

UC Davis

UC Davis Previously Published Works

Title

Increased risk of new persistent opioid use in pediatric and young adult patients with kidney stones

Permalink

<https://escholarship.org/uc/item/9mp8t6qt>

Journal

Canadian Urological Association Journal, 14(8)

ISSN

1911-6470

Authors

Hosier, Gregory W
McGregor, Thomas
Beiko, Darren
[et al.](#)

Publication Date

2020-08-01

DOI

10.5489/cuaj.6796

Peer reviewed



Increased risk of new persistent opioid use in pediatric and young adult patients with kidney stones

Gregory W. Hosier, MD, MSc¹; Thomas McGregor, MD¹; Darren Beiko, MD¹; Gregory E. Tasian, MD, MSc, MSCE²; Christopher Booth, MD^{3,4}; Marlo Whitehead⁴; D. Robert Siemens, MD^{1,3}

¹Department of Urology, Queen's University, Kingston, ON; ²Department of Pediatric Urology, Children's Hospital of Philadelphia, Philadelphia, PA, United States; ³Department of Oncology, Queen's University, Kingston, ON, Canada; ⁴Division of Cancer Care and Epidemiology, Queen's University Cancer Research Institute, Queen's University, Kingston, ON, Canada

Cite as: *Can Urol Assoc J* 2020;14(8):237-44. <http://dx.doi.org/10.5489/cuaj.6796>

Abstract

Introduction: Adolescents and young adults are a vulnerable patient population for development of substance use disorder. However, the long-term impact of opioid prescribing in young adult patients with renal colic is not known. Our objective was to describe rates of opioid prescription and identify risk factors for persistent opioid use in patients age 25 years or younger with renal colic from kidney stones.

Methods: Using previously validated, linked administrative databases, we performed a population-based, retrospective cohort study of opioid-naïve patients age 25 years or younger with renal colic between July 1, 2013 and September 30, 2017 in Ontario. All family practitioner, urgent care, and specialist visits in the province were captured. Our primary outcome was persistent opioid use, defined as filling a prescription for an opioid between 91 and 180 days after initial visit. Ontario uses a narcotic monitoring system, which captures all opioids dispensed in the province.

Results: Of the 6962 patients identified, 56% were prescribed an opioid at presentation and 34% of those were dispensed more than 200 oral morphine equivalents. There was persistent opioid use in 313 (8.1%) patients who filled an initial opioid prescription. In adjusted analysis, those prescribed an opioid initially had a significantly higher risk of persistent opioid use (odds ratio [OR] 1.85; 95% confidence interval [CI] 1.50–2.29) and opioid overdose (OR 3.45; 1.08–11.04). There was a dose-dependent increase in risk of persistent opioid use with escalating initial opioid dose. History of mental illness (OR 1.32; 1.02–1.71) and need for surgery (OR 1.71; 1.24–2.34) were also associated with persistent opioid use.

Conclusions: Among patients with kidney stones age 25 years or younger, filling an opioid prescription after presentation is associated with an increased risk of persistent opioid use 3–6 months later and a higher risk of serious long-term complications, such as opioid overdose.

Introduction

Prescription opioid misuse is a leading cause of unintentional injury and death among adolescents and young adults.¹

From 1992–2010, opioid-related deaths increased from 0.9% to 5.8% of all deaths among those aged 15–24 years in Ontario.² The increase in opioid-related mortality in this age group was second only to those aged 25–34 years.² The vast majority of adolescent and young adult (age 16–25) heroin users began drug use with prescription opioids.³ In a survey of 6220 students in grade 12 who were followed through to age 23, medical opioid use before high school graduation was associated with a 33% higher risk of future opioid misuse after high school.⁴ Consequently, pediatric and young adults represent a particularly vulnerable patient population for development of misuse after opioid exposure.

The incidence of pediatric urolithiasis has been steadily increasing in North America for the past several decades.^{5,6} Between 1997 and 2012, mean annual incidence of nephrolithiasis increased 1% annually from 206–239 per 100 000 persons.⁵ The increase in pediatric urolithiasis is mainly driven by an increase in the adolescent age group, with those aged 15–17 demonstrating the most dramatic increase.⁶ Alongside these changes in incidence, there has been an increase in the economic burden of pediatric urolithiasis of 20% after controlling for inflation.⁷

In a previous population-based study of all patients presenting with renal colic, we have previously reported 9% of opioid-naïve patients developed new persistent opioid use 3–6 months after initial presentation with kidney stones.⁸ Other studies have also demonstrated that adults, after undergoing ureteroscopy, have a high risk of continued opioid use.^{9,10} However, the long-term impact of opioid prescribing in pediatric and young adult patients with urolithiasis is not known. The present objective was to extend our previous observations on subsequent opioid-related outcomes and the risk factors for persistent opioid use in patients age 25 years or younger with urolithiasis.

