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Research

Influence of opioid prescribing standards on drug use among patients with long-term opioid use: a longitudinal cohort study

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Abstract

Background: In mid-2016, the College of Physicians and Surgeons of British Columbia (CPSBC) issued prescribing standards and guidelines relating to opioid drugs. We evaluated the impact of these regulatory standards and guidelines on prescription drug use among patients in the province with long-term opioid use.

Methods: We conducted a cohort study with monthly repeated measures using administrative health data in British Columbia. Patients with long-term prescription opioid use were followed for a 12-month prepolicy period and 10-month postpolicy period, and were compared with a historical control cohort. We excluded patients with a history of long-term care, palliative care or cancer. We estimated changes in use of opioids, high-dose opioids (> 90 mg of morphine equivalents/d), opioids with sedatives/hypnotics, and opioid discontinuation.

Results: The study population included 68 113 patients in the policy cohort and 68 429 patients in the historical control cohort. Following the introduction of the standards and guidelines, the average monthly use of opioids declined (adjusted difference –57 mg of morphine equivalents, 95% confidence interval [CI] –74 to –39) and discontinuation of opioids increased (odds ratio [OR] 1.24, 95% CI 1.16 to 1.32). Among patients prescribed high-dose opioids, switching to lower-dose opioids increased (OR 1.88, 95% CI 1.63 to 2.17), but discontinuation did not change significantly (OR 1.21, 95% CI 0.91 to 1.59).

Interpretation: The CPSBC's regulatory standards and guidelines were associated with modestly reduced opioid use and increased switching from high-dose to lower-dose opioids among patients with long-term use of prescribed opioids. Assessment of the potential impacts on health outcomes will be necessary for understanding the implications of the standards and guidelines.

The increasing number of opioid overdoses and deaths due to illicit drug overdoses in British Columbia led the provincial health officer to declare a public health emergency in April 2016.[1–3] Although the rise in deaths due to illicit drug overdoses was closely linked to the contamination of street drugs with fentanyl and other synthetic opioids,[3] the growth in opioid-related harms was likely related in part to high rates of opioid prescribing.[4–6] In mid-2016, the College of Physicians and Surgeons of British Columbia (CPSBC) issued regulatory prescribing standards and guidelines to help promote best prescribing practices for opioid treatment of pain.[7] The policy took effect on June 1, 2016, and contained both legally enforceable standards and recommended guidelines. The policy did not apply to patients with active cancer or those receiving palliative or end-of-life care.

The CPSBC issued the standards and guidelines in a context of uncertainty over the value of opioids in the treatment of chronic noncancer pain. A position paper that emerged from a 2014 National Institutes of Health workshop highlighted that "[d]ata to support the long-term use of opioids for chronic pain management are scant."[8] More recently, a pragmatic randomized trial comparing opioids to nonopioid medications for moderate to severe chronic back pain, or hip or knee osteoarthritis pain over 12 months showed that opioids were not superior to nonopioid medications at improving pain-related function,[9] and a systematic review showed that opioids compared to placebo were associated with only small

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decreases in pain and improvements in physical functioning in the treatment of chronic noncancer pain.[10] Our study aimed to evaluate whether the CPSBC's regulatory prescribing standards and guidelines influenced prescription drug use among British Columbians with long-term prescription opioid use.

Methods

Study setting and design

We used a longitudinal cohort study design with a historical control group. Longitudinal designs are characterized by repeated measures over time for people in the study, allowing for the study of "change in response over time and factors that influence change."[11] This design has been used to study drug effects[12,13] and the impacts of health policy.[14,15] The longitudinal data in our study captured monthly drug use, allowing us to study changes in drug use in response to the introduction of the opioid prescribing standards and guidelines, while controlling for patient covariates. The study cohort consisted of BC residents with long-term use of prescription opioids: buprenorphine patch, codeine, fentanyl, hydromorphone, meperidine, morphine, oxycodone, tapentadol or tramadol. We defined long-term opioid use as filling at least 2 opioid prescriptions during a 6-month period, with at least 1 fill in the first 3 months and 1 fill in the last 3 months, comprising at least 60 days' supply.

