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ORIGINAL RESEARCH ARTICLE

Opioid Prescribing in Canada following the Legalization of Cannabis: A Clinical and Economic Time-Series Analysis

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Abstract

Purpose On 17 October 2018 recreational cannabis became legal in Canada, thereby increasing access and reducing the stigma associated with its use for pain management. This study assessed total opioid prescribing volumes and expenditures prior to and following cannabis legalization.

Methods National monthly claims data for public and private payers were obtained from January 2016 to June 2019. The drugs evaluated consisted of morphine, codeine, fentanyl, hydrocodone, hydromorphone, meperidine, oxycodone, tramadol, and the non-opioids gabapentin and pregabalin. All opioid volumes were converted to a mean morphine equivalent dose (MED)/claim, which is analogous to a prescription from a physician. Gabapentin and pregabalin claims data were analyzed separately from the opioids. Time-series regression modelling was undertaken with dependent variables being mean MED/claim and total monthly spending. The slopes of the time-series curves were then compared pre- versus post-cannabis legalization.

Results Over the 42-month period, the mean MED/claim declined within public plans ($p < 0.001$). However, the decline in MED/claim was 5.4 times greater in the period following legalization (22.3 mg/claim post vs. 4.1 mg/claim pre). Total monthly opioid spending was also reduced to a greater extent post legalization ($Can267,000 vs. $Can95,000 per month). The findings were similar for private drug plans; however, the absolute drop in opioid use was more pronounced (76.9 vs. 30.8 mg/claim). Over the 42-month period, gabapentin and pregabalin usage also declined.

Conclusions Our findings support the hypothesis that easier access to cannabis for pain may reduce opioid use for both public and private drug plans.

1 Introduction

One of the most serious public health crises over the past decade in Canada has been opioid abuse, addiction, and overdoses. Indeed, between January 2016 and March 2019, an estimated 12,800 Canadians died from an opioid-related overdose [1]. A contributing factor has been the over-prescribing of opioids [2]. In one epidemiological study

Key Points for Decision Makers

There was a marked decline in the volume of opioids prescribed for patients covered under public drug plans following the legalization of recreational cannabis in Canada.

Similar findings were also observed for private payer plans; however, the absolute drop in opioid use was more pronounced than what was seen within public plans.

There was also a marked reduction in total monthly opioid spending by public and private drug plans following cannabis legalization.

Gabapentin and pregabalin prescribing volumes were also reduced, so patients with pain were not switching to these agents.

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focusing on British Columbia and Ontario, the annual rate of fentanyl, hydromorphone, morphine, and oxycodone prescribing (defined as the daily doses per 1000 population) was strongly correlated with mortality [3]. Death rates from opioid overdose were also significantly higher in jurisdictions with higher levels of opioid prescribing. The investigators concluded that new approaches and policies are needed to reduce opioid prescription volumes [3]. This is particularly relevant to Canada from a public health perspective because on a per-capita basis Canadians are among the highest consumers of opioids globally, with approximately 595 prescriptions per 1000 population from the years 2012–2016 [4]. Solutions to this public health crisis are complex and need to consider both the demand and the supply side of opioid prescribing in Canada [5]. This would include medical opioid utilization being reduced to lower levels whenever possible, with safer alternatives being explored.

The use of plant-derived cannabinoids for medical purposes has been growing in recent years, particularly for the management of long-term pain. There are studies suggesting that cannabinoids can reduce pain intensity, improve quality of life, and reduce or eliminate the need for opioid analgesics [6, 7]. In one prospective cohort study conducted in Israel [8], 1186 elderly patients with chronic pain from various causes were started on medical cannabis and followed for 6 months. Overall, 78.6% of patients had a moderate or significant improvement in their condition after 6 months of adjunctive cannabis therapy. Of equal importance, 14.4% of patients stopped using opioid analgesics and a further 3.7% reduced their dose. Other drugs eliminated included: other analgesics (7.3%), benzodiazepines (7.5%), and neuropathic pain drugs (4%). The retention rate of the initiated Cannabis therapy was high. Over the 6-month study horizon, 10.8% of patients discontinued their medical cannabis for various reasons, but only 1.4% were due to side effects [8].