Methods

Study design

We performed a population-based, retrospective cohort study of opioid-naïve patients age 25 years or younger diagnosed with urolithiasis in Ontario between July 1, 2013 and September 30, 2017. This was based on a parent study describing all patients in the province presenting with renal colic over the study period.⁸ The index stone event was defined as the first urolithiasis visit within the study time frame. Exclusion criteria were: 1) opioid prescriptions within one year before the index visit for urolithiasis; 2) those who required palliative care services within one year before or after the index visit for urolithiasis; and 3) patients with prior urolithiasis visits within the previous year. The Narcotic Monitoring System (NMS) in Ontario began in July 2012. Because we wanted to exclude patients with prior opioid use in the preceding year, we started our analysis time a year after this date. For all other data, the lookback period was at least eight years. This study was approved by the Queen's University Health Sciences and Affiliated Hospitals Research Ethics Board.

Data sources

Linked administrative databases were used through the Institute for Clinical Evaluative Sciences (ICES). These databases capture all family practitioner visits, emergency department visits, specialist clinic visits, inpatient stays, procedures, and opioid prescription data in the province. Each database is routinely used for research purposes and has been previously validated.¹¹ Records from the NMS were linked with the National Ambulatory Care Reporting System, Discharge Abstract Database, OHIP Physician Claims Database, the Ontario Drug Benefit plan, Registered Persons Database, Ontario Mental Health Reporting System, and Same Day Surgery Database. The quality and coding accuracy of these databases has been demonstrated in re-abstraction studies.¹²⁻¹⁴ Statistics Canada 2016 census data was used to infer income quintile by linking postal code of residence to the mean household income by dissemination area.

Outcomes

The primary outcome was persistent opioid use, defined as one or more dispensed opioid prescription(s) within 0–90 days after index urolithiasis visit (i.e., initial prescription) and one or more dispensed prescription(s) for opioids within 91–180 days after index urolithiasis visit (i.e., renewal prescription). Although this definition does not necessarily equate to opioid addiction, it is a potential risk factor for future substance use disorders as well as diversion, and the

timeframes described are consistent with other studies.^{15,16} Secondary outcomes were filling opioid prescriptions 180–365 days after the index visit, filling opioid prescriptions 365–730 days after the index visit, opioid addiction, opioid overdose, and hyperalgesia (as a surrogate for a chronic pain diagnosis) based on ICD-9 and ICD-10 codes.¹⁷⁻¹⁹ These outcomes were considered as positive if they occurred from index stone event to the time of data abstraction (September 30, 2018).

Covariates

Covariates included age, sex, income quintiles, Charlson comorbidity index, patient comorbidities (including mental health services utilization, given its strong association with substance misuse). Other variables included urban or rural geographic location (rural defined as <10 000 people per township), history of remote stone surgery (1–6 years prior to the index date), enrollment with a family practitioner (FP), prescriber specialty, number of emergency department (ED) visits during the acute stone episode, number of FP visits during the acute stone episode, number of days, and total oral morphine equivalents (OMEs) prescribed during the index stone episode.² Surgery-specific factors included type of surgery, number of surgeries, stent insertion, or episodes of sepsis related to the stone. Combined procedural codes were treated according to previously described algorithms.²⁰

To estimate the duration of the acute stone event from administrative data, we considered the date of index urolithiasis diagnosis plus 30 days after the last urolithiasis visit or 30 days after any procedure date. This was done because the time needed for stone passage is variable and may take anywhere from a few days to weeks. Additionally, following stone surgery, passage of stone fragments may take several weeks.

Statistical analysis

Univariate and multivariable logistic regression models were used to identify factors associated with persistent opioid use. A sensitivity analysis for those patients that had a stone intervention used the date of the last procedure as the index time. For all statistical methods, a two-sided p-value of <0.05 was considered statistically significant. As per institutional policy, cells with less than six patients were not reported and, in some cases, ranges were given due to privacy concerns. Data were analysed using SAS Stat 14.3 (SAS Institute Inc, Cary NC, U.S.).

Results

After exclusion, 6962 patients met study criteria (Fig. 1) and were followed for a median of three (interquartile range [IQR] 2–4) years. The median age of the cohort was 21 (IQR 19–24) years and 52% were women (Table 1). Overall, 56%

of patients were prescribed opioids during the acute stone period, of which 17% were dispensed seven or more days of opioids and 34% were dispensed more than 200 OME (Table 2). Among those initially prescribed opioids, 313 individuals (8%) continued to fill opioid prescriptions 3–6 months after the initial visit compared to 138 (4%) that were not prescribed opioids initially (Table 3). After adjusting for age, gender, mental health history, neighborhood income quintile, and Charlson index, those prescribed an opioid initially had a significantly higher risk of persistent opioid use (odds ratio [OR] 1.85; 95% confidence interval [CI] 1.50–2.29) and opioid overdose (OR 3.45; 1.08–11.04) compared to those without initial opioid exposure (Table 3). Analysis exploring the dose-response relationship of initial opioid prescription and persistent opioid use showed that those dispensed >300 OME had an increased risk of persistent use compared to those dispensed 1–99 OME (OR 2.21; 95% CI 1.49–3.29; $p < 0.0001$) (Table 4).

