

Perioperative opioid prescribing after male fertility procedures is associated with new persistent opioid use: retrospective analysis of a large claims database

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Objective: To assess the risk of new persistent opioid use in opioid-naïve men who underwent male fertility procedures.

Design: Retrospective cohort study using a claims database.

Setting: A database linking electronic medical record data and claims—assessing men who underwent fertility procedures between 2010 and 2021.

Patient(s): Opioid-naïve men who underwent fertility procedures (open or laparoscopic varicocele, spermatocele excision, and testicular excisional or incisional biopsy) without further surgical intervention requiring anesthesia in the 2 years after the index procedure. Those with and without perioperative opioid prescriptions were propensity score matched on age, race/ethnicity, smoking status, mental health diagnoses, and preoperative pain diagnoses.

Intervention(s): Perioperative opioid prescription.

Main Outcome Measure(s): The primary outcome was the incidence of new persistent opioid use (opioid prescription 3–9 months after the index fertility procedure). The secondary outcome was prolonged opioid use (opioid prescription 9–24 months after the index fertility procedure).

Result(s): A total of 387,565 men who underwent fertility procedures were identified, of whom 25.1% received an opioid prescription. After propensity score matching, 97,215 men were included; 4.7% of men who received a perioperative opioid prescription developed new persistent opioid use compared with 2.2% of those without a perioperative opioid prescription (risk ratio, 2.16; 95% confidence interval, 2.05–2.27; number needed to harm, 39). When assessing each unique fertility procedure independently, men who received perioperative opioids had statistically higher odds of developing new persistent opioid use for all procedure types. Men with new persistent opioid use were much more likely to go on and develop prolonged opioid use than men without new persistent opioid use.

Conclusion(s): Opioid prescription after male fertility procedures is associated with a significant risk of new persistent opioid use, emphasizing the importance of judicious opioid prescribing for male fertility procedures. (Fertil Steril® 2023;119:401-8. ©2022 by American Society for Reproductive Medicine.)

El resumen está disponible en Español al final del artículo.

Key Words: Analgesics (opioid), dependence (opioid), minor surgical procedures, infertility (male)

Overall, 5.9%–6.5% of patients who are prescribed an opioid after a minor surgical procedure develop new persistent opioid use (1). New persistent opioid use is defined as opioid-naïve patients developing the

need for narcotic prescriptions at least 90 days after the index procedure (2). It has been shown that the incidence of new persistent opioid use was similar among both major and minor surgeries, indicating that new persistent opioid use is likely independent of pain severity in the immediate postoperative period. Several factors contribute to the development of postsurgical new persistent opioid use, including preoperative

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tobacco use, substance use disorders, mood disorders, anxiety, and preoperative pain. However, in published studies, the strongest contributing factor to developing new persistent opioid use disorder has been the prescription of postoperative opioids (1).

Although pain management is an important aspect of postoperative care, liberal opioid prescribing can initiate or potentiate opioid addiction (3). Within urology, new persistent opioid use has been demonstrated after both ureteroscopy and vasectomy (4, 5). Most male fertility procedures are minimally invasive, such that postoperative opioid prescribing can be minimized or completely avoided without significant discomfort to the patient (6, 7). However, opioid prescription after these procedures remains common, and the relationship of infertility surgeries and long-term opioid use remains uncertain. We hypothesized that opioid use after a minor fertility procedure is associated with an increased incidence of long-term opioid dependence.

MATERIALS AND METHODS

Data Source and Study Design

Data used in this study were collected and analyzed in March 2022 from the TriNetX LLC Diamond Network, a US claims database that provides access to electronic medical records (diagnoses, procedures, medications, laboratory values, and genomic information) linked with insurance claims for approximately 212 million patients from 92 healthcare organizations covering 1.8 million sites and 99% of US health plans. Data regarding demographics, diagnoses from the International Classification of Diseases codes, procedures from the Current Procedural Terminology (CPT) codes, and medications were all recorded and used for analysis. Medication data were obtained from prescriptions, orders, inpatient medication reconciliations, and charted medications.

