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Impact of changes in opioid funding and clinical policies on rapid tapering of opioids in Ontario, Canada

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Abstract

Reports have emerged of abrupt tapering among recipients of long-term prescription opioids to conform new prescribing guidelines. We conducted a population-based, repeated cross-sectional time-series study among very high-dose (≥200 MME) opioid recipients in Ontario, Canada, to examine changes in the monthly prevalence of rapid tapering from 2014 to 2018, defined as recipients experiencing either a ≥50% reduction in daily doses or abrupt discontinuation sustained for 30 days. Interventional autoregressive integrated moving average models were used to test for significant changes following key guidelines and drug policies and programs. A sensitivity analysis examined rapid tapering sustained for 90 days. The monthly prevalence of rapid tapering events was stable from January 2014 to September 2016 (average monthly prevalence: 1.4%) but increased from 1.4% in October 2016 to 1.8% in April 2017 ($P = 0.001$), coincident with Ontario's Fentanyl Patch-for-Patch Return Program implementation. Transient spikes in the prevalence of rapid tapering also occurred 2 months after Ontario's delisting of publicly funded high-strength opioids and the release of updated Canadian Opioid Prescribing Guideline for Chronic Pain, reaching 2.3% in March 2017 and July 2017, respectively. However, this prevalence decreased to 1.2% in December 2018 ($P < 0.0001$). Although the prevalence of abrupt opioid discontinuation was lower, similar trends were observed. Our sensitivity analysis examining long-lasting rapid tapering found similar trends but lower prevalence, with no changes in complete discontinuation. These temporary increases in rapid tapering events highlight the need for improved communication and evidence-based resources for prescribers to minimize negative consequences of evolving policies and guidelines.

Keywords: Dose tapering, Opioids, Ontario, Evaluation, Time series, Drug policy

1. Introduction

Over the past 2 decades, the prevalence of high-dose opioid prescribing has increased, in part because of the late introduction of guidelines recommending dose thresholds for chronic non-cancer pain.[19] The use of high-dose opioids for chronic pain has increasingly raised concerns in light of evidence linking the practice to a variety of harms, including accidental overdose and death.[3,8,13,20,22,25] In an effort to promote safer opioid prescribing, recent guidelines in the United states and Canada, released in March 2016 and May 2017, respectively, now suggest that for the treatment of chronic noncancer pain, clinicians should generally avoid dose escalation above 90 mg of morphine or equivalent per day. For patients already receiving higher doses, guidelines also encourage gradual tapering of doses to the lowest effective dose.[4,11]

Numerous funding policies and programs have also been introduced over the past decade with the goals of reducing

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unsafe and inappropriate prescription opioid use and minimizing diversion. For example, in Ontario, a Fentanyl Patch-for-Patch (P4P) Return Program was launched in October 2016, mandating that individuals return their used fentanyl patches before receiving new patches.[30] In addition, in January 2017, Ontario's public drug program stopped funding high-strength opioids for non-palliative patients.[31]

Although new policies and guidelines are designed to minimize the potential harms of opioids, concerns have been raised that their overly aggressive implementation may have led to excessive changes in treatment patterns for some patients, particularly those managing chronic pain with very high-opioid doses. These concerns emerged in the United States and Canada beginning in 2016, with reports of some physicians tapering opioids too quickly, under the incorrect assumption that doing so was required by new guidelines.[1,7,12,14,16,17,24] Sudden dose reductions could lead some patients to experience withdrawal-related functional impairment, hyperalgesia, mood disturbances, and, in extreme cases, even suicidality.[2,7,12,17] Moreover, patients whose prescribed opioid doses are rapidly reduced or discontinued altogether might seek alternative, unregulated sources of opioids, increasing their risk of inadvertent overdose.[1,2,7,12,16,17,24] Recent studies support these concerns, finding increased risks of overdose and suicide among long-term opioid recipients who experienced sudden fluctuations in opioid dose or abrupt treatment discontinuation.[9,21,26,29]

We examined the impact of the introduction of new clinical opioid guidelines and opioid policies and programs on the prevalence of rapid opioid dose tapering events over time in Ontario, Canada.

2. Methods

2.1. Setting and design

We conducted a population-based, repeated cross-sectional study among long-term prescription opioid recipients receiving very high daily doses (≥200 morphine milligram equivalent [MME]) between January 2014 and December 2018 in Ontario, Canada.

