

Clinical indications associated with opioid initiation for pain management in Ontario, Canada: a population-based cohort study

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Abstract

Concerns over prescription opioids contributing to high levels of opioid use disorder and overdose have led policymakers and clinicians to seek means to reduce inappropriate and high-dose initial prescriptions. To inform such efforts, we sought to describe the clinical indications associated with opioid initiation and the characteristics of the initial prescriptions and patients through a retrospective population-based cohort study. Our cohort included Ontarians initiating prescription opioids for pain management between April 1, 2015, and March 31, 2016. We identified the apparent clinical indication for opioid initiation by linking prescription drug claims to procedural and diagnostic information on health service records on the day of, and 5 days preceding prescription. Outcomes included initial opioid type, prescription duration, and daily dose (in milligram morphine equivalents), stratified either by indication or indication cluster. Among 653,993 individuals, we successfully classified 575,512 (88.0%) people initiating opioids into 23 clinical indications in 6 clusters: dental (23.2%); postsurgical (17.4%); musculoskeletal (12.0%); trauma (11.2%); cancer/palliative care (6.5%); and other less frequent indications (17.7%). Individuals with postsurgical pain received the highest daily doses (40.5% with greater than 50 milligram morphine equivalent), and those with musculoskeletal pain received more initial prescriptions with a duration exceeding 7 days (34.2%). Opioids are initiated for a wide range of indications with varying doses and durations; yet, those who initiated opioids for postsurgical and musculoskeletal pain received the greatest doses and durations of therapy, respectively. These findings may help tailor and prioritize efforts to promote more appropriate opioid prescribing.

Keywords: Opioid analgesics, Prescribing, Drug policy

1. Introduction

The use of prescription opioids has increased considerably over the past 2 decades, particularly in Canada and the United States, which had the highest level of opioid consumption per capita

worldwide in 2015.^{12,19} High levels of opioid prescribing have raised concerns among clinicians and policymakers, given the limited evidence of long-term effectiveness of this class of drugs and research finding increased risks of adverse events including mortality with long-term use.^{14,22}

Previous research has associated long-term use of prescription opioids and dose escalation with worse outcomes.¹¹ In turn, recently published clinical practice guidelines for chronic noncancer pain management recommended non-opioid alternatives as first-line and have suggested threshold doses for patients newly started on opioids.^{1,6} However, opioids are prescribed for a range of acute and chronic pain conditions, including arthritis, back pain, postsurgical pain, and dental pain.²³ Studies in select populations have demonstrated that characteristics of opioid initiation and prescribing vary by clinical indication, which may reflect different anticipated needs for different indications as well as variations in training across specialties.²⁶ Therefore, there has been an emerging recognition that policies and programs developed to address appropriate prescribing of opioids may need to be tailored to each clinical indication. This requires an understanding of the relative contribution of each clinical indication to patterns of opioid initiation.²⁹ Previous studies investigating these indications have been limited to smaller populations.^{15,18,25,26}

Accordingly, we set out to determine the apparent clinical indications for opioid initiation at the population level and to describe the characteristics of the initial prescriptions and patients by indication.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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2. Methods

2.1. Setting

We conducted a population-based retrospective cohort study of all Ontarians who were newly dispensed an opioid between April 1, 2015, and March 31, 2016. Ontario is Canada's most populous province, with a population of 13.4 million in 2016, representing 38% of the Canadian population.²⁷ This study was approved by the institutional review board at Sunnybrook Health Sciences Centre, Toronto, Canada.

2.2. Data sources

We identified opioid prescription characteristics from the Narcotics Monitoring System (NMS), which captures information regarding all opioids dispensed from all retail pharmacies regardless of payer. Pharmacist data entry into the NMS is mandatory for all controlled substances.²⁰ We acquired cancer diagnoses from the Ontario Cancer Registry, and details regarding cancer treatment and palliative care from the cancer Activity Level Reporting database. We obtained hospital visit data (including diagnoses and procedures) from the Canadian Institute for Health Information's Discharge Abstract Database (CIHI DAD), emergency department visit and same day surgery data from CIHI's National Ambulatory Care Reporting System. We identified physician-billing data from the Ontario Health Insurance Plan (OHIP) Claims History Database, and used the OHIP Registered Persons Database (RPDB) to identify patients' place of residence and demographic characteristics. These databases have high levels of completeness and are regularly used in health services research.^{2,3,13} We linked data sets using unique encoded identifiers, and all analyses were performed at the Institute for Clinical Evaluative Sciences (ICES) using SAS software (version 9.4; SAS Institute Inc, Cary, NC).