Emergency medicine physicians were the most common opioid prescribers (55%), followed by FPs (32%), and urologists (10%) (Table 2). Prescriber specialty was not associated with new persistent opioid use (Table 4).

In multivariable analysis, several other factors were associated with continued opioid use (Table 4). This included higher patient comorbidity, prior mental health services use, history of prior stone surgery, and increasing number of ED visits. The duration of the initial stone event <60 days was associated with lower odds of persistent opioid use (OR 0.62; 95% CI 0.47–0.82).

Surgery was necessary in 11% of the cohort, with the most common surgery type being ureteroscopy (URS) (72%), followed by shock wave lithotripsy (SWL) (18%) and percutane-

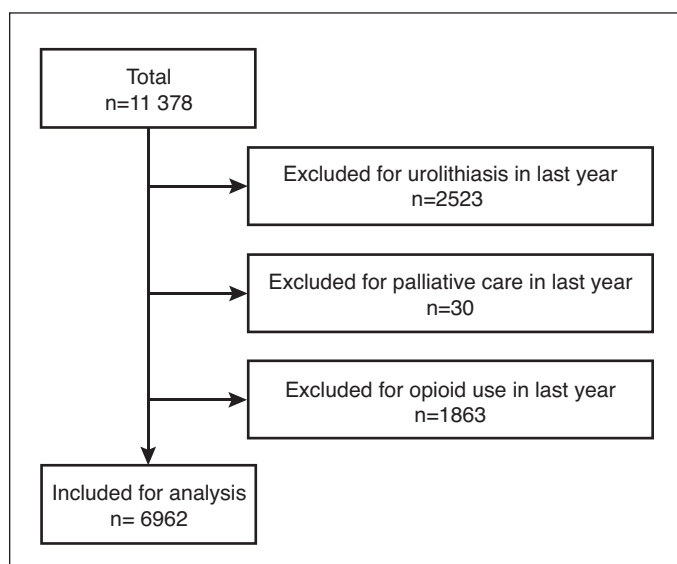


Fig. 1. Flow chart with exclusion criteria of patients age 25 years or younger with urolithiasis in Ontario from 2013–2017.

Table 1. Characteristics of patients with urolithiasis age 25 years or younger in Ontario from 2013–2017

Characteristic	Unexposed to initial opioids n (%) N=3085	Exposed to initial opioids n (%) N=3877	p
Patient-related			
Age at index renal colic			
0–11	250 (8)	63 (2)	<0.001
12–18	695 (23)	684 (17)	
19–21	782 (25)	1122 (29)	
22–25	1358 (44)	2008 (52)	
Sex			
Female	1598 (52)	2014 (52)	0.902
Male	1487 (48)	1863 (48)	
Neighborhood income quintile			
1	727 (24)	890 (23)	0.344
2	659 (21)	817 (21)	
3	604 (20)	743 (19)	
4	576 (19)	691 (18)	
5	508 (16)	721 (19)	
Charlson index			
0	3028 (98)	3856 (99.5)	<0.001
1–2	49 (1.6)	21 (0.5)	
3+	8 (0.3%)	0 (0)	
Geographic			
Urban	2603–2605 (84)	3429 (89)	<0.001
Rural	477 (16)	439 (11)	
Mental health history*			
Any	1,186 (38)	1,606 (41)	0.012
Anxiety treated by GP/FP	648 (21)	881 (23)	0.085
Anxiety treated by psychiatrist	339 (11)	459 (12)	0.269
Anxiety requiring hospitalization	38 (1)	51 (1)	0.758
Mood disorder treated by GP/FP	168 (5)	250 (6)	0.08
Mood disorder treated by psychiatrist	145 (5)	237 (6)	0.01
Mood disorder requiring hospitalization	60 (2)	81 (2)	0.671
Psychosis	21 (1)	41 (1)	0.096
Substance abuse	175 (6)	257 (6)	0.1
Self-harm	54 (2)	68 (1)	0.991
Enrolled with a family practice	2336 (76)	3081 (80)	<0.001
History of stone surgery 1–6 years pre-index	25 (1)	47 (1)	0.1

*Subcategories not mutually exclusive. ED: emergency department; FP: family physician; GP: general practitioner; PCNL: percutaneous nephrolithotomy; SWL: shock wave lithotripsy; URS: ureterorenoscopy.

