Studies on Implementation of Primary Care Services by Community Pharmacists

by

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Abstract

As one of the most accessible primary health care providers, pharmacists are in an excellent position to provide primary health care services. Although slow, the current transition from a dispensing-centered (transaction-based) pharmacy approach to a patient-centered (patient care based) approach is important in addressing the primary healthcare needs of Canadians. This is especially true in patients with chronic conditions, as they will visit the pharmacy more frequently to retrieve their prescriptions. As such, pharmacists have multiple opportunities to review their condition, adjust accordingly, and help patients achieve their health goals both pharmacologically and non-pharmacologically. Yet, this is dependent on the pharmacist being proactive in managing their patient's health, as many patients do not know how or when to ask for help.

The first chapter of this thesis introduces the types of primary care services pharmacists can provide that was investigated. It provides an outline of the following chapters and a rationale behind the importance and purpose of the investigations conducted.

The second chapter of this thesis investigates the effects of an innovative workflow model that places pharmacists at the front, allowing for immediate patient – pharmacist interaction, and observe the effects that this type of proactive workflow model has on managing hypertension and diabetes.

In chapters three and four, we address how pharmacists are able to play a role in combating the Canadian opioid epidemic. Naloxone, an opioid antagonist that is the primary treatment for

opioid poisoning, is an effective tool that even the general public would be able to administer to someone experiencing opioid poisoning. However, distribution of this crucial life-saving tool through pharmacies is haphazard across Canada. In chapter three, we investigate the current disparity in naloxone access in community pharmacies throughout Canada. Integrating these findings in chapter four, we provide recommendations for pharmacists on how and when they can proactively dispense naloxone to the general public.

Preface

Chapter two of this thesis has been submitted for publication as So R, Hamarneh YA, Oleksyn C, et al. “Impact of a “Pharmacist First” Innovative Workflow Plan in Patients with Hypertension and/or Diabetes”, to the *Canadian Pharmacists Journal / Revue des Pharmaciens du Canada.* This research project, of which this thesis is a part, received ethics approval from the University of Alberta Research Ethics Board, “Impact of an Innovative Workflow Plan for Pharmacists in Patients with Diabetes and/or Hypertension, No. Pro00094411, September 25, 2019. The study design was a collaborative work between myself, Dr. Ross Tsuyuki, and Dr. Yazid Al Harmarneh. I was responsible for data collection, analysis, and the manuscript composition, with assistance from Dr. Ross Tsuyuki and Dr. Yazid Al Harmarneh. Carlene Oleksyn and Mary Purschke also helped by demonstrating this model in real-time and providing an accurate description of this model in the manuscript.

The third chapter of this thesis was a collaborative research study led by myself and Dr. Ross Tsuyuki. This study has been published as So R, Hamarneh YA, Barnes M, et al. “The Status of Naloxone in Community Pharmacies Across Canada”, *Canadian Pharmacists Journal / Revue des Pharmaciens du Canada,* (online ahead of print). DOI: 10.1177/1715163520958435. My role was the lead author of a paper from a panel of experts from across Canada. I designed the study methods, collected the data, analyzed the data, wrote the manuscript, solicited comments from the co-authors. Co-authors were responsible for finding data in their respective provinces or territories, and helping retrieve information on jurisdictions with limited data, and providing feedback on the manuscript.

Chapter four was a clinical practice guidelines document led by Dr. Ross Tsuyuki. This paper has been published as Tsuyuki R, Arora V, Barnes M, et al. “Canadian National Consensus Guidelines for Naloxone Prescribing by Pharmacists”, *Canadian Pharmacists Journal / Revue des Pharmaciens du Canada,* (online ahead of print). DOI: 10.1177/1715163520949973. Coauthors, such as myself, acted as a panelist in this expert group and aided in manuscript revisions, which has been published in the Canadian Pharmacists Journal.

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I would like to first thank my supervisor Dr. Ross Tsuyuki, and co-supervisor, Dr. Yazid Al Hamarneh, for the opportunity of becoming a graduate student and the lifetime title of being their mentee. The immense pressure I now have as being your mentee will surely stay with me for the rest of my life and certainly push me to higher heights as I progress through my new journey in pharmacy. My debts to you both for your support, guidance (in both academia and life), and as a role model may never be repaid. The only way I could see this debt being forgiven is by becoming an exceptional pharmacist that is not afraid of taking on new challenges, continuing to advance the profession of pharmacy that you two have definitely pushed for, and finally learning a little bit more about alcohol so I am not clueless when listening to your discussions.

I would like to thank everyone at the EPICORE Centre for being the foundation I needed to support me throughout my studies. I can only hope that I was as helpful as a resource like you were to me. Although there was definitely a break-in period where I had to adjust to everyone's outgoing nature, you never stopped welcoming me and encouraging me to join in. I treat everyone here like family and my only regret is not getting to know each and every one of you better, but I hope it is not too late to start.

Finally, I want to thank my friends and family for believing in me, continually listening to my badgering of how scared I was of graduate school, and asking "What is pharmacology and does it have something to do with agriculture?" Thank you for always extending an ear out to me, pushing me out of my comfort zone to help me grow, and keeping me sane throughout our quarantine during this pandemic.

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Chapter 1 – Introduction

Pharmacists are the most accessible primary care providers.[1-4] Community pharmacies are often easier to access than primary care physician offices due to greater walk-in opportunities, longer operating hours, and often shorter wait times.[4] Indeed, according to a study by Berenbrok et. al, patients visited community pharmacies twice more often than a primary care physician, and this observed difference is even greater when examining non-metropolitan and rural areas.[1] Therefore, pharmacists are in a prime position to provide primary care services as they are easily accessible and see patients most frequently, especially in regions where access to a physician is limited.

By offering and providing primary care services, pharmacists will be able to transition from a dispensing-centered model to a more patient-centered focus model. Indeed, the continuous evolution of pharmacy practice has pushed pharmacists to focus on person-centered care.[5-6] However, this transition has been slow. One of the barriers is that current pharmacy practice is reactive, rather than proactive. Most pharmacists do not practice in a proactive fashion, that is, they will often wait to be approached by a patient for assistance. However, patients may not know who, when, or how to get help for their condition. What is needed is a proactive approach, in which a pharmacist assesses patients' needs, as more of these primary care services become available in community pharmacies, allowing them to play a more active role in managing patient's health conditions and helping achieving their health goals.