2.3. Study patients

We defined opioid users as those dispensed an eligible opioid (ie, an opioid formulation not used to treat opioid use disorder) between April 1, 2015, and March 31, 2016. We defined an individual's index date and prescription based on their first receipt of a prescription opioid in the accrual period.

We limited our analysis to prescriptions dispensed to individuals with a valid Ontario health card. We excluded individuals with opioid use before the index date, defined as any prescription for an eligible opioid between the index date and July 1, 2012, which is when all pharmacies were mandated to use the NMS. We excluded individuals currently or having previously been on treatment for opioid use disorder (defined as having been dispensed an opioid for the treatment of opioid use disorder since July 1, 2012, and before or on index date). We excluded patients who visited an emergency department or hospital for opioid toxicity (defined by ICD10 diagnosis codes T40.0-T40.4 or T40.6 in the National Ambulatory Care Reporting System or DAD databases) in the 2 years before the index date because this would reflect previous use of opioids.

Among the remaining new users of opioids, we excluded individuals dispensed an opioid formulation used only as an antitussive, thereby limiting our analysis to individuals newly initiating opioids for pain management.

2.4. Identifying the apparent clinical indication

We used a stepwise hierarchical approach to identify the most likely clinical indication for opioid initiation among individuals in the cohort. We developed the hierarchy based on the licensing

college of the initial prescriber and the degree of certainty that the procedural and diagnostic information on the related health care administrative data would warrant an opioid prescription. For example, we were most certain of indications for dental pain because the index prescription was directly linked to a dentist. For all other prescriptions written by physicians, our hierarchy was informed by clinical insight as to the likelihood that the diagnosis or procedure would lead to an opioid initiation.

In the first step of the hierarchical approach, we classified individuals whose index opioid was prescribed by a dentist, then those with evidence of palliative care in the past year, followed by those with evidence of active cancer in the past year into each of these 3 indications accordingly. For those remaining, we identified the diagnostic and procedural information on their most recent health care interaction on or in the 5 days preceding the first-opioid prescription. Health care interactions included inpatient hospitalizations, emergency department visits, outpatient surgical procedures, and physician office visits.

In the second hierarchical step, we classified individuals with a recent hospitalization or procedure into procedure-based indications according to the *Canadian Classification of Health Interventions* (CCI) procedure code on the identified health care record. In the third hierarchical step, remaining individuals were classified into diagnosis-based indications according to the *International Statistical Classification of Diseases and Related Health Problems 10th revision (ICD10)* or OHIP diagnostic code recorded. We classified individuals with diagnostic codes that would not normally warrant an opioid prescription into an "Unknown" group, and did the same with individuals who had no evidence of a health care encounter in the previous 5 days. We identified a total of 23 clinical indications, which were then grouped into 6 indication clusters. We provide more details on the approach and hierarchy used to assign indications along with associated procedure and diagnostic codes in the Supplementary Appendix (available online at <http://links.lww.com/PAIN/A570>).

2.5. Prescription and patient characteristics

Within each indication, we defined prescription characteristics at initiation, including the daily dose dispensed in milligram morphine equivalents (MMEs), the number of days supplied, opioid formulation type (immediate-release or long-acting), and type of opioid. Within each indication, we also identified the proportion of initial prescriptions that had a potentially inappropriate initial dose (defined as daily dose exceeding 50 MME) or a potentially inappropriate duration (defined as exceeding 7 days' supply). For daily dose, the threshold of 50 MME reflects how current U.S. and Canadian chronic noncancer pain guidelines suggest clinicians avoid initiating opioids above this daily dose, likely due to associations with adverse events such as road trauma and fatal overdose.^{1,6,8,9} For prescription duration, the threshold of 7 days reflects how these longer prescriptions may be associated with more long-term use.^{6,25,26}

For people dispensed 2 or more opioids on their index date, we counted the longest number of days supplied and summed the doses to calculate daily dose. Finally, we described patient demographic characteristics (including age, sex, neighbourhood income quintile, and urban/rural location of residence) by indication cluster. No formal statistical tests were performed.