Table 1 (cont'd). Characteristics of patients with urolithiasis age 25 years or younger in Ontario from 2013–2017

Characteristic	Unexposed to initial opioids n (%) N=3085	Exposed to initial opioids n (%) N=3877	P
Care-related			
# days acute stone episode			
<60	2671 (87)	2990 (77)	<0.001
60+	414 (13)	887 (23)	
# ED visits during acute renal colic episode			
0	2276 (74)	2386 (61)	<0.001
1	645 (21)	945 (25)	
2	115 (4)	327 (8)	
>2	49 (1)	219 (6)	
# GP visits during acute renal colic episode			
0	2096 (68)	2326 (60)	<0.001
1	675 (22)	975 (25)	
2	195 (6)	338 (9)	
>2	119 (4)	238 (6)	
Surgery-related			
Had surgery (within 180 days of index renal colic episode)			
No	2951 (96)	3255 (84)	<0.001
Yes	134 (4)	622 (16)	
Time to surgery from index visit			
<30	91 (68)	425 (68)	0.925
30+	43 (32)	197 (32)	
# of surgeries within 180 days of index renal colic			
1	44 (33)	154 (25)	0.106
2	76 (57)	376 (60)	
>2	14 (10)	92 (15)	
First surgery type			
SWL	29 (22)	110 (18)	0.043
PCNL	20 (15)	56 (9)	
URS	85 (63)	456 (73)	
Stent placement	93 (69)	464 (75)	0.215
Septic stone	45 (34)	235 (38)	0.361

*Subcategories not mutually exclusive. ED: emergency department; FP: family physician; GP: general practitioner; PCNL: percutaneous nephrolithotomy; SWL: shock wave lithotripsy; URS: ureterorenoscopy.

Table 2. Opioid dispensing information for patients with urolithiasis age 25 years or younger during the acute stone episode in Ontario from 2013–2017

Characteristic	N*	n (%)
Narcotic days supplied	3824	
1–2		1008 (26)
3–4		1315 (34)
5–7		862 (23)
>7		639 (17)
Total OME	3817	
1–99		908 (24)
100–150		859 (23)
150–199		733 (19)
200–299		704 (18)
300 +		613 (16)
Prescriber specialty	3329	
Emergency medicine		1822 (55)
Family practitioner		1058 (32)
Urology		326 (10)
Other		123 (3)

*N differs due to incomplete prescription information for some patients. The acute stone episode was defined as the date of index urolithiasis diagnosis plus 30 days after the last urolithiasis visit or 30 days after any stone procedure date. OME: oral morphine equivalents.

ing two interventions having an OR of 4.5 (95% CI 0.86–23.7; $p < 0.0001$) (Table 5). Time to surgery, ureteric stent placement, septic stone presentation, and surgery type (SWL vs. PCNL vs. URS) did not impact the primary outcome.

When we did a sensitivity analysis using varying definitions of persistent opioid use, we found that initial opioid exposure was associated with higher rates of two or more opioid prescriptions (as opposed to one) 3–6 months after the index visit (2 vs. 0.7%), filling opioid prescriptions 6–12 months after the index visit (12 vs. 8%), and filling opioid prescriptions 1–2 years after the index visit (20 vs. 13%; $p < 0.001$ for all) (Table 3).

Discussion

In this population-based cohort study of 6962 patients age 25 years or younger, we found that most patients with urolithiasis were prescribed an opioid at presentation and 8% continued to fill an opioid prescription 3–6 months after initial presentation. After adjusting for several factors, we found that those prescribed an opioid initially had a 1.85 times increased odds of new persistent opioid use 3–6 months after presentation. Importantly, we found an almost 3.5 times increased risk of overdose in pediatric and young adult patients exposed to opioids compared to those without initial opioid exposure. To our knowledge, this is the first study to show increased risk of serious, long-term complications in pediatric and young adult patients exposed to opioids. As the incidence of pediatric urolithiasis has been steadily increasing for the past several

ous nephrolithotomy (PCNL) (10%). Of those who underwent surgery, 68% had surgery within 30 days of the initial index stone visit. Need for surgery was a strong risk factor for persistent opioid use (OR 2.78; 95% CI 2.54–3.04; $p < 0.0001$) (Table 4). Need for multiple surgical interventions was associated with increasing risk of persistent opioid use, with those requir-

Table 3. New persistent opioid use and addiction outcomes in urolithiasis patients age 25 years or younger dispensed opioids from 2013–2017