Other studies have suggested that the legalization of cannabis can reduce prescription drug use for a wide range of conditions such as anxiety, depression, nausea, seizures, and especially chronic pain [9]. One study from the USA reported a 13% reduction in prescriptions for pain drugs in those states with legalized medical cannabis when compared to those states where cannabis remained illegal ($p < 0.01$). This corresponded to an annual cost savings of approximately $500 million over the first 4 years post legalization [10].

Medicinal cannabis became legal in Canada on 30 July 2001 [11]. Patients can access medicinal cannabis from the Federal government or a federally licensed seller, provided that it has been authorized by the patients' healthcare provider [11]. However, patients have to cover the cost of the medicinal cannabis drug. On 17 October 2018, recreational cannabis became legal in Canada [12], which resulted in increased access and may have reduced the stigma associated with its use, particularly with older patients. The impact of full cannabis legalization on the prescribing of opioids in Canada has not been formally evaluated. Therefore, the purpose of the current study was to assess trends in the amount and total cost of opioid prescribing in Canada prior to and following the legalization of cannabis. Our hypothesis was that cannabis legalization was associated with a statistically significant reduction in both the amount and total cost of opioid prescribing in Canada.

2 Methods

In Canada, approximately 35% of the population receives public drug coverage, another 60% has private drug insurance and the remaining 5% pay out of pocket [13]. Canada-wide monthly prescription-claims data for both public and private drug plans were obtained from IQVIA PharmaStat for January 2016 to June 2019. The public data accounted for 100% of all opioid claims from all provinces, except for Alberta and Nova Scotia, where only 80% and 82% of the claims were available. In addition, no public payer data were available for the province of Prince Edward Island. With respect to private drug insurance coverage, the data covered approximately 82% of plans nationally. The populations covered under both private and public drug plans consisted of patients with advanced cancer and other disorders where acute or chronic pain are characteristics of the condition. The IQVIA PharmaStat does not contain claims for medical cannabis prescriptions.

The data comprised the number of prescription claims, units per claim, and drug costs reimbursed per month. Drug costs per month include both the pharmacy fee and an allowable percentage markup, which is between 8% and 10%, depending on the drug plan. The agents consisted of morphine, codeine, fentanyl, hydrocodone, hydromorphone, meperidine, oxycodone, and tramadol. The dosage forms were oral, rectal, injectable, and transdermal. Methadone is also used for pain in Canada, but its primary indication is to treat opioid addiction. As a result, it was excluded from the analysis because it was not possible in our claims dataset to differentiate between the two indications for methadone. All opioid prescription volumes were then converted into a morphine-equivalent dosage (MED) per claim, which is analogous to a written prescription [14]. Gabapentin and pregabalin are anticonvulsants but are often used to treat neuropathic pain [15]. Claims data for gabapentin and pregabalin were also obtained to determine if any decrease in opioid prescriptions over the 42-month period was associated with an increase in gabapentin and pregabalin usage (as opioid substitutions). Separate analyses were performed for public and private claims. Gabapentin and pregabalin claim volumes and total costs were analyzed separately from the opioids.

All outcomes over the time-period were presented descriptively as means and medians via time series plots. Time-series regression modelling was undertaken with the opioid data. Dependent variables in the models were mean and median MED per claim and total monthly spending. The slopes of the time series curves were then compared pre- versus post-cannabis legalization. Any significant difference in the regression slopes would suggest that external factors were impacting opioid prescription volumes.

Methodological issues specific to time-series data include time-varying confounders, seasonal trends, concurrent events during the intervention, and autocorrelation of the data. There are several approaches available to evaluate time-series data, and these include Fitted Autoregressive Integrated Moving Average (ARIMA) models and interrupted time series (ITS) modelling [16, 17]. ITS is an effective method for evaluating time-series data, whereby slopes of a linear regression line are compared before and after the intervention of interest. However, ITS is typically not used for forecasting, and residual autocorrelation can be problematic with such models [17]. Indeed, standard regression models used by ITC assume that repeated observations are independent of each other. This assumption is often violated in time-series data because repeated observations are more similar to one another than those further apart [17]. In contrast, ARIMA models adjust for autocorrelation and are intended for forecasting [16].

