Opioid stewardship: implementing a proactive, pharmacist-led intervention for patients coprescribed opioids and benzodiazepines at an urban academic primary care centre

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ABSTRACT

In 2017, almost 4000 Canadians died from opioid-related causes. Coadministration of opioids and benzodiazepines is a risk factor for overdose. Few studies have evaluated leveraging pharmacists to address opioid-benzodiazepine coprescribing. Our aim was to develop and test a role for pharmacists as opioid stewards, to reduce opioid and benzodiazepine doses in coprescribed patients. We conducted Plan-Do-Study-Act cycles between November 2017 and May 2018 across two primary care centre clinics. A third clinic acted as a control. Our intervention included a pharmacist: (1) identifying patients through medical record queries; (2) developing care plans; (3) discussing recommendations with physicians and (4) discussing implementing recommendations. We refined the intervention according to patient and physician feedback. At the intervention clinics, the number of patients with pharmacist developed care plans increased from less than 20% at baseline to over 60% postintervention. There was also a fourfold increase in the number of patients with an active opioid taper. At the control clinic, the number of patients with pharmacist developed care plans remained relatively stable at less than 20%. The number of patients with active opioid tapers remained zero. At the intervention clinics, mean daily opioid dose decreased 11% from 50.5 milligrams morphine equivalent (MME) to 44.7 MME. At the control clinic, it increased 15% from 62.3 MME to 71.4 MME. The number of patients with a benzodiazepine taper remained relatively stable at both the intervention and control clinics at less than 20%. At the intervention clinics, mean daily benzodiazepine dose decreased 8% from 9.9 milligrams diazepam equivalent (MDE) to 9.3 MDE. At the control clinic, it decreased 4% from 10.8 MDE to 10.4 MDE. A proactive, pharmacist-led intervention for coprescribed patients increased opioid tapers and decreased opioid and benzodiazepine doses. Future work will help us understand whether sustaining the intervention ultimately reduces rates of opioid-benzodiazepine coprescribing.

PROBLEM

Canada ranks third in the world for prescription opioid use per capita.[1] From 2016 to 2017, the number of Canadians that died from opioid-related causes increased from 2861 to almost 4000.[2] Health Canada has declared the country in the midst of an opioid crisis.[2]

In an attempt to address the high rates of opioid prescribing, new national guidelines and provincial quality standards have been developed.[3] [4] The provincial quality standards include two quality statements specifically addressing high risk opioid prescribing and recommend opioids and benzodiazepines not be prescribed concurrently.[4] They also recommend opioid tapers be offered to patients every 3–6 months.[4]

As part of a broader strategy in our primary care organisation to reduce harm from opioids, we sought to implement a proactive, pharmacist-led intervention. This quality improvement (QI) intervention aimed to develop and test a role for pharmacists as opioid stewards, to reduce opioid and benzodiazepine doses in coprescribed patients at two clinics over 4 months. This project took place at the St. Michael's Hospital Academic Family Health Team (SMHAFHT), an urban, university-affiliated primary care organisation associated with a tertiary care medical centre in Toronto, Ontario, Canada. In Ontario, approximately 20% of residents receive primary care from a Family Health Team, primary care organisations where physicians work together with non-physician health professionals such as pharmacists and social workers.[5] SMHAFHT serves approximately 45 000 patients from a diverse inner-city population at six clinics. The team includes about 75 physicians, most of whom work part-time, and 3.5 full-time pharmacists.

BACKGROUND

Several studies have found that patients coprescribed opioids and benzodiazepines are at increased risk of emergency department (ED) visits, inpatient hospital admissions and death

related to opioid overdose.[6–9] In Ontario, it has been shown that over half of those who died from an opioid-related overdose had evidence of benzodiazepine use in their postmortem toxicology reports.[10] The increased risk of overdose results from the additive effects of both medications depressing the central nervous system and impairing the respiratory system.

We wondered about the potential role for pharmacists as opioid stewards in addressing coprescribing of opioids and benzodiazepines. This role could parallel pharmacists' work as antimicrobial stewards and centre on the same principles of optimising therapeutic effectiveness while minimising potential for adverse effects.[11] As in antimicrobial stewardship programmes, pharmacists can audit and provide feedback on patients' opioid regimens.[12] As medication experts with advanced knowledge of opioid pharmacotherapy, there may be a role for primary care pharmacists as opioid stewards, to support physicians in addressing coprescribed patients.