2.2. Data sources

We used the Ontario Narcotics Monitoring System database to identify all prescriptions dispensed in Ontario for opioids over our study period. This database captures all prescriptions for monitored and controlled substances dispensed from community pharmacies in Ontario regardless of payer. We used the Registered Persons Database to ascertain patient demographics (ie, age, sex, rural residence, and neighbourhood income quintile), the Ontario Health Insurance Planclaims database to classify all physician office visits and related billing codes, the Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System to identify all emergency department visits, the CIHI Discharge Abstract Database to identify all hospital admissions, and the Ontario Cancer Registry to identify all incident cancer diagnoses. All data were linked using unique, encoded identifiers and analyzed at ICES (www.ices.on.ca). Their use was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board.

2.3. Cohort creation

We created a cohort of all Ontarians who received a long-acting prescription opioid between January 2014 and December 2018. We extracted all opioid prescriptions (both long-acting and short-acting) dispensed to these individuals that overlapped the study period. We calculated daily opioid doses for each day of the study period using an algorithm that estimated opioid dose in MMEs and accounted for vacation supplies, early refills, and concurrent use of multiple opioid products (see Supplemental Appendix 1 for details, available at http://links.lww.com/PAIN/B442).

For each subject, we defined an anchor date to determine eligibility in the cohort and to calculate the reference opioid dose each person was receiving (schematic in **Fig. 1**). This was performed for each day in the study period. To be defined as receiving a very high daily opioid dose, we calculated a reference dose on the anchor date as the average daily opioid dose over a 30-day period (the anchor date and the previous 29 days). Those with a reference dose of ≥200 MME were defined as receiving a very high daily opioid dose and included in the cohort. We also restricted our cohort to long-term opioid recipients, defined as those receiving an opioid for at least 90 of the last 100 days preceding the anchor date. We excluded individuals receiving palliative care, individuals with a cancer diagnosis, and individuals who underwent chemotherapy or radiation for cancer in 6 months before the anchor date (codes in Supplementary Appendix 1 **Table 1**, available at http://links.lww.com/PAIN/B442), as well as individuals who received opioid agonist therapy with buprenorphine/naloxone or methadone in the 100 days before the anchor date. For each month of our study period, we defined a cohort that included all subjects meeting our inclusion criteria with an anchor date in the month of interest.

2.4. Rapid opioid dose tapering definition

To assess changes in daily opioid dose, for each subject we defined a taper evaluation date as 29 days after the anchor date. Comparisons between the reference opioid dose on the anchor date and the opioid dose on the taper evaluation date were made daily using a moving window over the study period. In the primary analysis, we defined rapid tapering in 2 ways: first, as a ≥50% reduction in opioid dose (anchor date vs taper evaluation date) sustained for at least 30 days after the taper evaluation date, and second, as abrupt discontinuation of opioids, defined as no subsequent prescription on the taper evaluation date and sustained for at least 30 days thereafter (schematic in **Fig. 1**). This definition aimed to capture tapering events that exceeded recommendations for safe opioid dose tapering from both the U.S. CDC Guideline for Prescribing Opioids for Chronic Pain (dose tapering of 10% of the dose per week) and the Canadian Guideline for Opioids for Chronic Non-Cancer Pain (dose reduction of 5-10% of the morphine equivalent dose every 2-4 weeks).[4,11]

We excluded rapid tapering events from our definition if a person died, was admitted to hospital, was dispensed an opioid agonist therapy prescription, or switched opioids (ie, hydromorphone vs fentanyl) between their anchor date and the taper evaluation date. Rapid tapers, where an individual switched opioid drugs, were excluded to prevent capturing instances of "opioid rotation," defined as a change in opioid therapy together with a reduced dose of 25 to 50% to minimize accidental overdose, which is recommended in the Canadian Opioid Guideline for patients who have persistent problematic pain or adverse effects from their current therapy.[4]