We identified a cohort of patients who met the criteria for long-term opioid use during an identification period of Dec. 1, 2014–May 31, 2015 (Figure 1). We refer to these patients as the policy cohort because their follow-up included a 12-month prepolicy period (June 1, 2015–May 31, 2016) and a 10-month postpolicy period (June 1, 2016–Mar. 31, 2017) during which the opioid prescribing standards and guidelines applied. We also identified a historical control cohort that met the criteria for chronic opioid use 1 year earlier (Dec. 1, 2013–May 31, 2014) (Figure 1). Follow-up for the historical cohort included a 12-month baseline period (analogous to the prepolicy period of the policy cohort) and a 10-month control period (analogous to the postpolicy period of the policy cohort), between June 1, 2014, and Mar. 31, 2016. The historical control cohort provided a comparison group not affected by the opioid prescribing standards and guidelines. It was possible for patients to be members of both cohorts if they met the inclusion criteria during the identification period for both cohorts. We excluded patients who lacked 1 year of medical services coverage, had a record of long-term residential or palliative care, or had a medical visit with a diagnosis of cancer in the year before follow-up (diagnostic codes are provided in Supplementary Table S1, Appendix 1, available at www.cmajopen.ca/content/7/3/E484/suppl/DC1). We censored patients during follow-up if they lost medical services coverage, entered long-term or palliative care, died or received a diagnosis of cancer.