In the current study, ARIMA models were built using claims data from the first 33 months (pre-legalization claims from January 2016 to September 2018) to forecast the median MED per claim in the 9 months that followed the legalization of cannabis. ARIMA models use autoregressive parameters, moving averages, and the number of differencing operators to describe a data series in which a pattern is presented over time [16]. Such models can be used to forecast future trends in the data from prior observations. When building an ARIMA model, the objective is to build a model that is parsimonious; the one that is the simplest, with the least assumptions and variables but with greatest explanatory power. This was the approach taken in the current study. Parameters for the ARIMA models were estimated by autocorrelation function (ACF) graphs and partial autocorrelation (PACF) correlograms. Statistical goodness-of-fit for the final models was assessed using the Akaike Information Criteria (AIC) and Bayesian Information Criteria (BIC) and through the evaluation of model residuals with the Portmanteau (Q) test for white noise. The final ARIMA models were then used to forecast the median MED per claim for the 9 months following cannabis legalization. The forecasted estimates were then graphically compared to what was observed (observed vs. expected). Monthly opioid expenditures were also compared for both public and private payers pre- versus post-cannabis legalization.

For the gabapentin and pregabalin time-series regression models, the dependent variable was mean monthly cost per claim over the 42-month time-period. Changes in the mean monthly cost per claim pre- versus post-cannabis legalization would be indicative of gabapentin and pregabalin drug volumes. A rise in the mean monthly cost per claim post legalization would suggest that at least some of the opioid prescriptions were being substituted by gabapentin and pregabalin. All of the statistical analyses were performed using Stata, release 16.0 (Stata Corp., College Station, TX, USA).

3 Results

Over the 42-month evaluation period, visual inspection of the time-series graphs revealed a steady decline in the volume of opioids prescribed (presented as a median MED per claim) for both public and private drug plans in Canada. However, after October 2018 when recreational cannabis because legal, the observed declines were greater than the predicted declines for both public and private drug plans, as determined by the ARIMA models (Fig. 1). The mean and median declines were obtained from the slopes of the time-series regression lines. A negative slope would be consistent with a reduction in the MED and cost per claim. When the slopes were quantified respectively over the entire time period, the mean and median decline in the MED per claim for public drug plans was 5.7 and 5.2 mg morphine equivalent, respectively. Similarly, the mean and median decline in the MED per claim for private drug plans was 39.6 and 4.7 mg morphine equivalent, respectively (Table 1). However, when the time-series regression slope was determined from January 2016 to September 2018 (the time period before cannabis legalization) and then compared to the slope from the months after legalization, the rate of decline in the MED per claim for both public and private drug plans was accelerated (Table 1). For public payers, the mean decline in the MED per claim was 4.1 mg (95% CI 2.22–6.00) pre-legalization compared to 22.3 (95% CI 9.23–35.4) mg post-legalization (an 18.2 mg absolute or 82% relative reduction in the MED per claim post legalization; $p < 0.05$). The absolute decrease in opioid utilization within private drug plans was even more pronounced. The mean decline in the MED per claim pre-legalization was 30.8 mg (95% CI 4.03–57.5) compared to 76.9 mg (95% CI 36.25–117.6; $p > 0.05$) post-legalization—an absolute reduction of approximately 46.1 mg in the MED per claim post-legalization, but the difference in the slopes did not reach statistical significance (Table 1).

For public payers, the decline in the utilization of opioids after October 2018 also resulted in cost savings. The monthly decline in opioid spending before cannabis legalization was approximately $Can95,140 per month. However,

after legalization, the monthly decline in spending became even more pronounced at $Can267,253 per month, representing an additional cost savings of $Can172,113 per month (Table 1 and Fig. 2). Cost savings post-cannabis legalization were also observed for private drug plans. The monthly reduction in opioid expenditures before cannabis legalization was approximately $Can76,111 per month. However, after legalization, the monthly decline in expenditures increased to $Can142,276 per month, an additional cost savings of $Can76,245 per month (Table 1).