TriNetX assumes responsibility for deidentification of the data in a process that adheres to Section §164.514(b) (1) of the Health Insurance Portability and Accountability Act Privacy Rule. Because this study used only deidentified patient records and did not involve collection, use, or transmittal of individually identifiable data, this study was exempt from the institutional review board.

Data from January 2010 through December 2021 were included. We additionally assessed the risk of developing new persistent opioid use over time to determine whether the risk of developing new persistent opioid use has changed with national efforts to curtail opioid abuse—we stratified our analysis into 2010 through 2015 and 2016 through 2021.

Cohorts

To evaluate the risk of new persistent opioid use associated with male fertility procedures, we included adult men aged 18–70 years who underwent selected male fertility procedures. The procedures assessed included the following groups: open varicocele excision or ligation (CPT 55530); laparoscopic varicocele ligation (55550); unilateral epididymovasostomy (54900); bilateral epididymovasostomy (54901); vasovasostomy (VV) (55400); incision biopsy of the testis (54505); unilateral or bilateral vasectomy (55250); and excision of spermatocele (54840).

Additional fertility procedures, such as testicular sperm aspiration, microscopic epididymal sperm aspiration, and percutaneous epididymal sperm aspiration, could not be assessed because these procedures have an unlisted CPT code (53899). Men were excluded if they underwent any additional surgical procedure (CPT Concept ID: 1003143) requiring anesthesia (CPT Concept ID: 1002796) between 1 and 9 months after the index fertility procedure.

We included only men who were opioid-naïve; men who received an opioid prescription within the past 1 year up to 2 weeks before the index fertility procedure were excluded. Additionally, men were excluded if they ever had a diagnosis of opioid abuse (F11.1) or opioid dependence (F11.2) at any time before the index procedure.

Included men were stratified into 2 cohorts: those who had received an opioid prescription <2 weeks before or 1 month after the index fertility procedure and those who had not received an opioid prescription in the perioperative period, which is consistent with cohorts in a prior study (1) (Fig. 1).

We defined opioid prescription as the recorded use, insurance claim, or prescription of opioids (CN101) as designated by the Veterans Affairs Drug classification system. The frequencies of outpatient services (CPT Concept ID: 1013626) and emergency department services (CPT Concept ID: 1013711) were also determined. The TriNetX database does not capture the dosages of opioids prescribed.

New Persistent Opioid Use Analysis

The primary outcome of interest was new persistent opioid use, defined as prescribing of an opioid prescription (CN101) between 3 and 9 months after the index procedure (8). We accounted for previously reported confounding variables known to be associated with opioid use through propensity score matching by logistic regression. We employed propensity scoring matching on the basis of age (continuous variable); race/ethnicity; smoking status; mental health diagnoses, including mood disorders (i.e., adjustment, anxiety, and mood disorders), homicidal and suicidal ideation, behavior disorders (i.e., attention deficit/hyperactivity disorder, conduct and disruptive behavior disorders, and impulse control disorders), personality disorders, schizophrenia and other psychotic disorders, and substance use disorders (i.e., alcohol and other substance-related disorders) (International Classification of Diseases 10th Revision [ICD-10] codes and complete list of mental health conditions included in [Supplemental Table 1](#), available online); and preoperative pain diagnoses, including back pain, neck pain, arthritis pain, pelvic/scrotal pain, and other pain disorders (ICD-10 codes and complete list of pain diagnoses included in [Supplemental Table 1](#)) (1). Given that varicocelelectomy may be performed to address chronic scrotal pain, cohorts who underwent open or laparoscopic index varicocelelectomy were matched on a diagnosis of male factor infertility (ICD-10 N46.9).

Sensitivity Analysis

Given that general opioid prescribing also occurs outside of surgical procedures, we created a control group of

TABLE 1

Unmatched cohort opioid prescribing rate.

