Patterns and trends in long-term opioid use for non-cancer pain in British Columbia, 2005–2012

Kate Smolina, PhD,[1] Emilie J. Gladstone, MPH,[1] Kimberly Rutherford, MD,[2] Steven G. Morgan, PhD[1]

ABSTRACT

OBJECTIVES: We aimed to calculate trends in incidence and prevalence rates of long-term opioid use for non-cancer pain, as well as to describe the characteristics of long-term opioid users and their patterns of opioid use.

METHODS: We used population-based linked health care and socio-demographic administrative data for British Columbia (BC) between 2005 and 2012. We included individuals who had at least one episode of long-term opioid use during the study period and who were not cancer or palliative care patients.

RESULTS: Long-term users comprised only 10% of all individuals prescribed opioids for non-cancer pain, but accounted for 64% of all opioid prescriptions and 87% of all morphine equivalents dispensed in BC during this period. While the incidence rate did not significantly change, the prevalence rate increased by 27% for men and 22% for women. In 2012, there were 3.80 (3.72–3.88) new long-term opioid users per 1,000 men and 4.42 (4.34–4.51) new users per 1,000 women. At the same time, there were 18.3 (95% CI 18.1–18.5) existing long-term users per 1,000 men and 21.7 users (95% CI 21.5–21.9) per 1,000 women. Overall, 2.4% of BC residents were long-term users of prescription opioids in 2012. Most long-term users had one continuous episode of use spanning multiple years. Almost two thirds took opioids every other day or more frequently.

CONCLUSION: There is a growing population of long-term opioid users for non-cancer pain in BC, with higher incidence and prevalence rates observed among women than among men.

KEY WORDS: Opioid analgesics; chronic pain; incidence; prevalence; inappropriate prescribing

La traduction du résumé se trouve à la fin de l'article.

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Millions of opioid prescriptions are written every year in Canada, with consumption levels quadrupling between 2002 and 2012.[1] While the prevalence of chronic pain in Canada has remained stable,[2] rates of opioid dispensing have increased in most provinces.[3] It is not known whether increased opioid dispensing in Canada is driven by increases in short-term use of opioids, long-term use, or both.

While the short-term analgesic effects of opioids are well established, a recent systematic review concluded that there is insufficient evidence to determine the effectiveness of long-term opioid therapy in improving chronic pain, while there is accumulating evidence of harm.[4] Specifically, use of opioids has been found to be associated with bone fractures, road trauma, emergency department visits and both intentional and unintentional toxicity deaths, with a strong dose-response relationship.[5–8]

Trends in total opioid dispensing alone provide limited insights into clinical practice and actual patterns of use by patients. More detailed information is needed about opioid prescribing practices and patterns of opioid use, particularly among long-term users in Canada. To date, there is limited information on this patient population because the vast majority of studies focused on opioids either are based on a sample of dispensations without any information on the individuals[9,10] or are limited to select population groups who are eligible for public drug coverage.[11–13]

The objective of this study is to calculate trends in incidence and prevalence rates of long-term opioid use for non-cancer pain in British Columbia (BC). We also describe the characteristics of long-term opioid users and their patterns of opioid use.

METHODS

Data sources

These analyses are based on data from de-identified, linked health datasets provided by Population Data BC with approval of relevant data stewards and of the University of British Columbia's Behavioural Research Ethics Board.[14–16] All inferences, opinions and conclusions drawn in this report are those of the authors, and do not reflect the opinions or policies of Population Data BC or the opinions or policies of the data stewards.

Our data on prescription drug dispensations came from British Columbia PharmaNet, an information system into which pharmacists must enter records of every prescription dispensed outside of acute care hospitals, regardless of the insurance status of

Author Affiliations

1. School of Population and Public Health, University of British Columbia, Vancouver, BC
2. Department of Family Practice, University of British Columbia, Vancouver, BC

Correspondence: Steven G. Morgan, PhD, School of Population and Public Health, University of British Columbia, 2206 East Mall, Vancouver, BC V6T 1Z3, Tel: 604-822-7012, E-mail: steve.morgan@ubc.ca

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the patient. Prescription records include information about the drug type, dose, quantity dispensed, formulation, days of therapy, and prescribing physician, among other fields.