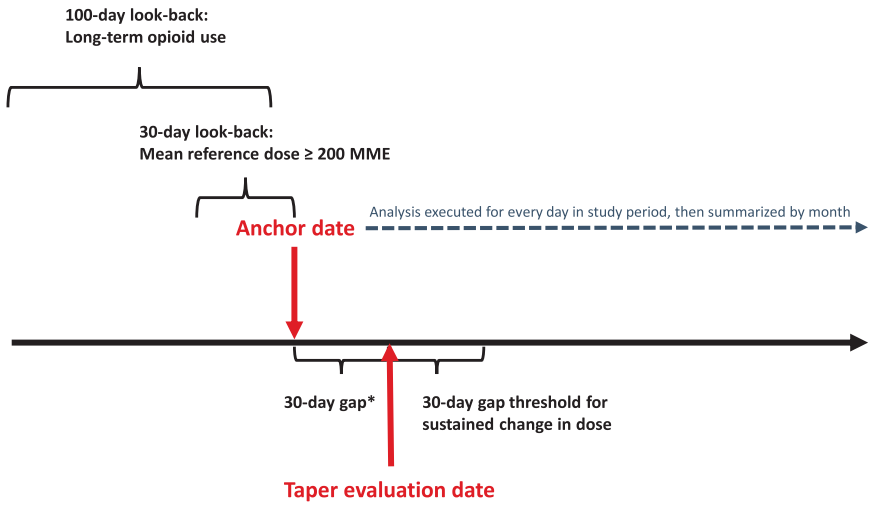

Figure 1. Schematic of cohort creation and definition of rapid dose tapering.

If a rapid taper was identified, this event was assigned to the month in which the taper evaluation date occurred. We also excluded individuals from the monthly denominator if they experienced a rapid taper in the previous month to avoid double counting a single rapid taper episode. For each month of our study period, we report the percent of individuals meeting eligibility criteria of our study (ie, long-term very high-dose opioid recipient) with evidence of rapid tapering of their opioid dose.

We conducted a sensitivity analysis in which we altered the definition of rapid tapering to require that dose reductions were sustained for at least 90 days after the taper evaluation date. In a secondary analysis, we replicated all analyses among a cohort of long-term high-dose opioid recipients using a ≥90 MME threshold for the reference daily opioid dose.

Table 1

Baseline characteristics of patients receiving long-term very high-dose (≥200 morphine milligram equivalent) opioids between January 2014 and December 2018.

Characteristic	Overall
	N=58,233
Age in y, median (IQR)	56 (47-66)
Age in y, categorical, n (%)	
0-18	25 (0.0%)
19-24	329 (0.6%)
25-44	10,656 (18.3%)
45-64	30,732 (52.8%)
65+	16,491 (28.3%)
Sex—Female, n (%)	29,114 (50.0%)
Urban residence, n (%)	48,537 (83.3%)
Neighbourhood income quintile, n (%)	
1—lowest	16,671 (28.6%)
2	12,964 (22.3%)
3	11,155 (19.2%)
4	9599 (16.5%)
5—highest	7632 (13.1%)

2.5. Patient characteristics

We report baseline patient characteristics among our cohort over the study period, including age, sex, urban residence, and neighbourhood income quintile (a proxy for socioeconomic status). If a person was identified as experiencing a rapid taper, their index date was defined as their first rapid taper date during the study period. Otherwise, index was assigned as a person's first anchor date in the study period.

2.6. Statistical analysis

In our monthly analysis, we fit interventional autoregressive integrated moving average (ARIMA) models to the data to test for significant changes in the prevalence of rapid tapering events when 4 distinct policies and guidelines were introduced, a method commonly used for population-based time-series analyses.[23,28] The ARIMA model requires 3 parameters: the p parameter (autoregressive term for the number of previous data points to account for), d parameter (number of model differences to achieve stationarity in the time series), and q parameter (order of moving average). To fit the ARIMA model, we first differenced the time series (ARIMA model d parameter equal to one) to achieve stationarity, which was confirmed visually and through the augmented Dickey–Fuller stationarity test. Once stationarity was confirmed, we selected the ARIMA model p parameter and q parameter for each time series by examining the autocorrelation function (ACF), partial ACF (PACF), and inverse ACF (IACF) correlograms. The p term varied for each time series based on the model diagnostic plots, whereas the q term was zero for all models. The final ARIMA model fit was assessed using the ACF, PACF, and IACF plots; white noise probability plots and the Ljung–Box χ^2 test for white noise; and r-square measure of fit. The ARIMA model forecasts were also examined on both the model fit to the truncated time series data (using data before interventions of interest) and complete time series data to ensure validity.

To evaluate the impact of the interventions, we included ramp intervention functions in the ARIMA model at March 2016 (corresponding to the release of the U.S. CDC Guideline for Prescribing Opioids for Chronic Pain), October 2016 (Ontario's Fentanyl P4P Return Program), and May 2017 (Canadian Guideline for Opioids for Chronic Non-Cancer Pain) to test for an immediate

slope change in trend after the intervention date of interest. We also included a step function at October 2016 to test for an immediate level shift (sustained decrease or increase) after the intervention date because of the mandatory nature of the programs and policies introduced at this time. The delisting of publicly funded high-strength opioids in Ontario (January 2017) was not included as an intervention date in the model because it occurred too close in time to the October 2016 intervention date. Therefore, any significant changes observed after October 2016 may be attributable to either the Fentanyl P4P Return Program or the subsequent delisting of publicly funded high-strength opioids in Ontario.