3. Results

Among 778,803 new users, 653,993 (84.0%) met our inclusion criteria (Fig. 1). Just over half (N = 339,525, 51.9%) were women,

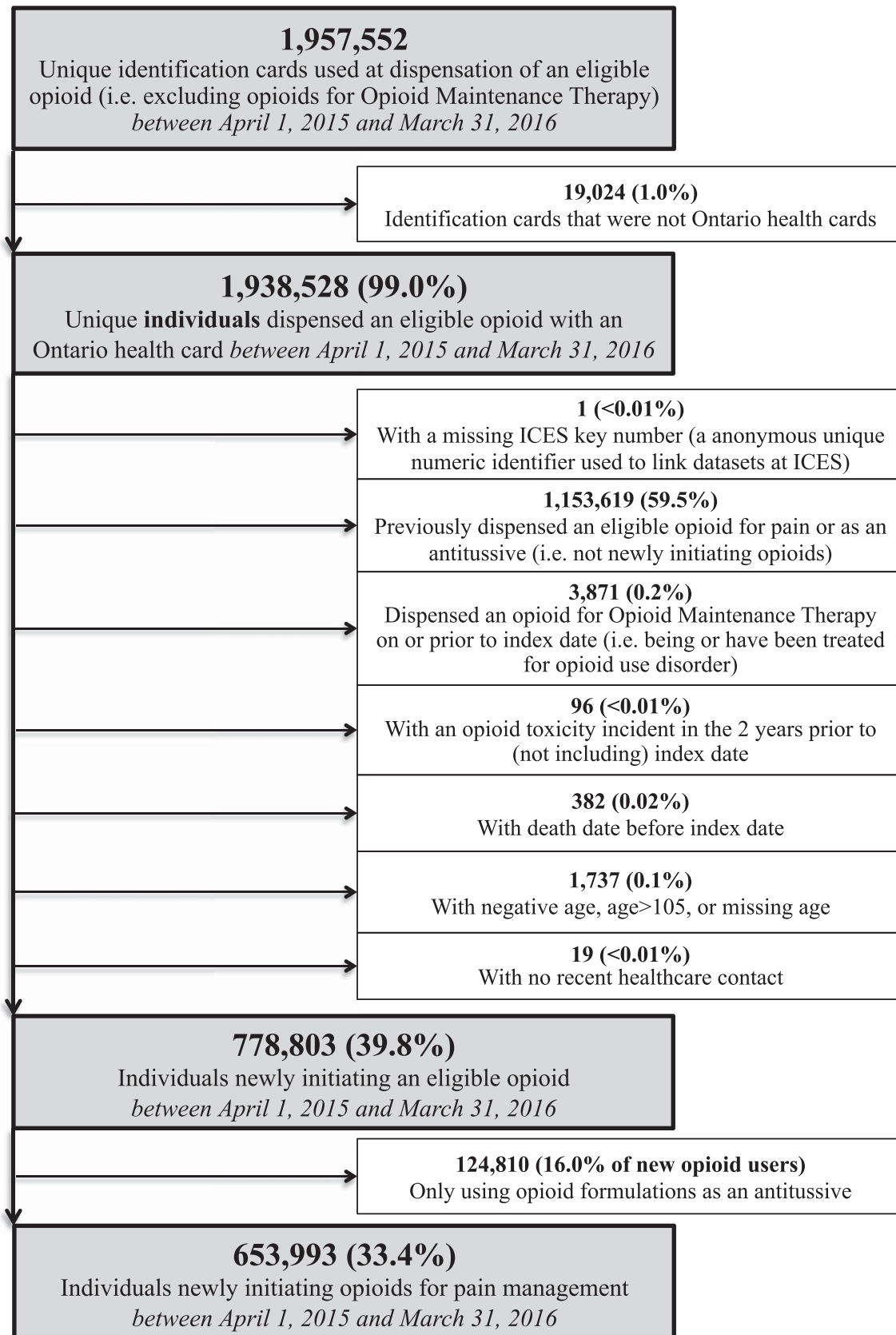


Figure 1. Cohort identification. This figure depicts the order in which inclusion and exclusion criteria were used to identify the study cohort of Ontarians newly initiating opioids between April 1, 2015, and March 31, 2016. ICES, Institute for Clinical Evaluative Sciences.

and the median age was 48 years (Q1-Q3, 29-63 years). The vast majority (N = 644,762, 98.6%) of new opioid users received only an immediate-release prescription on their index date, and the most common opioid prescribed to these individuals was codeine-combination products (N = 343,094; 53.2%). Among all new opioid users, the median daily dose on the index prescription was 34 MME (Q1-Q3, 21-45 MME) and 156,461 (23.9%) initial prescriptions had a daily dose above 50 MME. The median prescription duration was 4 days (Q1-Q3, 3-6 days); 113,523 (17.4%) had an initial duration exceeding 7 days.

