



Opioid prescribing after urologic surgery: we are part of the problem and part of the solution—an invited commentary on “an opioid prescription for men undergoing minor urologic surgery is associated with an increased risk of new persistent opioid use”

Matthew J. Ziegelmann¹, Bridget L. Findlay¹, Cameron J. Britton¹, Elizabeth B. Habermann²

¹Department of Urology, Mayo Clinic, Rochester, MN, USA; ²The Robert D. and Patricia E. Kern Center for the Science of Healthcare Delivery Surgical Outcomes Program, Mayo Clinic, Rochester, MN, USA

Correspondence to: Matthew J. Ziegelmann. Department of Urology, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905, USA.

Email: Ziegelmann.matthew@mayo.edu.

Provenance and Peer review: This article was commissioned by the editorial office, *Translational Andrology and Urology*. The article did not undergo external peer review.

Comment on: Welk B, McClure JA, Clarke C, *et al.* An Opioid Prescription for Men Undergoing Minor Urologic Surgery Is Associated with an Increased Risk of New Persistent Opioid Use. *Eur Urol* 2020;77:68-75.

Submitted Apr 17, 2020. Accepted for publication May 11, 2020.

doi: 10.21037/tau-2020-05

View this article at: <http://dx.doi.org/10.21037/tau-2020-05>

According to the United States (US) Center for Disease Control, an estimated 23,200 persons died in the US from prescription opioid overdose between 1999 and 2018 (1). In 2018 alone almost 15,000 prescription opioid-related deaths occurred, accounting for 32% of all drug overdose deaths (1). These concerns are not isolated to the US, as demonstrated by the United Nations' attempts to recognize and act upon global concerns related to drug misuse and abuse (2-4).

The opioid epidemic stems in large part from an overly optimistic outlook on addiction risks in patients with new exposure to opioid pain medications prescribed as part of routine medical care. A short letter published in the *New England Journal of Medicine* in 1980 set off a dramatic change in the medical community's approach to pain management with unforeseen consequences (5). In just five sentences, the authors made the unsubstantiated conclusion that addiction is a rare phenomenon in patients who receive prescription narcotic medications without prior history of abuse. Countless authors would go on to cite this paragraph as evidence to support substantial increases in opioid prescribing that were realized over the subsequent three decades (6). As “pain” became known anecdotally as the “fifth vital sign”, patient satisfaction became inextricably

linked to this outcome (7). This led to an environment in which healthcare providers were incentivized to provide higher quantities and doses of opioids to ensure higher scores on patient satisfaction surveys, often linked to physician payment plans (7,8). To add fuel to the fire, misguided motives driven by corporate profits further contributed to the drastic uptick in opioid prescribing (7).

There is ample evidence that surgeons have contributed to the current public health crisis through over-prescribing in the postoperative period. Surgeons prescribe approximately 3–10% of all opioid medications (9-11). In some instances, this initial exposure can result in prolonged medication use, misuse, or abuse even after recovery from the incident procedure. Rates of persistent or prolonged opioid use in previously opioid-naïve surgical patients vary widely from 0.01% to 15% depending on cohort and outcome definitions (12,13). Today more than ever, in the setting of astronomical health care expenditures, the potential downstream impact of opioid misuse is highly relevant. Lee *et al.* showed that new persistent opioid use postoperatively is associated with an average \$1,500 per patient increase in healthcare expenditures, resulting from more frequent hospital readmissions and ambulatory care visits (14).

In the January 2020 issue of *European Urology*, Welk *et al.* evaluated the prevalence of persistent opioid use in a cohort of over 91,000 male patients who underwent one of several “minor” urologic surgeries (vasectomy, transurethral resection of the prostate, urethrotomy, hydrocelectomy, spermatocelectomy, and circumcision) between 2013–2016 in Ontario, Canada using multiple linked-datasets (15). Analyses using these linked data sources are ripe for answering questions surrounding opioid prescribing patterns as there are mandatory reporting policies in place under the Canadian national healthcare system. To limit the impact of prior or chronic opioid exposure, patients with a history of opioid exposure within the preceding 180 days were excluded, along with those who were recently hospitalized or seen in the emergency department. This is similar to other definitions of “opioid-naïve” patients reported in the literature.

Within their cohort, 35% of the patients undergoing urologic procedures filled an opioid prescription within the first five days postoperatively. This is striking as the majority of these “minor” procedures are perceived to rarely if ever require opioids to manage pain, especially beyond the first few days after the procedure. The median morphine equivalents (MEQs) in those who received opioids was 113 mg, an amount that is significantly greater than reported and recommended for other minor/minimally invasive urologic procedures in modern-era guidelines (16,17). This likely stems in part from the timeframe over which this analysis was derived. Surgeons’ contribution to the opioid epidemic was only beginning to reach the forefront of public perception towards the end of the study period. In essence, the prescribing practices included in the current report represent findings in the era prior to our drive to promote opioid stewardship.