Characteristic	Unexposed to initial opioids n (%) N=3085	Exposed to initial opioids n (%) N=3877	p	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	p
Persistent opioid use 91–180 days post-index	138 (4.5)	313 (8.1)	<0.001	1.88 (1.53–2.31)	<0.0001	1.85 (1.51–2.29)	<0.0001
Two or more opioid scripts within 91–180 days post-index	21 (0.7)	82 (2.1)	<0.001	3.15 (1.95–5.10)	<0.0001	*	*
Any narcotic dispensed 6–12 months post-index	241 (7.8)	465 (12.0)	<0.001	1.61 (1.37–1.89)	<0.0001	1.55 (1.31–1.83)	<0.0001
Any narcotic dispensed 1–2 years post-index	410 (13.3)	766 (19.8)	<0.001	1.61 (1.41–1.83)	<0.0001	1.52 (1.33–1.74)	<0.0001
Opioid addiction	<6 (0.1)	18 (0.5)	0.013	3-4 (1–12)	<0.03	*	*
Opioid overdose	<6 (0.1)	14 (0.4)	0.059	2-3 (0.5–10)	<0.1	3.45 (1.08–11.0)	0.0366
Opioid hyperalgesia	8 (0.3)	16 (0.4)	0.278	1.59 (0.68–3.73)	0.282	*	*

*Numbers too small for multivariable analysis. Adjusted OR covariates: age, gender, mental health history, neighborhood income quintile, and Charlson comorbidity index. CI: confidence interval; OR odds ratio.

decades,⁵ these results highlight the importance of limiting opioids in this vulnerable patient population.

Rates of 8% new persistent opioid use seen in our study are slightly higher compared to other studies in post-surgical young adult patients. In previously opioid-naïve patients aged 13–21 years who underwent a range of surgical procedures, new persistent opioid use at 3–6 months after surgery was seen in 5% of patients.²¹ Similarly, 5% of adolescent patients 8–25 years old had persistent opioid use after cleft-palate surgery.²² Both these studies used the same definition of the primary outcome as our study. In the current study, 4.5% of patients not initially prescribed opioids filled one or more prescriptions 3–6 months after presentation. Although seemingly quite high, this is consistent with a cross-sectional survey study of over 43 000 citizens in the U.S., which found similar background rates of filling opioid prescriptions of approximately 5%.²³

The current results demonstrate several care- and patient-related factors associated with continued filling of opioid prescriptions and, in many ways, echo results demonstrated in adult patients. Initial opioid exposure in this study was associated with 1.85 increased odds of new persistent opioid use. This was similar to those seen in pediatric and young adult patients receiving opioids following various surgeries, including cholecystectomy (1.13 increased odds) and colectomy (2.33 increased odds).²¹ Consistent with previous reports, these results confirm a dose-dependent increase in the odds of persistent opioid use, with escalating opioid prescription's duration and dose.^{8,24,25} Higher comorbidity and lower socioeconomic status were also risk factors for persistent opioid use in the current study, which is consistent with adult postoperative surgical patients.^{15,16} These results further support the reduced use of opioids in pediatric and young adult urolithiasis patients.

We found that use of mental health services was a significant risk factor for persistent opioid use. In the adult

opioid literature, presence of mental health issues is a strong risk factor for development of new persistent opioid use.^{26,27} In a retrospective study of pediatric patients <21 years old exposed to opioids after surgery, substance abuse history was significantly associated with new persistent opioid use, but mental health history (anxiety and depression) was not.²¹ Differences between these findings and the current study may be due to the inclusion of patients up to 25 years of age.

Surgical stone intervention was an important risk factor for new persistent opioid use in our study, with 1.7 times increased odds of new persistent opioids use. Need for multiple surgical interventions was associated with further increased risk of new persistent opioid use and, unsurprisingly, those requiring surgery had higher rates of initial opioid exposure. Increased initial opioid exposure in those undergoing surgery is likely multifactorial and may be related to the indications for surgery (refractory pain, delayed stone passage), additional use of opioids in the postoperative setting (including for management of stent colic), and more frequent exposure to prescribers in those undergoing surgery.

We found increased new persistent opioid use in those with prolonged acute stone episode (>60 days). This may argue in favor of earlier intervention to allow for earlier resolution of pain and cessation of opioids. However, risk of new persistent opioid use was not different between those with early (<30 days after index visit) compared to late (>30 days after index visit) surgical intervention. Given the administrative nature of the data, it is difficult to draw conclusions from these somewhat contradictory findings. One interpretation may be that those with early surgical intervention represent patients with more severe/refractory pain, while those receiving delayed surgical intervention represent relatively asymptomatic patients. In support of this, there were higher rates of opioid dispensing during the acute stone event among those with a prolonged acute stone episode, but not those with delayed surgery.