Two notable primary care services involve the care of patients with hypertension/diabetes and the issue of opioid safety. Hypertension is the most prevalent chronic disease in Canada, affecting one in four Canadians aged 20 to 79. It is also the most important risk factor for premature death and disability as poor management increases the risk of developing

cardiovascular disease (CVD).[7] Diabetes is another risk factor that increases the risk of CVD and affects one in seven Canadians.[8] However, as epidemiological trends indicate, both hypertension and diabetes prevalence in Canada continue to increase.[7,9,10] Thus, the need for accessible primary health providers is even greater to help patients control their conditions, reach their health goals, and minimize risk of complications.

Pharmacists see patients with hypertension and diabetes frequently, and numerous studies have demonstrated that their interventions significantly improve health outcomes for patients with these chronic diseases.[11-15] Indeed, pharmacists are well-suited to aid in combating the rising prevalence of these chronic conditions and help manage them.

Opioid safety has been an important issue to address as opioids are responsible for approximately twelve deaths per day in Canada.[16] Furthermore, the deaths associated with opioid poisoning has only been exacerbated with the ongoing COVID-19 pandemic. Indeed, the mortality related to opioid poisoning in the first quarter (January 1 – March 31) has since doubled in the second quarter (April 1 – June 30), from 148 to 301.[17] Take-home naloxone (THN) kits have been pivotal in reversing opioid poisonings. Naloxone is an effective antagonist to opioids and providing THN kits to the public creates a portable tool that anyone can use. THN kits are available in all provinces and territories in Canada and have successfully reversed over 61,000 opioid-related poisoning events.[18] As approximately one in eight people are prescribed opioids, pharmacists could provide education about proper opioid usage and offer naloxone to them.[19] Indeed, approximately one-third of opioid related deaths are from prescription opioids, presenting an opportunity for pharmacist to intervene.[20] Despite this, co-dispensing naloxone with these opioids still remains significantly low.[21-23]

Given the magnitude of these issues, studying the implementation of these services by community pharmacists has great public health importance. The challenges for pharmacist management of hypertension/diabetes and the opioid crisis are many, however, a common theme is the lack of a proactive approach to these conditions. As such, the overall objective of this thesis is to explore aspects of the implementation of two primary care services by community pharmacists.

This will be accomplished through two projects:

1. Impact of a "Pharmacist First" Innovative Workflow Plan in Patients with Hypertension and/or Diabetes. This study looked at an innovative workflow and patient care model in patients with hypertension and/or diabetes.

2. The Status of Naloxone in Community Pharmacies Across Canada. This study reports on the status of naloxone use in community pharmacies across Canada.

The third project involves development of national consensus guidelines for naloxone prescribing.

3. Canadian National Consensus Guidelines for Naloxone Prescribing by Pharmacists. This is a national consensus guideline on naloxone prescribing by pharmacists.

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Chapter 2 - Impact of a "Pharmacist First" Innovative Workflow Plan in Patients with Hypertension and/or Diabetes

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Introduction:

Cardiovascular disease (CVD) is one of the leading causes of death in Canada.[1] The majority of cases are caused by modifiable risk factors such as hypertension and diabetes.[2] Hypertension is the most prevalent chronic disease, affecting one in four Canadian adults aged 20 to 79 and is the leading modifiable risk factor for premature morbidity and mortality worldwide.[3,4] Diabetes affects approximately one in seven Canadians.[5] Current epidemiological trends indicate new diagnoses of hypertension and diabetes continue to rise. Indeed, it has been projected that one in three Canadians will either have diabetes or pre-diabetes by 2020.[6] As well, approximately six in ten Canadians diagnosed with diabetes were also diagnosed with hypertension.[6]

Pharmacists are front line primary care providers who see patients with hypertension and diabetes frequently. Numerous trials have demonstrated that pharmacist intervention significantly improves health outcomes, such as effective management of blood pressure and glycemic control and better medication adherence.[7-10] Furthermore, their accessibility puts pharmacists in a prime position to systematically identify patients with poorly controlled cardiovascular risk factors and help in their management. However, there is a clear lack of implementation beyond this evidence. Barriers in the implementation of hypertension and

diabetes care by pharmacists may be related to the current workflow that is more suited towards dispensing rather than patient care.[11]

Carlene Oleksyn is a pharmacy owner in Spruce Grove, Alberta. She has developed an innovative workflow known as "Pharmacist First" (P1st), which focuses on immediate patient contact with the pharmacist. The pharmacist first assesses prescription appropriateness (both new prescriptions and refills), assesses the relevant laboratory tests, then discusses chronic disease control as well as answering any questions or concerns the patient has before passing it to be filled by a technician.[12] Rather than interacting with the patient only at the end of the care process, immediate pharmacist-patient interaction allows for pharmacy technicians to begin processing and dispensing the medication while the patient is being assessed by the pharmacist. As such, clinical issues or concerns can be identified up front and solved during this process. Not only does this reduce wait time, but also increases workflow efficiency while allowing pharmacists to build a rapport, conduct their assessment, and design a care plan. All pharmacists here have their additional prescribing authority, PracID, and injections authorization that only further increase the type of patient care they are able to provide.

P1st allows for increased opportunities to proactively identify therapeutic issues, counsel patients, and manage chronic conditions such as hypertension and diabetes. Additionally, this innovative workflow expands the provision of care through increased time and priority spent on assessments and patient education. As well, these consultations allow pharmacists to spend time with their patients to develop a comprehensive annual care plan (CACP) to help manage their chronic conditions, identify drug therapy problems, and establish a monitoring and treatment plan.[13]

The main aim for this study was to evaluate changes in blood pressure and glycemic control in patients with hypertension and/or diabetes receiving care at a pharmacy using that P1st workflow model.

Methods:

We conducted a retrospective chart review of patients with hypertension and/or diabetes in two community pharmacies who use the P1st approach in the Greater Edmonton Region. We included any patient with hypertension and/or type 1 or type 2 diabetes who have received care using the P1st workflow model. Patients were identified by running a report through the pharmacy software (Kroll™ Pharmacy Management Solution) to identify patients with hypertension and/or diabetes who received a CACP between January 2014 and March 2020.[14] We excluded patients with gestational diabetes and those who did not have any follow up visits.

Data was collected from patient records within the Kroll system by a trained graduate student from the University of Alberta. Information collected included: demographics (age, sex), patient assessment (blood pressure, diabetes type, duration, A1C), and pharmacist intervention (interventions made by the pharmacist, frequency of follow-up visits). Data was collected for baseline and all follow-up visits.

The primary outcome was the change in blood pressure (in those with hypertension) and the change in A1C (in those with diabetes) from baseline to the last recorded follow-up. The secondary outcome was the percentage of patients achieving their recommended blood pressure targets.