The final ARIMA model, intervention estimates, and model fit diagnostics are presented in Appendix 2, available at http://links.lww.com/PAIN/B442. This includes the ARIMA model summary table with estimates for each intervention function, indicating the magnitude of change associated with the intervention and its *P*-value. All analyses were conducted using SAS software (version 9.4; SAS Institute Inc., Cary, North Carolina) and used a type 1 error rate of 0.05 as the threshold for statistical significance.

3. Results

Over the 5-year study period, we identified 58,233 unique individuals receiving long-term opioid therapy at very high doses (≥200 MME; **Table 1**). Approximately half of the cohort members were female (N = 29,114; 50.0%), most were between the ages of 45 and 64 years (N = 30,732; 52.8%), and most resided in urban regions (N = 48,537; 83.3%) and low income neighbourhoods (N = 29,635; 50.9% in the 2 lowest neighbourhood income quintiles). The number of very high-dose opioid recipients declined over the study period from 29,413 individuals in January 2014 to 15,730 individuals in December 2018 (Supplementary Appendix 1, **Fig. 1**, available at http://links.lww.com/PAIN/B442).

3.1. Rapid tapering sustained for 30 days

In our primary analysis of rapid tapering events sustained for 30 days, we found that the monthly prevalence was generally stable between January 2014 and September 2016 (average monthly prevalence of 1.4%), with no changes observed after the U.S. CDC Opioid Guideline in March 2016 (slope change $P = 0.90$). This prevalence increased after October 2016 (slope change $P = 0.001$), from 1.4% in October 2016 to 1.8% in April 2017, representing a 0.4% absolute increase and approximately 95 additional individuals (**Fig. 2**, Supplementary Appendix 2, available at http://links.lww.com/PAIN/B442). The prevalence of rapid tapering events also peaked 2 months after Ontario's delisting of publicly funded high-strength opioids, from 1.7% in January 2017 to 2.3% in March 2017, representing an absolute increase of 0.6% (approximately 132 additional individuals). Similarly, this prevalence spiked in the 2 months after the release of the Canadian Opioid Guideline, from 1.8% in May 2017 to 2.3% in July 2017 (absolute increase of 0.5%; approximately 109 additional individuals) but declined thereafter (slope change $P < 0.0001$) to 1.2% in December 2018 (0.6% absolute decrease from 1.8% in May 2017; approximately 93 fewer individuals).

3.2. Abrupt discontinuations sustained for 30 days

These trends were consistent when studying abrupt opioid discontinuations that were sustained for at least 30 days. Specifically, after an average monthly prevalence of 0.7% between January 2014 and September 2016, the prevalence of abrupt opioid discontinuations rose considerably from 0.6% in October 2016 to 1.0% in April 2017 (slope change $P = 0.003$), representing a 0.4% absolute increase and approximately 94 additional individuals. Two spikes in the prevalence of abrupt opioid discontinuations also occurred 2 months after the delisting of publicly funded high-strength opioids, from 0.7% in January 2017 to 1.3% in March 2017 (absolute increase of 0.6% and approximately 133 additional individuals) and 2 months after the release of the Canadian Opioid Guideline, from 0.8% in May 2017 to 1.3% in July 2017 (absolute increase of 0.5% representing approximately 105 additional individuals). This prevalence declined after May 2017 (prevalence of 0.8%) reaching 0.6% in December 2018 (slope change $P < 0.0001$), representing a 0.2% absolute decrease and approximately 44 fewer individuals.

3.3. Sensitivity analysis: rapid tapering and abrupt discontinuations sustained for 90 days

When our definition of rapid tapering was adjusted to sustained dose reductions for at least 90 days, the monthly prevalence of rapid tapering was lower (average monthly prevalence of 0.8% between January 2014 and September 2016; **Fig. 3**, Supplementary Appendix 2, available at http://links.lww.com/PAIN/B442). This prevalence increased immediately after October 2016 (level shift $P = 0.0001$; average monthly prevalence of 1.0% between October 2016 and April 2017) and declined in the months after the release of the Canadian Opioid Guideline (slope change $P = 0.007$; 0.3% absolute decrease from a prevalence of 1.0% May 2017 to 0.7% in December 2018). There were no significant changes over time in the monthly prevalence of abrupt opioid discontinuations that were sustained for at least 90 days.

