

Health Reports

Association between mothers' postoperative opioid prescriptions and opioid-related events in their children: A population-based cohort study

by Jennifer Bethell, Mark D. Neuman, Brian T. Bateman, Karim S. Ladha, Andrea Hill, Guohua Li, Duminda N. Wijeyesundera, and Hannah Wunsch

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Association between mothers' postoperative opioid prescriptions and opioid-related events in their children: A population-based cohort study

by Jennifer Bethell, Mark D. Neuman, Brian T. Bateman, Karim S. Ladha, Andrea Hill, Guohua Li, Duminda N. Wijeyesundera, and Hannah Wunsch

Abstract

Background: Postoperative opioid prescriptions may be associated with risks of unintentional poisoning and drug diversion in other household members. The objective of this study was to explore the association between mothers' postoperative opioid prescriptions and incidence of opioid-related events in their children (aged 1 to 24 years).

Data and methods: This retrospective cohort study used individually linked administrative health data from Ontario, Canada. A population-based sample of 170,156 opioid-naïve mothers (aged 15 to 64) (see Figure 1) who underwent surgery between 2013 and 2017 in Ontario was linked through birth records to create a cohort of their 283,550 opioid-naïve children (aged 1 to 24). The association between postoperative opioid analgesic prescriptions filled by mothers within seven days of discharge after surgery and opioid-related events (emergency department presentations or inpatient admissions for opioid poisoning, or mental and behavioural disorders attributable to opioid use) in their children within one year of their mother's discharge was assessed.

Results: Overall, 60.4% of the children in the cohort had a mother who filled a postoperative opioid prescription. The incidence of opioid-related events in children in the year after a mother's surgery was low overall ($n=36/283,550$, 0.01%), but higher among children whose mother filled a postoperative opioid prescription ($n=29/171,139$, 0.02%, vs. $n=7/112,411$, 0.01%, $p=0.02$), including in an analysis adjusting for child's age, mother's age, rural residence, neighbourhood income quintile and mother's Charlson comorbidity index score (adjusted odds ratio, 2.42 [95% confidence interval (CI), 1.05 to 5.54], $p=0.04$).

Interpretation: Postoperative opioid prescriptions for mothers may contribute to opioid-related events in their children. These findings further underscore the importance of safe, effective opioid prescribing, as well as of patient and public education about the use, storage and disposal of these medications.

Keywords: surgery, analgesics, opioid, child, adolescent, young adult, prescription drug misuse, drug overdose

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In Ontario, in 2017, there were 1,276 emergency department visits for opioid poisoning among people younger than 25. Among those aged 15 to 24, the rate more than doubled between 2013 and 2017.¹ Both Canadian and American data suggest that people younger than 25 may be experiencing disproportionate opioid-related harms. This age group makes up roughly 1 in 10 of those who were dispensed an opioid, but accounts for 1 in 5 emergency department presentations for opioid poisoning.²⁻⁴ This difference may be related, in part, to illicit opioid use, but evidence also supports another explanation—that some youth access opioids that have been prescribed to others in the household. Survey data from both countries show that, among youth who use opioids, the most common source of these opioids was family or friends.^{5,6} Two case-control studies (also from Canada and the United States) have shown that opioid prescriptions to family members are associated with an increased risk of hospital-treated overdoses in children^{7,8} and young adults.⁸

Postoperative prescriptions are a potentially significant source of opioids. Pain after surgery is one of the most common reasons

for initiating opioid use,^{9,10} but these prescriptions tend to exceed patient need. Therefore, these medications often go unfinished,¹¹ and unused medications are then stored—unsecured—at home.¹² A systematic review of studies describing postoperative opioid oversupply found that, across six studies, 67% to 92% of patients reported having unused opioids, and 42% to 71% of opioids went unused.¹³

The objective of this study was to examine the association between mothers' postoperative opioid prescriptions and opioid-related emergency department presentations or inpatient admissions by their children (aged 1 to 24 years).