Descriptive statistics (mean (standard deviation), median (IQR) (range), frequency (proportion)) was used to analyze demographic and clinical characteristics. The primary and secondary

outcomes was analyzed using paired t-test. Results were considered statistically significant when $p < 0.05$. Statistical analyses were performed using STATA software (version 16.1; StataCorp LLC, College Station, TX).

This study was approved by the University of Alberta Health Research Ethics Board. Waiver of consent was granted as no direct contact or interaction with patients occurred and all identifiers were removed from the files prior to their review.

Data management was performed by the EPICORE Centre (www.epicore.ualberta.ca).[15]

Results:

We reviewed 217 patient records; 215 were included in the study (2 were excluded because they did not receive any follow-up visits). The mean age was 69.4 years (standard deviation 12.5), 51.2% were male, 57.7% had hypertension, 5.6% had diabetes, and 36.7% had both (Table 1). All patients with diabetes were type 2 (Table 1).

Table 1. Baseline Patient Demographics

	Pharmacy #1	Pharmacy #2	Total
Male (%)	58 (61.1)	52 (43.3)	110 (51.2)
Female (%)	37 (38.9)	68 (56.7)	105 (48.8)
Average Age in Years (SD)	63.5 (10.3)	74.2 (12)	69.4 (12.5)
Hypertension Only (%)	48 (22.3)	76 (35.3)	124 (57.7)
Diabetes Only (%)	6 (2.8)	6 (2.8)	12 (5.6)
Both hypertension and diabetes (%)	41 (19.1)	38 (17.7)	79 (36.7)

The median time for the first follow-up visit was 4.2 months (interquartile range 2.5 – 9.3).

The median overall follow-up duration was 19 months (interquartile range 10.4 – 29.8). The median number of follow-up visits per patient was 6 (interquartile range 4 – 11).

In the 201 patients with hypertension, systolic blood pressure was reduced from 139.83 mmHg at baseline to 131.26 mmHg ($p < 0.001$) at the most recent follow-up visit (Table 2). Diastolic blood pressure was reduced from 80.26 mmHg at baseline to 76.86 mmHg ($p < 0.001$) at the most recent follow-up (Table 2). In the 87 patients with diabetes, A1C changed from 7.369% to 7.216% ($p = ns$) (Table 2). Of the 79 patients with both hypertension and diabetes, 2 only had measurements for A1C (with no blood pressures recorded, and 4 only had measurements for blood pressure (with no A1Cs recorded).

Table 2. Blood Pressure and A1C Changes[1]

	Patient Type (n)	Baseline	Last Follow-Up
Systolic Blood Pressure, mmHg (SD)	With diabetes (77)	138.75 (17.78)	130.9* (11.34)
	Without diabetes (124)	140.53 (15.83)	131.48* (15.74)
	Overall (201)	139.83 (16.54)	131.26* (14.20)
Diastolic Blood Pressure, mmHg (SD)	With diabetes (77)	79.92 (10.37)	75.34* (9.28)
	Without diabetes (124)	80.47 (9.90)	77.96* (10.51)
	Overall (201)	80.26 (10.02)	76.86* (10.11)
A1C, % (SD)	With diabetes (87)	7.37 (1.43)	7.22 (1.29)

*Indicates statistical significance ($p < 0.05$) compared to baseline.

[1]Blood pressure and A1C changes in those with hypertension (n=201) and diabetes (n=87).

Of the 124 patients with hypertension only, 82.1% met the target systolic blood pressure, 93.5% met the target diastolic blood pressure, and 78.9% reached both targets (Table 3). For the 77 patients with both hypertension and diabetes, 53.2% met the target systolic blood pressure, 77.9% met the target diastolic blood pressure, and 46.7% reached both targets (Table 3).

Table 3. Patients Reaching Target Blood Pressure Recommendations

	Hypertension Only (n=124)	Both Hypertension and Diabetes (n=77)
Recommended Systolic Blood Pressure, mmHg	140	130
# (%) of Patients Meeting Systolic Blood Pressure Targets[1]	115 (82.1)	41 (53.2)
Recommended Diastolic Blood Pressure, mmHg	90	80
# (%) of Patients Meeting Diastolic Blood Pressure Targets[1]	116 (93.5)	60 (77.9)
# (%) of Patients Meeting Systolic and Diastolic Blood Pressure Targets[1]	97 (78.9)	36 (46.7)

[1]Values for the recommended blood pressure targets are taken from guidelines by Hypertension Canada.[16]

Discussion:

There is clear and strong evidence for the impact of pharmacist prescribing and care in patients with hypertension and diabetes.[7-9] What is missing is an implementation strategy that applies this evidence in real world practice. We found a significant reduction in systolic blood pressure (absolute difference 8.57 mmHg) and diastolic blood pressure (3.40 mmHg) in patients with hypertension in patients receiving care at a pharmacy using the P1st workflow model. These are clinically important reductions in blood pressure, suggesting that the P1st model of care, applied in a real-world setting, could be effective in improving patient outcomes.

In patients with hypertension only, most met the systolic and diastolic targets, with about 79% meeting both targets set by Hypertension Canada.[16] In patients with diabetes and hypertension, fewer met the systolic target (53%) and diastolic target (78%) and 48% achieved both targets.[16]

There was no significant reduction in A1C between baseline and the last follow-up visit (7.4% to 7.2%). However, depending on the functionality of patients, the A1C reported could actually be considered at target. According to Diabetes Canada, the recommended target ranges for A1C for adults over 65 years of age are between 7.1% - 8.0% for functionally dependent adults and ≤ 7.0% for functionally independent adults.[17] Considering the average age of the patient population and the A1C recommendation from Diabetes Canada, this could explain the observed non-significant trend. Furthermore, glycemic control in this group was already quite good, leaving little room for improvement. This also highlights that patients with poorer glycemic control should be targeted for this service.

