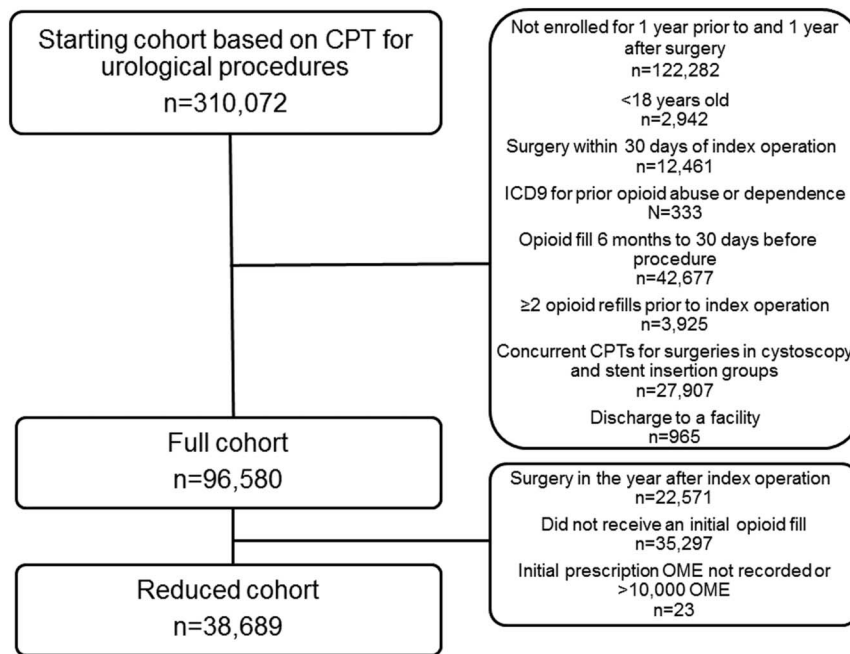
### Statistical Analysis

Descriptive statistics were calculated. Multivariable logistic regression of persistent and chronic use was performed with certain variables, including the difference in the initial amount from the procedure specific median OME, patient age, gender and race, procedure category, education level, poverty status, the Elixhauser comorbidity score, chronic pain or fatigue disorder, mental health disorder and state. We used an interaction term between procedure and difference from median OME to account for the modification of each procedure on the effect of the initial opioid amount on outcomes. Subset analysis was done excluding 34,435 patients 65 years old or older to ensure that enrollment in Medicare did not affect our results. Analysis was performed with STATA®, version 15.0 and SAS®, version 9.4.

## RESULTS

### Patient Characteristics and Initial Opioid Fills

The analytical cohort consisted of 96,580 patients. Supplementary table 1 (<https://www.jurology.com>) shows characteristics of the full and reduced cohorts. The table lists the rates of each opioid outcome by procedure. Overall 49,391 patients (51%) filled a prescription for a tablet opioid between 30 days preoperatively and 7 days after discharge home. Procedures for which less than 50% of patients received an initial prescription included radical cystectomy in 30%,



**Figure 1.** Cohort and exclusion criteria for full and reduced cohorts used for opioid outcomes after initial prescription

TURBT in 44%, TURP in 44%, cystoscopy in 3% and stent insertion in 38%. Of patients who underwent vasectomy and endoscopic treatment of kidney stones 66% and 57%, respectively, received opioids.

Hydrocodone was prescribed in 55% of patients (supplementary fig. 1, <https://www.jurology.com>). The median initial fill amount was 150 OME (IQR 125–225). Figure 2 shows the initial prescription total OME by procedure. Open nephrectomy, laparoscopic nephrectomy and open prostatectomy had

the largest median total dose at 225 OME. Vasectomy had the smallest median total dose at 135 OME (IQR 90–180). For reference 225 OME equal 45 tablets of 5 mg hydrocodone and 135 OME equal 27 tablets of 5 mg hydrocodone (supplementary table 2, <https://www.jurology.com>).

Figure 3 shows the difference in the initial OME from the procedure specific median by surgeon. The median OME per day filled across all procedures was 42 (IQR 30–56) (supplementary fig. 2, <https://www.jurology.com>).

