



## Platinum Priority – Brief Correspondence

Editorial by Katherine Theisen and Benjamin J. Davies on pp. 219–220 of this issue

# A Prospective Cohort Study of Postdischarge Opioid Practices After Radical Prostatectomy: The ORIOLES Initiative

Hiten D. Patel<sup>a,\*</sup>, Arnav Srivastava<sup>a</sup>, Neil D. Patel<sup>b</sup>, Farzana A. Faisal<sup>a</sup>, Wesley Ludwig<sup>a</sup>, Gregory A. Joice<sup>a</sup>, Zeyad R. Schwien<sup>a</sup>, Mohamad E. Allaf<sup>a</sup>, Misop Han<sup>a</sup>, Amin S. Herati<sup>a</sup>

<sup>a</sup> The James Buchanan Brady Urological Institute and Department of Urology, Johns Hopkins University School of Medicine, Baltimore, MD, USA; <sup>b</sup> Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University School of Medicine, Baltimore, MD, USA

### Article info

#### Article history:

Accepted October 4, 2018

#### Associate Editor:

Giacomo Novara

#### Keywords:

Opioid analgesics  
Surgery  
Surgical recovery  
Radical prostatectomy  
Postoperative pain  
Prostate cancer

### Abstract

Opioid pain medications are overprescribed, but few data are available to help in appropriate tailoring of postdischarge opioid prescriptions after surgery. Prior studies are retrospective and based on incomplete responses (<50%) to questionnaires, with small sample sizes for any particular surgery. The ORIOLES initiative was a prospective cohort study (2017–2018) designed to measure postdischarge opioid prescribing and use and clinical predictors of use for consecutive patients after radical prostatectomy. The objectives were to establish a postdischarge opioid reference value to meet the needs of >80% of patients and compare open and robotic surgery. A total of 205 adult patients were enrolled, with 100% completing follow-up. In units of oral morphine equivalents (OMEQ), a median of 225 mg was prescribed and 22.5 mg used. There was no difference by surgical approach or among patients with a history of pain-related diagnoses. Overall, 77% of postdischarge opioid medication was unused, with 84% of patients requiring  $\leq 112.5$  mg OMEQ. Only 9% of patients appropriately disposed of leftover medication. Approximately 5% reported continued incisional pain due to surgery at 30 d, but none required continued opioid medication use. Prescribing more opioids was independently associated with greater opioid use in adjusted models.

**Patient summary:** In this report, we looked at opioid medication use following discharge after radical prostatectomy. We found that 77% of opioid pain medication prescribed was unused, with 84% of patients using less than half of their prescription. Prescribing more opioids was associated with greater use; only 9% of patients appropriately disposed of leftover medication.

© 2018 European Association of Urology. Published by Elsevier B.V. All rights reserved.

\* Corresponding author. James Buchanan Brady Urological Institute, The Johns Hopkins University School of Medicine, 600 N. Wolfe Street, Baltimore, MD 21287, USA. Tel. +1 618 5344942; Fax: +1 410 9550833.

E-mail address: [hitenpatel@jhmi.edu](mailto:hitenpatel@jhmi.edu) (H.D. Patel).

More than 40 000 opioid-related deaths occur in the USA annually, with twice as many due to prescription opioid medications compared to heroin [1]. The trend is increasing across all age groups, with physicians serving as the primary

source of prescriptions for nonmedical use [2]. Surgical providers have contributed to the epidemic, with an estimated 5.9–6.5% of patients experiencing new persistent opioid use >90 d after major or minor surgery [3].



Unfortunately, few data are available to help in appropriate tailoring of postdischarge opioid prescriptions after surgery. Few studies have assessed actual postdischarge analgesia use. A recent systematic review identified only six studies involving 810 patients across all surgical fields, and noted that the majority of medication prescribed is ultimately unused [4]. In addition, these studies typically relied on questionnaire data from incomplete samples (<50% response rate) or did not report use by individual surgery type because of small sample sizes [5–7]. Therefore, guidelines attempting to make surgery-specific recommendations are based on poor evidence or, more often, none at all.

The ORIOLES initiative was implemented at Johns Hopkins Medical Institutions to prospectively measure postdischarge opioid prescribing and subsequent opioid use and disposal after a high-volume operation, radical prostatectomy (RP). The primary objective was to quantify the amounts prescribed and used to establish an appropriate prescribing reference value. Use by surgical approach (open vs robotic) was compared and predictors of opioid use were also evaluated.

The ORIOLES study (NCT03536065) was initiated to improve opioid prescribing practices for RP at the Johns Hopkins Hospital and Johns Hopkins Bayview Hospital. A provider-recommended oral morphine equivalent (OMEQ) reference value was determined to be 180 mg (Supplementary material).