Methods

Study sample

This retrospective cohort used population-based data from Ontario, Canada, which included residents eligible for universal health care coverage (nearly the entire population of roughly 14 million people) and captured inpatient admissions (Discharge

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Abstract Database [DAD]), same-day surgical procedures (Same Day Surgery [SDS] Database), opioid prescriptions (Narcotics Monitoring System [NMS]), emergency department presentations (National Ambulatory Care Reporting System), deaths (Office of the Registrar General – Deaths) and individual-level demographic information (Registered Persons Database). These datasets were linked using unique encoded identifiers and analyzed at ICES (a not-for-profit research institute formerly known as the Institute for Clinical Evaluative Sciences). The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board.

The cohort was defined using the DAD and SDS surgical records^{14,15} of females aged 15 to 64 years who had a hospital stay of seven days or less and were discharged home. The accrual period (discharge dates between July 2013 and March 2017) was selected to coincide with the introduction of the NMS in 2012, as well as with the necessary one-year review of these data (see exclusions below). Only one surgical record was retained for each individual. For those with multiple surgeries during the study period, only the first was considered for inclusion. The records of these individuals were then linked to those of their children (aged 1 to 24 years at the time of surgery) using the ICES-derived MOMBABY database, which has linked the inpatient records of delivering mothers and their newborns for births in Ontario since 1988. There are no comparable linkages for fathers or other household members. Young adults—up to age 24—were also included in the cohort, as 62.6% of Canadians aged 20 to 24 still live with their parents, but the proportion declines precipitously thereafter.¹⁶ If the same individual appeared in both cohorts, she was excluded from the mother cohort (and all of her children were subsequently removed from the children cohort). Mothers and all of their children were excluded if either had (1) filled any opioid prescription (including

for methadone or buprenorphine) within one year prior to the surgery (i.e., to create an opioid-naïve cohort), (2) experienced an opioid-related event¹⁷ within one year prior to the surgery (see appendix) or (3) died within one year of the surgery (i.e., to ensure complete follow-up).

Measures

Exposure, i.e., a mother's postoperative opioid analgesic prescription, was defined as a prescription for oral tablet forms of codeine, fentanyl, hydromorphone, meperidine, morphine, oxycodone, pentazocine, tapentadol or tramadol filled within seven days of the surgery (i.e., on the surgery discharge date or within the six subsequent days). The first prescription filled during these seven postoperative days was defined as the index prescription. If more than one opioid prescription was filled on the first day, all records were retained. The primary outcome was an opioid-related event¹⁷ within one year of the mother's surgery discharge date or index prescription date (as applicable). Opioid-related events included emergency department presentations and inpatient admissions for opioid poisoning, or mental and behavioural disorders resulting from opioid use (see appendix for a list of diagnosis codes). Information on age, sex and residential postal code of the mothers and children at the time of surgery was also retained. Postal codes were used to assign rural residence (community with a population of fewer than 10,000 people) and neighbourhood income quintile.¹⁸ Mothers' Charlson comorbidity scores were determined using data from the index surgical record,¹⁹ and their surgeries were categorized by year, as either inpatient or outpatient, and according to the Canadian Classification of Health Interventions.²⁰ Index prescriptions were described according to days' supply and total morphine milligram equivalent (MME)²¹ dose and categorized by type (codeine, hydromorphone, morphine, oxycodone, tramadol, other or multiple).

What is already known on this subject?