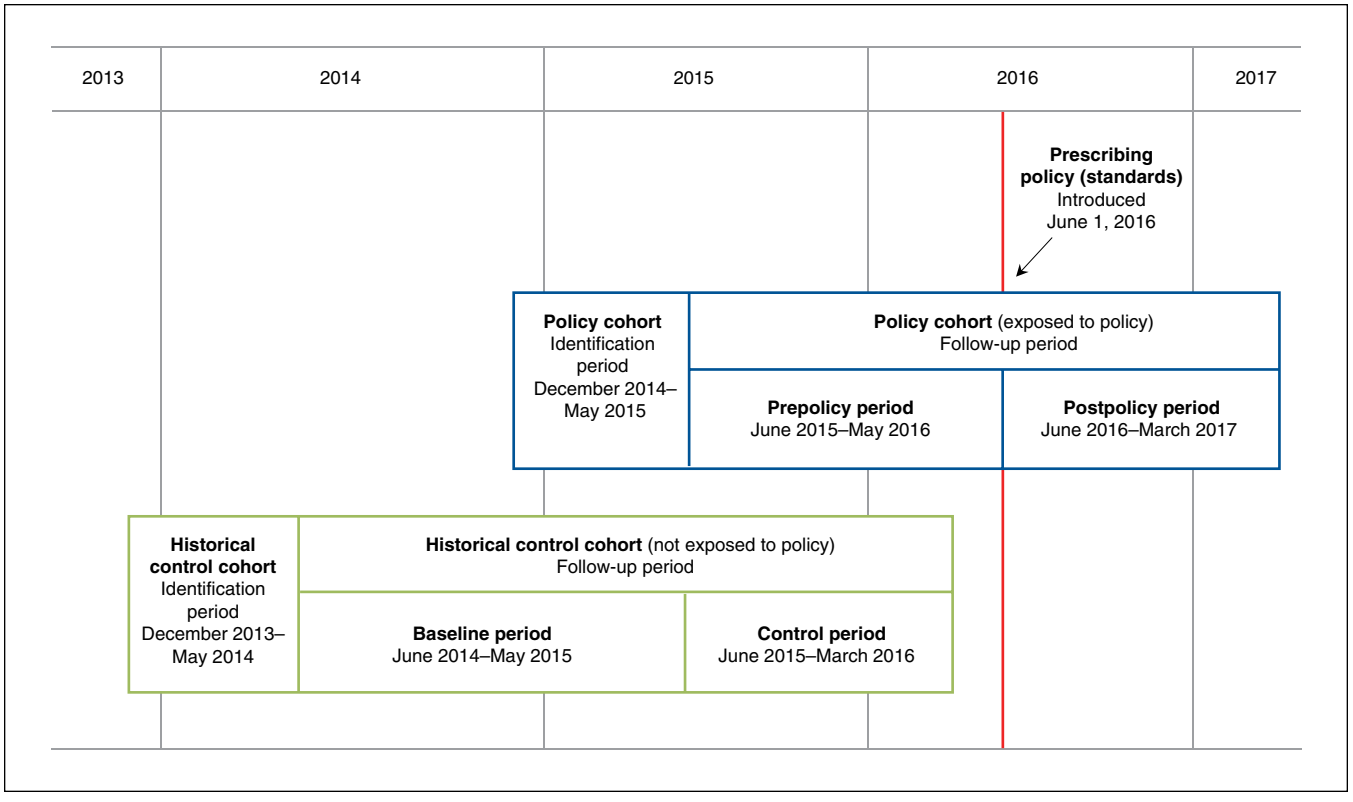

Figure 1: Longitudinal cohort study design with cohort identification and follow-up periods for policy cohort and historical control cohort. Patients were selected for either cohort during a 6-month identification period. The policy cohort was followed for a 12-month period before the College of Physicians and Surgeons of British Columbia issued regulatory opioid prescribing standards and guidelines and a 10-month postpolicy period. Historical control subjects were followed for an analogous 12-month baseline period and 10-month control period, but were not exposed to the policy.

Data sources

We used linked data from the BC Ministry of Health's Health*ideas* data warehouse, including deidentified patient-level, data from the BC Medical Services Plan, BC PharmaNet, the BC Vital Statistics Agency and the Canadian Institute for Health Information Discharge Abstract Database. These data sets include most of the province's population but exclude about 4% of the population covered by federally insured drug plans for First Nations, members of the military, veterans, members the Royal Canadian Mounted Police and inmates in federal penitentiaries. The BC Ministry of Health and the BC Vital Statistics Agency approved access to and use of BC data (www.popdata.bc.ca/data).

Outcome measures

Outcomes included monthly use of opioid analgesic medication, discontinuation of opioids, discontinuation of high-dose opioids, switching from high-dose to lower-dose opioids, and discontinuation and initiation of concurrent use of opioids and sedatives/hypnotics (identified by Anatomic Therapeutic Chemical codes N05C, N03AE and N05BA[17]). To determine a patient's monthly opioid analgesic use, we calculated each prescription's daily dosage in milligrams of morphine equivalents[16] and assumed that use was evenly distributed across the prescribed days' supply. We defined discontinuation as occurring if no additional prescription was filled within 90 days of the end of the prescription. We deemed a patient to have discontinued high-dose opioid therapy if no additional opioid prescription of any dosage was filled within 90 days, or to have switched to a lower dosage if a prescription with a daily dosage of 90 mg or less of morphine equivalents, but no prescription greater than 90 mg of morphine equivalents/d, was filled within 90 days. We defined concurrent use of opioids and sedatives/hypnotics as overlapping days' supply of these medications. We deemed a patient to have discontinued concurrent use after 90 days with no concurrent supply.

Covariates

We defined patient variables to control for confounding in adjusted analyses. Demographic variables included sex, age category, low-income status and rural residence. We included medical history variables based on diagnoses from outpatient and inpatient records in the 365 days before follow-up: psychiatric illness, mechanical neck or back problems (excluding low back pain), mechanical low back pain, osteoarthritis, rheumatoid arthritis, diabetic neuropathy, peripheral neuropathy (excluding diabetic neuropathy), lumbar radiculopathy, alcohol dependence or abuse, opioid use disorder and Romano comorbidity score (an index of the patient's comorbidities based on previous diagnoses).[18,19] Diagnostic codes and definitions for chronic pain conditions are provided in Supplementary Tables S2 and S3, Appendix 1.[20–28] We also included variables for prescription drug use in the 180 days before follow-up: opioid substitution therapy (≥ 1 prescription), use of sedative/hypnotic medication (including benzodiazepines) (≥ 1 prescription), maximum daily opioid analgesic dosage prescribed (≤ 50, > 50 to 90, > 90 to 200 or > 200 mg of morphine equivalents) and intensity of opioid analgesic use (60 to < 90 or ≥ 90 days' supply prescribed).