Persistent use in previously *opioid-naïve* patients, defined as filling at least two separate opioid prescriptions between 9–15 months after the incident urologic procedure, was seen in 1.6% of patients overall. Of those patients who filled an opioid prescription postoperatively, 2.02% had evidence of persistent use at 9–15 months after the index procedure, compared with 1.35% of patients who did not immediately fill an opioid prescription [adjusted odds ratio 1.43 (95% CI: 1.26–1.62, $P < 0.001$). There was also a 3-fold higher rate of emergency room visits and/or hospital admissions for opioid overdose in those patients who filled an opioid prescription postoperatively.

The rate of persistent opioid use identified by Welk *et al.*

is notably lower than previous reports detailing outcomes in urologic surgery populations, where it has been estimated that 6–9% of patients show evidence of persistent use at three-months after surgery (13,18,19). Using a similar dataset and rigorous methodology, Hosier and colleagues found a 9% rate of persistent opioid use at three-months postoperatively (after initial perioperative exposure) in a cohort of nearly 102,000 patients who underwent treatment for urolithiasis from 2013–2017 (20). In contrast, as Welk *et al.* emphasize, their definition of persistent is more restrictive compared to other studies, requiring at least two separate opioid medication prescription refills at 9–15 months after surgery (15). The more restrictive definition likely accounts for some of the discrepancy seen in the rate of persistent use relative to other reports, but the conclusions drawn by Welk *et al.* remain extremely concerning. Specifically, receiving an opioid prescription within the immediate postoperative period, even after minor urologic procedures, was associated with a 43% increased odds of new persistent use beyond one year after surgery.

One could also surmise that opioid fills beyond 9–12 months postoperatively may be associated with an entirely unrelated circumstance. For example, a patient may undergo another procedure, or may develop an illness or injury resulting in the need for opioid medications. However, even at 3–6 months after surgery, Welk *et al.* identified a 33% increase in the odds of repeatedly filling opioid prescriptions in those patients who were exposed to opioids in the immediate postoperative period (15). To further assess the influence of other medical/surgical illness, the authors performed a sensitivity analysis to account for hospitalizations or other operative procedures occurring during the similar timeframe. This once again supported their outcomes [odds ratio 1.45 (95% CI: 1.28–1.65; $P < 0.01$) favoring a higher likelihood of persistent use in patients initially exposed to opioids postoperatively]. Additional models evaluated the impact of physician prescribing habits (i.e., those who were most likely to always or never prescribe opioids), medical comorbidities, and even a negative control assessment using the diagnoses of shingles or malignancy, lending further support to the rigor of their dataset and the reliability of the reported outcomes.

These findings are extremely important, and lend credence to our efforts to minimize opioid exposure for our patients whenever possible. Yet, there are limitations to the current analysis that must be acknowledged (15). For example, the quantity of opioids consumed by patients who

filled their prescriptions is unknown. Previous work has shown that up to 60% of opioids prescribed at discharge from urologic surgery remained unused, suggesting a disconnect between patient needs and provider assumptions regarding postoperative pain (21). Further, non-opioid alternative interventions to minimize and manage pain control were not explored, despite their ability to contribute to pain management (15). Wide-spread clinician concerns regarding patient satisfaction and postoperative pain control are not unfounded, and urologists and other surgical specialists must balance optimizing pain control while minimizing risks of adverse medication-related outcomes for their patients. Patient satisfaction scores may be linked to certain measures of surgical quality, but, by the same token, opioid prescribing does not appear to be highly-linked with higher patient satisfaction scores in most instances (22).

Urologists are at the forefront in developing novel treatment protocols for postoperative pain. For example, multiple enhanced recovery after surgery (ERAS) protocols have been proposed to optimize perioperative and postoperative outcomes with the use of local anesthetic blocks, anti-inflammatories (ibuprofen, meloxicam, celecoxib), and anticonvulsants (gabapentin, pregabalin) (23,24). Our group has also seen early success with implementation of an opioid guideline to promote standardization amongst larger groups of surgeons (25). These and other novel non-opioid pain regimens seem especially relevant for minor endo-urologic and penile/scrotal cases where the degree and duration of anticipated postoperative pain is minimal, and they are just as likely to optimize patient satisfaction when compared to opioid-based regimens. Future work will enhance our ability to minimize untoward downstream effects while ensuring the best outcomes during the recovery process for our patients.

In conclusion, Welk *et al.* are to be congratulated for their important work assessing risks for persistent or prolonged opioid use in patients who undergo minor urological procedures. Their findings serve as an important reminder of the role urologists have in curbing the opioid epidemic. The challenge we face moving forward is toeing the line between appropriate postoperative pain management and the inherent risks with opioid medications as we seek to provide the highest level care for our patients.

Acknowledgments

Funding: None.

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/tau-2020-05>). MJZ reports personal fees from Paradigm Medical Communications, outside the submitted work. The other authors have no conflicts of interest to declare.

Ethical Statement: the authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Cite this article as: Ziegelmann MJ, Findlay BL, Britton CJ, Habermann EB. Opioid prescribing after urologic surgery: we are part of the problem and part of the solution—an invited commentary on “an opioid prescription for men undergoing minor urologic surgery is associated with an increased risk of new persistent opioid use”. *Transl Androl Urol* 2020;9(3):997-1000. doi:10.21037/tau-2020-05