Our medical services data included provider type, service type, cost of service, and one primary diagnosis code (ICD-9) for every fee-for-service medical visit by all patients in our dataset. Our hospital services data came from the Discharge Abstract Database, which tracks discharges from all hospitals in BC. Hospital records contain information about reason for admission, length of stay, level of care, procedures received, and up to 25 diagnoses (ICD-10).

We obtained demographic information from registration files for BC's universal, public health insurance program. We estimated household income based on a combination of household-specific and area-based income data.[17] For 78% of the study population, we had validated, household-specific income information from BC's income-based public drug subsidy system. For the remaining 22% of the population, we estimated household income based on the median household income for the Census Dissemination Area in which people lived. Dissemination Areas are contiguous geographic areas with populations ranging from approximately 400 to 700 persons.

Study population

Our study population included individuals covered by British Columbia Medical Services Plan (and therefore residents of BC) for at least one year between January 1, 2004 and December 31, 2013. To ensure complete data capture, we only included those living in BC for at least 275 days in a given year. Our datasets did not capture information for individuals whose prescription drug coverage fell under federal jurisdiction (military, registered First Nations people and Inuit, and federal penitentiary inmates, who collectively make up approximately 4% of the BC population).

Definitions of key variables

Opioid analgesic drugs included in this study are listed in Appendix A, along with conversion factors used to calculate morphine equivalent (ME) values. We were able to calculate MEs for 98.6% of all captured dispensations. We excluded dispensations of methadone and buprenorphine because, in BC, these drugs are primarily prescribed as treatment for opioid dependence and, in part due to licensing regulations, are more rarely prescribed for the treatment of chronic pain. We also excluded opioid medications used as anesthetics (e.g., sufentanil), antipropulsives (e.g., diphenoxylate), muscle relaxants (e.g., methocarbamol) and cough suppressants (e.g., codeine combinations).

For the purposes of this analysis, we defined incident long-term opioid users as individuals who started an episode of long-term use in a given year but did not have an episode of long-term opioid use in the previous year. Individuals could be classified as incident users more than once if they had multiple episodes of long-term use that were at least a year apart. We defined prevalent users as those who had at least one episode of long-term use in a given year and also used opioids on a long-term basis in the previous year.

To be classified as an episode of long-term opioid use, a patient had to have filled one or more prescriptions containing at least 90 days of opioid therapy, with no gaps in prescriptions (periods during which previous prescriptions would have run out if taken consecutively) lasting longer than 182 days (six months). As such, an episode began when the first opioid prescription was dispensed, with no opioid drugs available to the patient in the previous six months based on their dispensation history. An episode ended on the date when the dispensed supply would have run out for the last prescription after which there was a minimum of six months with no further opioid dispensations. Some individuals had multiple episodes of long-term use with periods of six months or longer between episodes. This definition is similar to that used in the CONSORT study of long-term opioid users.[18,19]

Using this definition of long-term use of opioids, some episodes could have been for continuous use whereas others could have been for sporadic or intermittent use. We therefore categorized episodes of long-term opioid use into four groups based on the frequency of drug use. Frequency – in percentage of days covered – was calculated as the total number of days of prescribed opioid treatment dispensed to a patient during the episode divided by the total episode duration in calendar days. The groups were empirically derived based on data distribution and defined as follows: occasional users (<20%), regular users (20%–49%), chronic users (50%–89%) and every-day users (≥90%).