Table 4. Factors associated with new persistent opioid use among urolithiasis patients age 25 years or younger initially prescribed opioids in Ontario from 2013–2017 (N=3877)

Characteristic	Rate (%)	Univariate analysis OR (95% CI)	p	Multivariable analysis OR (95% CI)	p
Patient-related					
Age, years					
0–11	2	0.21 (0.03–1.51)	0.18	0.16 (0.02–1.22)	0.22
12–18	9	1.24 (0.87–1.75)		1.20 (0.83–1.70)	
19–21	7	Ref		Ref	
22–25	9	1.20 (0.91–1.6)		1.06 (0.8–1.4)	
Sex					
Female	9	1.22 (0.97–1.5)	0.09	1.15 (0.90–1.48)	0.26
Male	7	Ref		Ref	
Neighborhood income quintile					
1 (low)	9	Ref	0.60	Ref	0.573
2	8	0.86 (0.62–1.22)		0.90 (0.63–1.28)	
3	7	0.76 (0.53–1.09)		0.80 (0.55–1.16)	
4	7	0.75 (0.52–1.09)		0.74 (0.50–1.08)	
5 (high)	9	0.93 (0.66–1.31)		0.99 (0.69–1.42)	
Geographic					
Rural	10	1.35 (0.97–1.88)	0.2141	1.24 (0.87–1.76)	0.4943
Urban	8	Ref		Ref	
Charlson index					
0	8	Ref	0.0130	Ref	0.0070
≥1	24	3.6 (1.31–9.90)		4.51 (1.51–13.49)	
Mental health history					
No	7	Ref	0.0025	Ref	0.0338
Yes	10	1.43 (1.13–1.80)		1.32 (1.02–1.71)	
Substance abuse					
No	8	Ref	0.9522	Ref	0.2456
Yes	8	1.01 (0.64–1.61)		0.74 (0.45–1.23)	
Enrolled with FP					
No	9	1.24 (0.95–1.63)	0.1176	1.31 (0.98–1.74)	0.0676
Yes	8	Ref		Ref	
History of prior stone surgery					
No	8	0.32 (0.16–0.65)	0.0015	0.34 (0.16–0.72)	0.0050
Yes	21	Ref		Ref	
Care-related					
Duration urolithiasis episode					
<60 days	6	0.45 (0.35–0.57)	<0.0001	0.62 (0.47–0.82)	0.0008
>60 days	13	Ref		Ref	
# ED visits for urolithiasis after index visit					
0	6	0.24 (0.17–0.35)	<0.0001	0.49 (0.32–0.74)	0.0059
1	8	0.32 (0.21–0.47)		0.5 (0.33–0.79)	
2	13	0.57 (0.36–0.90)		0.68 (0.42–1.09)	
>2	21	Ref		Ref	

CI: confidence interval; ED: emergency department; FP: family physician; OR: odds ratio.

Limitations of this study include the retrospective nature of the study. Information around the size and location of stones was not captured, as we were using administrative data. The definition of persistent opioid use of filling prescriptions 3–6

months after an acute pain event does not necessarily imply that the full prescription was actually used, nor does it equate to dependence or addiction. However, continued filling of opioid prescriptions cannot be ignored as a significant risk fac-

Table 4 (cont'd). Factors associated with new persistent opioid use among urolithiasis patients age 25 years or younger initially prescribed opioids in Ontario from 2013–2017 (N=3877)

Characteristic	Rate (%)	Univariate analysis OR (95% CI)	p	Multivariable analysis OR (95% CI)	p
Care-related (cont'd)					
# FP visits for urolithiasis after index visit					
0	7	0.40 (0.27–0.59)	<0.0001	0.77 (0.50–1.18)	0.5925
1	8	0.49 (0.32–0.74)		0.83 (0.53–1.31)	
2	11	0.67 (0.41–1.10)		0.93 (0.56–1.56)	
>2	16	Ref		Ref	
Had surgery					
No	7	Ref	<0.0001	Ref	0.0009
Yes	14	2.30 (1.77–2.99)		1.7 (1.24–2.34)	
Opioid-related					
Total oral morphine equivalents during acute stone episode					
1–99	5	Ref	<0.0001	Ref	<0.0001
100–149	6	1.07 (0.71–1.62)		1.0 (0.65–1.52)	
150–199	7	1.29 (0.85–1.95)		1.18 (0.77–1.80)	
200–299	8	1.62 (1.09–2.42)		1.35 (0.90–2.04)	
>300	17	3.79 (2.64–5.44)		2.21 (1.49–3.29)	
Specialty of initial prescriber					
Emergency medicine	7	0.95 (0.61–1.48)	0.4886	1.37 (0.84–2.25)	0.3340
Family practitioner	9	1.2 (0.76–1.90)		1.62 (0.97–2.7)	
Other	9	1.18 (0.56–2.48)		1.05 (0.47–2.38)	
Urology	8	Ref		Ref	

CI: confidence interval; ED: emergency department; FP: family physician; OR: odds ratio.