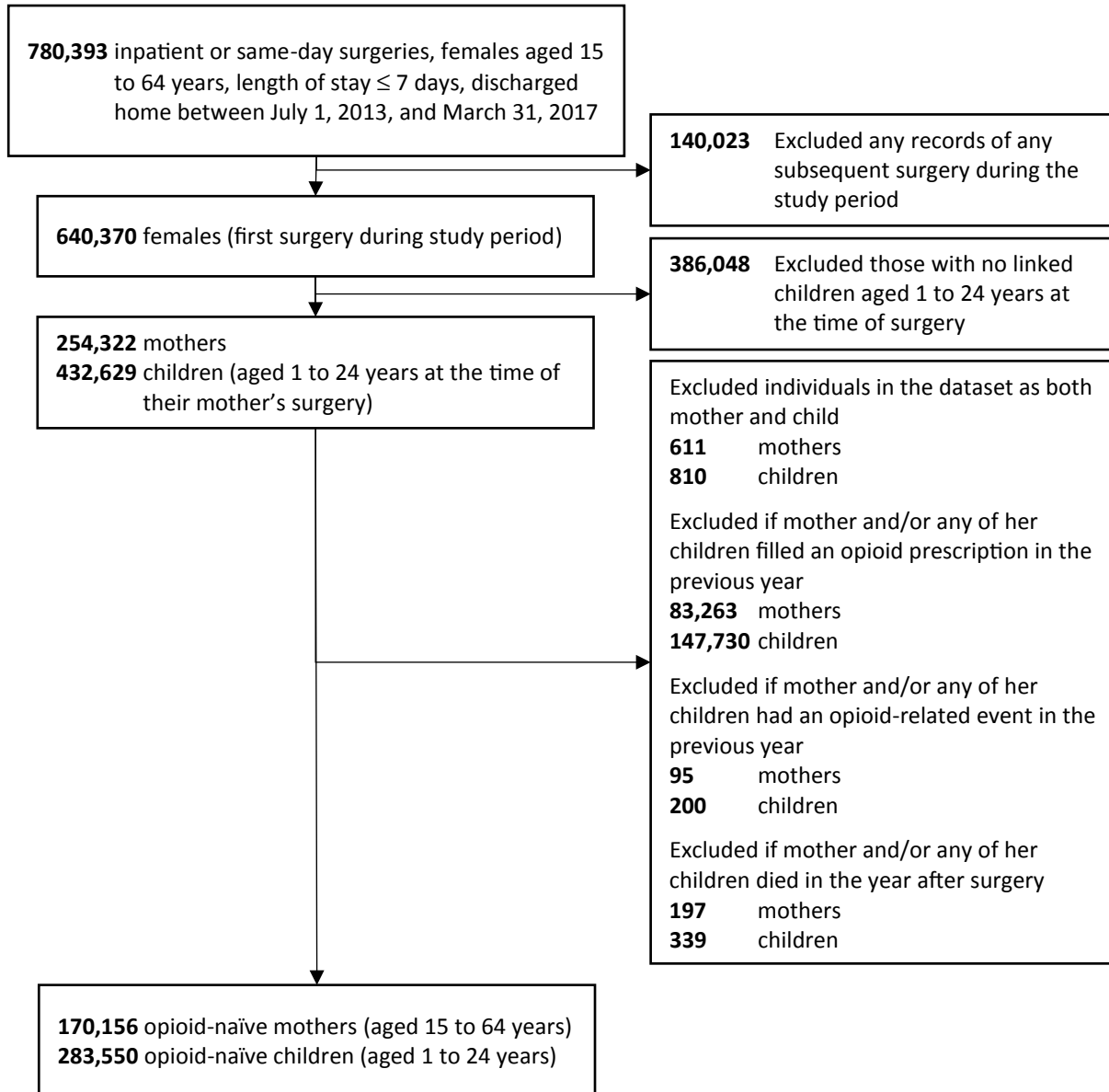
- People younger than 25 may be at risk for opioid-related harms related to unintentional poisoning with and diversion of opioids prescribed to someone else in the household.
- Postoperative prescriptions are a potentially significant source of opioids in the household, as pain after surgery is one of the most common indications for initiating opioids, and these prescriptions often go unfinished and are then stored—unsecured—at home.

What does this study add?

- Postoperative opioid prescriptions for mothers may contribute to opioid-related events in their children.
- These findings further underscore the importance of safe, effective opioid prescribing, as well as of patient and public education on the use, storage and disposal of these medications.