Among the study population, we identified individuals with cancer or those receiving palliative care services based on at least one hospital record with a cancer/palliative care diagnosis listed as the reason for admission or at least two physician billing claims no more than one year apart; the earliest record was taken as the date of diagnosis. We defined cancer diagnosis as all malignant neoplasms, neoplasms of uncertain behaviour or unspecified nature, carcinomas in situ, and other and unspecified malignant neoplasms of skin. We excluded episodes during which a patient received a cancer diagnosis or palliative care services. We also excluded episodes that began within a year after the last record of cancer diagnosis or palliative care services.

Other variables

We used the Johns Hopkins Adjusted Clinical Group (ACG version 10.0) case-mix adjustment system with ICD codes drawn from each individual's medical and hospital records during a given calendar year.[20] We used counts of the number of major Aggregated Diagnostic Groups (ADGs) as overall health status measures. We also used selections from the 264 Expanded Diagnostic Clusters (EDCs) of the ACG system to flag specific co-morbidities for which opioids are commonly prescribed. EDCs group similar diagnosis codes for related conditions (see Appendix B for specific codes).

We assigned ethnicity using a validated algorithm to identify surnames of Chinese and South Asian origin.[21] Chinese and South Asian are the dominant ethnic minorities in BC and respectively comprise 40% and 26% of the province's visible minority population.[22] Both of these ethnic groups demonstrated distinct prescription drug utilization patterns in prior survey-based studies conducted in BC.[23,24] Finally, we categorized neighbourhood urbanization based on the Local Health Area in which people lived.

Analyses

We examined the patterns of long-term opioid use by episode category, year and sex. We also calculated incidence, prevalence and discontinuation rates for long-term users over time. Incidence and prevalence were defined as the rates of occurrence of new and existing long-term users respectively. To compare rates between

men and women, we computed the incidence rate ratio (IRR). To account for population aging over time, all rates were directly age standardized to the 2008 British Columbia population. The 95% confidence intervals were estimated assuming that the observed number of events followed a Poisson distribution. We calculated discontinuation rate as percentage loss of incident and prevalent users in a current year who did not continue to be users in the following year.

Because of the six-month clearance period required to identify an episode's beginning and end, as well as a year-long time period to identify cancer cases, we could not completely capture all episodes that occurred in 2004 or 2013 and thus our data underestimate the number of long-term users for these years. Therefore, we do not include 2004 and 2013 in the presentation of our results. All analyses were performed using Stata version 13.1 and SAS version 9.3.

RESULTS

Of the 1.93 million residents of British Columbia who have received at least one opioid dispensation between 2005 and 2012, we identified a total of 270,672 episodes of long-term opioid use among 200,974 individuals. These long-term users – who comprised only 10% of all individuals prescribed opioids – accounted for 64% of all opioid prescriptions and 87% of all MEs dispensed in BC during this period.

Table 1 details the demographic characteristics of these individuals for the start year of their first episode of long-term use during the study period. Approximately 55% were women. Mean age was 59 among women and 54 among men. Individuals in the two lowest income quintiles accounted for 56% of all long-term users. Just over half (53%) had at least one chronic, non-cancer pain condition and 40% had at least one mental health condition.

Table 2 summarizes age-standardized incidence and prevalence rates for long-term opioid users in BC from 2005 to 2012. While the incidence rate did not significantly change, the prevalence rate increased by 27% for men, at an average annual rate of 3.53% (95% CI 2.75–4.31) and by 22% for women, at an average annual rate of 2.76% (95% CI 2.06–3.46). In 2012, there were 3.80 (3.72–3.88) new long-term opioid users per 1,000 men and 4.42 (4.34–4.51) new users per 1,000 women. At the same time, there were 18.3 (95% CI 18.1–18.5) existing long-term users per 1,000 men and 21.7 (95% CI 21.5–21.9) per 1,000 women. The incidence rate ratio was significantly higher for women compared to men for both incidence (1.16, 95% CI 1.11–1.22) and prevalence (1.22, 95% CI 1.19–1.25).