We identified 23 clinical indications for initiating opioids grouped into 6 indication clusters: dental pain (N = 151,874, 23.2%), postsurgical pain (N = 113,605, 17.4%), musculoskeletal pain (N = 78,155, 12.0%), trauma-related pain (N = 73,069, 11.2%), cancer or palliative care (N = 42,832, 6.5%), and other types of pain (N = 115,977, 17.7%) (Table 1). Overall, 78,481 (12.0%) individuals could not be linked to an indication. Among these individuals, 39,803 (50.7%) had no health care record identified, whereas the remainder (49.3%) had a health care record identified that would not normally warrant opioid initiation (eg, anxiety and hypertension; see Supplementary Appendix for details; available online at <http://links.lww.com/PAIN/A570>).

Individuals who initiated opioids for dental pain were typically younger (median age 31 years, Q1-Q3 20-52 years), whereas those who initiated for musculoskeletal pain (median age 56 years, Q1-Q3 44-69 years), and cancer and palliative care (median age 66 years, Q1-Q3 55-77 years) were typically older than those in the other indication clusters (range in medians from 45 to 49 years). The neighbourhood income quintile profiles of patients were fairly evenly distributed across indication clusters.

Within each indication cluster, we identified a number of highly prevalent clinical indications. Although specific dental indications could not be identified in our data, the overwhelming majority of patients initiating an opioid for dental pain received their prescription from a dentist (144,118 of 151,874 [94.9%], representing 22.0% of the entire cohort) (Table 2). Other common clinical

indications were common excisions (4.2%), joint and muscle pain (7.1%), back pain (4.8%), dislocations, sprains and strains (4.0%), cancer (5.3%), and abdominal or pelvic pain (6.0%).

The characteristics of initial prescriptions varied considerably by indication. Patients initiating for dental pain received prescriptions with a lower daily dose (median 30 MME, Q1-Q3 of 23-45) and shorter durations (median 3 days, Q1-Q3 of 3-5) relative to other indications (Table 2). Individuals initiating opioids after knee, hip, or shoulder surgery received higher daily doses (median 60 MME, Q1-Q3 of 45-90; 64.7% with initial daily dose above 50 MME), as did those initiating following caesarean section (median 50 MME, Q1-Q3 of 33-68; 50.3% with initial daily dose above 50 MME), relative to other indications. Clinical indications with a higher-than-average proportion of potentially risky prescription durations were joint and muscle pain (37.7% with durations >7 days); dislocations, sprains, and strains (33.3% with durations >7 days); palliative care (34.9% with durations >7 days); back pain (29.2% with durations >7 days); and headaches and migraines (28.1% with durations >7 days).

Finally, the type of opioids prescribed at initiation varied, with immediate-release codeine-combination products being the most common across all clinical indications (Table 3). Immediate-release hydromorphone prescribing occurred most commonly among individuals initiating opioids for cancer and palliative care (9,831, 23.5%), whereas morphine prescribing occurred more often among those initiating postsurgery (13,677, 12.3%).

4. Discussion

In this population-based study of 653,993 new users of prescription opioids, we found wide diversity of the apparent clinical indications for which people initiate opioids for pain management. Dental pain accounted for nearly one-quarter of all new opioid prescriptions, which were generally of short duration and low dose. By contrast, 1 in 6 new opioid users were treated for postsurgical pain, and these patients generally started on higher doses (over 40% were

Table 1
Patient characteristics of individuals newly initiated on opioids for pain, by major clinical indication cluster.