With institutional review board approval, data on opioid prescriptions were prospectively tracked for consecutive patients undergoing RP enrolled in a randomized trial with

an unrelated endpoint (NCT03006562; PREVENTER) from August 2017 to January 2018 (Supplementary Fig. 1). The anticipated initial sample size was 200 patients assuming 1:3 enrollment from open ( $n = 50$ ) and robotic ( $n = 150$ ). Data, outcomes, and statistical analysis are described in the Supplementary material, with tablet equivalents referring to 5 mg of oxycodone.

A total of 205 consecutive patients (56 open, 149 robotic) across nine surgeons were prospectively evaluated. Patients had similar baseline demographic, clinical, and disease characteristics by surgical approach (Supplementary Table 1). Perioperative outcomes were also comparable except for lower blood loss among robotic patients (Supplementary Table 2). A detailed comorbidity evaluation showed a relative healthy cohort, but 20% had a pain-related diagnosis (Supplementary Table 3). Greater than 90% of patients received oxycodone, with an overall OMEQ mean of 227 mg and median of 225 mg (30 tablets; Table 1, Fig. 1A).

The rate of complete 30-d follow-up was 100%. The mean OMEQ used was 52.5 mg (23% of OMEQ prescribed; median 22.5 mg [3 tablets]) with no difference between open and robotic surgery (Table 1, Supplemental Table 4, Fig. 1B,C). Only 9% of patients appropriately disposed of leftover medication by 30 d (drop off or flushed) while 87% had medication at home. A total of ten patients (4.9%) reported continued incisional pain at 30 d, but none reported continued opioid medication use.

In multivariable models, surgical approach, operative time, comorbidity, and history of a pain-related diagnosis were not significant predictors of greater OMEQ used (Supplementary Table 4). Only African-American race was

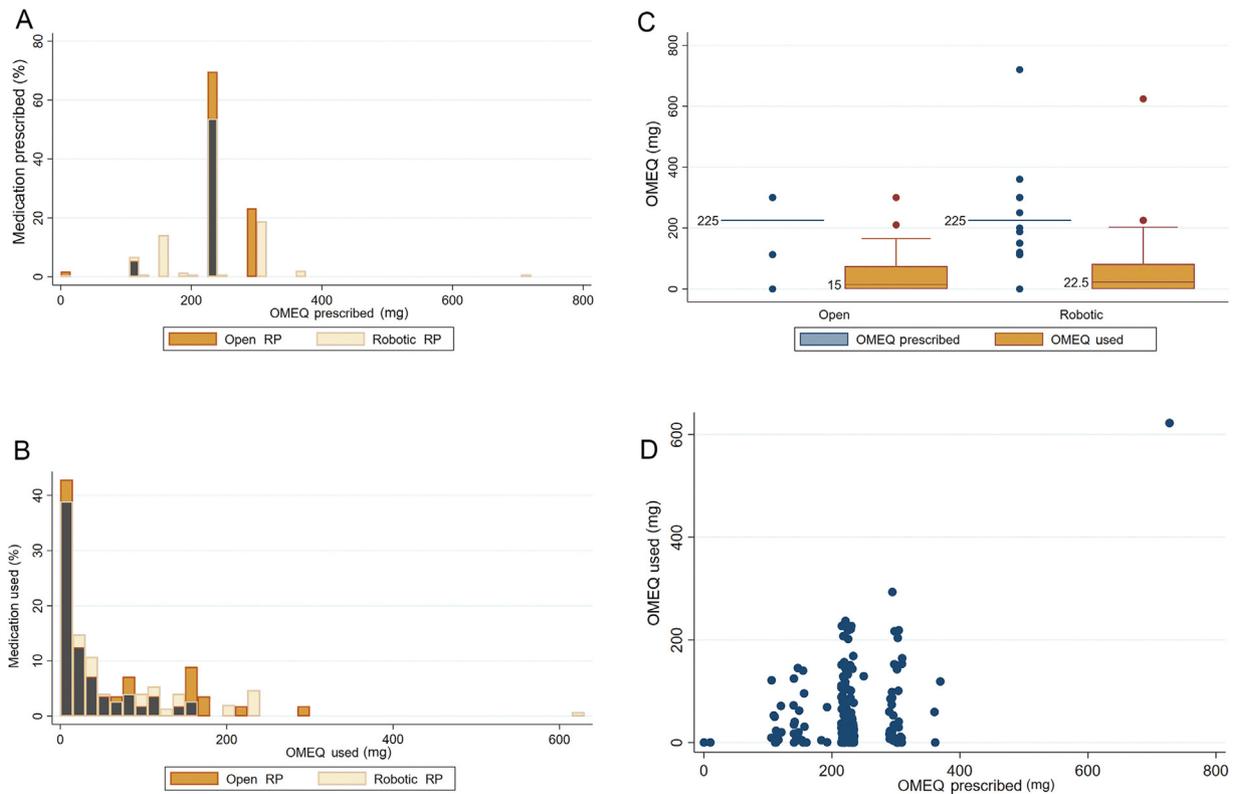
**Table 1 – Postdischarge analgesia prescribed and used and method of disposal by surgical approach for RP in ORIOLES**