Our findings are consistent with the findings of the randomized trial, the R_xEACH study, which demonstrated that pharmacist intervention (assessment, education, prescribing, and regular follow-up) in patients at high risk for CVD was associated with significant reduction in blood pressure, A1C and estimated cardiovascular risk.[7] R_xEACH demonstrated that a proactive pharmacist approach that allowed patients to spend more time with their pharmacists was much more successful in managing CVD risk factors than usual care.[7]

The findings from our study are also consistent with the findings from Santschi et al, who found from a systematic review of 39 randomized controlled trials that pharmacist intervention significantly reduced blood pressure by 7.6/3.9 mmHg when compared to usual care.[9]

The P1st model is an implementation strategy that appears to produce results consistent with the evidence in the literature that indicates proactive, pharmacist-led interventions are successful in managing CVD and its risk factors.[7,9,18,19] Indeed, when pharmacists are able to practice to their full scope (prescribing, administering injections, ordering and interpreting laboratory tests, and

disease management) better outcomes have been reported when caring for patients with chronic conditions.[7,20,21]

There are a number of limitations with the current study. The lack of randomization and a control group makes it difficult to determine a causal relationship. There was no standardized measure of blood pressure, nor a pre-specified follow-up schedule. Measurements recorded from patient records could be from the patient's home, physician's office, or at the pharmacy. Our follow-up duration was relatively short, and as a retrospective chart review, documentation was sometimes limited. We were not able to capture components of pharmacist interventions due to limited documentation and as a result, we could not determine that pharmacists were practicing to their full scope. Although we examined two independent community pharmacies for this study, it is possible that the effects observed are simply the exceptional pharmacists themselves. Furthermore, patient selection was based on having a CACP and therefore, it is not clear if changes are a result of the P1st workflow model or the care plan itself. Nevertheless, our study provides some promising evidence for a new, proactive model of care that should be investigated further.

Further research should evaluate the P1st to a traditional workflow model in a randomized control trial, examine multiple community pharmacies, have standardized follow-ups, analyze the patient journal, and have consistent documentation of patients' health measurements throughout the study. This will help us better evaluate this innovative workflow model and establish if it is more effective than traditional workflow models in improving patient outcomes.

Conclusion:

As the healthcare professionals who see patients with chronic diseases the most frequently, pharmacists are well positioned to provide care and help patients achieve their health goals. In this study, we observed a significant reduction in systolic and diastolic blood pressure for patients being treated under the P1st workflow model. Adapting this model of care has the potential to significantly improve patient health outcomes.

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Chapter 3 - The Status of Naloxone in Community Pharmacies Across Canada

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Introduction

Opioids are responsible for approximately 12 deaths per day in Canada.[1] Virtually all (94%) of these deaths could be prevented, as they are caused by accidental opioid use.[1,2] The burden of the "Opioid Crisis" goes beyond the immediate impact on the individual, their families and their community to affect the health care system as a whole. Indeed, opioid-related harms cost the health care system $3.5 billion dollars per year, or approximately $100 for every Canadian regardless of age.[3]

Harm reduction strategies have been implemented in order to tackle this crisis.[4] The distribution of the opioid antagonist, naloxone, as a take-home kit is a prime example of these strategies. Naloxone has shown great success in treating and reversing opioid-induced respiratory depression (OIRD), the main cause of opioid-related premature morbidity and mortality.[5-7] Take-

home naloxone (THN) kits allow non-health care providers to administer the opioid antagonist to anyone experiencing OIRD.[8]

In Canada, all provinces and territories provide free THN kits.[8] However, distribution varies markedly between provinces and territories, as these programs are managed at the provincial level.[8] For example, an individual can receive a free THN kit at over 1000 distribution sites in Alberta, but they can only access free THN kits at 4 distribution sites in New Brunswick.[8] Such variations create disparities in naloxone access throughout Canada, which in turn creates barriers to obtaining this crucial tool. Indeed, it has been reported that more than 98% of individuals who are at high risk (patients with a history of OIRD, opioid-related substance use disorder, high-dosage opioid prescription or prescribed a benzodiazepine concurrently with an opioid) cannot readily access free THN kits.[8,9] Thus, there is a need for an innovative way to address this disparity.

Community pharmacists are extremely accessible primary health care providers who are located in the heart of Canadian communities (urban, rural and remote) and see patients who use opioids frequently. As such, they are well positioned to proactively and systematically identify individuals who are at high risk for OIRD, provide THN kits and educate in a non-stigmatizing environment.[10,11] In fact, pharmacies have already shown great success as naloxone distribution sites.[6,12] Despite this evidence, community pharmacies are still not universally included as free THN kit distribution sites in Canada.[8]

Community pharmacists can play a vital role in tackling the opioid crisis. A better understanding of the current pharmacy distribution system for naloxone and the associated policies surrounding that will help to enhance the current role that pharmacists in each region can play in the fight

against this major public health crisis. The purpose of this paper is to report the current naloxone distribution policies and practice for community pharmacists in Canada.

Methods

Two search methods were used to gather information about naloxone distribution policies and practice in Canada. First, a search of the databases PubMed and ScienceDirect was conducted to find current literature on naloxone distribution in Canada and pharmacist attitudes towards naloxone dispensing. The follow MeSH headings were used: *naloxone dispensing, naloxone distribution, naloxone pharmacist remuneration, community naloxone, take home naloxone* and *naloxone kit program*. These search terms were also combined with the phrase "*in Canada"* or "*in X"* (where *"X"* represents a province or territory in Canada) to aid in specificity. When information was insufficient, such as statistics and remuneration in each jurisdiction, a Google search with the same MeSH terms was conducted to extract relevant data from grey literature. We sent the information we gathered to pharmacy professional bodies across the country, as well as known experts in the field to capture additional information and verify what we had found through our search.

TABLE 1 Comparison of naloxone distribution and costs in Canada between provinces and territories

	BC[8,12-15]	AB[8,13-18]	SK[8,13,14]	MB[8,13,14]	QU[8,13,14,19]	ON[8,13,14,20,21]	NFL[8,13,14]	PEI[8,13,14]	NS[8,13,14,22]	NB[8,13,14]	YU[8,13,14]	NWT[8,13,14]	NU[8,13,14]
No. (%) of pharmacies distributing free THN kits	728/1358 (52.8)	1205/1457 (82.7)	No program	6/426 (1.4)	1633/1907 (85.6)	2729-3500/5051 (54-69.3)	No program	No program	285/307 (92.8)	No program	i	10/10 (100)	No program*
No. (year) of THN kits distributed by pharmacies	3523 (2018)	7608 (01/2019-09/2019)	NA	i	13,268 (2019)	125,606 (2018)	NA	NA	5700 (2017-2019)	NA	i	59 (2019)	NA
Forms of naloxone available in free THN kits	Injectable only	Injectable only	NA	Injectable only	Injectable and nasal spray	Injectable and nasal spray	NA	NA	Injectable only	NA	Injectable only	Nasal spray only	NA
Criteria for dispensing THN kits in pharmacies	At risk or likely to witness overdose	At risk or likely to witness overdose	NA	At risk or likely to witness overdose	At risk or likely to witness overdose	At risk or likely to witness overdose	NA	NA	At risk or likely to witness overdose	NA	Anyone	Anyone	NA
Remuneration for pharmacies ($)	$0	Dispensing (up to $12.30/kit)	$0	$0	Dispensing (up to $9.64) Counselling ($18.59)	Training fee ($25) Professional fee ($10)	$0	$0	Administration fee ($25)	$0	Training fee	Training fee ($15)	NA
Cost to patients to purchase injectable naloxone at nonparticipating pharmacies	$45-$55 (injectable)	$40-$50 (injectable)	$40-$50 (injectable)	$30-$50 (injectable)	$0	$0	$50 (injectable)	$50 (injectable)	i	$40-$50 (injectable)	$55 (injectable)	$0	NA
Cost to patients to purchase naloxone nasal spray at nonparticipating pharmacies	$175-$200 (nasal)	$150-$180 (nasal)	$160-$200 (nasal)	$170-$200 (nasal)	$0	$0	$200 (nasal)	$180 (nasal)	i	$150-$190 (nasal)	$200 (nasal)	$0	NA