	Overall, N = 653,993	Dental, N = 151, 874 (23.2%)	Postsurgical pain, N = 113, 605 (17.4%)	Musculoskeletal pain, N = 78, 155 (12.0%)	Trauma, N = 73, 069 (11.2%)	Cancer and palliative, N = 42, 832 (6.5%)	Other types of pain, N = 115, 977 (17.7%)	Unknown, N = 78, 481 (12.0%)
Age								
Median (IQR)	48 (29-63)	31 (20-52)	45 (29-60)	56 (44-69)	49 (32-63)	66 (55-77)	45 (31-60)	53 (36-69)
0-17	49,461 (7.6%)	21,454 (14.1%)	13,554 (11.9%)	741 (0.9%)	4130 (5.7%)	405 (0.9%)	6373 (5.5%)	2804 (3.6%)
18-24	70,963 (10.9%)	37,916 (25.0%)	8065 (7.1%)	2354 (3.0%)	6108 (8.4%)	460 (1.1%)	10,458 (9.0%)	5602 (7.1%)
25-44	176,901 (27.0%)	39,352 (25.9%)	34,963 (30.8%)	17,109 (21.9%)	20,746 (28.4%)	3703 (8.6%)	39,869 (34.4%)	21,159 (27.0%)
45-64	205,919 (31.5%)	37,611 (24.8%)	36,204 (31.9%)	31,380 (40.2%)	25,296 (34.6%)	14,803 (34.6%)	36,609 (31.6%)	24,016 (30.6%)
65+	150,749 (23.1%)	15,541 (10.2%)	20,819 (18.3%)	26,571 (34.0%)	16,789 (23.0%)	23,461 (54.8%)	22,668 (19.5%)	24,900 (31.7%)
Sex								
Female	339,530 (51.9%)	75,068 (49.4%)	57,768 (50.8%)	40,663 (52.0%)	33,868 (46.4%)	23,396 (54.6%)	64,952 (56.0%)	43,815 (55.8%)
Male	314,463 (48.1%)	76,806 (50.6%)	55,837 (49.2%)	37,492 (48.0%)	39,201 (53.6%)	19,436 (45.4%)	51,025 (44.0%)	34,666 (44.2%)
Income quintile								
1 (lowest)	117,236 (17.9%)	25,781 (17.0%)	19,145 (16.9%)	14,588 (18.7%)	13,639 (18.7%)	7060 (16.5%)	22,106 (19.1%)	14,917 (19.0%)
2	123,429 (18.9%)	27,186 (17.9%)	21,005 (18.5%)	15,407 (19.7%)	14,334 (19.6%)	8040 (18.8%)	22,625 (19.5%)	14,832 (18.9%)
3	130,256 (19.9%)	30,010 (19.8%)	22,420 (19.7%)	15,940 (20.4%)	14,537 (19.9%)	8577 (20.0%)	23,270 (20.1%)	15,502 (19.8%)
4	142,975 (21.9%)	33,766 (22.2%)	25,702 (22.6%)	16,757 (21.4%)	15,817 (21.6%)	9291 (21.7%)	24,936 (21.5%)	16,706 (21.3%)
5 (highest)	136,735 (20.9%)	34,310 (22.6%)	24,778 (21.8%)	15,125 (19.4%)	14,381 (19.7%)	9659 (22.6%)	22,494 (19.4%)	15,988 (20.4%)
Location of residence								
Rural	80,519 (12.3%)	15,969 (10.5%)	15,555 (13.7%)	10,649 (13.6%)	9281 (12.7%)	5598 (13.1%)	13,069 (11.3%)	10,398 (13.2%)
Urban	573,111 (87.6%)	135,811 (89.4%)	97,987 (86.3%)	67,460 (86.3%)	63,757 (87.3%)	37,212 (86.9%)	102,850 (88.7%)	68,034 (86.7%)

For certain indications, certain demographic variables were missing. In these cases, the percentages may not add to 100% and the individual numbers may not add to the total for that clinical indication. IQR, interquartile range.

Table 2

Frequency and characteristics of initial opioid prescriptions for pain, by major and minor clinical indication.