3.4. Secondary Analysis: Rapid tapering and abrupt discontinuations sustained for 30 days among long-term high-dose opioid recipients (≥90 MME)

In our secondary analysis among a broader cohort of long-term high-dose opioid recipients (≥90 MME), the findings were similar to the primary analysis. The prevalence of both rapid tapering and abrupt discontinuations sustained for 30 days increased after October 2016 (slope change $P < 0.0001$) and decreased after May 2017 (slope change $P < 0.0001$), with a similar peak in prevalence observed in March 2017 and July 2017 (**Fig. 4**, Supplementary Appendix 2, available at http://links.lww.com/PAIN/B442). Findings were consistent with the primary analysis when we required dose reductions sustained for 90 days (**Fig. 5**, Supplementary Appendix 2, available at http://links.lww.com/PAIN/B442).

4. Discussion

In this large, population-based study of Ontarians prescribed a high dose of opioids for chronic noncancer pain, we found that rapid opioid dose tapering events temporarily increased in response to changing drug policies, programs, and guidelines in 2016 to 2017. However, the absolute changes were relatively small and of short duration. Significant increases in the prevalence of rapid tapering sustained for at least a month initially occurred after October 2016, coinciding with the implementation of Ontario's Fentanyl P4P Return Program, and short-term spikes in prevalence emerged in March 2017 and July 2017, 2 months after Ontario's delisting of publicly funded high-strength opioids and the Canadian Guideline for Opioids for Chronic Non-Cancer Pain. When examining abrupt discontinuation of opioid therapy

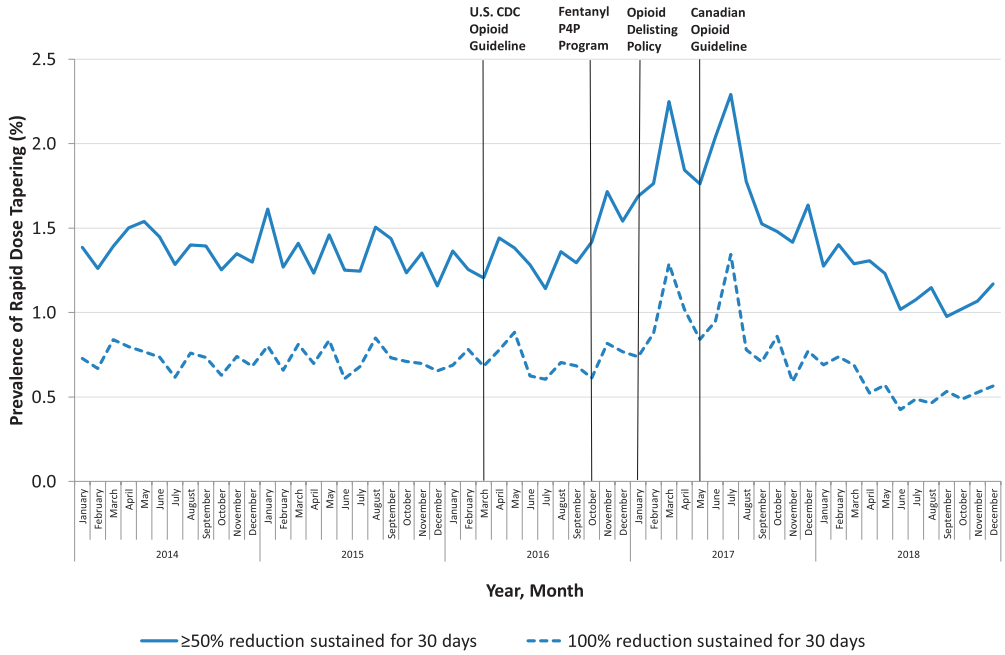

Figure 2. Prevalence of rapid dose tapering sustained for 30 days among very high-dose opioid recipients (≥200 morphine milligram equivalent).

sustained for a month, we observed similar trends but the prevalence was generally lower.

These findings document changes in practice that may have subjected a subset of patients with chronic pain to opioid withdrawal, putting them at risk of hazardous outcomes. However, these changes seemed to be limited in magnitude and duration, with the prevalence of rapid tapering declining significantly in the last year of our study period and returning to baseline levels observed before 2016. This decline aligned with a reduction in the prevalence of long-term high-dose opioid recipients during the study period more generally. In addition, in our sensitivity analysis examining tapering events sustained for 3 months, the prevalence of rapid tapering was generally lower, and there were no changes observed in the prevalence of individuals having their opioid therapy discontinued entirely, suggesting that many of the rapid dose reductions were short-term.