Table 5. Factors associated with persistent opioid use in those age 25 years or younger initially prescribed opioids 0–90 days after surgery for urolithiasis in Ontario from 2013–2017 (N=756)

Characteristic	Rate (%)	Univariate analysis OR (95% CI)	p	Multivariable analysis OR (95% CI)	p
Time to surgery					
<30 days	10	Ref	0.1823	Ref	0.1740
30 days or more	7	0.61 (0.30–1.26)		0.59 (0.27–1.27)	
# of surgeries					
1	5	Ref	<0.0001	Ref	<0.0001
2	6	1.30 (0.51–3.32)		4.52 (0.86–23.7)	
>2	28	7.46 (2.85–19.57)		29.92 (4.92–181.94)	
Surgery type					
URS	10	Ref	0.8556	Ref	0.4392
PCNL	7	0.74 (0.25–2.16)		0.52 (0.17–1.61)	
SWL	10	0.99 (0.44–2.22)		1.27 (0.46–3.52)	
Stent					
No	7	Ref	0.2282	Ref	0.1878
Yes	10	1.63 (0.74–3.58)		0.32 (0.06–1.74)	
Septic stone					
No	9	Ref	0.7286	Ref	0.4797
Yes	10	1.12 (0.60–2.07)		0.77 (0.38–1.58)	

Outcome of persistent opioid use 91–180 days measured from time of last surgery. CI: confidence interval; OR: odds ratio; PCNL: percutaneous nephrolithotomy; SWL: shock wave lithotripsy; URS: ureterorenoscopy.

tor for future substance use disorder or diversion. Furthermore, it is not possible to infer the indications for persistent opioid use, whether it is for ongoing pain from complications of urolithiasis, other pain conditions, or due to opioid misuse. However, the higher incidence of new persistent use among kidney stone patients with initial opioid exposure compared to those without initial exposure, as well as the dose-dependent relationship between escalating initial opioid dose and higher new persistent opioid use raise concern that initial opioid prescription may prime patients for future opioid misuse. Strengths of the study include our relatively large cohort size for a pediatric and young adult study. Additionally, the use of a province-wide opioid reporting system ensures near complete capture of opioid dispensing information.

Conclusions

Among patients with urolithiasis age 25 years or younger, filling an opioid prescription after stone presentation is associated with an increased risk of persistent opioid use 3–6 months later and a higher risk of serious, long-term complications, including opioid overdose. These results support and highlight the urgent need for appropriate opioid reduction strategies for those with renal colic, especially young patients, who represent a particularly vulnerable population.

Competing interests: Dr. Tasian has been an advisory board member for Allena Pharmaceuticals, Alnylam, Dicerna Pharmaceuticals, and Novome Biotechnology; and has received grants/honoraria from Lumenis. Dr. Siemens has given educational talks for Ferring and has participated in clinical trials supported by Astellas, Janssen, and Pfizer. The remaining authors report no competing personal or financial interests related to this work.

Acknowledgement: This study was supported by the Institute for Clinical Evaluative Sciences (ICES), which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care (MOHLTC). Parts of this material are based on data and information compiled and provided by CIHI. The opinions, results, and conclusions reported in this paper are those of the authors and are independent from the funding sources and CIHI. No endorsement by ICES or the Ontario MOHLTC is intended or should be inferred. Dr. Siemens 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.