Fertility procedure	Total	No perioperative opioids	Perioperative opioids prescribed
Vasectomy	355,879	268,280 (75.3%)	87,599 (24.6%)
Spermatocectomy	12,553	8,406 (66.9%)	4,147 (33.0%)
Open varicocelectomy (laparoscopic approach excluded)	12,535	8,833 (70.4%)	3,702 (29.5%)
Vasovasostomy or unilateral or bilateral vasoepididymostomy	2,273	1,575 (69.2%)	698 (30.7%)
Testicular incisional biopsy	2,310	1,749 (75.7%)	561 (24.2%)
Laparoscopic varicocelectomy	2,015	1,400 (69.4%)	615 (30.5%)
All surgeries	387,565	290,243 (74.9%)	97,322 (25.1%)

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opioid-naïve men who did not undergo any surgery but who presented for fertility care (and, thus, were likely to be from a similar baseline population as our patients who underwent fertility surgeries). We included men who underwent semen analysis who had not undergone any surgery requiring anesthesia or the fertility procedures of interest in this study for 3 years prior or 2 years after the initial semen analysis, never had a diagnosis of opioid abuse (F11.1) or opioid dependence (F11.2), and had no opioid prescription 1 year prior or 3 months after the index semen analysis—thus, these men were opioid-naïve and without a perioperative indication for new opioid use. The incidence of new opioid use was assessed between 3 and 9 months after the index semen analysis and was compared with new persistent opioid rates in men who underwent the fertility procedures with and without perioperative opioids.

Prolonged Opioid Use Analysis

The secondary outcome of interest was whether new persistent opioid use (3–9 months after the index procedure) would result in prolonged opioid use (9–24 months after the index procedure). To assess this, we combined all aforementioned fertility procedures and compared 5 cohorts: men with no initial opioids immediately before or after the index procedure and no opioid prescription in the 3–9-month follow-up; men with no initial opioids immediately before or after the index procedure but had at least 1 opioid prescription in the 3–9-month follow-up; men with initial opioid prescription either 2 weeks before or 1 month before the index procedure and no opioid prescription in the 3–9-month follow-up; men with initial opioid prescription either 2 weeks before or 1 month before the index procedure and had at least 1 opioid prescription in the 3–9-month follow-up; and men with no surgical procedures 2 years before an index semen analysis and no opioid prescriptions in the 9 months after the index semen analysis. Men were excluded if they ever had a diagnosis of opioid abuse (F11.1) or opioid dependence (F11.2) at any time before the index procedure. Additionally, men were excluded if they had any surgical procedure (CPT Concept ID: 1003143) requiring anesthesia (CPT Concept ID: 1002796) between 1 month and 2 years after the index fertility procedure.

The outcome of prolonged opioid use was defined as receipt of an opioid prescription (CN101) between 9 and 24 months after the index procedure. Confounding variables

were controlled for using propensity score matching for age, race/ethnicity, type of fertility procedure, smoking status, mental health diagnoses, and preoperative pain diagnoses. The risk ratios (RRs) and mean number of opioid prescriptions among men who received opioid prescription were generated in the 9–24-month period after the index period.

Statistical Analysis

We used 1:1 greedy nearest-neighbor propensity score matching to control for confounding variables through the TriNetX platform. A sensitivity analysis was performed by serially excluding matching variables or variable groups and comparing the RR of developing new persistent opioid when all variables were included in the propensity matching analysis. Statistical analysis was performed using Python and R software. We determined that the 2 groups had minimal differences after balancing because the standardized differences between propensity scores were <0.1 (9).

RESULTS

A total of 387,565 men aged 18–70 years who underwent a fertility procedure and who met the eligibility criteria were included initially. Most men underwent a vasectomy ($n = 355,879$, 91.8%); spermatocoe excision was the second most common procedure in our cohort ($n = 12,553$, 3.2%), and open varicocele was the third ($n = 12,535$, 3.2%) (Table 1). A total of 2,273 men underwent VV or vasoepididymostomy (VE), 2,310 men underwent testicular incisional biopsy, and 2,015 men underwent laparoscopic varicocelectomy. Overall, 290,243 men (74.9%) did not receive a perioperative opioid prescription, whereas 97,322 (25.1%) did receive an opioid prescription. Opioid prescribing was most frequent for men who underwent spermatocectomy (33.0%), followed by VV or VE (30.7%), and then laparoscopic varicocelectomy (30.5%) and open varicocelectomy (29.5%). The procedures that least often resulted in perioperative opioid prescription were incisional testicular biopsy (24.2%) and vasectomy (24.6%). Men who did or did not receive an opioid prescription in the perioperative period were of similar age at baseline (38.3 ± 7.7 and 38.5 ± 7.4 years), with a range of 18–70 years (Supplemental Table 2, available online).