Table 1. Characteristics of individuals with at least one episode of long-term opioid use from 2005 to 2012

	Women, N = 110,136		Men, N = 90,838	
	n	%	n	%
Age (years)				
<35	10,368	9.4	9258	10
35–44	15,420	14	16,130	18
45–54	22,416	20	23,392	26
55–64	19,920	18	19,516	21
65+	42,012	38	22,542	25
Mean (SD)	59 (18)		54 (16)	
Income quintile				
1 (low)	38,761	35	25,154	28
2	25,534	23	22,216	24
3	17,377	16	16,732	18
4	14,793	13	14,330	16
5 (high)	12,134	11	10,253	11
Missing	1537	1.4	2153	2.4
Relationship status				
Single	60,820	55	42,556	47
Marriage-like	49,316	45	48,282	53
Neighbourhood urbanization				
Metro	61,748	56	51,148	56
Mixed	38,496	35	31,032	34
Rural	9637	8.8	8459	9.3
Missing	255	0.2	199	0.2
Ethnicity				
Chinese	1898	1.7	1249	1.4
European and other	104,327	95	83,671	92
South Asian	3911	3.6	5918	6.5
Major ADGs				
0	34,224	32	27,309	30
1–2	57,116	52	47,576	52
3+	16,137	15	14,126	16
Co-morbidities				
Abdominal pain	23,443	21	11,556	13
Anxiety	34,424	31	21,217	23
Depression	25,579	23	14,691	16
Fractures	10,626	10	8874	10
Low back pain	42,449	39	39,397	43
Neck pain	7042	6.4	6260	6.9
Rheumatoid arthritis	6337	5.8	2873	3.2
Substance use	5599	5.1	8902	10

Note: ADG = aggregated diagnosis group; SD = standard deviation.

Table 2. Age-standardized incidence and prevalence rates of long-term opioid users, 2005 vs. 2012, British Columbia

	2005		2012		Overall % change†	Annual % change (95% CI)	IRR‡ (95% CI)
	Cases	Rate per 1000* (95% CI)	Cases	Rate per 1000* (95% CI)			
Incidence							
Men	7554	3.83 (3.74–3.92)	8570	3.80 (3.72–3.88)	–0.9	1.54 (–0.02 to 3.08)	Ref.
Women	9269	4.58 (4.49–4.68)	10,344	4.42 (4.34–4.51)	–3.5	–0.60 (–0.80 to 2.02)	1.16 (1.11–1.22)
Prevalence							
Men	28,372	14.4 (14.2–14.6)	41,562	18.3 (18.1–18.5)	27	3.53 (2.75–4.31)	Ref.
Women	35,975	17.8 (17.6–18.0)	50,494	21.7 (21.5–21.9)	22	2.76 (2.06–3.46)	1.22 (1.19–1.25)
Overall prevalence (total)							
Men	35,926	18.2 (18.0–18.4)	50,132	22.1 (21.9–22.3)	21	3.13 (2.44–3.83)	Ref.
Women	45,244	22.4 (22.2–22.6)	60,838	26.1 (25.9–26.3)	16	2.34 (1.71–2.97)	1.21 (1.19–1.24)

Note: CI = confidence interval; IRR = incidence rate ratio.
* Age-standardized.
† Calculated as: (1 – [rate in 2012]/[rate in 2005]) × 100.
‡ Adjusted for year.

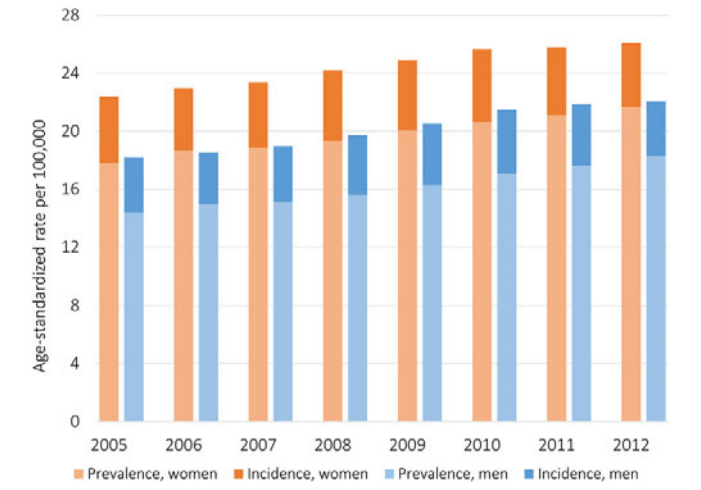

Figure 1. Long-term users of prescription opioids in British Columbia by sex, 2005–2012