This paper has been peer-reviewed

References

- Johnston LD, Miech RA, O'Malley PM, et al. Monitoring the future national survey results on drug use, 1975–2015: Overview, key findings on adolescent drug use [Internet]. 2019 [cited 2020 Jan 9]. Available at: <http://monitoringthefuture.org/pubs.html#monographs>. Accessed June 18, 2020.
- Gomes T, Mamdani MM, Dhalla IA, et al. The burden of premature opioid-related mortality. *Addiction* 2014;109:1482-8. <https://doi.org/10.1111/add.12598>
- Lankenau SE, Teti M, Silva K, et al. Initiation into prescription opioid misuse among young injection drug users. *Int J Drug Policy*. 2012;23:37-44. <https://doi.org/10.1016/j.drugpo.2011.05.014>
- Miech R, Johnston L, O'Malley PM, et al. Prescription opioids in adolescence and future opioid misuse. *Pediatrics* 2015;136:e1169-77. <https://doi.org/10.1542/peds.2015-1364>
- Tasian GE, Ross ME, Song L, et al. Annual incidence of nephrolithiasis among children and adults in South Carolina from 1997–2012. *Clin J Am Soc Nephrol* 2016;11:488-96. <https://doi.org/10.2215/CJN.07610715>
- Alfandary H, Haskin O, Davidovits M, et al. Increasing prevalence of nephrolithiasis and BMI among children: A population-based study. *J Urol* 2018;199:1044-9. <https://doi.org/10.1016/j.juro.2017.10.023>
- Kusumi K, Becknell B, Schwaderer A. Trends in pediatric urolithiasis: Patient characteristics, associated diagnoses, and financial burden. *Pediatr Nephrol* 2015;30:805-10. <https://doi.org/10.1007/s00467-014-3012-3>
- Hosier GW, McGregor T, Beiko D, et al. Persistent opioid use among patients with urolithiasis: A population-based study. *Eur Urol Focus* 2020;6:745-51. <https://doi.org/10.1016/j.euf.2019.08.011>
- Tam CA, Dauw CA, Ghani KR, et al. New Persistent opioid use after outpatient ureteroscopy for upper tract stone treatment. *Urology* 2019;134:103-8. <https://doi.org/10.1016/j.urology.2019.08.042>
- Kang C, Shu X, Herrell SD, et al. Opiate exposure and predictors of increased opiate use after ureteroscopy. *J Endourol* 2019;33:480-5. <https://doi.org/10.1089/end.2018.0796>
- Goel V, Williams J, Anderson G, et al. Patterns of health care in Ontario. ices.on.ca [Internet]. [cited 2019 Mar 29]. Available at: <https://www.ices.on.ca/flip-publication/patterns-of-health-care-2d-edition/files/assets/common/downloads/ICES.pdf>. Accessed June 18, 2020.
- CIHI. CI for HI. CIHI data quality study of the DAD 2017–2018 discharge abstract database. 2018 Apr 27 [cited 2019 Mar 29]. Available at: <https://secure.cihi.ca/estore/productFamily.htm?pf=PFC1762&lang=en&media=0>. Accessed June 18, 2020.
- CIHI. CIHI data quality study of the DAD 2017–2018 national ambulatory care reporting system. [Cited 2019 Mar 29]. Available at: <https://www.cihi.ca/sites/default/files/document/current-year-information-nacs-2017-2018-en-web.pdf>. Accessed July 7, 2020.
- Iron K, Goel V, Williams J. Concordance of hospital discharge abstracts and physician claims for surgical procedures in Ontario. *Work Pap 42 Inst Clin Eval Sci* 1995.
- Clarke H, Soneji N, Ko DT, et al. Rates and risk factors for prolonged opioid use after major surgery: Population-based cohort study. *BMJ* 2014 2014;348:g1251. <https://doi.org/10.1136/bmj.g1251>
- Johnson SP, Chung KC, Zhong L, et al. Risk of prolonged opioid use among opioid-naïve patients following common hand surgery procedures. *J Hand Surg Am* 2016;41:947-57.e3. <https://doi.org/10.1016/j.jhsa.2016.07.113>
- Gladstone E, Smolina K, Morgan SG, et al. Sensitivity and specificity of administrative mortality data for identifying prescription opioid-related deaths. *CMAJ* 2016;188:E67-72. <https://doi.org/10.1503/cmaj.150349>
- Spooner L, Fernandes K, Martins D, et al. High-dose opioid prescribing and opioid-related hospitalization: A population-based study. Schanzer DL, editor. *PLoS One* 2016;11:e0167479. <https://doi.org/10.1371/journal.pone.0167479>
- Ellison J, Walley AY, Feldman JA, et al. Identifying patients for overdose prevention with ICD-9 classification in the emergency department, Massachusetts, 2013–2014. *Public Health Rep* 2016;131:671-5. <https://doi.org/10.1177/0033354916661981>
- Ordon M, Urbach D, Mamdani M, et al. The surgical management of kidney stone disease: A population-based time series analysis. *J Urol* 2014;192:1450-6. <https://doi.org/10.1016/j.juro.2014.05.095>
- Harbaugh CM, Lee JS, Hu HM, et al. Persistent opioid use among pediatric patients after surgery. *Pediatrics* 2018;141:e20172439. <https://doi.org/10.1542/peds.2017-2439>
- Bennett KG, Harbaugh CM, Hu HM, et al. Persistent opioid use among children, adolescents, and young adults after common cleft operations. *J Craniofac Surg* 2018;29:1. <https://doi.org/10.1097/SCS.0000000000004762>
- McCabe SE, West BT, Morales M, et al. Does early onset of non-medical use of prescription drugs predict subsequent prescription drug abuse and dependence? Results from a national study. *Addiction* 2007;102:1920-30. <https://doi.org/10.1111/j.1360-0443.2007.02015.x>
- Shah A, Hayes CJ, Martin BC. Characteristics of initial prescription episodes and likelihood of long-term opioid use – United States, 2006–2015. *MMWR Morb Mortal Wkly Rep* 2017;66:265-9. <https://doi.org/10.15585/mmwr.mm6610a1>
- Deyo RA, Hallvik SE, Hildebran C, et al. Association between initial opioid prescribing patterns and subsequent long-term use among opioid-naïve patients: A statewide retrospective cohort study. *J Gen Intern Med* 2017;32:21-7. <https://doi.org/10.1007/s11606-016-3810-3>
- 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. <https://doi.org/10.1001/jamasurg.2017.0504>
- Sekhri S, Arora NS, Cottrell H, Baerg T, et al. Probability of opioid prescription refilling after surgery: Does initial prescription dose matter? *Ann Surg* 2018;268:271-6. <https://doi.org/10.1097/SLA.0000000000002308>

Correspondence: Dr. Gregory W. Hosier, Department of Urology, Queen's University, Kingston, ON; gregory.hosier@gmail.com