After propensity score matching, a total of 97,215 men were included in each cohort. The baseline and post-propensity score-matched baseline characteristics for

TABLE 2

Risk of new persistent opioid use stratified by procedure in a propensity score–matched cohort.

	Open varicocelelectomy ^a	
	No perioperative opioids	Perioperative opioid Rx
No. of men	3,686	3,686
Opioid Rx in the 3–9-mo follow-up, n(%)	71 (1.93%)	186 (5.05%)
Risk ratio (95% CI)	—	2.62 (2.00–3.43)
Mean ± SD, No. of Rx ^b	1.48 ± 1.21	1.32 ± 0.88
	VV or VE	
	No perioperative opioids	Perioperative opioid Rx
No. of men	662	662
Opioid Rx in the 3–9-mo follow-up, n(%)	14 (2.11%)	33 (4.98%)
Risk ratio (95% CI)	—	2.36 (1.27–4.36)
Mean ± SD, No. of Rx ^b	1.07 ± 0.27	1.03 ± 0.17
	Vasectomy	
	No perioperative opioids	Perioperative opioid Rx
No. of men	87,598	87,598
Opioid Rx in the 3–9-mo follow-up, n(%)	1,945 (2.22%)	3,998 (4.56%)
Risk ratio (95% CI)	—	2.06 (1.95–2.17)
Mean ± SD, No. of Rx ^b	1.35 ± 0.96	1.42 ± 1.13
	Testicular incisional biopsy	
	No perioperative opioids	Perioperative opioid Rx
No. of men	541	541
Opioid Rx in the 3–9-mo follow-up, n(%)	12 (2.22%)	43 (7.95%)
Risk ratio (95% CI)	—	3.58 (1.91–6.72)
Mean ± SD, No. of Rx ^b	1.25 ± 0.45	1.58 ± 1.26
	Spermatocoele excision	
	No perioperative opioids	Perioperative opioid Rx
No. of men	4,133	4,133
Opioid Rx in the 3–9-mo follow-up, n(%)	129 (3.12%)	322 (7.79%)
Risk ratio (95% CI)	—	2.50 (2.04–3.05)
Mean ± SD, No. of Rx ^b	1.52 ± 1.20	1.53 ± 1.18
	Laparoscopic varicocelelectomy ^a	
	No perioperative opioids	Perioperative opioid Rx
No. of men	595	595
Opioid Rx in the 3–9-mo follow-up, n(%)	14 (2.35%)	29 (4.87%)
Risk ratio (95% CI)	—	2.07 (1.11–3.88)
Mean ± SD, No. of Rx ^b	1.07 ± 0.27	1.14 ± 0.44

Note: For each procedure, men who did not receive a prescription for opioids after surgery were compared with men who did receive a prescription for opioids after surgery. Risk ratios and 95% CIs were generated via propensity score–matched cohorts matched on age, race/ethnicity, smoking status, mental health diagnoses, and preoperative pain diagnoses. Bolded to indicate significance. CI, confidence interval; Rx = prescription; SD = standard deviation; VE = vasospermidystomy; VV = vasovasostomy.

^a Propensity score matched on male factor infertility diagnosis as well.

^b Patients with 0 instances excluded from calculations.

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each procedure are presented in [Supplemental Table 3](#) (available online).

Overall, across all fertility procedures, 4.6%–8.0% of men who received a perioperative opioid prescription developed new persistent opioid use, whereas 1.9%–3.1% of those without a perioperative opioid prescription developed new persistent opioid use. When evaluating all fertility procedures together, 4.7% of men who received a perioperative opioid prescription went on to develop new persistent opioid use, whereas 2.2% of those who did not receive a perioperative opioid prescription developed new persistent opioid use (RR, 2.16; 95% confidence interval [CI], 2.05–2.27; number

needed to harm, 39). When excluding men who underwent vasectomy and assessing only men who underwent male fertility procedures, 6.0% of those who received perioperative opioids went on to develop new persistent opioid use compared with 2.4% of those who did not receive perioperative opioids (RR, 2.54; 95% CI, 2.19–2.95). When assessing each procedure individually, men who underwent open varicocelelectomy were at higher risk of developing new persistent opioid use when perioperative opioids were prescribed (RR, 2.62; 95% CI, 2.00–3.43). Men who underwent VV or unilateral or bilateral VE and who received perioperative opioids also were more likely to develop new persistent opioid use

TABLE 3

Risk of persistent opioid use for all procedures stratified by perioperative and postoperative opioid prescribing.