Statistical analysis

Frequencies and proportions (with chi-square tests) means and standard deviations (with t-tests) and medians and interquartile ranges (IQR) were reported to describe characteristics of the mothers and children. The association between mothers' postoperative opioid prescriptions and the risk of opioid-related events in their children was assessed using logistic regression, first unadjusted, then adjusted for child's age, mother's age, rural residence and neighbourhood income quintile—variables selected based on previous findings.^{1-4,22} Four sensitivity analyses were conducted: (1) to account for the potential clustering of children (by mother), one child was randomly selected per mother; (2) to assess for likely diversion (rather than unintentional poisoning), the analysis was restricted to children aged 12 to 24 years; (3) to acknowledge the unique postoperative context of the first year

Figure 1**Selection of a surgical cohort of opioid-naïve mothers (aged 15 to 64 years) and their opioid-naïve children (aged 1 to 24 years), Ontario, Canada, 2013 to 2017**

Source: Authors' compilation.

postpartum (i.e., mother's new baby or child's new sibling), children of mothers who underwent a caesarean section were excluded; and, (4) to account for the possibility of opioid-related deaths, the cohort was recreated without applying the final exclusion, and opioid-related deaths were included in the outcome. Statistical significance was interpreted at $p < 0.05$. Analyses were carried out

using SAS software, Version 9.4 (SAS Institute, Cary, North Carolina).

Results

Cohort characteristics

After exclusions were applied (see Figure 1), the cohort consisted of 283,550 children (see Table 1) linked to 170,156

mothers (see Table 2). Overall, 60.4% of the children had mothers who filled a postoperative opioid prescription. The children of mothers who filled a prescription were older, had older mothers, and were more likely to live in non-rural areas and higher-income neighbourhoods. The most commonly dispensed opioids were oxycodone, codeine, tramadol and hydro-morphone, which together accounted for

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Table 1
Cohort characteristics, opioid-naïve children (aged 1 to 24 years) of opioid-naïve mothers who underwent surgery in Ontario, Canada, July 2013 to March 2017

Characteristic	Total/overall (n=283,550)		Mother filled postoperative opioid prescription (n=171,139)		Mother did not fill postoperative opioid prescription (n=112,411)		P-value [‡]
	mean	standard deviation	mean	standard deviation	mean	standard deviation	p-value [‡]
Age, child, years	10.6	6.6	11.0	6.8	10.0	6.8	<0.001
Age, mother, years	40.2	8.3	40.7	8.2	39.4	8.4	<0.001
	number	percent	number	percent	number	percent	p-value [‡]
Sex, male	146,951	51.8	88,505	51.7	58,446	52.0	0.15
Residence							
Rural	38,571	13.6	22,480	13.1	16,091	14.3	<0.001
Non-rural	244,979	86.4	148,659	86.9	96,320	85.7	N/A
Neighbourhood income quintile							
First (lowest)	49,852	17.6	28,307	16.5	21,545	19.2	<0.001
Second	51,700	18.2	30,502	17.8	21,198	18.9	N/A
Third	57,094	20.1	34,490	20.2	22,604	20.1	N/A
Fourth	64,581	22.8	39,998	23.4	24,583	21.9	N/A
Fifth (highest)	57,930	20.4	36,559	21.4	21,371	19.0	N/A
Missing	2,393	0.8	1,283	0.7	1,110	1.0	N/A

[‡] chi-square (categorical) or t-tests (means)

Note: N/A stands for not applicable (single p-value is reported from chi-square test of cross-tabulated categorical variables).

Sources: 1. Inpatient admissions (Discharge Abstract Database), 2. Same-day surgical procedures (Same Day Surgery Database), 3. Opioid prescriptions (Narcotics Monitoring System), 4. Emergency department presentations (National Ambulatory Care Reporting System), 5. Deaths (Office of the Registrar General – Deaths) and individual-level demographic information (Registered Persons Database), 6. Mother–baby linked database (ICES-derived MOMBABY database).

92.6% of postoperative opioid prescriptions. The median prescription duration was three days (IQR: 3 to 5 days) and the median total MME was 150.0 (IQR: 112.5 to 225.0).