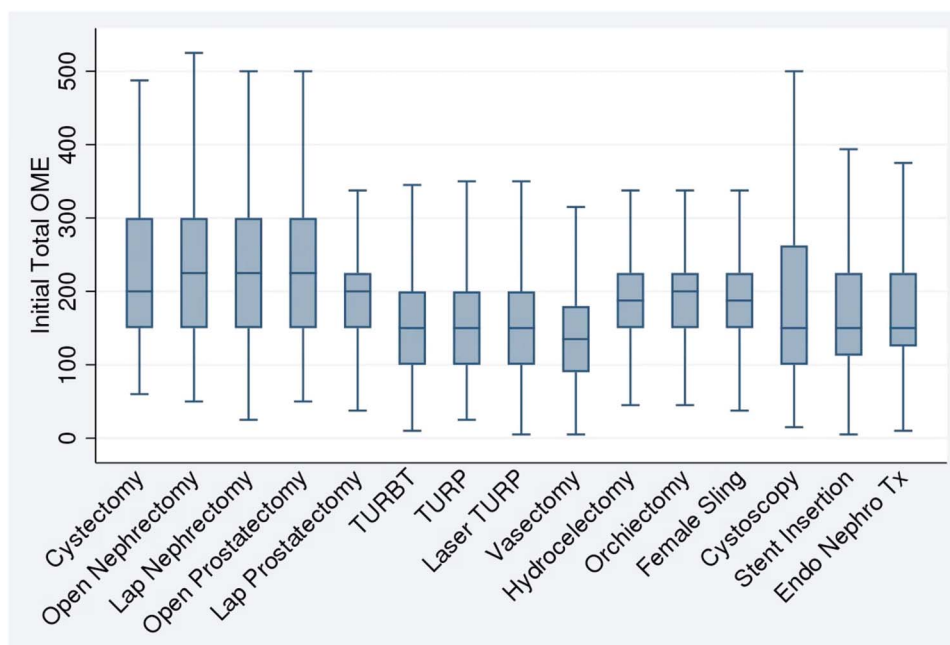
#### Number of patients with each opioid outcome by procedure type

Procedure Category	Full Cohort (96,580 pts)		Reduced Cohort (38,689 pts)		
	No. Pts	No. Initial Opioid Fill (%)*	No. Pts	No. Persistent Opioid Use (%)†	No. Chronic Opioid Use (%)‡
Prostatectomy:					
Laparoscopic	7,013	5,507 (78.5)	4,514	190 (4.2)	20 (0.4)
Open	1,324	1,000 (75.5)	792	30 (3.8)	4 (0.5)
Cystectomy:					
Radical	264	78 (29.6)	50	6 (12.0)	1 (2.0)
Laparoscopic	2,292	1,625 (70.9)	1,189	98 (8.2)	18 (1.5)
Open	1,375	938 (68.2)	693	69 (10.0)	21 (3.0)
TURBT	1,580	705 (44.6)	483	40 (8.3)	9 (1.9)
TURP	6,622	2,921 (44.1)	2,240	129 (5.8)	35 (1.6)
Laser TURP	4,162	2,099 (50.4)	1,591	114 (7.2)	13 (0.8)
Vasectomy	9,758	6,420 (65.8)	5,960	247 (4.1)	10 (0.2)
Hydrocelectomy	3,540	2,863 (80.9)	2,439	124 (5.1)	15 (0.6)
Orchiectomy	1,777	1,487 (83.7)	1,196	74 (6.2)	12 (1.0)
Female sling	18,776	14,227 (75.8)	11,348	771 (6.8)	69 (0.6)
Cystoscopy	20,854	681 (3.3)	409	65 (15.9)	27 (6.6)
Stent insertion	5,328	2,002 (37.6)	828	70 (8.5)	17 (2.1)
Endoscopic nephrolithiasis treatment	11,915	6,838 (57.4)	4,957	373 (7.5)	54 (1.1)

\* Less than 30 to more than 7 days after discharge.

† Refill 91 to 180 days after discharge.

‡ Ten or more refills, or supply for 120 days or more in year after discharge and 0.136% risk in nonsurgical population.<sup>13</sup>



**Figure 2.** Initial prescription OME by procedure type. *Lap*, laparoscopic. *Endo Nephro Tx*, endoscopic nephrolithiasis.