	Semen analysis only, no surgery
No. of men	4,163
Opioid Rx in the 9–24-mo follow-up, n(%)	288 (6.9%)
Risk ratio (95% CI)	1.26 (1.06–1.49)
Mean ± SD, No. of Rx ^a	1.69 ± 2.10
	No perioperative opioid Rx/no opioids in 3–9 mo
No. of men	4,195
Opioid Rx in the 9–24-mo follow-up, n(%)	231 (5.5%)
Risk ratio (95% CI)	—
Mean ± SD, No. of Rx ^a	1.48 ± 1.67
	Perioperative opioid Rx/ no opioids in 3–9 mo
No. of men	4,193
Opioid Rx in the 9–24-mo follow-up, n(%)	390 (9.3%)
Risk ratio (95% CI)	1.69 (1.44–1.98)
Mean ± SD, No. of Rx ^a	1.52 ± 1.20
	No perioperative opioid Rx/opioid Rx in 3–9 mo
No. of men	4,139
Opioid Rx in the 9–24-mo follow-up, n(%)	1031 (24.9%)
Risk ratio (95% CI)	4.52 (3.95–5.18)
Mean ± SD, No. of Rx ^a	3.22 ± 4.2
	Perioperative opioid Rx/ opioid Rx in 3–9 mo
No. of men	4,195
Opioid Rx in the 9–24-mo follow-up, n(%)	1192 (28.4%)
Risk ratio (95% confidence interval)	5.16 (4.51–5.90)
Mean ± SD, No. of Rx ^a	2.95 ± 4.15

Note: Each group was compared for the risk ratios to men who received no opioid after surgery and no opioids in the 3–9-month follow-up. Risk ratios and 95% confidence intervals were generated from propensity score–matched cohorts matched on age, race/ethnicity, smoking status, mental health diagnoses, and preoperative pain diagnoses. Bolded to indicate significance. CI, confidence interval; Rx = prescription; SD = standard deviation.

^a Patients with 0 instances excluded from calculations.

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(RR, 2.36; 95% CI, 1.27–4.36). A similar risk of developing new persistent opioid use after perioperative opioid prescribing was noted in men who underwent vasectomy (RR, 2.06; 95% CI, 1.95–2.17), testicular incisional biopsy (RR, 3.56; 95% CI, 1.91–6.72), spermatocele excision (RR, 2.50; 95% CI, 2.04–3.05), and laparoscopic varicocelectomy (RR, 2.07; 95% CI, 1.11–3.88) (Table 2).

We assessed whether the risk of developing new persistent opioid use differed over time; from 2010 to 2015, men were prescribed perioperative opioids 21.8% of the time after fertility procedures with an increased risk of new persistent opioid use if they had received a perioperative opioid prescription (RR, 2.40; 95% CI, 2.23–2.57). From 2016 to 2021, rate of perioperative opioid prescriptions increased to 27.9%; however, men had a less strong risk of developing new persistent opioid use (RR, 1.87; 95% CI, 1.75–2.02).

There was no significant difference in the mean number of opioid prescriptions in the 3–9-month follow-up window when comparing men with no perioperative opioids prescribed with those with perioperative opioid prescriptions ($P > .05$). We also assessed whether engagement with the healthcare system created a detection bias for later diagnosis of persistent opioid use. When assessing follow-up visits in the 3–9 months, there was no significant difference in the frequency of follow-up between the 2 groups (25.8% for men who received perioperative opioids and 25.5% for those who did not receive perioperative opioids, $P = .16$). For those who received perioperative opioids, the duration of continuous enrollment >24 months was 90%, and that for those who did not receive an opioid prescription was 91%. On serial exclusion of matching variables or variable groups, none of the variables greatly changed the RR of developing new persistent opioid use when compared with that when all variables were included in the propensity matching analysis (Supplemental Table 4, available online).