Statistical analysis

We used generalized linear models to estimate changes in monthly use of opioid analgesic medications following the introduction of the standards and guidelines as absolute differences, and to estimate changes in discontinuation, switching or initiation as odds ratios (ORs). All statistical models included adjustment for the patient-level covariates to control for confounding, and used generalized estimating equations to adjust for correlations among multiple observations from the same patients.[29]

We estimated absolute differences or ORs for changes to the level and trend of each outcome following the opioid prescribing standards and guidelines among patients in the policy cohort compared to the historical control cohort by including interactions in each model between cohort status (policy cohort v. historical control cohort) with level effect and trend effect variables.[14,15] An interaction between cohort status and level effect in the model tested for level changes in drug use, which represented a sudden change after the policy was issued. An interaction between cohort status and trend effect in the model tested for trend (slope) changes, which represented a gradual change in drug use occurring in each month of the postpolicy period (Supplementary Figure S1, Appendix 1 depicts potential level and trend changes following a change in policy). We modified our approach for the outcome of monthly opioid use by including a 3-month transition period and using a shorter postpolicy period, because days' supply from prescriptions predating the opioid prescribing standards and guidelines might carry forward for about 3 months and attenuate this measure (more detail about statistical analyses is provided in Appendix 1).

Ethics approval

This study was approved by the University of British Columbia Clinical Research Ethics Board.

Results

Patient characteristics

The study population included 68 113 patients in the policy cohort and 68 429 patients in the historical control cohort (Table 1); 47 416 patients were in both cohorts because they met the inclusion criteria at baseline for both (during the identification period for each cohort). Patients were followed for 1–22 months; 61 677 patients (90.6%) in the policy cohort and 62 183 patients (90.9%) in the historical control cohort were followed for at least 16 months. Patient characteristics were similar across the 2 cohorts (Table 1). However, slightly fewer patients in the policy cohort than in the historical control cohort had been prescribed high-dose or very high dose opioids before follow-up. The most common chronic pain conditions among the study population were mechanical low back pain, mechanical neck and back pain (excluding low back pain) and osteoarthritis (Table 1).

Table 1: Characteristics of patients with long-term opioid use in British Columbia, historical control cohort versus policy cohort*

Characteristic	No. (%) of patients		ASD, %
	Historical control cohort *n* = 68 429	Policy cohort *n* = 68 113	
Demographic			
Sex			
Female	36 894 (53.9)	36 903 (54.2)	0.5
Male	31 535 (46.1)	31 210 (45.8)	0.5
Age, yr			
< 25	473 (0.7)	388 (0.6)	1.5
25–39	6376 (9.3)	5925 (8.7)	2.2
40–54	20 946 (30.6)	19 848 (29.1)	3.2
55–64	18 779 (27.4)	19 249 (28.3)	1.8
65–74	11 670 (17.0)	12 391 (18.2)	3.0
75–84	6921 (10.1)	7015 (10.3)	0.6
≥ 85	3264 (4.8)	3297 (4.8)	0.3
Low income	13 222 (19.3)	12 683 (18.6)	1.8
Place of residence			
Rural	10 766 (15.7)	10 726 (15.7)	0.04
Urban	57 663 (84.3)	57 387 (84.2)	0.04
Medical history in 365 d before follow-up			
Psychiatric illness	14 994 (21.9)	14 152 (20.8)	2.8
Chronic pain condition			
Mechanical neck or back pain†	9738 (14.2)	9815 (14.4)	0.5
Mechanical low back pain	12 900 (18.8)	13 477 (19.8)	2.4
Osteoarthritis	6778 (9.9)	6723 (9.9)	0.1
Rheumatoid arthritis	1619 (2.4)	1566 (2.3)	0.4
Diabetic neuropathy	239 (0.3)	262 (0.4)	0.6
Peripheral neuropathy	230 (0.3)	262 (0.4)	0.8
Lumbar radiculopathy	182 (0.3)	221 (0.3)	1.1
Alcohol dependence or abuse	1307 (1.9)	1311 (1.9)	0.1
Opioid use disorder	821 (1.2)	931 (1.4)	1.5
Romano comorbidity score			0.8
0	36 447 (53.3)	36 000 (52.8)	
1	17 146 (25.1)	16 965 (24.9)	0.3
2	7074 (10.3)	7320 (10.7)	1.3
≥ 3	7762 (11.3)	7828 (11.5)	0.5
Prescription history in 180 d before follow-up			
Opioid substitution therapy	943 (1.4)	909 (1.3)	0.4
Maximum daily opioid analgesic dosage dispensed, MME			
Lower (≤ 50)	41 679 (60.9)	42 565 (62.5)	3.3
Intermediate (> 50 to 90)	12 987 (19.0)	12 753 (18.7)	0.7
High (> 90 to 200)	8598 (12.6)	8144 (12.0)	1.9
Very high (> 200)	5165 (7.5)	4651 (6.8)	2.8
Intensity of opioid analgesic use‡			
Lower (< 90 days' supply)	10 648 (15.6)	10 471 (15.4)	0.5
Higher (≥ 90 days' supply)	57 781 (84.4)	57 642 (84.6)	0.5
Sedative/hypnotic medication use	30 291 (44.3)	28 737 (42.2)	4.2