Opioid-related events

Opioid-related events in children in the first year after a mother’s surgery were rare (n=36/283,550, 0.01%). However, the incidence of opioid-related events was higher among the children of mothers who filled a postoperative opioid prescription (n=29/171,139, 0.02% vs. n=7/112,411, 0.01%; unadjusted odds ratio [OR] 2.72 [1.19 to 6.21] p=0.02), including in the adjusted analysis (adjusted OR 2.42 [95% CI, 1.05 to 5.54], p=0.04) (see Table 3). Sensitivity analyses produced similar results, although some associations lost statistical significance (see Table 3). Nevertheless, the unadjusted, adjusted and sensitivity analyses’ odds ratio estimates all fell between 2 and 3. The differences observed were not entirely explained by adjustment variables or clustering (by mother) and also held for specific sub-populations within the cohort.

Discussion

Incidence of opioid-related events in children in the first year after their mother’s surgery was low overall, but comparable to previously published estimates.¹ However, the children of mothers who filled a postoperative opioid prescription had an increased risk of an opioid-related event during this time. These results mirror findings from two previous case–control studies that found that the presence of household opioid prescriptions more than doubles the risk of opioid overdose.^{7,8} However, the focus on surgery identifies a specific context for opioid prescribing and intervention.

Strengths of this study include a large, population-based cohort assembled through a unique mother–child linkage. The results likely generalize to other populations, particularly where the over-prescribing of opioids after surgery appears to be common.²³ In particular, beyond the Canadian context, recent data show that comparable proportions of Canadian and American patients are dispensed a postoperative opioid prescription. However, American patients received significantly higher total quan-

ties of opioids,¹⁹ suggesting an even greater opportunity for diversion.

However, this study has limitations. First, there was no direct measure of whether children lived with their mother or accessed their mother’s prescription opioids. Second, similar to previously published estimates for this age group and time period,¹ opioid-related events were rare. Health administrative data are widely used for researching and reporting opioid-related harms,¹⁻⁴ but include only those who present to hospital. These data likely underestimate the actual extent of opioid diversion in this population, particularly for older children who may be less likely to present to hospital in the context of opioid use¹⁻⁶ or self-harm.²⁴ Furthermore, given the infrequency of the outcome, the analyses were not elaborated upon, including to disaggregate events by intent (e.g., self-harm or unintentional poisoning), assess risk according to opioid prescription characteristics (e.g., type of opioid, dose–response relationship or number of refills), analyze trends over time, test hypotheses of mediation or stratify analyses to examine specific subpopulations of mothers and children—all of

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Table 2
Cohort characteristics, opioid-naïve mothers who underwent surgery in Ontario, Canada, July 2013 to March 2017