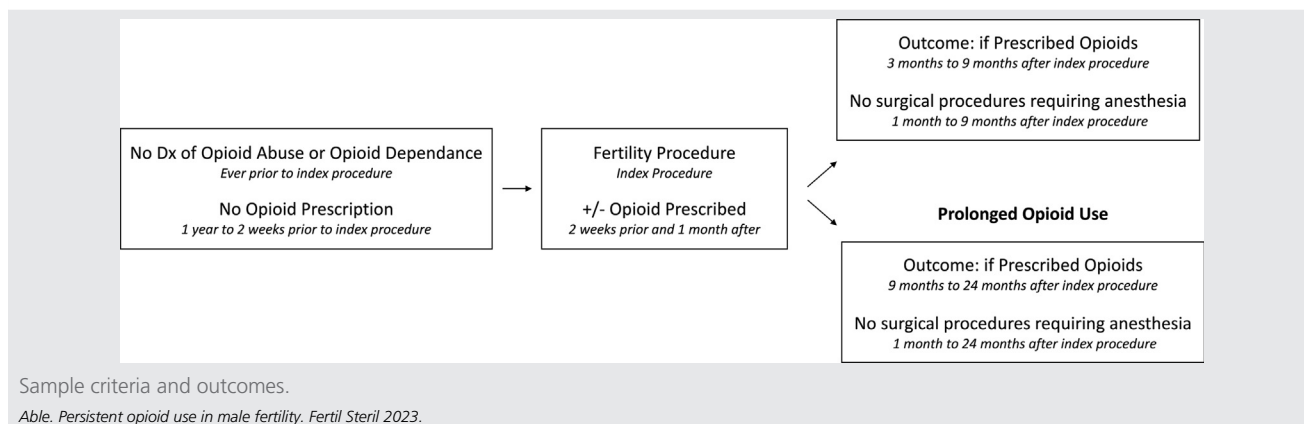
Next, we compared men who underwent fertility procedures with a cohort of control men who underwent initial semen analysis without a surgical procedure 3 years prior or 2 years after their index semen analysis. The rates of opioid prescriptions at 3–9 months were higher in the control group who did not undergo a procedure than in men who received no opioid prescriptions in the perioperative period (2.65% vs. 2.15%, respectively) (RR, 0.81; 95% CI, 0.76–0.87). The rates of opioid prescriptions at 3–9 months were higher in men who received opioid prescriptions perioperatively (4.60%) than in control men who had not undergone a surgical procedure (2.72%) (RR, 1.69; 95% CI, 1.59–1.80) (Table 3).

When assessing prolonged opioid use 9–24 months after the index procedure, we found that men who received perioperative opioid prescriptions and who required opioids in the 3–9-month period after the index procedure had the highest rates of new persistent opioid use (28.4%) compared with those who received no perioperative opioids or opioids at 3–9 months after the index procedure (5.5%) (RR, 5.16; 95% CI, 4.51–5.90). Men with no perioperative opioid prescriptions but with opioid prescriptions at 3–9 months postoperatively also exhibited high rates of new persistent opioid use (24.9%). The rates were lower in men who initially were prescribed opioid after surgery but did not require opioids 3–9 months postoperatively (9.3%). Finally, in men who did not undergo surgical procedures but only had an initial semen analysis, the rate of opioid use 9–24 months after the initial semen analysis (6.9%) was higher than in men who underwent a fertility procedure and who received no opioids perioperatively or 3–9 months after (5.5%) (RR, 1.26; 95% CI, 1.06–1.49) (Table 3 and Supplemental Table 5, available online).

DISCUSSION

We demonstrate a strong association between opioid prescribing after fertility procedures and future new persistent opioid use. To our knowledge, this is the first study to assess the risk of new persistent opioid use after varicocelectomy, spermatocele excision, VV, VE, or testicular incisional biopsy

FIGURE 1



and the largest study to assess the rates of new persistent opioid use in men who underwent vasectomy (5, 10, 11).