Subsequently, overall prevalence rate of long-term users (including incident and prevalent users in a given year) rose as well. Expressed as a proportion, 2.0% of BC residents in 2005 were long-term opioid users compared with 2.4% in 2012 – a relative increase of 19% over eight years. Figure 1 illustrates the growing population of long-term opioid users in BC.

In any given year, the existing population of long-term opioid users (both men and women) consisted of approximately 19% who were new users that year and 81% who continued from the previous year to use opioids. On average, 12% of new users and 17% of prevalent users did not go on to be users in the following year. In other words, the overall discontinuation rate among all long-term opioid users in a given year was 16%.

Every year, approximately 5% of all long-term episodes were occasional; the rest were equally split between regular (31%), chronic (31%) and every-day users (33%). However, as Figure 2 shows, individuals with prevalent episodes tended to have a higher frequency of use in terms of percentage of episode days for which an opioid was available. This relative distribution did not change over time. There were no sex differences between or within episode types.

Over the study period, the majority (79%) of users had only one continuous episode; this ranged from 71% among occasional users to 87% among every-day users. Median episode duration was 645 calendar days, while the median number of days of therapy during an episode was 300.

Median [interquartile range, IQR] daily dose during the episode of long-term use was 4 [3–5] ME for occasional users, 8 [5–11] ME for regular users, 17 [11–28] ME for chronic users and 79 [33–197] ME for every-day users.

For more than half (56%) of all episodes among the study population, codeine was the most frequently prescribed opioid during the episode, followed by oxycodone (16%), tramadol (9%), hydromorphone (8%) and morphine (7%). The number of different opioids used during the episode increased with frequency of drug use during the episode (Figure 3).

DISCUSSION

In this study, we found that there is a growing prevalent population of long-term opioid users in British Columbia, with new long-term users emerging every year at a stable rate. In 2012, 2.4% of BC residents were long-term users of prescription opioids, with the majority of them being prevalent users who accounted for most of the opioid consumption in the province. Most long-term users had one continuous episode of use spanning multiple years. Almost two thirds took opioids every other day or more frequently.

The demographic and clinical characteristics of our study population are consistent with previous research on long-term opioid users.[18,19] We found that the majority of users have one continuous episode of opioid use, often spanning multiple years. This is in line with US studies of discontinuation rates among chronic opioid users, which have found that the majority of patients who received at least 90 days of continuous opioid therapy over a six-month period remained on opioid therapy years later.[25,26]

We found that an increasing proportion of BC residents are becoming long-term opioid users. This is driven by a discontinuation rate among users that is lower than the incidence of new users: for every 19 new long-term users in a given year, 16 existing long-term users will discontinue therapy. We could not examine the factors that contributed to long-term

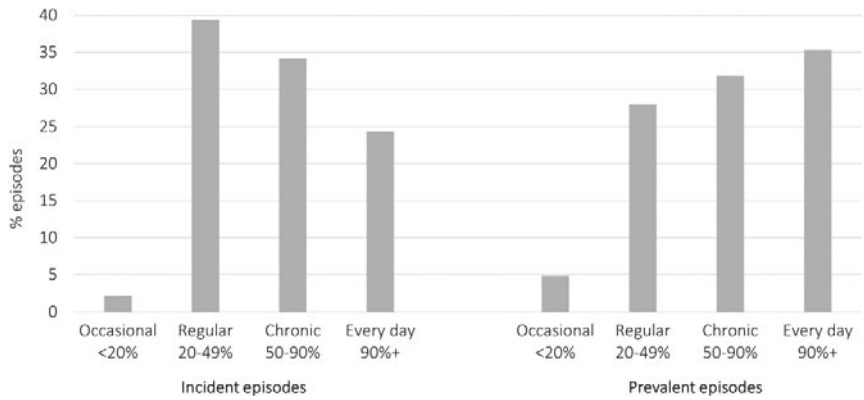

Figure 2. Episode types of incident and prevalent episodes, British Columbia, 2012