Characteristic	Total/overall (n=170,156)		Filled postoperative opioid prescription (n=100,521)		Did not fill postoperative opioid prescription (n=69,635)		P-value [‡]
	mean number	standard deviation percent	mean number	standard deviation percent	mean number	standard deviation percent	p-value [†] p-value [‡]
Age, mother	40.3	8.8	40.9	8.7	39.3	8.9	<0.001
Number of linked children							
1	86,269	50.7	48,143	47.9	38,126	54.8	<0.001
2	61,378	36.1	38,276	38.1	23,102	33.2	N/A
3 or more	22,509	13.2	14,102	14.0	8,407	12.1	N/A
Residence							
Rural	22,113	13.0	12,738	12.7	9,375	13.5	<0.001
Non-rural	148,043	87.0	87,783	87.3	60,260	86.5	N/A
Neighbourhood income quintile							
First (lowest)	29,300	17.2	16,322	16.2	12,978	18.6	<0.001
Second	31,024	18.2	17,836	17.7	13,188	18.9	N/A
Third	34,665	20.4	20,516	20.4	14,149	20.3	N/A
Fourth	39,289	23.1	23,742	23.6	15,547	22.3	N/A
Fifth (highest)	35,063	20.6	21,719	21.6	13,344	19.2	N/A
Missing	815	0.5	386	0.4	429	0.6	N/A
Surgery							
Outpatient	89,409	52.5	56,601	56.3	32,808	47.1	<0.001
Inpatient	80,747	47.5	43,920	43.7	36,827	52.9	N/A
Charlson comorbidity index							
0	157,284	92.4	91,357	90.9	65,927	94.7	<0.001
1	4,100	2.4	2,603	2.6	1,497	2.1	N/A
2+	8,772	5.2	6,561	6.5	2,211	3.2	N/A
Intervention							
Nervous system	3,367	2.0	2,474	2.5	893	1.3	<0.001
Eye and ocular adnexa	3,832	2.3	256	0.3	3,576	5.1	N/A
Ear and mastoid (process)	956	0.6	732	0.7	224	0.3	N/A
Orocraniofacial region	9,767	5.7	7,505	7.5	2,262	3.2	N/A
Respiratory system	538	0.3	352	0.4	186	0.3	N/A
Cardiovascular system	1,565	0.9	1,205	1.2	360	0.5	N/A
Lymphatic system	284	0.2	203	0.2	81	0.1	N/A
Digestive, hepatobiliary and abdominal	21,746	12.8	16,534	16.4	5,212	7.5	N/A
Genitourinary system	47,839	28.1	24,524	24.4	23,315	33.5	N/A
Musculoskeletal system	21,724	12.8	18,237	18.1	3,487	5.0	N/A
Skin, subcutaneous tissue and breast	14,723	8.7	11,432	11.4	3,291	4.7	N/A
Caesarean section delivery	42,241	24.8	16,445	16.4	25,796	37.0	N/A
Other	1,574	0.9	622	0.6	952	1.4	N/A
Year of surgery							
2013 (July to December)	25,507	15.0	14,473	14.4	11,034	15.8	<0.001
2014	50,540	29.7	29,431	29.3	21,109	30.3	N/A
2015	44,975	26.4	26,732	26.6	18,243	26.2	N/A
2016	39,792	23.4	24,238	24.1	15,554	22.3	N/A
2017 (January to March)	9,342	5.5	5,647	5.6	3,695	5.3	N/A
Index opioid							
Type							
Codeine	34,527	34.3
Hydromorphone	10,759	10.7
Morphine	5,419	5.4
Oxycodone	35,457	35.3
Tramadol	12,379	12.3
Other	218	0.2
Multiple	1,762	1.8

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Table 2
Cohort characteristics, opioid-naïve mothers who underwent surgery in Ontario, Canada, July 2013 to March 2017

Characteristic	Total/overall (n=170,156)		Filled postoperative opioid prescription (n=100,521)		Did not fill postoperative opioid prescription (n=69,635)		P-value [‡]
	mean/ median	standard deviation/IQR	mean/ median	standard deviation/IQR	mean/ median	standard deviation/IQR	p-value [‡]
Days' supply							
Mean (SD)	4.3	3.2
Median (IQR)	3	3-5
Total MME							
Mean (SD)	184.2	129.1
Median (IQR)	150.0	112.5-225.0

... not applicable

[‡] chi-square (categorical) or t-tests (means)

Notes: IQR stands for interquartile range, MME stands for morphine milligram equivalent, SD stands for standard deviation and N/A stands for not applicable (single p-value is reported from chi-square test of cross-tabulated categorical variables).

Sources: 1. Inpatient admissions (Discharge Abstract Database), 2. Same-day surgical procedures (Same Day Surgery Database), 3. Opioid prescriptions (Narcotics Monitoring System), 4. Emergency department presentations (National Ambulatory Care Reporting System), 5. Deaths (Office of the Registrar General – Deaths) and individual-level demographic information (Registered Persons Database), 6. Mother–baby linked database (ICES-derived MOMBABY database).