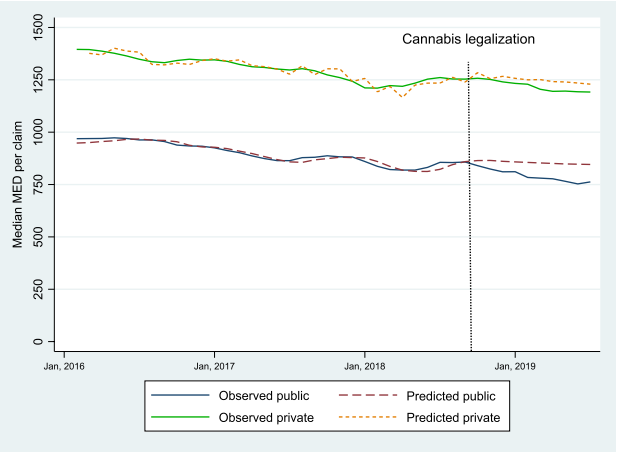

Fig. 1 Median morphine equivalent dose (mg) per claim for Canadian public and private drug plans: observed vs. predicted

ARIMA models were then constructed with the public and private payer time-series data from January 2016 to September 2018 only. The best fitting models for the public and private data, those with the lowest AIC and BIC statistics, the final models were ARIMA (1,1,1) and ARIMA (2,1,1) respectively. The final models were then used to forecast the median MED per claim in the 9 months that followed the legalization of cannabis, and these were compared to what was observed. The model predicted forecasts for median MED per claim were greater to what was observed in all the 9 months following legalization (Fig. 3). Indeed, these data suggest that external factors contributed to a decline in opioid volumes from October 2018 until June 2019, the end of the evaluation period.

One factor could be a reduction in the national prevalence of chronic pain. If the prevalence of chronic pain is on the rise in Canada, then patients may be receiving alternative agents such as gabapentin and pregabalin. To test this hypothesis, gabapentin and pregabalin prescription claims data for both public and private payers were evaluated over the same 42-month period. Gabapentin and pregabalin utilization was expressed as a median cost per claim. The findings revealed that the utilization of both gabapentin and pregabalin, within both public and private payers, also declined (Fig. 4). However, it was interesting to note that the decline began approximately 5 months before cannabis legalization.

Table 1 Opioid MED and cost per claim post- versus pre-cannabis legalization

Outcome	Public payers, mean (SE)	Private payers, mean (SE)
Monthly decline in MED (mg) per claim from January 2016–June 20, 19[g,h]	5.7 (0.70)[a]	39.6 (8.2)[a]
Monthly decline in MED (mg) pre-legalization[f]	4.1 (0.92)[a]	30.8 (13.1)[c]
Monthly decline in MED (mg) post-legalization	22.3 (5.5)[b]	76.9 (17.2)[d]
Difference in MED monthly decline per month (post vs. pre)	18.2	46.1
Outcome (median, SE)	Public payers	Private payers
Monthly decline in MED (mg) per claim from January 2016–June 20, 19[g,h]	5.2 (0.42)[a]	4.7 (0.44)[a]
Monthly decline in MED (mg) pre-legalization	5.0 (0.60)[a]	5.2 (0.64)[a]
Monthly decline in MED (mg) post-legalization	10.3 (4.2)[e]	7.6 (3.7)[f]
Difference in MED monthly decline per month (post vs. pre)	5.3	2.4
Total opioid spending per month	Public payers	Private payers
Monthly decline in total spending over entire time period	$108,929 (7407)[a]	$84,467 (4392)[a]
Monthly decline in spending pre-legalization	$95,140 (59,863)[c]	$76,111 (6114)[a]
Monthly decline in spending post-legalization	$267,253 (10,195)[a]	$142,276 (41,831)[a]
Difference in total opioid spending per month (post vs. pre)	$172,113	$76,245

SE standard error, *MED* morphine equivalent dose

[a]$p < 0.001$, [b]$p = 0.005$, [c]$p = 0.003$, [d]$p = 0.025$, [e]$p = 0.047$, [f]$p = 0.081$. The p-values are associated with the slopes of the time series regression line

[g]The mean and median declines were obtained from the slope of the time series regression line. A negative slope was consistent with a reduction in the MED and cost per claim

[h]Cannabis received full legalization in Canada on 17 October 2018

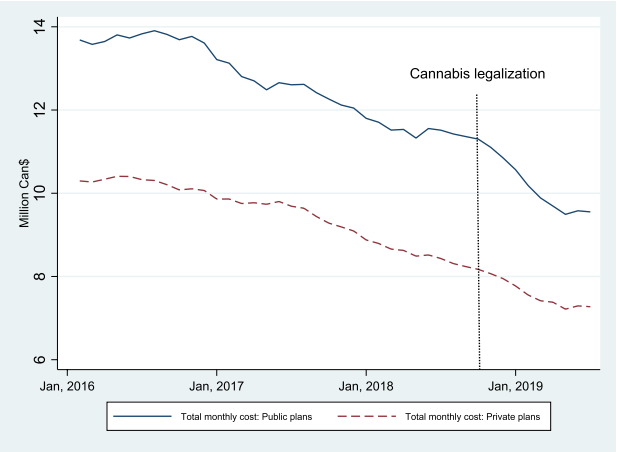

Fig. 2 Total monthly cost of opioid prescriptions for Canadian public and private drug plans