	Open RP	Robotic RP	<i>p</i> value <sup>a</sup>
Patients ( <i>n</i> )	56	149	
<b>Opioid prescribing pattern</b>			
Opioid medication prescribed, <i>n</i> (%)			
Oxycodone	55 (98)	137 (92)	0.2
Hydromorphone	0 (0)	5 (3.4)	
Tramadol	0 (0)	6 (4.0)	
No opioid	1 (1.8)	1 (0.7)	
Mean number of pills prescribed (SD)			
Oxycodone 5 mg only	32.58 (7.41)	29.34 (7.07)	0.02
OMEQ prescribed	232 (53.7)	224 (72.0)	0.5
<b>Opioid/analgesia use and disposal</b>			
Mean number of pills used (SD)			
Acetaminophen	40 (71.4)	106 (71.1)	1
NSAID	18 (32.1)	46 (30.9)	0.9
OMEQ	50.5 (67.5)	53.19 (78.6)	0.8
Proportion overprescribed (%)	78	76	–
Used all opioid medication Rx, <i>n</i> (%)	1 (1.8)	8 (5.4)	0.3
Never filled an opioid Rx, <i>n</i> (%) <sup>b</sup>	13 (23)	10 (6.7)	<0.01
Opioid disposal, <i>n</i> (%)			
Not disposed, have at home	31 (74)	120 (92)	0.02
Disposed, medication drop-off	4 (9.5)	6 (4.6)	
Disposed, flushed	4 (9.5)	2 (1.5)	
Disposed, thrown out	2 (4.8)	3 (2.3)	
Disposed, other method	1 (2.4)	0 (0.0)	

RP = radical prostatectomy; SD = standard deviation; OMEQ = opioid morphine equivalents; NSAID = nonsteroidal anti-inflammatory drug; Rx = prescription.

<sup>a</sup> Student's *t* test for continuous variables and a  $\chi^2$  test for categorical variables.

<sup>b</sup> One surgeon performing open RP routinely provided the postoperative opioid prescription in hand rather than sending it directly to the pharmacy.



**Fig. 1 – (A) Total oral morphine equivalents (OMEQ) prescribed and (B) total OMEQ used after radical prostatectomy (RP) by surgical approach. (C) Box plot of OMEQ prescribed and used. (D) Scatter plot of the association between the total amount prescribed and the total amount used for patients in the ORIOLES initiative.**

associated with greater use (+30.8 mg OMEQ, 4 tablets;  $p = 0.04$ ). Notably, greater OMEQ prescribed was significantly associated with greater OMEQ used after multivariable adjustment and in mixed models regardless of outlier exclusion (Supplementary Table 5, Fig. 1D, and Supplementary Fig. 2). For each additional OMEQ prescribed, 22% (95% confidence interval 5.7–38%) was used. Sensitivity analyses confirmed associations of similar effect size.

The reach of the opioid epidemic includes postsurgical care; the majority of opioid medication prescribed is not used, contributing to subsequent persistent use [4]. However, there are few data to guide surgery-specific prescribing. In our prospective cohort study, 77% of prescribed medication was never used after RP, with no differences in OMEQ prescribed and used between open and robotic surgery. A cutoff of  $\leq 112.5$  mg OMEQ used ( $\leq 15$  tablets) accounted for 83.9% of the cohort and could constitute an appropriate reference standard to reduce opioid prescriptions by 50% from the current average (30 tablets), and is notably less than the provider-recommended 180 mg OMEQ reference value (24 tablets).

We also demonstrated that a pain-related diagnosis was not sufficient to identify patients who would require higher use of opioid medication after discharge. Instead, prescribing a higher quantity of opioid medication was independently associated with greater opioid medication use (22% use per additional OMEQ prescribed). This finding has not been previously demonstrated to the best of our knowledge.

It suggests that patients may use additional opioid medication simply because they have more available rather than because of surgical or clinical factors. The association with African-American race is probably due to unmeasured confounding (eg, socioeconomic status), and lack of association with over-the-counter medications due to a general recommendation that patients rely on acetaminophen before their prescribed opioid.