Table 3
Association between mothers' postoperative opioid prescription and opioid-related events in their children aged 1 to 24 years within one year of surgery

Model	Number with outcome events	Population	Odds ratio			P-value
			Estimate	95% confidence interval		
				From	To	
Crude/unadjusted	36	283,550	2.72	1.19	6.21	0.02
Adjusted [†]	36	281,157	2.42	1.05	5.54	0.04
Sensitivity analyses						
Restricting to one randomly selected child per mother	..	170,156	2.63	0.98	7.05	0.05
Restricting to children aged 12 to 24 years	..	119,856	2.12	0.92	4.87	0.08
Restricting to children of mothers whose surgery was not a caesarean section	..	225,426	2.07	0.91	4.75	0.08
Including children and children of mothers who died within one year of surgery and opioid-related deaths in the outcome	..	283,889	2.72	1.19	6.21	0.02

[†] Adjusted for child's age, mother's age, rural residence, neighbourhood income quintile and mother's Charlson comorbidity index score

Note: Cells containing "... " cannot be reported to minimize re-identification risk (i.e., differences of n<6 between number of events in sensitivity analyses and main analyses).

Sources: 1. Inpatient admissions (Discharge Abstract Database), 2. Same-day surgical procedures (Same Day Surgery Database), 3. Opioid prescriptions (Narcotics Monitoring System), 4. Emergency department presentations (National Ambulatory Care Reporting System), 5. Deaths (Office of the Registrar General – Deaths) and individual-level demographic information (Registered Persons Database), 6. Mother–baby linked database (ICES-derived MOMBABY database).

which merit further research. Still, these data provide some insights into prescription opioid availability for nonmedical use, which is an area that typically relies on survey data and represents a key data gap in addressing public health issues associated with opioid analgesics.²⁵ Third, there may be residual confounding. However, a previous case–control study that assessed the association between opioid prescriptions to family members and opioid overdoses and included a range of covariates reported almost identical unadjusted and adjusted odds ratios.⁸ Regardless, the potential impact of opioid use in other household members²⁶ could not be assessed with these data.

Opioids are important for managing pain after surgery. However, concerns over the potential negative impacts of excessive opioid prescribing in this context have prompted efforts to reduce these prescriptions, including through interventions implemented at the individual, health care system and policy levels. These findings suggest that postoperative opioid prescriptions may contribute to opioid-related events among others in the household. These results have implications for both clinical practice and future research. First, taken in context with the tendency for postoperative opioid prescriptions to exceed patient need,¹¹⁻¹³ these results

reinforce the importance of “right-sized” postoperative opioid prescriptions and further highlight the roles of prescribers, dispensers and public health campaigns in educating patients and the public about the safe use, storage and disposal of these medications.^{27,28} For research purposes, better evidence is needed to establish optimal postoperative opioid prescribing practices and develop interventions to support their implementation.²⁹

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Appendix

Table A
Definition of opioid-related event outcome

ICD-10-CA code	Description
T40.0	Poisoning by opium
T40.1	Poisoning by heroin
T40.2	Poisoning by other opioids
T40.3	Poisoning by methadone
T40.4	Poisoning by other synthetic narcotics
T40.6	Poisoning by other and unspecified narcotics
F11.0	Mental and behavioural disorders due to use of opioids, acute intoxication
F11.1	Mental and behavioural disorders due to use of opioids, harmful use
F11.2	Mental and behavioural disorders due to use of opioids, dependence syndrome
F11.3	Mental and behavioural disorders due to use of opioids, withdrawal state
F11.4	Mental and behavioural disorders due to use of opioids, withdrawal state with delirium
F11.5	Mental and behavioural disorders due to use of opioids, psychotic disorder
F11.6	Mental and behavioural disorders due to use of opioids, amnesic syndrome
F11.7	Mental and behavioural disorders due to use of opioids, residual and late-onset psychotic disorder
F11.8	Mental and behavioural disorders due to use of opioids, other mental and behavioural disorders
F11.9	Mental and behavioural disorders due to use of opioids, unspecified mental and behavioural disorder

Notes: Any emergency department presentation (via the National Ambulatory Care Reporting System) or inpatient admission (via the Discharge Abstract Database) record listing any one of the above International Statistical Classification of Diseases and Related Health Problems, 10th revision, Canada (ICD-10-CA), codes as a primary or any other diagnosis.

Source: Authors' compilation.

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