Our rates of new persistent opioid use are in line with prior studies assessing opioid use after minor procedures. Brummett et al. (1) found the rates of new persistent opioid used to be 5% in patients who underwent minor surgeries, such as the following: varicose vein removal; laparoscopic cholecystectomy; laparoscopic appendectomy; transurethral prostate surgery; parathyroidectomy; and carpal tunnel procedure. When comparing the rates of new persistent opioid use specifically in men who underwent vasectomy, our rates are slightly lower than the results from the study by Barham et al. (10) (incidence of new persistent opioid use of 7.8% in the opioid cohort compared with 1.5% in the nonopioid cohort). Our results for new persistent opioid use after perioperative opioid prescribing (4.6%) are similar to the rates reported by Berger et al. (11) for men after vasectomy (4.1%). Overall, our findings demonstrate a consistency with already published studies assessing new persistent opioid use in men who underwent vasectomy.

Although the rates of new persistent opioid use are relatively low, these rates are similar to or exceed the rates of other known complications after male fertility procedures. Of men with a perioperative opioid prescription, 4.6%–8.0% develop new persistent opioid use (compared with 1.9%–3.1% who did not receive an opioid prescription). The vasectomy failure rates are $\leq 1\%$, the symptomatic hematoma and infection rates are 1%–2%, and the chronic scrotal pain rates are 1%–2% (12). Varicocele recurrence and hydrocele occur in 1.1% and 0.4%, respectively, of men with microsurgical varicolectomy and 4.3% and 2.8% of men with laparoscopic varicolectomy (13). In VVs, complications such as wound infection, prolonged pain, hematoma, and testicular loss are rare, and the rates of late failure range between 0 and 12% (14, 15). Thus, when counseling patients about the risks and benefits of a procedure, urologists already counsel about the risk of complications and should counsel their patients about the similar level of risk of new persistent opioid use, especially if opioids are prescribed in the perioperative period.

The American Urological Association position statement on opioid use urges providers to counsel patients and

caregivers about the safe use, proper storage, and disposal of opioid medications with every opioid prescription. Where possible, the American Urological Association statement encourages the use of nonnarcotic pain medications when appropriate and to prescribe the “lowest dose and lowest potency” to adequately control pain when narcotics are indicated and to use the “Opioid Analgesic Patient Counseling Guide” when counseling patients (16).

Although opioid prescribing in moderation may seem relatively harmless, a study assessing perioperative opioid use in men who underwent surgeries at the Veterans Health Administration found that postoperative opioid prescribing was associated with higher rates of opioid use disorders (5.0% with and 2.4% without postoperative opioid prescribing) and opioid overdoses (2.1% with and 1.0% without postoperative opioid prescribing) (17). Our study demonstrated that postoperative new persistent opioid use was strongly associated with prolonged opioid use up to 24 months—for men who required opioids in the 3–9-month postoperative period, as many as 25%–28% of them would continue to require opioid prescriptions at 9–24 months. Although persistent pain can be real (and sometimes difficult for surgeons to manage), urologists may have to critically look at these patients who are continuing to need opioids for minor procedures when multiple months out. A more active approach of bringing these patients back to the office, talking with them, and assessing whether nonnarcotic pain medications or alternative strategies may be more beneficial could help to stem a long-term dependence on narcotics rather than simply re-prescribing an additional course of opioids. Given that the limitations of this database do not allow for individual details, future studies are likely needed to describe this population who needs opioids in the 3–9-month postoperative period and to describe the risk factors that are additionally predictive of developing long opioid use.

Our study has notable strengths and weaknesses. Using a large claims database, we were able to include 380,000 men (31,000 fertility procedures when excluding vasectomies), increasing the power of the analysis. As with all retrospective studies, this study is dependent on the completeness and

quality of the recorded data; however, the ICD-10 codes have been shown to be valid in determining patient outcomes (18). One strength of this database is that the electronic medical record data are linked with insurance and pharmaceutical claims data; thus, if an individual were to receive opioids at an institution not included within the TriNetX network, this would still be captured as part of the pharmaceutical claims data, suggesting that although only approximately 25% of men in each group saw a provider in either a clinic or emergency department in the 3–9 months, most opioid prescriptions would be captured. The weaknesses of our study include that the TriNetX database does not capture the amount of opioid consumption or the dosages of opioids prescribed. Additionally, we could not determine whether postoperative opioid pain medications were related to another procedure or diagnosis; however, we eliminated all patients with claims related to another surgery requiring anesthesia after the index procedure. Finally, the analytics available within the TriNetX database interface only allow for propensity score matching rather than multivariate regression analysis, which would provide information about the influence of the included independent variables in addition to the exposure of interest—thus, we are limited to only making conclusions about the exposure after created our matched cohorts.