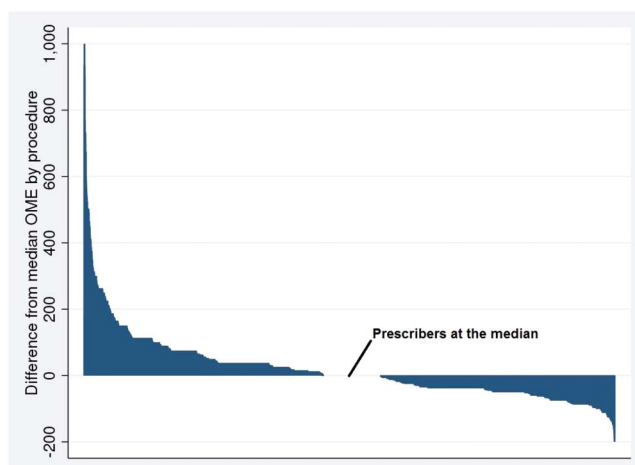
### Persistent and Chronic Opioid Outcomes

Supplementary table 3 (<https://www.jurology.com>) shows persistent and chronic use associated with a 100 unit increase in the initial OME from the median by procedure and other significant factors on regression analysis. Persistent opioid use, defined as a fill on day 91 through 180 after discharge if opioids were initially filled, was noted in 2,399 patients (6.2%). A 100 unit increase from the median initial dose increased the risk of persistent use in patients who underwent TURP (OR 1.13, 95% CI 1.03–1.24), vasectomy (OR 1.18, 95% CI 1.05–1.32), orchiectomy (OR 1.21, 95% CI 1.05–1.39), a female

sling procedure (OR 1.09, 95% CI 1.03–1.15), cystoscopy (OR 1.29, 95% CI 1.12–1.50) and stent insertion (OR 1.20, 95% CI 1.05–1.38).

Chronic opioid use, defined as 10 or more opioid refills, or an opioid supply of 120 days or more in the year following discharge if opioids were filled initially, was found in 325 patients (0.8%). An increase from the median filled initial dose was associated with chronic use in patients treated with open nephrectomy (OR 1.30, 95% CI 1.14–1.48), TURBT (OR 1.64, 95% CI 1.22–2.20), TURP (OR 1.36, 95% CI 1.15–1.60), vasectomy (OR 1.69, 95% CI 1.33–2.16), a female sling procedure (OR 1.28, 95% CI 1.15–1.42), cystoscopy (OR 1.26, 95% CI 1.07–1.47), stent insertion (OR 1.28, 95% CI 1.04–1.56) and endoscopy for nephrolithiasis (OR 1.34, 95% CI 1.14–1.56). Supplementary table 4 (<https://www.jurology.com>) shows full models of outcomes. Supplementary table 5 (<https://www.jurology.com>) provides an analysis by state.

Supplementary table 6 (<https://www.jurology.com>) shows the category of the provider prescribing opioids after the initial prescription. Urologists provided 12% of prescriptions while medical specialists provided the most prescriptions at 28%.



**Figure 3.** Initial prescription total OME of 12,000 randomly sampled surgeons. Procedure specific median initial OME was subtracted from median initial OME of each provider.

### DISCUSSION

Using a national private insurance database, we identified variability in post-discharge opioid fills for urological procedures. For many minor procedures an increase in the initial dose was associated with long-term opioid use. These results have

important implications for the prescription of opioids after surgery.

Existing studies confirm variation in opioid prescribing practices across surgical specialties.<sup>5,14</sup> Studies of institutional experience describe these results in urology even among providers in the same practice.<sup>15–18</sup> Most patients receive more medication than they require.<sup>6</sup> Excessive prescribing creates a massive pool of opioids available to reach unintended individuals. The urological literature lacks national prescription patterns with the only current study revealing variation after kidney stone procedures.<sup>19</sup> In our work there was variation in the OME prescribed for all procedures. Our initial oral morphine equivalent prescription IQR varied by approximately 150 OME or 30 tablets of 5 mg hydrocodone for major procedure and by 100 OME or 20 tablets of 5 mg hydrocodone for minor procedures.