Our chief finding that altered drug funding policies, programs, and clinical practice guidelines were associated with potential destabilization of patients receiving long-term opioid therapy warrants discussion. It is possible that some rapid dose reductions and instances of abrupt therapy discontinuation represent appropriate cessation of opioid prescriptions that

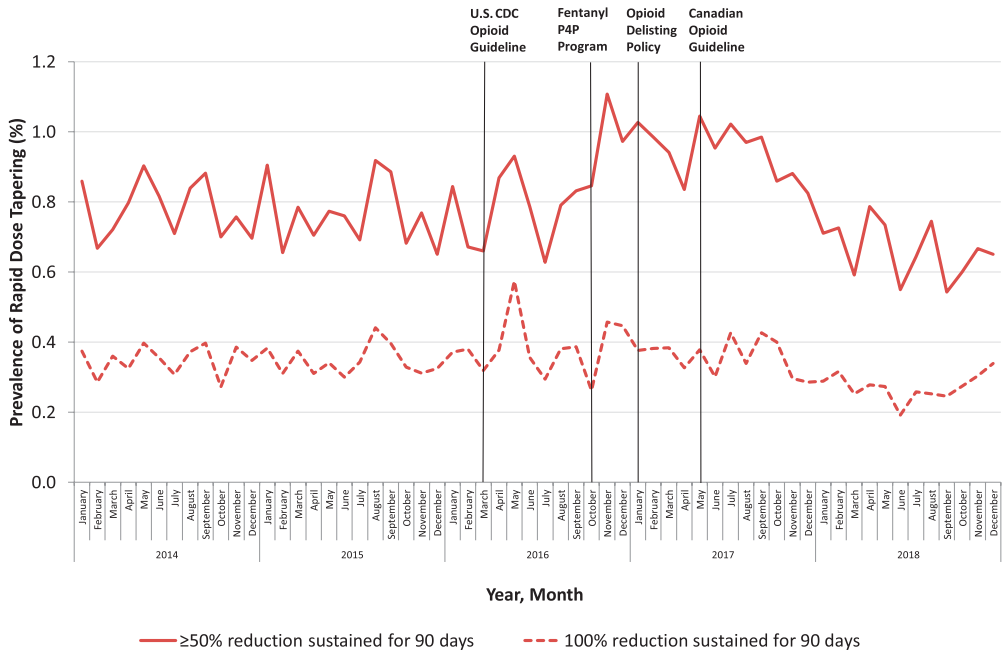

Figure 3. Prevalence of rapid dose tapering sustained for 90 days among very high-dose opioid recipients (≥200 morphine milligram equivalent).