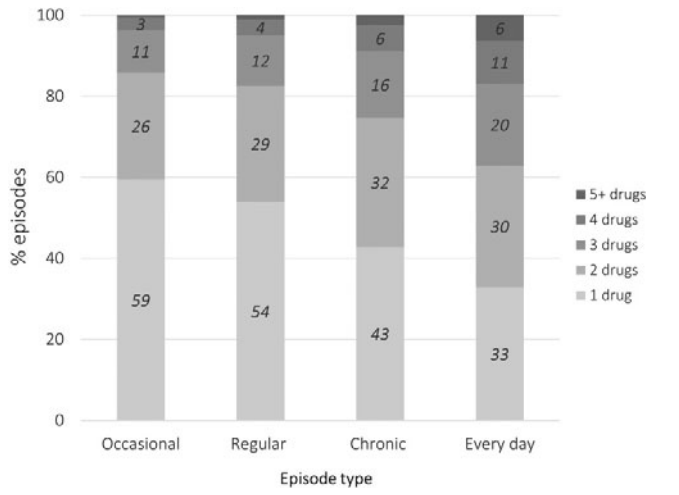

Figure 3. Number of different opioid drugs used during an episode, by type of episode

opioid use becoming more common. The most likely explanation is the increased attention to pain management by the medical community, and the accompanying encouragement to diagnose and treat pain in patients.

Our incidence and prevalence rates, as well as annual rates of change, are of comparable magnitude but considerably lower than those reported for two US health care plan enrollees.[18,19] This is consistent with overall higher opioid consumption in the US compared to Canada.[1,27] We could not identify any Canadian references for comparison. To put these rates in perspective on a population level, our reported incidence of non-cancer, non-palliative long-term opioid use of 3.8 per 1,000 men and 4.4 per 1,000 women in 2012 is comparable to incidence of cancer in BC in that year, at 3.9 per 1,000 men and 3.3 per 1,000 women.[28]

Furthermore, from the population health perspective, the prevalence of 2.4% is indicative of an exposure that is common enough to warrant serious concerns regarding adverse events. While opioids have been shown to work well on a short-term basis, their effectiveness during long-term therapy is uncertain.[4] In light of the growing population of long-term opioid users, further research into the effectiveness and safety of such therapy is needed to better understand the clinical implications for this patient population.

We found that incident users used opioids less frequently than prevalent users, whose opioid dispensations represented an intake of up to multiple pills per day. This pattern is expected as patients transition from being new users to persistent users, given that opioid use is associated with development of tolerance and dependence.[29] It is also noteworthy that the top 25% of every-day users received a dose of 200 ME or higher per day, suggesting either extremely high tolerance or diversion in this patient group. We further observed that as the frequency of opioid intake increased, so did the number of different opioid medications. While this may signal potentially problematic polypharmacy, it may also reflect physician efforts to limit tolerance by using drug rotation, and thus, appropriate clinical practice.

Strengths and limitations

Our results are strengthened by the comprehensiveness of our prescription drug data used, which is the biggest in terms of whole-of-population coverage currently available in Canada. Further, our study captures almost all residents of British Columbia, thus providing complete and representative population-level estimates. We could not capture any opioids dispensed during hospital stays. However, the majority of opioids are dispensed in retail pharmacies in Canada.[9] Dispensation does not equate to consumption, and we may be overestimating the actual level of exposure to prescription opioids. This may particularly apply to individuals categorized as "every-day users" because at least some of the opioids dispensed to them may be diverted. Given the geographic variability in opioid prescribing practices, we are not certain to what extent our results are generalizable to other jurisdictions.