Several groups have examined long-term opioid outcomes after procedures. Using the same definitions of chronic opioid use as in our study, Sun et al found a higher incidence of chronic use after some procedures than in a nonsurgical cohort.<sup>13</sup> While they included TURP in analysis, they did not find a significantly higher rate of chronic use. Shah et al studied urological patients in California and concluded that the risk of opioid dependence was approximately 0.1% in postoperative year 1.<sup>20</sup> The rate of chronic use in our series was higher at 0.8% but Shah used ICD-9 codes to identify dependence and likely underestimated opioid disorders.

In 2014 in the United States 930,400 urological procedures were performed, which our data suggest would have led to 7,443 patients with chronic opioid use.<sup>21</sup> Our study also demonstrated that more than 25% of patients across all procedures were prescribed more than 50 OME per day, a dose associated with an increased risk of overdose and mortality.<sup>22</sup> Notably we used 2 definitions of long-term use based on the number of prescriptions with persistent more lenient and chronic more strict. As our data did not capture nonprescription opioids, which are likely obtained by many chronic users, the true incidence of opioid dependence is likely between these 2 values. However, to our knowledge the relationship between the definitions of persistent and chronic use remains unknown.

Evidence suggests that acute postoperative pain is independent of prolonged opioid use. Brummett et al analyzed major and minor procedures using the same definition of persistent use as in our study and found that each type was associated with increased odds of persistent use.<sup>4</sup> Our results suggest the same conclusion since endoscopic procedures such as TURP and stent insertion were associated with persistent and chronic use. Despite this risk approximately 40% of

patients who underwent these procedures received opioids.

Pain after endoscopy is often related to catheters, stents or bladder spasms. It is unclear whether parenteral administration of opioids is efficacious against spasmodic or stent related pain and it may not be necessary after ureteroscopy and stent insertion.<sup>23</sup> Given the availability of nonnarcotics and the increased risk of chronic use, we encourage careful consideration when prescribing opioids for post-discharge analgesia in these patients.<sup>24,25</sup>

Surgeons must be aware of risk factors for opioid abuse when prescribing in the post-operative period. A history of mental health and substance disorders is consistently associated with adverse opioid outcomes in the literature and in our study.<sup>4,10,20</sup> Nephrolithiasis is associated with opioid use and minimizing additional factors is important to avoid addiction.<sup>26</sup> While opioids should not be withheld to address pain, careful selection of dose and maximization of adjunct medication is critical.

There are conflicting data on whether the dose of a single prescription affects outcomes. Using Optum Sekhri et al found that increased initial OME did not affect opioid refills within 30 days of an operation.<sup>10</sup> However, studies of longer term outcomes have shown that the initial opioid dose as well as the number of days supplied increased the risk of long-term use.<sup>27</sup> We found a risk in increasing the initial prescription amount above the median for certain procedures. Many minor procedures had an increased risk of 10% to 60% for 100 unit increases in OME, indicating the importance of opioid stewardship for benign disease.

Practice standardization is a cornerstone of quality interventions and the results of our study support future policy. While the AUA (American Urological Association) has released a statement recommending the limitation of opioids to the lowest amount possible, procedure specific guidelines are lacking.<sup>28</sup> The Mayo Clinic has published guidelines for urological procedures with similar pain levels.<sup>29</sup> Overton et al recommended 75 OME after robotic radical prostatectomy,<sup>30</sup> which was below the fifth percentile in our study. Transurethral and endoscopic procedures are important targets for guidelines since they vary in prescription rate and size. Audits and feedback may prove useful to identify high prescribers, increase individual awareness and allow for external intervention when necessary. With the expansion of prescription drug monitoring programs the basic infrastructure required to audit already exists.

Our study has several limitations. With claims data we could only investigate the amount of opioids

filled by patients and not necessarily the amount prescribed by providers. Some patients may not have filled the prescription and, thus, we likely underestimated the percent for whom opioids were prescribed.

To account for prescriptions from other members of the surgical team we did not limit our analysis to prescriptions by the index surgeon. However, this method could not account for prescriptions provided by other providers such as primary care physicians.