Published literature supports the role for pharmacists as opioid stewards.[13–15] One study examining perspectives of ED practitioners found that the intervention of choice for reducing co-prescribing of opioids and benzodiazepines was a pharmacist consult.[13] Subsequently, two studies evaluating pharmacist interventions found that rates of opioid and benzodiazepine coprescribing decreased by 24.6% and 65.5%, respectively.[14 15] These studies, however, are not without limitations. Neither study had pharmacists leading the intervention.[14 15] Pardo *et al* required a physician to initiate the consult by a pharmacist, while Homsted *et al* had the medical centre's QI team develop a list of patients to assess.[14 15] Neither study addressed patients chronically coprescribed opioids and benzodiazepines.[14 15] Pardo *et al* focused on patients at the point of new instances of coprescribing, while Homsted *et al* focused on patients on high dose opioids, some of which happened to be coprescribed.[14 15] Both studies took place within the American healthcare system.[14 15] Neither study included details on the nature of pharmacists' recommendations or provided guidance on how to implement pharmacist-led interventions.[14 15] Through this QI intervention, we aimed to improve on previous studies by having an embedded primary care pharmacist lead all assessments in a predefined patient population and be reproducible within the Canadian healthcare system.

MEASUREMENT

We collected process, outcome and balancing measures monthly at baseline (November 2017 to January 2018) and during and after the intervention (February 2018 to May 2018) (figure 1).

Process measures

We reviewed chart documentation to determine the per cent of coprescribed patients who: (1) had a pharmacist developed pain care plan, (2) were offered an opioid and/or benzodiazepine taper by any provider and (3) had an
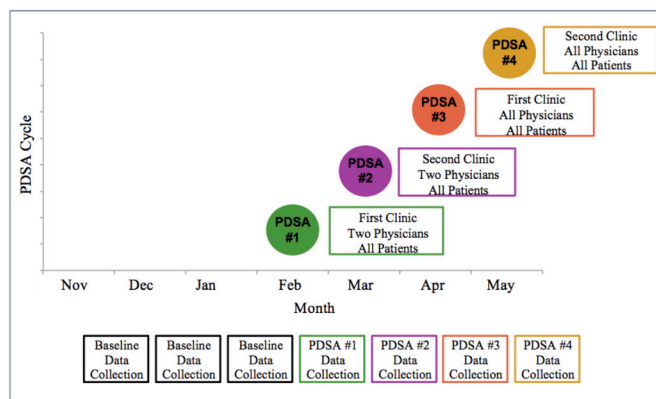
Figure 1 Graphical representation of PDSA cycles performed for all patients coprescribed opioid(s) and benzodiazepine(s) at the two intervention clinics. PDSA, Plan-Do-Study-Act.

active opioid and/or benzodiazepine taper. We qualitatively assessed pharmacist care plans and whether they were acted on.

Outcome measures

As this was a patient safety initiative aiming to reduce potential harms associated with being coprescribed opioids and benzodiazepines, we calculated patients' mean total daily opioid doses, mean total daily benzodiazepine doses and the number of coprescribed patients rather than clinical outcomes. Total daily doses were calculated according to the prescriptions' directions for use. For directions with instructions to 'use as needed', the daily dose was calculated by dividing the total prescribed quantity by the day supply. Total daily opioid doses were converted to milligrams morphine equivalent (MME) using 'Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain's Oral Opioid Analgesic Conversion Table'.[3] Total daily benzodiazepine doses were converted to milligrams diazepam equivalent using 'Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain's Benzodiazepine Equivalent Table'.[3] If multiple prescriptions were issued within the month, the most recent prescription was used to calculate mean total daily doses.

Balancing measures

We collected data on substance use (ie, illicit drug use, alcohol use, smoking status), opioid-related injury (ie, overdose, suicide, death), pain (ie, pain scores, functioning) and physician-patient relationship (ie, ongoing professional relationship) as documented in the patients' electronic medical record (EMR) profile and chart notes.

Baseline measures

Baseline measures are summarised in figures 2–4.