Note: ASD = absolute standardized difference, MME = milligrams of morphine equivalents.
*Patient characteristics were evaluated before follow-up.
†Excluding low back pain.
‡Based on days' supply dispensed.

Impact on drug use

The average monthly dosage of opioids was 1625 mg of morphine equivalents during the prepolicy period in the policy cohort and 1770 mg of morphine equivalents in the historical control cohort (Table 2). We observed a small decrease in the level of monthly opioid use following the introduction of the opioid prescribing standards and guidelines in the policy cohort relative to the historical control cohort (adjusted difference –57 mg of morphine equivalents, 95% confidence interval [CI] –74 to –39) and a decreasing trend in opioid use (Table 2). The trend lines for monthly opioid use for both cohorts declined over time, in part because some patients in both cohorts stopped opioids over time (Figure 2). However, the decline in opioid use associated with the policy can be observed in the divergence of trend lines during the postpolicy period.

The average monthly rate of discontinuation was 2.6% in the policy cohort and 2.5% in the historical control cohort in the prepolicy period. Following the introduction of the prescribing standards and guidelines, we found an increase in the level of opioid discontinuation in the policy cohort relative to the historical control cohort (adjusted OR 1.24, 95% CI 1.16 to 1.32) (Table 2 and Figure 2). In contrast, we did not find a clear association between the introduction of the opioid prescribing policy and the rate of discontinuation of high-dose opioids: the level of discontinuation of high-dose opioids increased nonsignificantly (adjusted OR 1.21, 95% CI 0.91 to 1.59), whereas there was small, nonsignificant monthly decline in discontinuation of high-dose opioids (adjusted OR 0.98, 95% CI 0.94 to 1.03) (Table 2). Figure 3 appears to reflect this mixed finding, as the crude rate of discontinuation of high-dose opioids in the policy cohort increased temporarily following the introduction of the policy and then returned to prepolicy levels. However, the level of switching from high-dose to lower-dose opioids showed a clear increase during the postpolicy period (adjusted OR 1.88, 95% CI 1.63 to 2.17) (Table 2 and Figure 3).

Discontinuation of concurrent use of opioids and sedatives/hypnotics increased in the postpolicy period (adjusted OR 1.37, 95% CI 1.27 to 1.49). However, the potential change in initiation of concurrent use of opioids and sedatives/hypnotics following the policy was unclear, with the impact on the level suggesting an increase (adjusted OR 1.10, 95% CI 1.02 to 1.18) and the impact on trend suggesting a monthly decline (adjusted OR 0.98, 95% CI 0.97 to 0.99) (Table 2 and Supplementary Figure S2).

Table 2: Impact of opioid prescribing standards and guidelines on drug use among patients with long-term opioid use