CONCLUSION

There is a growing population of long-term opioid users for non-cancer pain in British Columbia, with higher incidence and prevalence rates observed among women than among men. Research into the effectiveness and safety of long-term opioid use is needed to better understand the clinical implications for this patient population.

Appendix A. Opioid equivalents

Opioid	To convert dose to oral morphine equivalent, multiply by	Equivalence to oral morphine 30 mg
Codeine	0.15	200 mg
Dextropropoxyphene	0.1	300 mg
Hydromorphone	5	6 mg
Morphine	1	30 mg
Oxycodone	1.5	20 mg
Pentazocine	0.165	182 mg
Pethidine	0.1	300 mg
Tapentadol	0.30	100 mg
Tramadol	0.05	600 mg
Transdermal Fentanyl	52 mg morphine = 12 mcg/h 97 mg morphine = 25 mcg/h 152 mg morphine = 37 mcg/h 202 mg morphine = 50 mcg/h 247 mg morphine = 62mcg/h 292 mg morphine = 75 mcg/h 337 mg morphine = 87 mcg/h 382 mg morphine = 100 mcg/h	

Appendix B. Co-morbidities

Condition	EDC code(s)
Abdominal pain	GSU10
Anxiety	PSY01
Depression	PSY09
Fractures	MUS04, MUS10
Low back pain	MUS14
Neck pain	MUS13
Rheumatoid arthritis	RHU05
Substance use	PSY02

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RÉSUMÉ

OBJECTIFS : Nous avons cherché à calculer les tendances dans les taux d'incidence et de prévalence de l'usage à long terme d'opioïdes contre la douleur non cancéreuse, ainsi qu'à décrire les caractéristiques des consommateurs à long terme d'opioïdes et leurs types d'usage d'opioïdes.

MÉTHODE : Nous avons utilisé les données administratives sociodémographiques et de soins de santé liées à la population de la Colombie-Britannique (C.-B.) de 2005 à 2012. Nous avons inclus les personnes ayant eu au moins un épisode d'usage à long terme d'opioïdes durant la période de l'étude et qui n'étaient pas des patients cancéreux ni aux soins palliatifs.

RÉSULTATS : Les consommateurs à long terme ne représentaient que 10 % des personnes à qui l'on avait prescrit des opioïdes contre la douleur non cancéreuse, mais ils avaient reçu 64 % des prescriptions d'opioïdes et 87 % de tous les équivalents de morphine distribués en C.-B. durant la période de l'étude. Le taux d'incidence n'a pas changé de manière significative, mais le taux de prévalence a augmenté de 27 % chez les hommes et de 22 % chez les femmes. En 2012, il y avait 3,80 (3,72–3,88) nouveaux consommateurs à long terme d'opioïdes pour 1 000 hommes et 4,42 (4,34–4,51) nouvelles consommatrices pour 1 000 femmes. Simultanément, il y avait 18,3 (IC de 95 % 18,1–18,5) consommateurs à long terme existants pour 1 000 hommes et 21,7 consommatrices à long terme existantes (IC de 95 % 21,5–21,9) pour 1 000 femmes. Dans l'ensemble, 2,4 % des résidents de la C.-B. étaient des consommateurs à long terme d'opioïdes d'ordonnance en 2012. La plupart des consommateurs à long terme avaient eu un épisode continu de consommation sur plusieurs années. Près des deux tiers prenaient des opioïdes tous les deux jours ou plus souvent.

CONCLUSION : Il existe une population croissante de consommateurs à long terme d'opioïdes contre la douleur non cancéreuse en C.-B., et l'on observe des taux d'incidence et de prévalence plus élevés chez les femmes que chez les hommes.

MOTS CLÉS : opioïdes analgésiques; douleur chronique; incidence; prévalence; prescriptions inappropriées