Only 9% of patients appropriately disposed of excess medication after 30 d, with 87% reporting retention at home despite no requirement for pain alleviation. Improving appropriate disposal of leftover opioid medication is a relevant objective in conjunction with reducing prescribing. Pain requirements for individual patients vary; some groups, including Michigan-OPEN, suggest that 75% may be an appropriate threshold on which to base postsurgical prescriptions [8]. While prior studies noted that pain improves relatively quickly after robotic RP, there are concerns about undertreatment of pain, lower patient satisfaction, and difficulty with access after discharge for patients requiring additional medication [9]. Given these concerns, data from ORIOLES are now being used to set a clinical prescribing guideline at Johns Hopkins to facilitate patient education and recovery in a post-intervention phase.

Our study should be considered in the context of a few potential limitations. Daily opioid medication use was not tracked. In addition, although pain-related diagnoses were

thoroughly assessed, a better definition of the high-risk subset may exist. Finally, the study was conducted at two hospitals within Johns Hopkins Medicine with more robotic than open procedures, which may limit the generalizability. Despite the limitations, the study provides the first prospective assessment of postdischarge analgesia use for consecutive patients undergoing RP.

In conclusion, 77% of postdischarge opioid medication for RP was unused in ORIOLES, with 84% of patients requiring  $\leq 112.5$  mg OMEQ. Although no patients required opioid mediation by 30 d after surgery, only 9% reported appropriate disposal. Prescribing a greater quantity of medication was independently associated with greater opioid use, while surgical and clinical characteristics were not helpful in predicting greater use. Further prospective studies are needed to tailor postdischarge opioid prescribing for other procedures.

**Author contributions:** Hiten D. Patel had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** H.D. Patel, N.D. Patel, Han, Allaf, Herati.

**Acquisition of data:** H.D. Patel, Faisal, Ludwig, Joice, Schwen.

**Analysis and interpretation of data:** H.D. Patel, Srivastava, N.D. Patel.

**Drafting of the manuscript:** H.D. Patel, Srivastava, N.D. Patel.

**Critical revision of the manuscript for important intellectual content:** H.D. Patel, Srivastava, N.D. Patel, Faisal, Ludwig, Joice, Schwen, Allaf, Han, Herati.

**Statistical analysis:** H.D. Patel, Srivastava.

**Obtaining funding:** None.

**Administrative, technical, or material support:** None.

**Supervision:** Allaf, Han, Herati.

**Other:** None.

**Financial disclosures:** Hiten D. Patel certifies that all conflicts of interest, including specific financial interests and relationships and affiliations relevant to the subject matter or materials discussed in the manuscript (eg, employment/affiliation, grants or funding, consultancies, honoraria, stock ownership or options, expert testimony, royalties, or patents filed, received, or pending), are the following: None.

**Funding/Support and role of the sponsor:** None.

**Acknowledgments:** We would like to acknowledge the investigators and staff of the PREVENTER trial (NCT03006562) for assisting with data collection and patient follow-up.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.eururo.2018.10.013>.

## References

- [1] Hedegaard H, Warner M, Miniño AM. Drug overdose deaths in the United States, 1999–2016. NCHS Data Brief, no 294. Hyattsville, MD: National Center for Health Statistics; 2017.
- [2] Substance Abuse, Mental Health Services, Administration. Results from the 2013 National Survey on Drug Use and Health: Summary of National Findings. NSDUH series H-48, HHS publication no. (SMA) 14-4863. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014.
- [3] Brummett CM, Waljee JF, Goesling J, et al. New persistent opioid use after minor and major surgical procedures in US adults. *JAMA Surg* 2017;152:e170504.
- [4] Bicket MC, Long JJ, Pronovost PJ, Alexander GC, Wu CL. Prescription opioid analgesics commonly unused after surgery: a systematic review. *JAMA Surg* 2017;152:1066–71.
- [5] Bates C, Laciak R, Southwick A, Bishoff J. Overprescription of post-operative narcotics: a look at postoperative pain medication delivery, consumption and disposal in urological practice. *J Urol* 2011;185: 551–5.
- [6] Bartels K, Mayes LM, Dingmann C, Bullard KJ, Hopfer CJ, Binswanger IA. Opioid use and storage patterns by patients after hospital discharge following surgery. *PLoS One* 2016;11:e0147972.
- [7] Hill MV, McMahan ML, Stucke RS, Barth Jr RJ. Wide variation and excessive dosage of opioid prescriptions for common general surgical procedures. *Ann Surg* 2017;265:709–14.
- [8] Howard R, Waljee J, Brummett C, Englesbe M, Lee J. Reduction in opioid prescribing through evidence-based prescribing guidelines. *JAMA Surg* 2018;153:285–7.
- [9] Woldu SL, Weinberg AC, Bergman A, et al. Pain and analgesic use after robot-assisted radical prostatectomy. *J Endourol* 2014;28:544–8.