Analysis	No. of patients		Measures in prepolicy period*		Impact on outcome level†	Impact on outcome trend†
	Historical control cohort	Policy cohort	Historical control cohort	Policy cohort		
			Monthly MME, mean ± SD		Adjusted difference (95% CI)‡	Adjusted difference (95% CI)‡
Opioid analgesic use	68 429	68 113	1770 ± 4200	1625 ± 3860	–57 (–74 to –39)	–6.8 (–9.9 to –3.8)
Discontinuation			Monthly discontinuation, %		Adjusted OR (95% CI)‡	Adjusted OR (95% CI)‡
Discontinuation of opioid use§	66 203	65 791	2.5	2.6	1.24 (1.16 to 1.32)	1.00 (0.98 to 1.01)
Discontinuation among high-dose opioid users¶	13 922	12 409	0.6	0.6	1.21 (0.91 to 1.59)	0.98 (0.94 to 1.03)
Discontinuation of concurrent opioid and sedative/hypnotic use**	28 483	26 506	9.2	9.4	1.37 (1.27 to 1.49)	0.99 (0.97 to 1.00)
Switching			Monthly switching, %		Adjusted OR (95% CI)‡	Adjusted OR (95% CI)‡
Switching from high-dose to lower-dose opioid¶	13 922	12 409	2.5	2.6	1.88 (1.63 to 2.17)	0.99 (0.97 to 1.01)
Initiation			Monthly initiation, %		Adjusted OR (95% CI)‡	Adjusted OR (95% CI)‡
Initiation of concurrent opioid and sedative/hypnotic use**	54 934	56 441	2.1	2.0	1.10 (1.02 to 1.18)	0.98 (0.97 to 0.99)

Note: CI = confidence interval, MME = milligrams of morphine equivalents, OR = odds ratio, SD = standard deviation.
*Calculated based on all monthly observations during the 12-month prepolicy period for the policy cohort and corresponding period for the historical control cohort.
†"Impact on outcome level" measures a sudden change following implementation of a policy, whereas "impact on outcome trend" measures gradual change occurring each month following implementation of a policy.
‡Adjusted for patient-level covariates, including demographic variables, medical history and prescription drug use.
§Analysis of discontinuation of opioids included only patients who had a prescription with sufficient days' supply to end in a given month.
¶Analyses of discontinuation of high-dose opioids and switching from high-dose to lower-dose opioids included patients who had received a high-dose prescription (with a daily dosage > 90 mg of morphine equivalents) ending in a given month.
**Concurrent use was defined as overlapping supply according to the date and days' supply dispensed. Analysis of discontinuation of concurrent use of opioids and sedatives/hypnotics included patients with concurrent use and an opioid or sedative/hypnotic prescription ending in a given month; analysis of initiation of concurrent use of these medications included only patients without concurrent use in the 180 days before the current month.