A letter "i" denotes insufficient information. Data sources are indicated by references and consultation with experts.

NA, no information was available; THN, take-home naloxone.

*Although there is no territorial program for THN distribution through pharmacies, the Indigenous majority population is eligible for coverage of both intranasal and injectable naloxone from pharmacies through the Non-Insured Health Benefits (NIHB) program. Of pharmacies in the territory, 83% (5/6) offer naloxone.

Table 1 describes the current state of naloxone distribution in community pharmacies across Canada and the costs associated with dispensing. It is clear that availability of free THN kits varies markedly across the country. Community pharmacies are not included as a distribution site for free THN kits in almost half of the Canadian provinces and territories (Saskatchewan, Newfoundland and Labrador, Prince Edward Island and New Brunswick). In contrast, British Columbia, Alberta, Ontario, Nova Scotia and the Northwest Territories have a majority of their community pharmacies participating as a distribution site offering free THN kits. The types of THN kits (nasal vs. injectable) also vary between jurisdictions, with only 2 provinces (Ontario and Quebec) and one territory (Northwest Territories) offering a free nasal spray option. In 2018, the jurisdiction dispensing the largest number of free THN kits (125,606) through community pharmacies was Ontario.[8]

Remuneration to pharmacists for providing naloxone services was very limited and varied greatly between jurisdictions. Only Quebec and Ontario offer reimbursement for both naloxone dispensing and training on injectable use. Alberta and Nova Scotia only offer remuneration for dispensing, while the Northwest Territories offers reimbursement only for training.[8]

The cost of naloxone at pharmacies that do not offer free THN kits ranged from $30 to $50 for the injectable form and $150 to $200 for the nasal spray, depending on jurisdiction. Quebec, the Northwest Territories and Nunavut are the only jurisdictions to list naloxone in their drug formularies, allowing patients to walk into any pharmacy and receive it, as long they meet the criteria for dispensing. Although not listed in the drug formulary, naloxone is free in all community pharmacies across Ontario.

Discussion

Accessibility of naloxone varies greatly across Canada. Indeed, many provinces and territories currently do not offer free THN kits in community pharmacies, reducing accessibility to this crucial tool. Furthermore, only 2 provinces and 2 territories have over 80% of their community pharmacies participating in the program. In areas with poor access to naloxone, the perceived OIRD-to-death ratio is much higher, indicating an opportunity for growth and expansion of the free THN program.[12,13]

The "standard" form of naloxone available in free THN kits is the injectable form, which is administered intramuscularly. Although injectable naloxone is available in all jurisdictions (except the Northwest Territories) throughout Canada at THN kit distribution sites, this route of administration may act as a barrier for use by the general public. Indeed, injectable routes are well suited for medical professionals who have had extensive training, but emergency administration by the general public, especially in a crisis, can be stressful.[12,14] Use of a nasal spray form, which has been observed to reverse OIRD when administered by the general public and is equally effective as the intramuscular form, may increase uptake of naloxone distribution and acceptance.[14,15] However, cost may be a barrier in adopting intranasal naloxone, as the primary form found in free THN kits, as this product is approximately 3 to 4 times more expensive than the injectable version.[16]

Recent studies have observed current naloxone distribution in community pharmacies and have indicated that naloxone dispensing in high-risk populations is still minimal.[11,17,18] The current criteria for obtaining naloxone is insufficient, as it relies on self-identification of individuals being at risk or likely to witness OIRD. Criteria also vary between jurisdictions. A study in

Ontario, consisting of 67,910 individuals who dispensed naloxone, found that only 40.7% of prescription opioid agonist therapy (OAT) patients and 1.6% of prescription opioid recipients received a THN kit.[13] This signifies an extensive subgroup of patients receiving prescription opioids or OAT in this population that needs to be addressed, as this group is the most likely to be at risk of OIRD.

The inclusion of community pharmacies as THN distribution sites will create more accessible, credible venues and will aid in reducing health disparities.[19,20] Furthermore, including more community pharmacies as distribution sites will allow pharmacists to systematically and *proactively* identify patients in the high-risk categories to co-dispense naloxone with their opioid prescriptions and opioid agonist therapy. Pharmacy-based interventions have been shown to be effective in reducing opioid-related harms and promoting safe use.[12,13,19,21]

Pharmacists are more willing to participate in these intervention practices provided they receive proper training and remuneration.[19] Indeed, a study in Colorado identified fear of offending patients and enabling riskier behaviour as potential barriers in naloxone co-dispensing.[20] In an environment of declining pharmacy reimbursement and increasing administrative and regulatory requirements, the lack of remuneration has been observed to reduce pharmacists' enthusiasm on naloxone distribution.[12] Standardization of naloxone availability and form is needed alongside appropriate training and remuneration across the country to enable pharmacists to play a greater role in addressing the public health crisis posed by opioids.

Conclusion

Inconsistent inclusion of community pharmacies as free THN distribution sites limits the accessibility of a crucial, life-saving tool. This disparity is seen across the country and is unfair to Canadians, as they deserve equal and universal health care, regardless of jurisdiction. Including community pharmacies as distribution sites will also provide opportunities for pharmacists to proactively screen for high-risk patients, who already visit frequently and who may not self-identify as benefitting from possession of a naloxone kit. Indeed, a practice guideline in this issue of the journal recommends co-dispensing THN with *all* opioid prescriptions.[31] Future research is needed to evaluate the effects of pharmacist intervention in increasing uptake of THN kits, especially in high-risk populations and its impact as a harm reduction strategy.