4 Discussion

The findings of this 42-month time-series analysis (which included the month when cannabis was legalized) revealed a steady and statistically significant decline in the mean and median MED per claim for public payer drug plans. However, when comparing the pre- versus post-legalization time periods, the decline in the mean MED per claim was approximately 5.4 times greater in the period following legalization (22.3 vs. 4.1 mg per claim). In addition, total public payer monthly opioid spending reductions averaged $Can95,000 per month before October 2018 compared to $Can267,000 per month following the legalization of cannabis. Similar findings were also observed within private drug plans, but the absolute magnitude of the decline in opioid use was more pronounced (76.9 vs. 30.8 mg per claim) post-legalization. Gabapentin and pregabalin usage were also reduced over the same time-period, suggesting that these agents were not used in place of opioids. Therefore, the legalization of cannabis coincided with a marked drop in opioid volumes prescribed in Canada.

One important observation from our data was the steady decline in opioid prescribing volumes in general, from January 2016 until October 2018, the month that recreational cannabis was legalized in Canada. This decline may have been due to an increased awareness by Canadian physicians of the risks associated with opioid overprescribing through government actions, educational initiatives by the Canadian Medical Association, and the publication of Canadian guidelines for opioid therapy in May 2017 [18–20]. However, the magnitude of the opioid-prescribing-volume decline after October 2018 was 5.4 and 2.5-fold higher than expected in public and private drug plans, respectively. Indeed, there were no major government policy announcements or educational initiatives after this date that could have accounted for the sharp decline in opioid-prescribing volumes.

One factor potentially contributing to the observed decline in opioid-prescribing volumes may have been a reduction in the national prevalence of chronic pain. However, a study using Community Health Survey data to measure the prevalence of chronic pain in Canada was recently

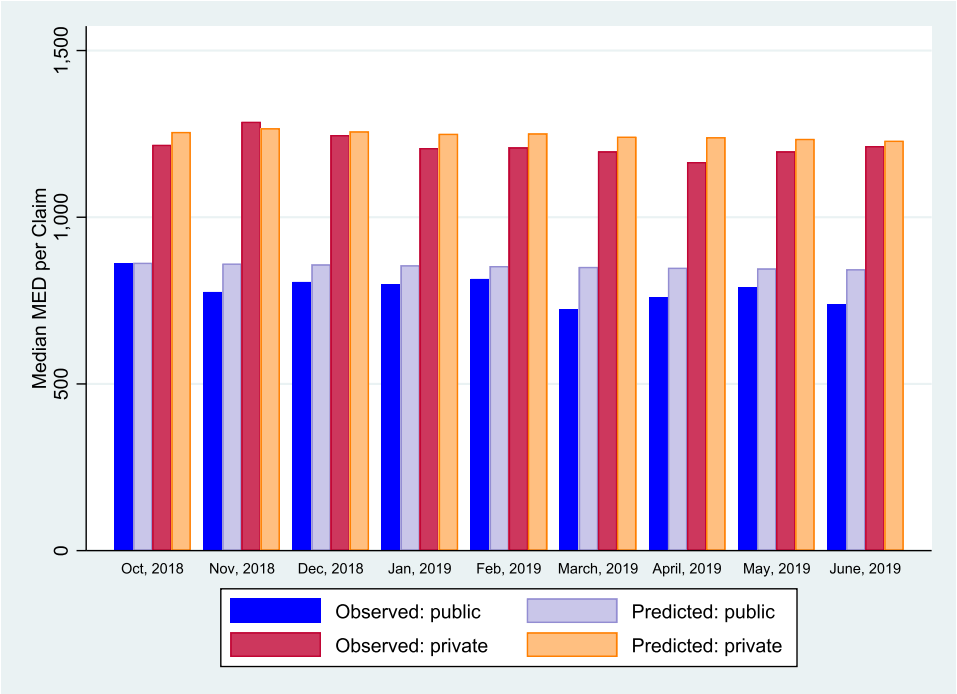

Fig. 3 ARIMA model forecasts on the median MED per claim for the nine months following cannabis legalization: observed vs. predicted within public and private plans