Although uncommon, some patients may have had alternative medication insurance not captured by Optum. We performed subset analysis excluding patients eligible for Medicare to confirm that dual enrollment did not affect our results.

Curiously, radical cystectomy had a low initial prescription rate. While there were relatively few patients in this group, there was a large number of surgeons. Many patients with longer LOS may have had time to wean off opioids prior to discharge. Cystoscopy was associated with high rates of persistent and chronic use in those with an initial prescription. Patients with underlying opioid risk factors were likely selected for because cystoscopy had an initial prescription rate of only 3%.

Our study did not capture opioids from nonprescription sources and it likely underestimates opioid dependence. Different mental health and medical disorders might have varying effects on opioid use, which were not accounted for in our

regression. We did not control for the medical condition that indicated the procedure or for disseminated cancer. The contribution of complications to long-term use was not analyzed and it has been under explored in the literature. We did not include adjunct medications for pain control or the distance from health care resources, which may affect the initial amount of opioids. As we excluded patients with recent opioid exposure, our results may not be applicable to this population. In particular, patients with nephrolithiasis who are opioid naïve are likely different than those with opioid exposure.

Finally, as a retrospective study, we were limited to the time frame of available data. We could not evaluate the effect that recent interventions such as prescription drug monitoring programs have had on practice. However, this study demonstrates that a significant risk of long-term opioid use exists in patients who undergo urological interventions.

## CONCLUSIONS

Variation exists in post-discharge opioid fills following urological operations. A long-term risk of opioid use is associated with several factors, including higher initial prescription amounts after certain procedures. This study provides evidence for procedure specific interventions to increase standardization, especially among minor urological operations.

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## EDITORIAL COMMENTS



The opioid epidemic in the United States continues to intensify with a reported 47,600 deaths in 2017, an increase of 12% over the previous year.<sup>1</sup> Although many of these deaths were due to synthetic opioid and heroin abuse, 36% occurred from prescription opioid abuse. As urologists most of our patients are opioid naïve, meaning that the postoperative prescription provided serves as the initial opioid exposure of the patient. Further, since patients use less than half of the opioids typically prescribed,<sup>2</sup> this practice creates a significant reservoir of pills available for diversion and abuse.

These authors present national prescribing practices and the associations with persistent and long-term use following common urological procedures. Overall half of the patients filled a perioperative prescription. There was also substantial variation in the amount prescribed for each procedure with the IQR often spanning 100 OME. The reported 6.2% persistent use rate (3 to 6-month post-discharge fills) is similar to that previously reported (reference 4 in article). This degree of variation in the fill rate and

the amount of opioids prescribed for individual procedures is unlikely to be driven by patient factors. It indicates a significant opportunity for urologists to improve opioid stewardship.

Although opioids are likely to remain part of a multimodal approach to postoperative pain management for some procedures, urologists must critically examine procedures for which opioids can be omitted or those for which prescriptions can be greatly reduced. To ensure continued high level patient care these changes should be part of a comprehensive approach using patient counseling, nonopioid and non-pharmacological analgesics, education of other medical providers and safe disposal of unused medications.

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Postoperative opioid prescribing has recently come under greater scrutiny. Several studies have

identified significant overprescribing following urological procedures but limited data are available to

evaluate long-term outcomes. This study addresses that gap, examining trends in opioid prescribing following urological surgeries from 2010 to 2014 in national claims data and focusing on the outcome of new chronic opioid use.

Brummett et al previously evaluated new persistent opioid use following general surgeries with TURP as the only urological procedure included (reference 4 in article). However, this study focused specifically on urological procedures and concluded that 6.2% of previously opioid naive patients demonstrated new persistent opioid use (opioid claim 91 to 180 days after operation, similar to the definition and findings of Brummett et al) and 0.8% demonstrated chronic opioid use (10 or more refills, or a supply for 120 days or more in the year following

the operation). This novel definition of chronic use is particularly stringent and identifies a concerning number of patients in whom new and apparently problematic opioid use develops each year.

While the study timeline does not account for potential effects of recent increased regulation and awareness of prescribing patterns, the findings allow urologists to more accurately counsel patients on the risks of postoperative opioid use, and motivate continuing efforts to improve care and identify patients at high risk.

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