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Chapter 4 - Canadian National Consensus Guidelines for Naloxone Prescribing By Pharmacists

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The opioid problem

- Canada is experiencing a public health crisis related to the alarming number of cases of opioid-induced respiratory depression (OIRD) due to prescription and illicit opioids.[1]
- From January to September 2019, there were 2913 opioid-related deaths across Canada, with the highest rates (per 100,000 population) in British Columbia, Alberta and Ontario.[2] In all of 2018, there were 4623 opioid-related deaths, with the number of deaths having increased from 4144 in 2017 and 3025 in 2016.
- From January to September 2019, there were 3663 hospitalizations for opioid-related poisoning across Canada, with 5349 hospitalizations reported in all of 2018.[2]

- According to Statistics Canada, the number of deaths due to OIRD is so great it has affected overall life expectancy.[3] For the first time in more than 40 years, life expectancy has not increased in Canada, with a decrease reported in British Columbia and Alberta from 2016 to 2017. Life expectancy decreased by 0.28 and 0.05 years in British Columbia and by 0.21 and 0.08 years in Alberta for men and women, respectively.

- Prescription opioids such as codeine, morphine, oxycodone and hydromorphone are frequently used for treating pain, one of the most common reasons for seeking health care in Canada.[4]

- Approximately 1 in 8 (~4.7 million) people in Canada were prescribed opioids in 2018, representing a large number of people at risk for opioid-related toxicities and OIRD.[4]

- OIRD is characterized by sedation, hypotension and respiratory depression, potentially resulting in respiratory failure and death.[5]

- The use of naloxone has been instrumental in preventing opioid-related deaths by counteracting depression of the central nervous and respiratory systems related to opioid toxicity.[6]

- Currently, take-home naloxone (THN) kits are publicly funded across all Canadian provinces and territories.[1]

- In most provinces (with the exception of British Columbia, Saskatchewan and Alberta), naloxone is classified as a Schedule II drug, thereby requiring pharmacist intervention for sale. In the other provinces and territories, it is classified as unscheduled.[1]

- As frontline health care professionals, pharmacists are ideally and uniquely positioned to assess patients who are receiving opioid therapy, providing a critical point of care in the patient journey for distributing naloxone. However, Canadian guidelines to advise pharmacists in identifying the appropriate patients for naloxone distribution and education do not exist.
- A steering committee of 8 pharmacists from relevant practice and professional settings across Canada was convened to develop guidelines to provide the first recommendations for pharmacists on the use and distribution of naloxone.

Effectiveness of naloxone distribution programs

- THN programs have been shown to effectively reduce opioid-related deaths.
    - In a systematic review of 22 observational studies to assess the effectiveness of THN programs, a fatal outcome was reported in 1 out of 123 OIRD cases (0.8%; 95% confidence interval = 0.4, 1.2). This is in comparison to 1 fatal outcome for every 20 cases of OIRD that has been documented in populations without naloxone intervention.[7]
    - In Canada specifically, a British Columbia THN program providing low-barrier access to naloxone kits at no cost greatly reduced the number of deaths due to OIRD during a time when there was an increase in the number of fentanyl-related toxicities.[8-10]
        - This THN program, launched in 2012, originally provided naloxone through harm reduction sites and community organizations where there

was a high prevalence of OIRD. In December 2017, the program incorporated selected community pharmacies to provide naloxone to other places and populations with limited access to THN kits.

  - Distribution records from participating pharmacies indicated that 3523 kits were distributed by 562 pharmacies between January 1, 2018, and December 31, 2018. As of June 15, 2019, 656 community pharmacies were participating.

  - Qualitative interviews were performed to determine key strengths and challenges of the program. Key strengths included standardized procedures, standardized THN kits across the province, a centralized distribution model, close-knit teams and adequate training and resources. Key challenges included complicated pharmacy structures, lack of remuneration for pharmacists, communication gaps and logistical challenges such as lag in data entry.

  - Inclusion of community pharmacies had several benefits: providing an opportunity to address stigma, increasing access to THN, screening patients for naloxone and providing education and highlighting pharmacists as key providers in addressing the opioid crisis.

- Distribution of naloxone through community-based programs for substance users is associated with a decreased risk of OIRD at the community level.[6] An observational time series analysis of opioid-related death and acute care utilization rates from 2002 to 2009 in 19 Massachusetts communities showed a reduction in death rates where opioid

education and nasal naloxone distribution programs were implemented (adjusted death rate ratio: 0.54, 95% CI 0.39, 0.76 in high-implementation THN program areas).

- Evaluations of THN programs have shown that they also encourage bystanders to take action when education is included.[11] In a cross-sectional study of community support groups for family members of opioid users, attendees were highly motivated to receive training and use naloxone to rescue people when witnessing opioid-related toxicity.
- Moreover, THN programs have been found to be cost-effective in the provision of naloxone to people using heroin.[12]
- Therefore, increasing the availability and targeted distribution of naloxone is a critical component of continuing efforts to reduce OIRD deaths in Canada.

Pharmacists to the rescue: increasing naloxone distribution to those at risk

- About one-quarter to one-third of opioid-related deaths in Ontario involve prescription opioids.[13,14] In addition, approximately 80% of people assessed at an emergency department for opioid toxicity had received an opioid prescription in the previous 3 years.
- The large population being prescribed opioids must therefore also be targeted with OIRD prevention strategies to reduce the risk of opioid-related deaths.
- Pharmacists are uniquely positioned to distribute THN and educate people who are prescribed opioids.
- Despite the availability of these kits, naloxone dispensing by pharmacies is highly variable.

- A population-based study examining the uptake of THN in the Ontario Naloxone Program for Pharmacies in 2017 showed that only 55.6% of community pharmacies dispensed naloxone.[13]
    - However, one-third (33.7%) of those THN kits were dispensed by the top 1% of naloxone-dispensing pharmacies.
    - There was less uptake among prescription opioid recipients and those with past opioid exposure, regardless of their risk of OIRD.
    - Over the 21-month study period, only 3918 of 55,000 (about 7%) of patients receiving high-dose opioids prescriptions (>90 mg morphine equivalents per day) were given THN in 2017.
- Therefore, a need for pharmacists to increase the dispensing of THN kits to those prescribed opioids to prevent OIRD and possibly death is critical.

Patient selection for THN kits

- Typically, patient selection guidelines for dispensing naloxone recommend using key risk factor criteria such as a history of OIRD or substance use disorder, higher opioid doses and concurrent benzodiazepine use[15-18]
- However, risk factor information is not easy to acquire, as the stigma related to substance use disorders may prevent people from disclosing this information accurately.
    - People may also use multiple pharmacies to acquire medications, making it difficult to determine whether they are taking benzodiazepines or other

medications that increase their risk. They may also obtain these substances through the illicit market.