Analysis

Our QI initiative was pragmatic and included all physicians and patients at the two intervention clinics. Accordingly, our sample size was not calculated in advance and
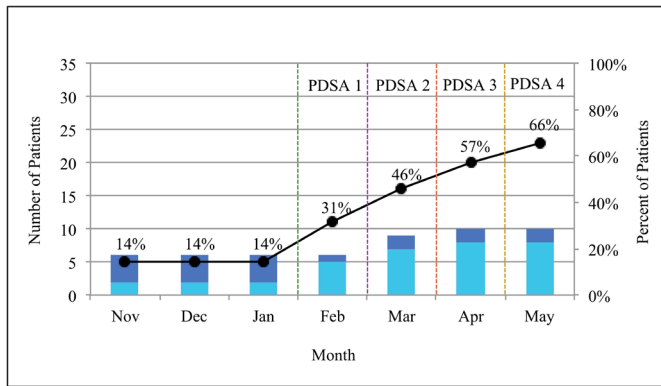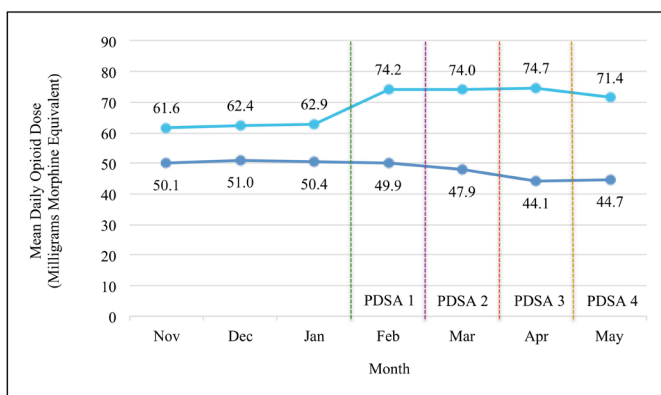
Figure 2 Process measures over four PDSA cycles for all patients coprescribed opioid(s) and benzodiazepine(s) at the two intervention clinics. ▮, patients offered an opioid taper; ▮, patients with an active opioid taper; ●, patients with pharmacist involvement in their pain management; PDSA, Plan-Do-Study-Act.

our outcomes were not powered. We expressed descriptive summary statistics of continuous variables as means (±SD). We summarised categorical variables as proportions. We used run charts for the analysis of non-random patterns of change.

DESIGN
Patient eligibility

We identified participants prescribed at least one opioid and at least one benzodiazepine through EMR queries (online supplementary appendix 1) and manual chart reviews. Patients were eligible if they met the following inclusion criteria: (1) patient at the clinics of interest during the project timeframe; (2) opioid prescription for >3 months within the last 12 months; (3) benzodiazepine prescription for >3 months within the last 12 months and (4) concurrent opioid and benzodiazepine prescriptions prescribed within the last 12 months. We defined concurrent prescriptions as an opioid and benzodiazepine

Figure 3 Mean daily opioid dose (milligrams morphine equivalent) over four PDSA cycles for all patients coprescribed opioid(s) and benzodiazepine(s) at the two intervention (dark blue) and one control (light blue) clinic(s). ●, intervention clinics; ●, control clinic; PDSA, Plan-Do-Study-Act.
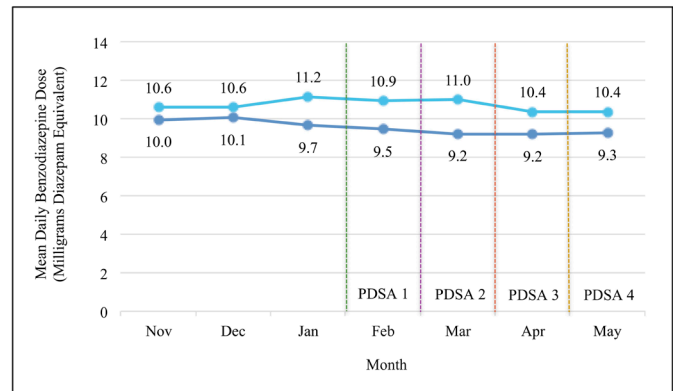
Figure 4 Mean daily benzodiazepine dose (milligrams diazepam equivalent) over four PDSA cycles for all patients coprescribed opioid(s) and benzodiazepine(s) at the two intervention (dark blue) and one control (light blue) clinic(s). ●, intervention clinics; ●, control clinic; PDSA, Plan-Do-Study-Act.

prescription having at least 1 day of overlap. We defined expected duration of the prescription as the number of days the prescription quantity would last according to the directions for use. For directions that included instructions to use 'as needed', we calculated day supply according to time elapsed between renewals. Participants were excluded if they met the following criteria: (1) opioid or benzodiazepine use discontinued; (2) less than daily opioid or benzodiazepine use; (3) inactive patient during the study period (eg, out of the country, documented failed efforts to contact); (4) receiving opioid substitution therapy (ie, methadone, buprenorphine/naloxone); (5) cancer pain; (6) palliative status or (7) EMR data unavailable. In addition, two patients were excluded from the control group because their mean daily opioid doses were outliers at >600 MME; this exclusion enabled a more comparable baseline between our control and intervention groups.