Indication/indication cluster	Number (%)	Median daily dose (IQR)	No. (%) with daily dose >50 mg MME	Median days' supplied (Q1-Q3)	No. (%) with days' supplied >7
Overall	653,993	34 (21-45)	156,461 (23.9%)	4 (3-6)	113,523 (17.4%)
Dental	151,874 (23.2%)	30 (23-45)	21,158 (13.9%)	3 (3-5)	5721 (3.8%)
Dentist prescribed	144,118 (22.0%)	30 (23-45)	19,626 (13.6%)	3 (3-5)	5037 (3.5%)
Physician prescribed	7756 (1.2%)	34 (23-45)	1532 (19.8%)	3 (2-5)	684 (8.8%)
Postsurgical pain	113,605 (17.4%)	45 (29-64)	45,993 (40.5%)	4 (3-5)	12,361 (10.9%)
Common excision	27,370 (4.2%)	38 (25-50)	8476 (31.0%)	4 (3-5)	2555 (9.3%)
Knee, hip, and shoulder surgery	18,320 (2.8%)	60 (45-90)	11,855 (64.7%)	5 (4-7)	4182 (22.8%)
Hernia repair	10,900 (1.7%)	45 (28-56)	3735 (34.3%)	3 (3-5)	591 (5.4%)
Caesarean section	6039 (0.9%)	50 (33-68)	3035 (50.3%)	3 (2-4)	224 (3.7%)
Other surgery	50,976 (7.8%)	45 (27-60)	18,892 (37.1%)	4 (3-5)	4809 (9.4%)
Musculoskeletal pain	78,155 (12.0%)	30 (17-45)	17,479 (22.4%)	5 (3-10)	26,768 (34.2%)
Joint and muscle	46,462 (7.1%)	30 (15-45)	10,947 (23.6%)	5 (4-10)	17,515 (37.7%)
Back	31,693 (4.8%)	30 (18-45)	6532 (20.6%)	5 (3-10)	9253 (29.2%)
Trauma	73,069 (11.2%)	34 (19-50)	18,263 (25.0%)	4 (3-7)	15,475 (21.2%)
Dislocations, sprains, and strains	26,341 (4.0%)	28 (15-45)	5287 (20.1%)	5 (3-10)	8775 (33.3%)
Fracture and major trauma	22,581 (3.5%)	42 (27-56)	7539 (33.4%)	4 (3-5)	3235 (14.3%)
Burns, wounds, and superficial trauma	14,722 (2.3%)	34 (20-45)	3116 (21.2%)	4 (3-5)	2086 (14.2%)
Other trauma	9425 (1.4%)	34 (23-47)	2321 (24.6%)	4 (3-5)	1379 (14.6%)
Cancer and palliative	42,832 (6.5%)	38 (23-54)	12,979 (30.3%)	4 (3-7)	9318 (21.8%)
Cancer	34,856 (5.3%)	38 (25-56)	11,160 (32.0%)	4 (3-7)	6538 (18.8%)
Palliative care	7976 (1.2%)	30 (18-53)	1819 (22.8%)	5 (3-10)	2780 (34.9%)
Other types of pain	115,977 (17.7%)	33 (19-45)	27,209 (23.5%)	4 (3-5)	18,747 (16.2%)
Abdominal/pelvic pain	38,919 (6.0%)	38 (23-50)	10,442 (26.8%)	3 (2-5)	5048 (13.0%)
Infection	18,977 (2.9%)	28 (15-45)	3091 (16.3%)	5 (3-7)	4202 (22.1%)
Nephrolithiasis/cholecystitis	15,052 (2.3%)	45 (28-57)	5853 (38.9%)	3 (2-5)	953 (6.3%)
Eyes, ears, nose, and throat	14,860 (2.3%)	25 (14-45)	1848 (12.4%)	4 (3-7)	2819 (19.0%)
Chest pain	10,628 (1.6%)	29 (15-45)	2127 (20.0%)	5 (3-7)	2645 (24.9%)
Nonsurgical deliveries	5848 (0.9%)	38 (25-50)	1565 (26.8%)	3 (2-4)	290 (5.0%)
Headache and migraine	5335 (0.8%)	23 (14-38)	593 (11.1%)	5 (3-9)	1497 (28.1%)
Other pain	6358 (1.0%)	35 (23-50)	1690 (26.6%)	4 (3-7)	1293 (20.3%)
Unknown	78,481 (12.0%)	27 (14-45)	13,380 (17.0%)	5 (3-10)	25,133 (32.0%)

IQR, interquartile range; MME, milligram morphine equivalent.

prescribed more than 50 MME, and at least 25% were prescribed 90 MME or more). Finally, although just 1 in 10 patients initiated opioids for back, joint, or muscle pain, these patients generally received longer durations of therapy, with more than one-third receiving initial prescription durations of greater than 7 days.

Previous studies have generally not been designed to characterize the indication for opioid initiation at population level using robust, linked health administrative databases.^{15,18,25,26} Four American studies, in particular, are based on prescriptions written, not those dispensed, and were limited to smaller populations (ie, a specific clinic or insurance provider) and could not account for access to opioids from other sources.^{15,18,25,26} Our study confirms most findings from the literature (apart from 1 previous study that identified chronic noncancer pain as the most common pain indication)²⁵; we found that acute indications (ie, dental, postsurgical, and trauma-related pain) accounted for the majority of all opioid initiations,¹⁵ that opioid initiation was more commonly attributed to joint and muscle pain than back pain,²⁶ and that dental pain was a significant contributor to new opioid exposure.¹⁸ However, our study also highlights the broad set of indications for which opioids are initiated, and provides important information on other significant contributors to new opioid exposure. In particular, we found that postsurgical pain accounts for nearly 1 in 6 new opioid starts, which tend to be of short duration at relatively higher doses and to older adults. Although the contribution of prescriptions for dental pain in a primary care setting

has previously been identified,¹⁸ our finding of the significant contribution of prescriptions by dentists is particularly novel and important. Although the dose and duration of these prescriptions are relatively limited, the concentration of dental prescriptions among younger patients—a group at potentially greater risk of prescription opioid misuse, illicit use, and recreational experimentation—^{10,30} highlights the importance of policy efforts to ensure that dentist prescribing remains appropriate and necessary.^{16,17,21}