- In addition, the criteria do not consider the risk to other family members who live in the home.
- Many patients do not perceive their need for THN; therefore, a proactive, structured approach by pharmacists is needed.
- The benefit of having naloxone kits available in cases of emergency outweighs the drawbacks of dispensing those that end up not being used.
- Given the difficulties in assessing the potential risk of OIRD, naloxone kits should be distributed to anyone who is prescribed an opioid.

Recommendation:

All patients receiving an opioid should be dispensed take-home naloxone and counselled by a pharmacist.

Practice implementation tips

- Pharmacists must be proactive in addressing the need for naloxone.
    - People may not feel comfortable asking for naloxone due to stigma, including feelings of shame around opioid use or addiction.
    - Long-term opioid users may have a false sense of security.

    - People may associate OIRD with illicit use only, not prescription opioids, and may not have considered the possibility of accidental or intentional ingestion of opioid medications by family members.
    - People may not be aware that THN kits are available at no cost from community pharmacists, although a valid Health Card may be required in some provinces and territories.
    - Pharmacists need to accept and feel confident in their role as educators on prevention of OIRD.
    - It is important for pharmacists to take the lead by approaching those who may benefit from naloxone.
- Given the stigma associated with opioid use, pharmacists need to be sensitive when discussing the use of naloxone.
    - Use of language that reduces the stigma can help in increasing openness within discussions. For example, pharmacists can describe overdose in a technical way such as "opioid-induced respiratory depression," which can be described as "slowed breathing" (an adverse effect that can occur in any person, regardless of the opioid used or the reason for use).
    - Pharmacists can make it clear that they counsel *all* people who have an opioid prescription on the use of naloxone: "We give this to all patients using these medications." This normalizes the dispensing of THN kits for patients using opioids.

- Strategically placed signage at prescription pick-up and drop-off can act as a conversation starter with patients and demystify stigma around age, gender, ethnicity and diversity.

- The discussion around naloxone can be built into the patient consultation on the adverse effects of opioids. For example, use of naloxone can be introduced when discussing that people cannot drive, may get constipation, and may experience heavy sedation with opioid use.

- Following a script can be helpful in discussing the use of naloxone. See Figures 1 and 2 for step-by-step instructions that can aid in interactions with those who are eligible.

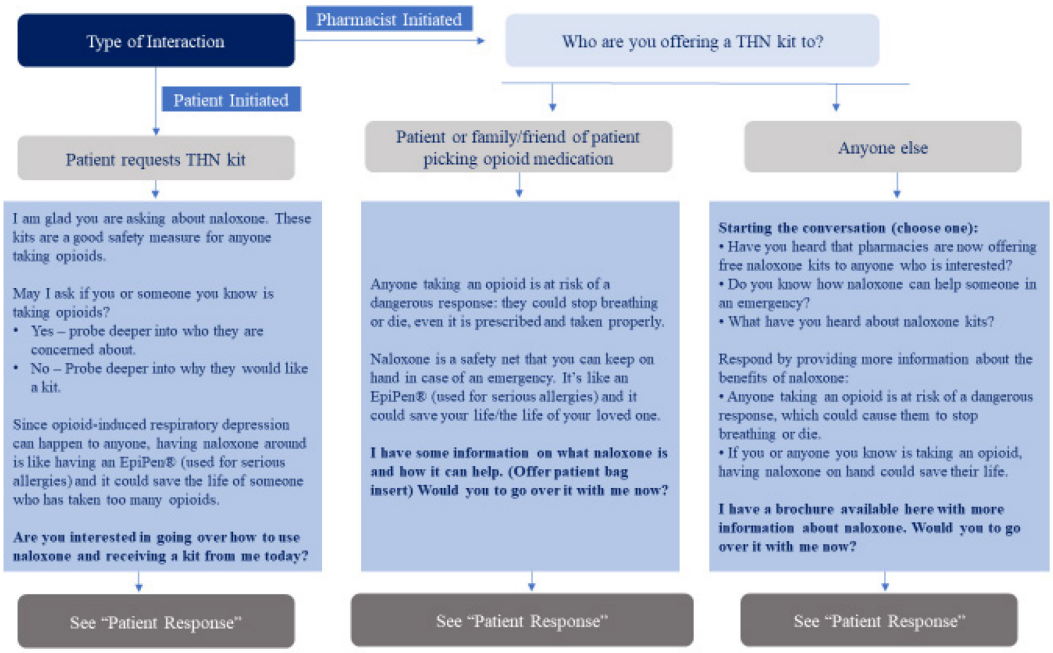

Figure 1 Clinical tool: Pharmacist script based on type of interaction.

THN, take home naloxone

Adapted with permission from the Ontario Pharmacists Association.[16]