Intervention

We employed Plan-Do-Study-Act (PDSA) methodology to implement and refine the pharmacist-led intervention from February 2018 to May 2018 (figure 1).

Our intervention consisted of four components: (1) the principal investigator (TT) conducted EMR queries (online supplementary appendix 1) and manual chart reviews to proactively identify coprescribed patients; (2) the primary care pharmacist (JH) reviewed patients' medical histories and developed individualised pain care plans; (3) the primary care pharmacist engaged the physician to discuss plan recommendations and (4) the physician and/or primary care pharmacist, based on physician preference, met with the patient to discuss plan implementation.

STRATEGY
Interviews

The principal investigator conducted five interviews with physicians to refine subsequent PDSA cycles' intervention. Interviews lasted, on average, 13 min (range, 9–21

min). The principal investigator conducted three interviews with patients to refine subsequent PDSA cycles' intervention. Interviews lasted, on average, 28 min (range, 21–39 min). The principal investigator took field notes throughout each physician and patient interview and analysed them for themes. Themes for suggested improvements, and examples of proposed suggestions, can be seen in online supplementary appendix 2.

Refinement of intervention

PDSA Cycle 1: The pharmacist communicated with physicians via the EMR and provided recommendations for individual patients via chart notes. The feedback from physicians revealed a preference to meet with the pharmacist in-person to discuss recommendations rather than correspond strictly electronically.

PDSA Cycle 2: The pharmacist met with physicians in-person. A unique meeting was scheduled for each individual patient discussion. The feedback from physicians revealed a preference to discuss all coprescribed patients in a single meeting.

PDSA Cycle 3: The pharmacist scheduled a single meeting to discuss all of a physician's coprescribed patients. Physicians suggested increasing pharmacist visibility at the clinic and providing additional education for physicians on the role of pharmacists.

PDSA Cycle 4: In addition to meeting with physicians and patients, the pharmacist attended multidisciplinary meetings, provided project updates, delivered drug presentations and informed physicians of the pharmacist's ability to meet with patients. Feedback from patients revealed that participants viewed education and referrals for non-pharmacotherapy options as priority items for the pharmacist to discuss in patient meetings and incorporate into care plans.

RESULTS
Patient demographics

The automated EMR query identified 71 potentially coprescribed patients at the intervention clinics and 35 at the control clinic. Manual audit confirmed that 35 and 20 patients were eligible for participation at the intervention and control clinic(s) respectively. Top reasons patients were excluded from the EMR query results were that their opioid or benzodiazepine had already been discontinued or their frequency of use was less than daily. Table 1 provides a summary of baseline patient characteristics. At baseline, patients at the control clinic had slightly higher mean daily opioid doses than those at the intervention clinics.

Pharmacist recommendations

We identified 35 patients who were coprescribed at the intervention clinics. The primary care pharmacist was able to engage with physicians for 34 patients, as 1 patient left the practice prior to their assigned PDSA cycle. The pharmacist made care plans for 23 (66%) patients during the PDSA cycle for which they were assigned. The remaining

Table 1 Baseline characteristics of patients coprescribed opioid(s) and benzodiazepine(s) at the control and intervention primary care centre clinic(s)

Patient characteristic	Control patients* (n=20)	Intervention patients* (n=35)
Sex, female	65	69
Age (mean), years (SD)	60 (±8.4)	57 (±12.3)
Psychiatric comorbidity	75	83
Depression	55	49
Anxiety	40	43
Substance use disorder	25	34
Post-traumatic stress disorder or history of trauma	<25†	26
Bipolar disorder or schizophrenia	<25†	23
Current cigarette use	50	49
Current illicit drug use	40	37
ODSP client	65	37
History of overdose	<25†	31

*Results are percentages of patients except where indicated otherwise.
†Exact percentage suppressed due to small sample size.
ODSP, Ontario Disability Support Program.