The U.S. and Canadian clinical guidelines for opioids in chronic non-cancer pain published in 2016 and 2017, respectively, suggest that clinicians should avoid initiating opioids at daily doses above 50 MME.^{1,6} Our study found that, in the period immediately before the guidelines were published, nearly one-quarter of Ontarians newly initiating opioids received a daily dose exceeding this threshold, and that this was even higher in certain indications such as knee, hip, and shoulder surgeries, and caesarean sections. Moreover, at least one-quarter of individuals initiating opioids for knee, hip, and shoulder surgeries received an initial daily dose equal to or exceeding 90 MME, which guidelines now recommend avoiding even after initiation. Given that these higher doses have been associated with more adverse events, including overdose deaths, depression, road trauma, and falls,^{7,9} our findings suggest that improvements to safe opioid prescribing could be achieved by focusing on dose initiation patterns among surgeons. In addition to high daily doses being a concern, recent evidence suggests

Table 3
Opioid types and formulations dispensed to individuals newly initiating opioids for pain, by major clinical indication cluster.

	Overall (N = 653,993)	Dental (N = 151,874)	Postsurgical pain (N = 113,605)	Musculoskeletal pain (N = 78,155)	Trauma (N = 73,069)	Cancer and palliative (N = 42,832)	Other types of pain (N = 115,977)	Unknown (N = 78,481)
Long-acting only	N = 4039 (0.6%)	N = 77 (0.1%)	N = 215 (0.2%)	N = 1119 (1.4%)	N = 534 (0.7%)	N = 290 (0.7%)	N = 506 (0.4%)	N = 1298 (1.7%)
Tramadol	1276 (31.6%)	≤5*	13-17 (6.0%-7.9%)*	465 (41.6%)	177 (33.1%)	60 (20.7%)	120 (23.7%)	437 (33.7%)
Hydromorphone	772 (19.1%)	≤5*	71-75 (33.0%-34.9%)*	156 (13.9%)	116 (21.7%)	99 (34.1%)	89 (17.6%)	236 (18.2%)
Oxycodone	538 (13.3%)	55 (71.4%)	64 (29.8%)	101 (9.0%)	30 (5.6%)	28 (9.7%)	71 (14.0%)	189 (14.6%)
Morphine	369 (9.1%)	≤5*	19-23 (8.8%-10.7%)*	81 (7.2%)	40 (7.5%)	37 (12.8%)	53 (10.5%)	134 (10.3%)
Fentanyl	262 (6.5%)	0	≤5*	42 (3.8%)	21-25 (3.9%-4.7%)*	43 (14.8%)	37 (7.3%)	114 (8.8%)
Codeine	148 (3.7%)	≤5*	0	38 (3.4%)	30 (5.6%)	7 (2.4%)	15-19 (3.0%-3.8%)*	53 (4.1%)
Other	679 (16.8%)	15 (19.5%)	35 (16.3%)	240 (21.4%)	120 (22.5%)	16 (5.5%)	117 (23.1%)	136 (10.5%)
Immediate-release only	N = 644,762 (98.6%)	N = 151,791 (99.9%)	N = 111,439 (98.1%)	N = 76,064 (97.3%)	N = 71,837 (98.3%)	N = 41,884 (97.8%)	N = 115,260 (99.4%)	N = 76,487 (97.5%)
Codeine combination	343,094 (53.2%)	121,393 (80.0%)	36,563 (32.8%)	39,104 (51.4%)	36,842 (51.3%)	15,648 (37.4%)	51,266 (44.5%)	42,278 (55.3%)
Oxycodone combination	128,879 (20.0%)	22,079 (14.5%)	27,801 (24.9%)	16,838 (22.1%)	17,204 (23.9%)	7260 (17.3%)	25,518 (22.1%)	12,179 (15.9%)
Hydromorphone	61,455 (9.5%)	1144 (0.8%)	15,926 (14.3%)	7302 (9.6%)	7225 (10.1%)	9831 (23.5%)	11,884 (10.3%)	8143 (10.6%)
Tramadol	56,541 (8.8%)	5324 (3.5%)	12,189 (10.9%)	9816 (12.9%)	7145 (9.9%)	4323 (10.3%)	10,349 (9.0%)	7395 (9.7%)
Morphine	33,941 (5.3%)	1048 (0.7%)	13,677 (12.3%)	2125 (2.8%)	3130 (4.4%)	2693 (6.4%)	8174 (7.1%)	3094 (4.0%)
Oxycodone	13,134 (2.0%)	1322 (0.9%)	6749 (6.1%)	500 (0.7%)	299 (0.4%)	1338 (3.2%)	1913 (1.7%)	1013 (1.3%)
Other	14,863 (2.3%)	1067 (0.7%)	509 (0.5%)	929 (1.2%)	729 (1.0%)	1216 (2.9%)	6943 (6.0%)	3470 (4.5%)
Both long-acting and immediate-release	5192 (0.8%)	6 (0.0%)	1951 (1.7%)	972 (1.2%)	698 (1.0%)	658 (1.5%)	211 (0.2%)	696 (0.9%)