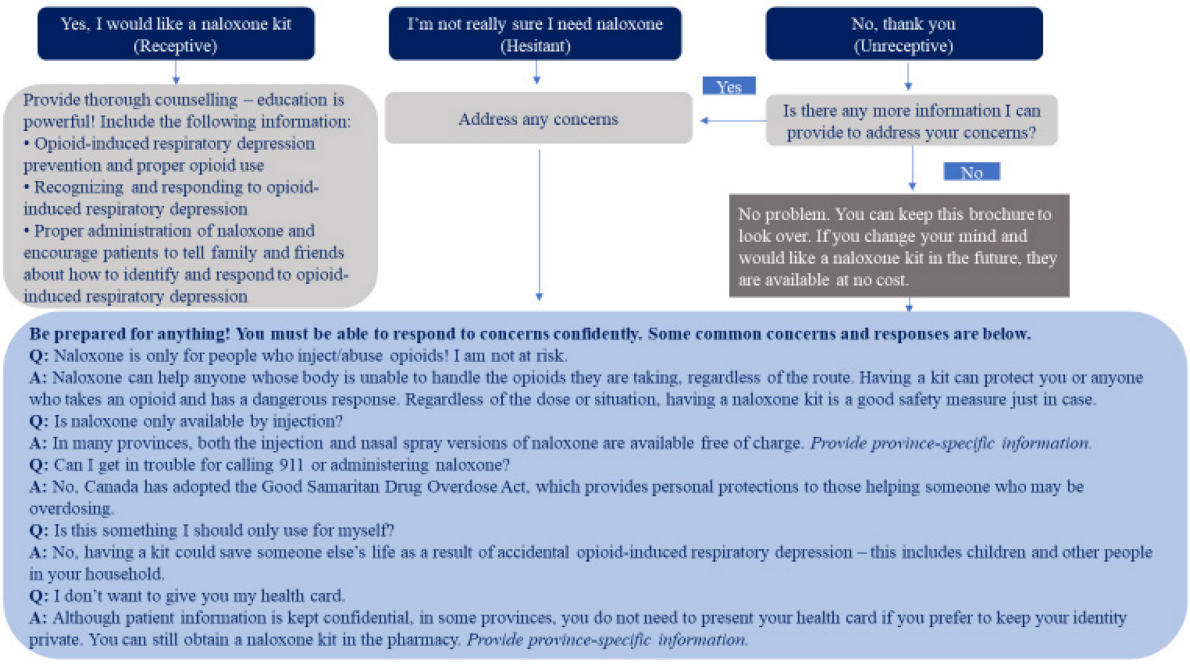

Figure 2 Clinical tool: Pharmacist script based on patient response

Adapted with permission from the Ontario Pharmacists Association.[16]

Patient follow-up

- It is important to follow up with patients to make sure naloxone kits have not expired.
    - An alert could be set as a refill reminder to notify pharmacists to call patients. Note that replacement naloxone kits are also free to patients through THN programs in most provinces and territories.
    - The follow-up communication points provide a critical opportunity to reinforce naloxone education.

- If a naloxone kit has not been dispensed previously, changes in opioid prescriptions or the addition of a benzodiazepine, or other risk factor changes, are important opportunities to revisit offering a naloxone kit.

Recommendation:

Reminders should be set to follow up with people after 3 months and at 1 year after dispensing take-home naloxone. Ongoing yearly follow-up is recommended to ensure THN kits have not expired and reinforce overdose prevention education.

Conclusions

- THN is a critical intervention to reduce opioid deaths; however, current distribution of the kits is insufficient to provide access to all those at risk.
- Pharmacists are accessible and uniquely placed to screen patients and provide THN to prevent opioid-related deaths.
- The federal and provincial/territorial governments have removed barriers to accessing naloxone by expanding pharmacist scope of practice, thereby promoting their ability to intervene effectively.
- Patients prescribed opioids do not typically ask for naloxone and may be unaware of or fail to disclose the risk of OIRD for themselves and/or others in their household.
- We therefore recommend that pharmacists provide naloxone proactively to all patients receiving opioids.

- Follow-up with patients after 3 months and at 1 year after dispensing naloxone is recommended. Ongoing yearly follow-up is also recommended to ensure the kit has not expired and to reinforce OIRD prevention education.
- Implementation strategies for initiating naloxone discussions with patients are suggested here but require further refinement and evaluation.

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Chapter 5 - Conclusions

Pharmacists are the most accessible health care provider, which suggests that they could be central figures in the provision of primary healthcare services. From these studies, we have found:

1. Preliminary evidence of the effectiveness of a proactive, innovative workflow model of care, P1st. Patients with hypertension receiving care at a pharmacy utilizing this model demonstrated significant reductions in both systolic and diastolic blood pressure.
2. Insight into the barriers to greater naloxone use for patients receiving prescription opioids. A great disparity in naloxone access and distribution policies in community pharmacies across Canada. This signals a need to address these policies in order to allow pharmacists to participate in addressing this aspect of the opioid crisis.
3. National guidelines for pharmacists to proactively prescribe naloxone to patients receiving opioids.

There is significant potential for pharmacists to play a greater clinical role in helping patients with health problems and helping them achieve their health goals. However, implementation has been poor due to existing barriers that prevent or slow this transition from dispensing-centered to patient centered care. Such barriers, as indicated by Lounsbery et al, include lack of compensation, additional staff, and medical information.[1] Minard et al indicated that resistance to this transition stemmed from difficulties in documentation, increased workload, and workflow restrictions.[2] As well, many pharmacists indicated that the lack of explicit instruction of how to translate patient centered care into day-to-day activities caused pharmacists to be hesitant, and therefore, be less proactive in offering these clinical services.[3]

Implications of Our Findings:

1. Our findings contribute to the plethora of literature that demonstrate pharmacists can manage patients with chronic conditions, such as those with hypertension.[4,5] Our study adds to the concept that a proactive, more patient-focused workflow model can improve patient care.
2. Pharmacists are able to contribute to safer opioid use, but current policies are haphazard, inequitable and need to be changed to allow for pharmacists to provide naloxone kits to their patients receiving opioids. It will be important to investigate the effects of incorporating more community pharmacies throughout Canada as distribution sites, as well as the effect of pharmacists being more proactive and dispensing naloxone alongside opioids to all patients.
3. Our guidelines provide explicit guidance and information for pharmacists for who, when, and how to provide naloxone to patients. Indeed, this is the foundation where pharmacists can begin to become more proactive and involved with the health needs of their patients' who are using opioids.

Future Research:

1. Future research should include a randomized control trial comparing the P1st innovative workflow model to the traditional workflow model to determine the impact on disease parameters and patient satisfaction. Indeed, this will allow us to make greater causal inferences about this framework and observe the benefits and drawbacks of the P1s workflow model compared to the traditional workflow model. An economic analysis

conducted alongside the trial would help to understand the benefits versus the increased staffing costs.

2. It is evident that advocacy work is needed to address disparities in naloxone availability between provinces and territories. Accessibility should be equal in all jurisdictions, especially when comparing rural to metropolitan areas. Issues to be addressed include: availability of free take home naloxone kits in all pharmacies and fair remuneration for pharmacists to provide and educate patients and their families on the use of naloxone.
3. A prospective implementation study to incorporate the naloxone guidelines for pharmacists into practice will allow us to assess its effectiveness in increasing naloxone dispensing and opioid education and awareness. This study could add automatic reminders in pharmacy management software for pharmacists to dispense naloxone when opioid prescriptions are filled. Alongside, explicit instructions for pharmacists on how to initiate the conversation and how to deal with difficult situations/questions could be established to further encourage a proactive pharmacist approach in dispensing naloxone. Comparing naloxone dispensing between pharmacies with these added reminders and instructions to others without will allow us to assess effectiveness. However, difficulties may arise in negotiating software amendments to include these reminders.

The scope of pharmacy continues to evolve as the health needs of the population grow. The ability of pharmacists to be an integral part in patients' health and management is crucial in reducing premature morbidity and mortality. It is now up to pharmacists to be up to the task of being a proactive healthcare professional by assisting patients with their health care needs.

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