11 patients did not receive pharmacist-developed care plans as their prescriber declined the primary care pharmacist intervention. The pharmacist endorsed continuation of current therapy for 11 patients and recommended therapy changes for 12 patients. The two most common reasons for continuation of current therapy were that the patient was on a stable or low dose. The most common recommended changes were to reduce doses and switch to alternative drug therapy (eg, initiating an opioid taper via an opioid rotation). Other recommendations were to initiate additional therapy, increase doses and obtain drug coverage. Online supplementary appendix 3 demonstrates the pharmacist's individual patient care plan development process.

Physicians accepted 24 (75%) of the 32 recommendations made by the pharmacist to change therapy. We defined acceptance as the physician documenting agreement with the recommendation and taking subsequent action to enable implementation (eg, scheduling a patient appointment with the pharmacist to discuss implementation, prescribing according to the recommendation). The remaining eight (25%) recommendations had yet to be addressed by the physicians at the end of this initiative. Of the 24 recommendations accepted by physicians, 13 (54%) were subsequently accepted by patients, 7 (29%) were rejected by patients and 4 (17%) were scheduled to be discussed at upcoming appointments and therefore had no resolution at the end of this initiative.

Effect of pharmacist intervention

At the intervention clinics, there was an increase in the per cent of patients with a pharmacist developed pain care plan, the per cent offered an opioid taper and the per cent with an active opioid taper (figure 2). At the control clinic, which had a pharmacist but did not have the proactive pharmacist-led intervention, the per cent of patients with a pharmacist developed care plan remained relatively stable at less than 20%. The control clinic had an increase in the per cent offered an opioid taper, but no increase in the per cent with an active opioid taper (0%). The number of patients offered and accepting a benzodiazepine taper remained relatively stable at less than 20% at both the intervention and control clinics. Among all the patients at the intervention clinics, there was an 11% reduction in mean daily opioid dose and an 8% reduction in mean daily benzodiazepine dose (figures 3 and 4, respectively). At the control clinic, there was a 15% increase in mean daily opioid dose and a 4% decrease in mean daily benzodiazepine dose (figures 3 and 4, respectively). At the intervention clinics, all 35 patients remained coprescribed. At the control clinic, 18 of the original 20 patients remained coprescribed. One instance of stopping coprescribing occurred secondary to accidental discontinuations by the patient. Once discovered, the physician elected not to restart benzodiazepine therapy.

Balancing measures

Substance use and pain assessments were infrequently recorded using quantitative means (eg, urine drug test, Ransford pain drawing); however, no signal for an increase in substance use or worsening in function was identified in prescriber chart notes. No increase in opioid-related accidents occurred. Two breakdowns in physician-patient relationships occurred. In both cases, the pharmacist's recommendation had yet to be discussed with the patient.

LESSONS AND LIMITATIONS

A pharmacist-led opioid stewardship intervention increased the per cent of patients offered and attempting opioid tapers. A corresponding decrease in patients' mean daily dose of opioids was observed. In contrast, the control clinic without the pharmacist-led intervention experienced no change in the per cent of patients attempting opioid tapers and an increase in patients' mean daily opioid dose. No reduction in the number of coprescribed patients was observed at the intervention clinics. This likely reflects the need for gradual dose reductions for patients chronically prescribed opioids and benzodiazepines to prevent withdrawal. Physicians and patients accepted the pharmacist-led intervention despite its proactive approach, which differs from the traditional physician-initiated referral model for pharmacist assessment.

At the intervention clinics, patients' mean daily doses of opioids and benzodiazepines decreased by 11% and 8%, respectively. These dose reductions are clinically significant as they align with national guidelines that recommend initial opioid and benzodiazepine dose reductions by 5%–10% of the starting dose.[3] Further dose reductions likely require extended follow-up (to capture the full effects of ongoing tapers) and additional pharmacist reviews (to encourage further rotations and tapers). Additionally, the reduction in daily opioid dose was clinically significant as it brought the average daily opioid dose below 50 MME. This has been highlighted as a key threshold as opioids produce a graded response, where the greatest analgesic benefits occur at lower doses, yet the risk of fatal overdose continues to increase as dose increases.[3 9 16]