* In cases where the number in the cell is less than 6, this number has been suppressed to ensure confidentiality. In cases where there is only 1 record being suppressed, another record has been suppressed to provide a range to avoid residual disclosure.

prescribing less than 7 days of opioid at initiation, ideally less than or equal to 3 days, as these shorter prescription durations are associated with less long-term use.^{6,25,26} In this study, we found that although opioids initiated postsurgery were typically of higher dose, they tended to have shorter durations, with only 1 in 10 individuals receiving more than a 7-day supply of drug. By contrast, more than one-third of people initiating opioids for musculoskeletal pain received an initial prescription duration exceeding 7 days' supply, which may contribute to the high degree of sustained opioid use among people initiated for musculoskeletal pain.²⁴ In addition, these differences in patterns by clinical indication may reflect variations in intended duration of opioid use, but could also suggest opportunities for improved opioid initiation practices in some populations. Finally, although rare, our findings also highlight that opioids are used to treat conditions such as headaches and migraines, for which opioid-related harms have been reported to outweigh any evidence of benefit.^{4,28}

Our study has several limitations. First, given the retrospective study design and data sources, we cannot confirm whether the diagnosis or procedure codes identified before the index prescription are responsible for opioid initiation. However, the use of similar approaches to identify opioid indications in studies with limited population samples,^{24,26} and the proximity of the health care encounters to opioid dispensing, increases our confidence in our approach for defining indications associated with opioid initiation. Second, we only have historical dispensing data from July 2012 onwards, so cannot ascertain more remote opioid prescriptions. In some instances, the identified initial prescription may not be an individual's first-opioid exposure. Nevertheless, because it was patients' first use of a prescription opioid in at least 2.5 years, any

previously acquired tolerance would have been lost.³¹ Third, we cannot account for people recently moving into the province because there is often a lag period for them to gain access to the health care system.⁵ Fourth, we could not identify a pain indication among 12% of patients in our cohort. Although our algorithm was designed to capture all potential pain indications where suitable information was captured in our databases, some physicians may list a generic diagnosis on the billing record, which would not provide us with the detailed information required to allocate a pain indication. Therefore, in these cases, we are unable to appropriately allocate these individuals to an indication group. Notably, half of these individuals had no evidence of a physician encounter in the preceding 5 days, thus filled prescriptions that were at least 5 days old. Finally, some patients may have had multiple indications and we could only identify 1 indication because our approach to identifying indications was hierarchical. However, we developed a hierarchy intended to classify indications according to the most appropriate indication for opioid use.

As we aim to optimize opioid prescribing, patients' first-opioid prescriptions are critically important. Across all clinical indications, a high percentage of people received daily doses above 50 MME and prescription lengths over 7 days, which have been associated with potential adverse events and long-term opioid use. Given this, our findings highlight the need to prioritize certain indications in the promotion of more appropriate opioid prescribing. Knowing the nature of opioid prescribing postsurgically and for musculoskeletal pain, particular attention may be warranted to determine the appropriateness and safety of opioid use in these indications. Future efforts to inform such resource allocation efforts ought to consider which specific pain indications are associated with downstream risks of sustained use, opioid use disorder, and opioid toxicity.

Conflict of interest statement

M.M. Mamdani has received honoraria from Boehringer Ingelheim, Pfizer, Bristol-Myers Squibb, and Bayer. D.N. Juurlink has received payment for lectures and medicolegal opinions regarding the safety and effectiveness of analgesics, including opioids. He is a member of Physicians for Responsible Opioid Prescribing, a volunteer organization that seeks to reduce opioid-related harm through more cautious prescribing practices. No other authors have any conflicts of interest to declare.

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Appendix A. Supplemental digital content

Supplemental digital content associated with this article can be found online at <http://links.lww.com/PAIN/A570>.

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