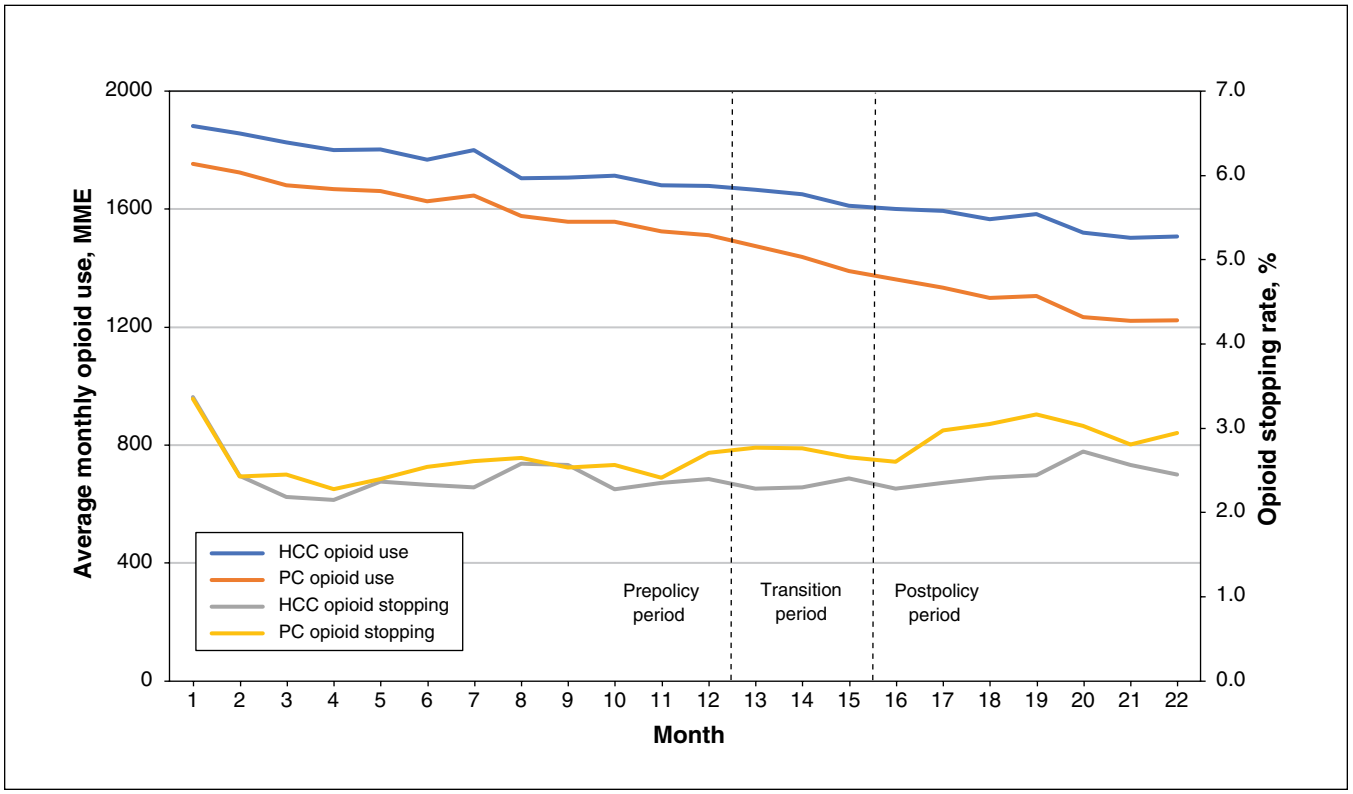

Figure 2: Average monthly opioid analgesic use and opioid discontinuation rate in the policy cohort (PC) versus the historical control cohort (HCC). The analysis of opioid use included a 3-month transition period after prescribing standards were introduced to account for medication supply that would carry forward from the prepolicy period; this did not apply to the discontinuation analysis. Note: MME = milligrams of morphine equivalents.