The increase in opioid tapers in the intervention group may be related to both physician and patient factors. The pharmacist intervention likely enhanced awareness of the risks of co-prescribing for both patients and physicians. Both groups may have gained new knowledge about the process of tapering and potential alternatives from education provided by the pharmacist. Pharmacist-developed individualised care plans likely made implementing tapers easier for physicians to discuss and patients to accept. Last, dedicated patient visits with a pharmacist focusing on the singular priority of high risk opioid use likely provided more time for the patient to discuss their taper plan and enhanced their comfort with accepting the taper. Fewer patients attempted benzodiazepine tapers than opioid tapers. This may be due to the pharmacist placing less focus on deprescribing benzodiazepines. It could also be due to patients being less aware of benzodiazepine risks given lower media attention received compared with opioids or the high prevalence of psychiatric comorbidities. Throughout the project, the pharmacist suggested initiation of selective serotonin and norepinephrine reuptake inhibitors for psychiatric comorbidities and neuropathic pain management as opioid and/or benzodiazepine sparing agents. This recommendation had the highest patient rejection rate.

Previous studies evaluated the traditional model of physician-initiated referral for pharmacist assessment of patients vulnerable to high risk opioid treatment.[14 15] These studies targeted new instances of coprescribing or high opioid doses regardless of coprescription with benzodiazepines.[14 15] Neither study characterised the temporal overlap or chronicity of coprescribing.[14 15] Further, these studies either did not specify the pharmacist's specialisation or limited pharmacist involvement to those with expertise in pain management or mental health.[14 15] To overcome these limitations, we employed a primary care pharmacist-initiated approach prioritising patients with long-term, concurrent opioid and benzodiazepine therapy. Our project's physician acceptance rate for pharmacist recommendations (75%) was consistent with that observed by Pardo *et al* (81%).[14] While prior studies did not report patient acceptance rates, our project had a patient acceptance rate for pharmacist recommendations of 54%. Our physician and patient acceptance rates are

anticipated to increase as patients in later PDSA cycles had recommendations made but had yet to be seen in follow-up by the project end date. Prior studies found that rates of opioid and benzodiazepine coprescribing decreased by 24.6% and 65.5%, respectively.[14 15] In contrast, we found no decrease in the number of coprescribed patients at the intervention clinics. This is likely due to the initiative addressing patients who had been chronically coprescribed, who require gradual dose reductions over a longer time-period, rather than acute instances of coprescribing.

Strengths of our initiative include its methodology, novel intervention and use of a control clinic. PDSA methodology enabled us to develop and refine an intervention that was integrated into a primary care pharmacist's existing workflow—a pharmacist without specialised training in pain management or psychiatry. In Canada, there is only one pharmacy practice residency programme focusing on mental health and additions and no specialty psychiatric pharmacy practice residency programmes. Our use of a pharmacist without specialised training allows for greater generalisability in team-based primary care organisations across Canada. We included a control clinic to separate the potential effects of the intervention from those in the external environment.

A potential limitation of our project is that opioid and benzodiazepine doses were calculated according to prescribing records rather than dispensing or administration data as access to dispensing databases is restricted to clinical use in Ontario. Additionally, the success of the single pharmacist intervention may represent the skills of the individual, limiting generalisability to all primary care pharmacists. Further, we were limited in our assessment of patient pain, patient function and other balancing measures and so were unable to glean a full picture of intervention effects, intended or unintended. Further qualitative work should explore barriers and facilitations to prescriber assessments and documentation of substance use, pain and function.

CONCLUSION

A proactive, pharmacist-led intervention in primary care resulted in clinically significant dose reductions in mean daily opioid and benzodiazepine doses over a 4-month period for patients prescribed both medications. As pharmacist involvement in patients' pain care plans increased, so too did the per cent of patients with active opioid tapers. The intervention was acceptable to patients, family physicians and the participating pharmacist and was integrated into routine work. The intervention was tested at two of six clinics in an urban academic primary care centre. Future work will spread the intervention to the remaining clinics to evaluate the intervention with a larger number of patients over a longer period of time. This will help us understand whether dose reductions ultimately result in a decrease in coprescribing and impact clinical outcomes. Our improvement initiative highlights a new role for primary care pharmacists as opioid stewards. This role for pharmacists may increase the healthcare system's capacity to address the opioid crisis and prevent further lives lost.

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