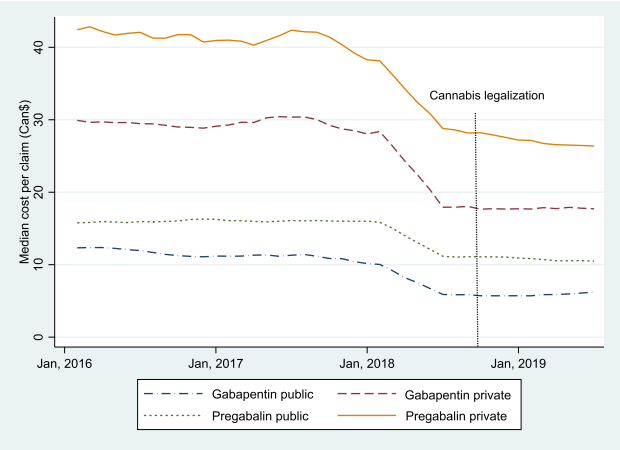

Fig. 4 Median cost per claim for gabapentin and pregabalin for Canadian public and private drug plans

published [21]. The prevalence of chronic pain in the general Canadian population increased in all provinces, in all age groups, and among people with no other chronic medical problems. At a national level, a 5.7% increase in chronic pain was reported, from 16.3% in 2000 to 21.0% in 2014 [21]. Therefore, it is unlikely that changes in the prevalence of chronic pain post-legalization are responsible for the drop in overall opioid consumption.

ARIMA models developed from time-series data are commonly used in econometrics to forecast future trends in the data from prior observations [16]. ARIMA models developed from the public and private opioid prescription volume data were used to forecast the median MED per claim for the 9 months following cannabis legalization. The predicted median MED per claims for all 9 months post-legalization was greater than what was observed. If the legalization of cannabis had no impact on the mean and median MED per claim, then the observed values should have been comparable to the ARIMA model forecasted estimates. However, other factors may also have contributed to the decline over the same time period.

Consistent with other studies [9, 10, 22, 23], our findings support the hypothesis that easier access to cannabis for medical and recreational purposes may have reduced opioid use and potentially reduce opioid expenditures for both public and private payers. Given the high cost of drugs to treat patients with cancer and other chronic diseases, financial toxicity has become a major concern for clinicians and health-policy makers [24]. The findings of the current study suggest that cannabis has the potential to partially offset some of the costs of supportive care drugs to treat pain. To properly address the cost and benefits of these interventions, a cost-effectiveness analysis comparing opioids to cannabis for the management of acute and chronic pain is warranted. Nevertheless, the successful implementation of cannabis into pain-management strategies will require educating both patients and physicians on its appropriate use. The need for education was illustrated in one investigation conducted in the USA, where 2774 people were surveyed across all 50 states [25]. A total of 1248 (46%) reported substituting cannabis for prescription drugs without medical guidance. Respondents indicated the most common drug classes to be substituted were opioids (35.8%), anxiolytics (13.6%), and antidepressants (12.7%). Similar findings have also been reported in studies conducted in Canada [26].

Educational strategies on the use of cannabis for medical purposes should not be limited to patients. In one recent survey of healthcare providers in the USA, most respondents (> 50%) believed that medical cannabis was helpful for treating medical conditions such as cancer and terminal illness [27]. However, knowledge gaps remained about its effectiveness in managing other medical conditions and there was an acknowledged need for accurate information about the potential for drug interactions [27]. Therefore, future research is needed to identify the best strategies for educating both patients and healthcare providers on the effective use of cannabis for medical purposes. Such strategies might include point-of-care decision support tools, as opposed to the more traditional forms of passive information dissemination [28].