In conclusion, new persistent opioid use is a known risk factor for future opioid abuse and opioid overdose. Perioperative opioid prescription after fertility procedures is associated with double the risk of new persistent opioid use in opioid-naïve men. For every 39 men who are prescribed an opioid after a fertility procedure, 1 man will develop persistent opioid use. Up to 28% of men with new persistent opioid use will go on to have prolonged opioid prescriptions up to 2 years after the index procedure. Lastly, the rates of new persistent opioid use are on par with the most frequent adverse events after fertility procedures. It is imperative that urologists counsel their patients about this risk when prescribing perioperative opioids and consider ways to mitigate the risk by using multimodal, nonnarcotic medications.

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La prescripción perioperatoria de opioides después de procedimientos de fertilidad masculina se asocia con un nuevo uso persistente de opioides: análisis retrospectivo de una gran base de datos de reclamaciones.

Objetivo: Evaluar el riesgo de un nuevo uso persistente de opioides en hombres sin experiencia previa con opioides que se sometieron a procedimientos de fertilidad masculina.

Diseño: Estudio de cohorte retrospectivo utilizando una base de datos de reclamaciones.

Entorno: Una base de datos que vincula datos de registros médicos electrónicos y reclamaciones, que evalúa a hombres que se sometieron a procedimientos de fertilidad entre 2010 y 2021.

Paciente(s): Hombres sin tratamiento previo con opioides que se sometieron a procedimientos de fertilidad (varicocelectomía abierta o laparoscópica, escisión de espermatocelo y biopsia por escisión o incisión testicular) sin intervención quirúrgica adicional que requiera anestesia en los 2 años posteriores al procedimiento índice. Aquellos casos con y sin recetas perioperatorias de opiáceos fueron emparejados por puntuación de propensión por edad, raza/etnicidad, tabaquismo, diagnósticos de salud mental y diagnósticos de dolor preoperatorio.

Intervención(es): Prescripción perioperatoria de opioides.

Principales resultados medibles: El resultado primario fue la incidencia del nuevo uso persistente de opioides (prescripción de opioides de 3 a 9 meses después del procedimiento de índice de fertilidad). El resultado secundario fue el uso prolongado de opioides (prescripción de opioides de 9 a 24 meses después del procedimiento de índice de fertilidad).

Resultado(s): Se identificó un total de 387.565 hombres que se sometieron a procedimientos de fertilidad, de los cuales el 25,1% recibió prescripción de opioides. Después de emparejar el puntaje de propensión, se incluyeron 97,215 hombres; el 4,7 % de los hombres que recibieron una receta de opioides perioperatorios desarrollaron un nuevo uso persistente de opioides en comparación con el 2,2 % de los que no tenían una receta de opioides perioperatorios (cociente de riesgos, 2,16; intervalo de confianza del 95 %, 2,05–2,27; número necesario para dañar, 39). Al evaluar cada procedimiento de fertilidad único de forma independiente, los hombres que recibieron opioides perioperatorios tenían probabilidades estadísticamente más altas de desarrollar un nuevo uso persistente de opioides para todos los tipos de procedimientos. Los hombres con un nuevo uso persistente de opioides tenían muchas más probabilidades de continuar y desarrollar un uso prolongado de opioides que los hombres sin un nuevo uso persistente de opioides.

Conclusión(es): La prescripción de opioides después de los procedimientos de fertilidad masculina se asocia con un riesgo significativo de nuevo uso persistente de opioides, lo que enfatiza la importancia de la prescripción juiciosa de opioides para los procedimientos de fertilidad masculina.