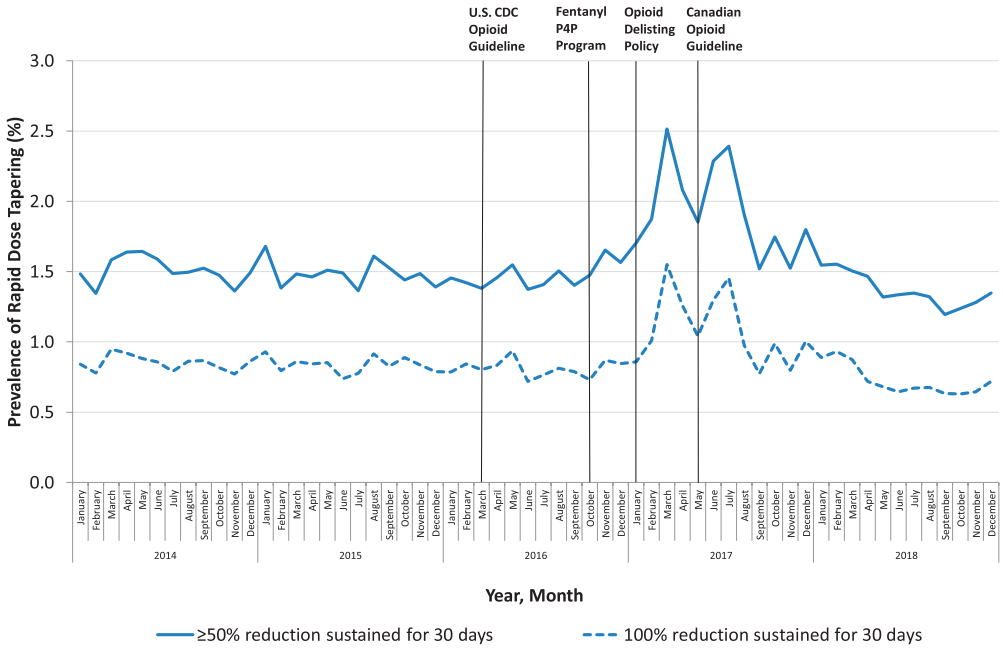

Figure 4. Prevalence of rapid dose tapering sustained for 30 days among high-dose opioid recipients (≥90 morphine milligram equivalent).

were being diverted, particularly around the timing of Ontario's Fentanyl P4P Return Program that was intended to address fentanyl patch diversion.[33] However, it is also probable that some individuals prescribed fentanyl and other high-strength opioids were negatively affected by reductions in opioid supply on implementation of policies affecting these medications. Moreover, a Canadian survey found that half of the Canadian physicians who prescribed opioids for noncancer pain reported initiating opioid tapering among their high-dose opioid patients after the release of the 2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain, with more than a third misinterpreting the recommendations as a mandate to taper doses.[5] This implies that increased rapid tapering events observed in this study were likely influenced by tapering practices after the release of these guidelines, in line with patient reports of the practice.[1,7,12,14,17,24]

Importantly, we found that sustained tapers for more than 90 days were more rare, indicating that many of the patients whose doses were rapidly tapered over a 30-day period managed to increase their opioid doses again within a relatively short period. Furthermore, the declining trends in rapid tapering observed at the end of our study period are reassuring and possibly influenced

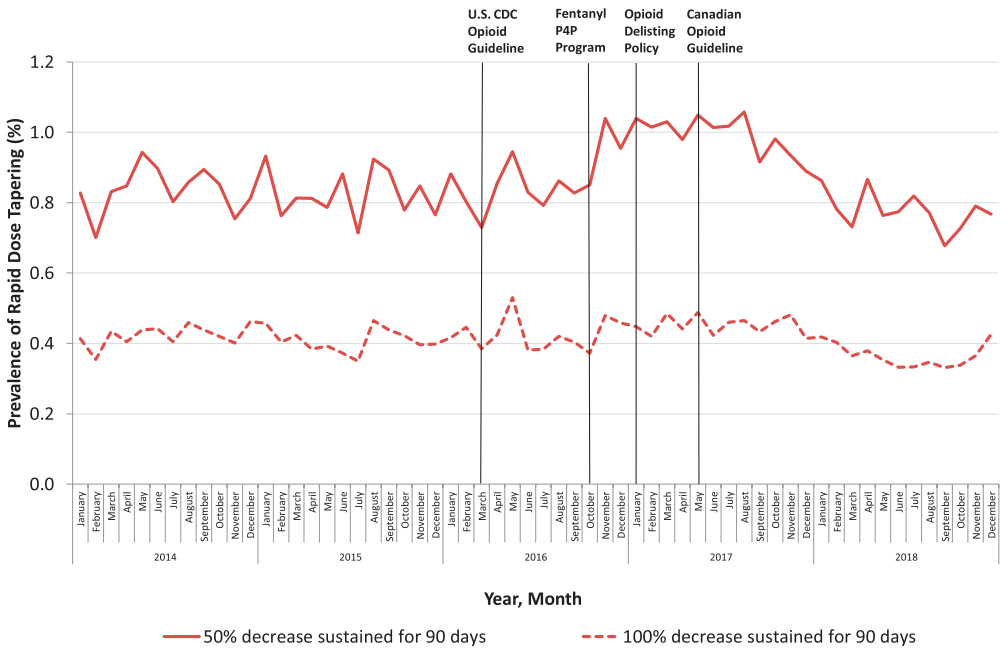

Figure 5. Prevalence of rapid dose tapering sustained for 90 days among high-dose opioid recipients (≥90 morphine milligram equivalent).

by increased media coverage and ongoing communications surrounding this contentious practice and its potential harmful effects on patients.[1,7,12,14,16,17,24] These observed temporary shifts in practice emphasize the need for educational initiatives and good communication when guidance and policies related to opioid prescribing are introduced to ensure proper interpretation and implementation.[5,10]