The legalization of cannabis in Canada may have even broader implications. Cannabis legalization may also have a direct impact on the Canadian opioid-dependence crisis. One study from the USA examined medical marijuana policies and hospitalizations related to marijuana and opioid use for pain [29]. Hospital admission and discharge records from 1997 to 2014 were examined from 28 states that had legalized medical marijuana. The analysis determined that the legalization of medical cannabis was associated with a 23% ($p = 0.008$) reduction in hospital admissions for opioid dependence and a 13% reduction in admissions for overdoses ($p = 0.025$). Furthermore, there was no evidence to suggest that cannabis legalization led to an increase in marijuana-related hospitalizations [29].

In another study, time-series analysis was used to compare opioid analgesic overdose death rates between 13 states with legalized medical cannabis to states where medical cannabis remained illegal [30]. Overall, states with legalized medical cannabis had a 24.8% lower annual opioid overdose mortality rate (95% CI − 37.5 to − 9.5; $p = 0.003$) relative to states without legal medical cannabis laws [30]. Therefore, the published data suggest that cannabis legalization in Canada may provide benefits beyond opioid prescription volume decreases and cost savings to public and private drug plans.

4.1 Limitations

There are several limitations inherent in the current study that need to be addressed. Firstly, even though the

time-series analysis revealed that the legalization of cannabis coincided with a marked decrease in prescription opioid use across Canada, it does not imply causation. Other factors such as a heightened awareness by Canadian physicians of the risks associated with overprescribing opioid analgesics or improved physician education may have contributed to the decline in opioid use [19–21]. Our data were from the national opioid claim level, and not the individual patient level. Hence, we could not adjust our findings by patient factors. This must also be acknowledged as a study limitation. Cannabis prescribing data post-legalization was not available for comparison, nor did we survey patients who were receiving opioid analgesics for pain. Therefore, it is unknown which agents (if any) were being substituted for opioids in such patients post-legalization. The opioid prescription claims data were not complete. Only 80% and 82% claims data were available for public payers in Alberta and Nova Scotia. In addition, no public-payer data were available for the province of Prince Edward Island and private-payer data covered only 82% of plans nationally. The decline in the mean MED per claim post-legalization within private drug plans did not reach statistical significance, which may have been due to the variability in the data and the evaluation of only 8 months post-legalization. Longer follow-up data are required in both public and private drug plans to determine if the rate of the MED decline per claim is sustained.

Many of the agents evaluated were available as lower-cost generic formulations. As a result, it should also be acknowledged that price reductions in these agents after the legalization of cannabis may have contributed to the observed drop in monthly expenditures. Pain, anxiety, and depression often present as a medical triad; however, we did not evaluate the prescribing patterns of anxiolytics and antidepressants over the 42-month evaluation period. Cannabis as a potential adjunct therapy to opioids for pain management is associated with an acquisition cost. However, the cost of cannabis was not included in the economic analysis. Our findings must also be interpreted with some caution because there are several potential sources of bias that may have contributed to the observed decline in opioid prescribing. For instance, as the Canadian government was liberalizing its marijuana laws, other policies could have affected opioid use. There is also controversy in the literature on the impact of cannabis consumption on opioid use. While some studies suggest that the medical use of cannabis reduces opioid consumption [25, 26], others have reported the opposite [31, 32]. Clearly more research is needed in this area.

Notwithstanding these limitations, our study results are encouraging as they may reflect a behaviour change in opioid prescribing and utilization. We strongly recommend further clinical studies and educational programs in large well-defined medical populations to monitor the benefits of cannabis for specific medical conditions and to educate patients and healthcare professionals, with the goal being to offer patients in need alternatives to opioids.

5 Conclusions

The findings of this study add to the growing body of evidence that easier access to cannabis for patients with pain may reduce opioid use and partially offset expenditures for both public and private drug plans.

Declarations

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Conflicts of interest LM and BPE are employees of Scientus Pharma Inc. All authors had full access to the data, participated in the design of the study, interpretation of the results, and preparation of the final manuscript. There are no other conflicts of interest to declare.

Ethics approval Not applicable.

Consent to participate Not applicable.

Consent for publication All authors have provided their consent for publication.

Availability of data and material All original data are available from the primary author upon request.

Code availability Not applicable.

Authors' contributions GD: Study design, data analysis, preparation of the manuscript. CD: Study design, contribution from a clinical perspective, revisions to the manuscript. BP: Study design, contribution from a clinical perspective, revisions to the manuscript. LM: Study design, data analysis, preparation of the manuscript. BPE: Study design, contribution from a clinical perspective, revisions to the manuscript.

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