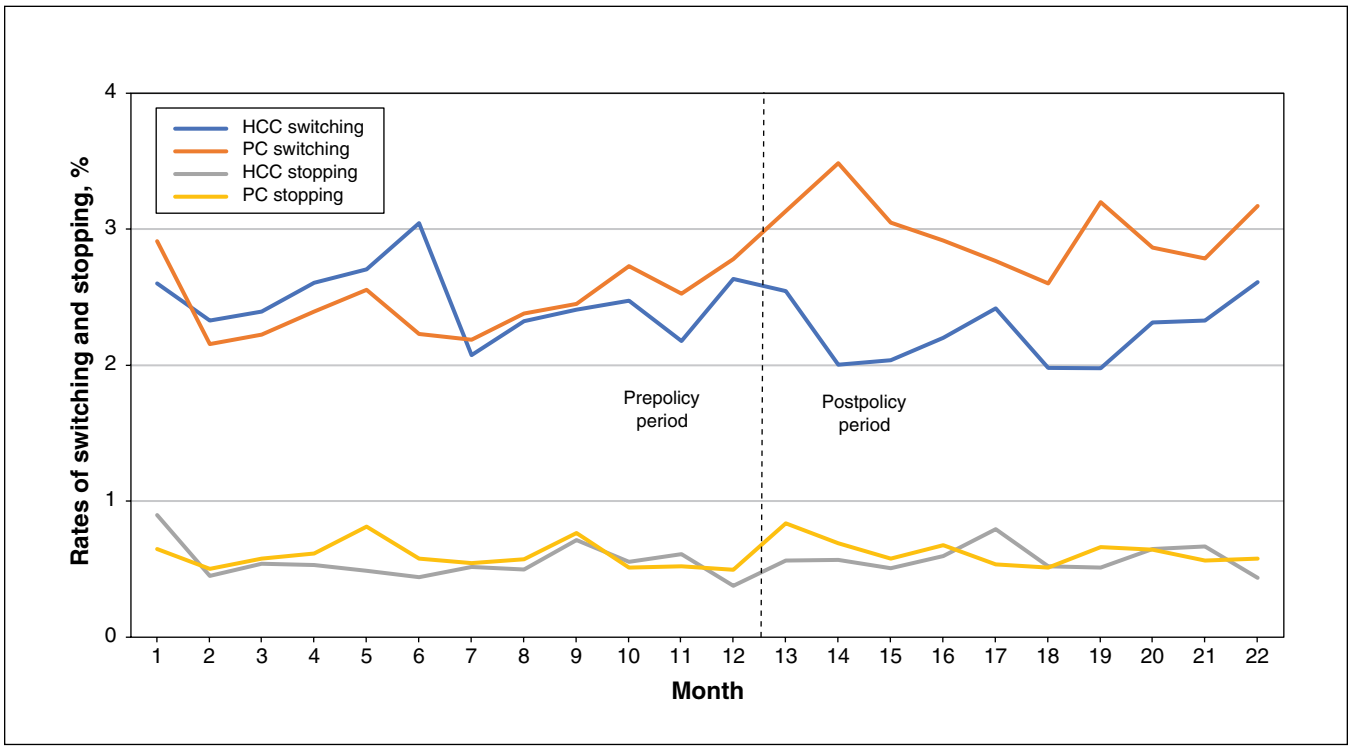

Figure 3: Monthly rates of switching from high-dose (> 90 mg of morphine equivalents/d) to lower-dose (≤ 90 mg of morphine equivalents/d) opioid medication and rates of stopping high-dose opioid medication in policy cohort (PC) versus historical control cohort (HCC).

Interpretation

The CPSBC's opioid prescribing standards and guidelines were associated with a modest reduction in opioid use among patients with long-term prescription opioid use in British Columbia. Introduction of the standards and guidelines was followed by a small reduction in the level and trend of use of prescription opioid analgesics, reflecting both increased discontinuation of opioids and increased switching from high-dose to lower-dose opioids. The rate of opioid discontinuation among patients with high-dose opioid prescriptions did not change significantly following introduction of the policy. Introduction of the standards and guidelines was associated with increased discontinuation of concurrent use of opioids and sedative/hypnotic medications, but not with a clear change in initiation of concurrent use of opioids and sedative/hypnotic medications.

The increased rate of switching from high-dose to lower-dose opioids appears to reflect the CPSBC's advice to avoid prescribing daily dosages above 90 mg of morphine equivalents in most cases and to prescribe opioids at the "lowest effective dosage."[7] Similarly, the prescribing standards discouraged prescribing of sedatives/hypnotics to patients receiving long-term opioid therapy,[7] and this appears to be reflected in the increased discontinuation of concurrent use of opioids and sedatives/hypnotics in the postpolicy period. Previous research suggests that use of higher-dose opioids and concurrent use of opioids and sedative/hypnotic medications are risk factors for overdose.[30–32] Revisions of the standards and guidelines (now simply a "practice standard") have retained elements similar to those mentioned above.[33]

Our findings are consistent with those of 2 previous studies of the impact of opioid prescribing guidelines on drug use. A study of workers' compensation claimants in Washington State showed that an opioid prescribing guideline reduced the prevalence of opioid use among claimants.[34] Similarly, a study of Ontario residents aged 15–64 years who were eligible for public drug coverage suggested that the introduction of Canadian clinical practice guidelines, in May 2010, reduced the rate of opioid use in that province.[35]

Limitations

We did not evaluate the impact of the policy on pain management or health outcomes. The definition of long-term opioid use used to define our study cohort likely captured some patients who were not long-term users of opioids. We used prescription drug dispensing data, which may differ from actual medication use (e.g., overlapping supply of opioids and sedatives/hypnotics could differ from concurrent use for some patients). Opioid use may have been influenced by factors not controlled for in our study, such as news reports and cointerventions. Cointerventions included the release of the Centers for Disease Control and Prevention guideline for prescribing opioids for chronic pain, in March 2016,[36] the declaration of a public health emergency by the BC provincial health officer, in April 2016,[1] and the CPSBC's policy to allow prescribing of buprenorphine/naloxone by physicians not officially authorized to prescribe methadone for opioid use disorder (which took effect 1 mo after the standards and guidelines were issued).[37]

Conclusion

The regulatory opioid prescribing standards and guidelines introduced by the CPSBC in mid-2016 were associated with modestly reduced opioid analgesic use, increased discontinuation of opioids, increased switching from high-dose to lower-dose opioid use, and increased discontinuation of concurrent use of opioids and sedative/hypnotic medications among patients with long-term use of prescribed opioids in British Columbia. Assessment of potential impacts on health outcomes will be necessary for understanding the implications of the standards and guidelines.

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