Our findings are consistent with a U.S. study that found increased annual trends in rapid opioid dose tapering events after the release of the 2016 U.S. CDC Guideline for Prescribing Opioids for Chronic Pain, particularly among patients receiving high doses of opioids.[15] Our study found that although the publication of the U.S. CDC Guideline did not seem to affect rapid tapering events in Canada, the release 1 year later of the Canadian Guideline for Opioids for Chronic Non-Cancer Pain led to a similar phenomenon in Ontario. Our study period also extended beyond that of the U.S. study and found a general decline in the prevalence of rapid dose tapering events in 2018, likely influenced by greater awareness and caution against this practice by both pain experts and the U.S. Food and Drug Administration.[1,7,12,14,17,24] Our study also provides additional insight into an evaluation of Ontario's delisting of publicly funded high-strength opioids that reported a small but significant reduction in weekly opioid doses among patients receiving these medications.[27] Although this study found no evidence of complete opioid discontinuation in the 6 months after the policy,[27] our findings indicate there may have been some short-term disruptions in therapy for some patients. Although few other studies have examined temporal changes in rapid tapering among opioid recipients, U.S. studies have reported short times to opioid discontinuation that may reflect rapid tapering, and these incidents were notably associated with a greater risk of subsequent overdose and death.[21,26,29] Generally, these changes in prescribing patterns have occurred across several jurisdictions during a time of novel programs, policies, and clinical guidelines, which may have led to varying degrees of destabilization for some patients.

Given the risks associated with rapid tapering of opioid doses and our finding that changing policies can lead to increased prevalence of this practice, a multifaceted approach is needed to address this issue. Statements from the U.S. Food and Drug Administration and international pain experts strongly caution against forced rapid dose tapers and advise that any practices in dose tapering are both consensual and personalized to each patient.[6,17] Particularly, given the clinical and safety benefits of reducing high daily opioid doses for patients with chronic pain, it is recommended that dose reductions are appropriate and undertaken in interdisciplinary settings that ensure patients are not thereby harmed by destabilization.[18,32] However, to accomplish this, supports and services must be integrated into the healthcare system for patients undergoing opioid dose tapering, including improvements in the availability of chronic pain treatment services and financially accessible nonopioid treatment options to manage pain with less reliance on opioids.[5,10]

This study is strengthened by including all prescription opioids dispensed in Ontario, Canada's most populous province representing 14 million individuals. However, it is important to contextualize these findings within the rapidly shifting clinical and policy environment in Ontario and the limitations of dispensing data. First, a baseline rate of rapid tapering was apparent in the monthly analysis before the introduction of policies and guidelines of interest. This is likely related to switching between different opioids and formulations, inaccuracies in the pharmacy dispensed administrative data, and/or the PRN (as needed) use of opioids. However, we modelled changes from this baseline rate to determine the impact of our interventions of interest, assuming that the factors contributing to the baseline rate would remain consistent over our study period. Second, local initiatives that were introduced over our study period could have influenced the observed trends, and these external factors could not be incorporated into this analysis. Importantly, we excluded tapering events if a person was hospitalized or died during the dose evaluation period because this would affect the ability to capture prescriptions dispensed and calculate changes in daily doses. However, it is possible that some of these individuals had their opioid doses rapidly tapered and consequently were hospitalized or died because of this practice, which may have underestimated the prevalence reported. Finally, we are unable to determine the circumstances surrounding a rapid taper in our study and whether these tapers were implemented in some cases to prevent prescription diversion.

5. Conclusion

Opioid-related policies and guidelines introduced in 2016 and 2017 were associated with temporary increases in the prevalence of rapid opioid dose tapering events in Ontario, Canada. These changes seem to be relatively rare and of short duration, and some may have been appropriate in cases where medication was being diverted. However, the findings highlight the need for effective communication when new policy and guideline changes are being introduced to prevent interruptions in prescribed opioid therapy that could compromise patient safety. Given the known complexity and limited resources for safely tapering an individual's opioid dose, efforts should be made to ensure prescribers have appropriate evidence-based resources to successfully implement safe opioid dose tapers alongside improvements in access and affordability of alternative treatment options to manage pain and opioid use disorder.

Conflict of interest statement

M.M. Mamdani has received honoraria from Novo Nordisk, Allergan, Neurocrine, and Celgene. D.N. Juurlink is a volunteer member of Physicians for Responsible Opioid Prescribing and has received payment for expert testimony related to opioids. T. Gomes, M. Tadrous, D.N. Juurlink, and M. Mamdani have received grant funding from the Ontario Ministry of Health and Long-Term Care. The remaining authors have no conflicts of interest to disclose.

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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/B442.

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