Availability of Naloxone in Canadian Pharmacies: A Population-Based Survey

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ABSTRACT

Background The antidote naloxone is lifesaving when administered shortly after opioid overdose. In March 2016, the Canadian government made naloxone available without prescription to help combat a growing number of opioid overdoses and deaths. However, anecdotal reports suggest difficulty in procuring the drug. We examined the availability of naloxone at community pharmacies across Canada.

Methods We identified all community pharmacies in Canada (n=10,295) using regional pharmacy association data. From these, we randomly selected 506 pharmacies, stratified using proportionate allocation by population size. We thereafter excluded pharmacies in Alberta and Manitoba because these provinces released data indicating which pharmacies distribute naloxone during data collection. We contacted pharmacies by telephone during standard working hours to enquire about the availability of naloxone, the associated cost and the need for a prescription. When a pharmacy did not have naloxone available, we ascertained whether it could be procured within 7 days.

Results We contacted 429 community pharmacies. Of these, only 103 (24.0%) had naloxone on hand. Availability was highest in British Columbia (33 of 65; 50.8%), followed by The Maritimes (11 of 35; 31.4%), Ontario (52 of 193; 26.9%) and Central and Northern Canada (5 of 21; 23.8%). In Quebec, only 1 of 115 (0.8%) pharmacies had naloxone available. Of pharmacies without naloxone on hand, fewer than 1 in 5 anticipated that they would be able to provide it within one week (63 of 326; 19.3%).

Interpretation Despite its nonprescription status, most community pharmacies in Canada do not have naloxone on hand. Availability varies by region but appears particularly poor in Quebec. Of pharmacies without naloxone on hand, fewer than 1 in 5 anticipated the ability to provide it within 1 week. Our findings emphasize the need for increased availability of naloxone in pharmacies across Canada.

INTRODUCTION

North America is in the midst of a crisis of opioid addiction, overdose and death(1-7) related in part to liberal opioid prescribing(8-11) and recent increases in clandestinely-produced fentanyl and its analogues in the illicit drug supply.(6,7,12-14) In addition to more cautious prescribing of opioids and public education, harm-reduction strategies are increasingly advocated to counter the opioid crisis, including opioid agonist therapies (such as methadone and buprenorphine), greater access to addiction care, supervised consumption sites and widespread availability of the antidote naloxone.(15)

Naloxone is a competitive opioid receptor antagonist that acts within minutes of administration to reverse the respiratory and central nervous system depression associated with opioid overdose.(16,17) Naloxone is an exceedingly safe medication, with opioid withdrawal as the primary adverse effect. Naloxone has value in several patient groups, including those who procure ~~prescription and clandestine products~~opioids through illicit means and ~~in~~ those receiving high-dose prescription opioids for pain. Both groups ~~who~~ are at an increased risk of opioid-related death.(18,19) As a harm reduction strategy, the recent Centre for Disease Control Guideline for Prescribing Opioids for Chronic Pain suggests that opioid doses of greater than 50 milligrams of morphine (or equivalent) per day be accompanied by the co-receipt of naloxone.(15) This recommendation is of particular importance for those receiving higher doses of prescription opioids,(18,20-22) those with a history of opioid overdose, the majority of whom continue to receive subsequent opioid prescriptions placing them at increased risk for repeat overdose,(23) and those with acutely reduced opioid tolerance, such as after release from addiction treatment programs(24,25) or incarceration.(26)

Providing naloxone in the community has been shown to be highly effective, with several studies illustrating a reduction in rates of opioid-related mortality and thousands of opioid overdose rescues

following the introduction of community-based opioid education and naloxone distribution programs. (28,31-36) Moreover, take-home naloxone is acceptable to patients receiving opioids for chronic pain.(37,38) Recipients state that receiving education about the risks of opioids and having naloxone available in the event of overdose would be beneficial, and that they would not be offended when offered the product.

While naloxone is readily available to patients with an opioid use disorder through addiction clinics, public health departments and supervised consumption sites, access to these is not uniform across Canada. These services are often concentrated in large city centres where high rates of intravenous opioid use and opioid overdose are present. Furthermore, naloxone may not be available through these sources to patients receiving opioids for chronic pain, despite the tremendous number of such patients and the fact that roughly 1 in 4 of these patients misuse opioids in some way.(19)

In response to a growing body of evidence for the widespread access to naloxone as a means of reducing the toll of the opioid crisis, Health Canada reclassified the antidote's status ~~of naloxone~~ in March 2016, making it available without the requirement for a prescription.(39) However, the planned rollout of naloxone into community pharmacies has not been systematically studied, and anecdotal reports suggest the antidote can be difficult to procure. As healthcare professionals with regular and direct patient contact, pharmacists are uniquely positioned to promote the broad availability of naloxone for those with addiction as well as patients with chronic pain receiving prescription opioids at high doses. In this study, we characterized the availability of naloxone in Canada using a telephone-based survey of community pharmacies.

METHODS

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Identification of pharmacies

We used publicly available regional pharmacy association data and online repositories to identify the contact information of all community pharmacies in Canada (N=10,295). Jurisdictions were defined using Canadian Federal Census data and included the 13 Canadian provinces and territories (British Columbia, Alberta, Saskatchewan, Manitoba, Yukon Territories, Nunavut, Northwest Territories, Ontario, Quebec, Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador).

We initially selected a sample size of 500 pharmacies across Canada stratified using proportionate allocation according to each jurisdiction's population based on the most recent federal census. We chose 500 on the basis of ~~pragmatism~~feasibility, because contacting all of the more than 10,000 pharmacies in Canada by phone would not have been practical. Our sample represents nearly 5% of all community pharmacies in Canada. Territories were grouped together due to their small population size. We ensured that a minimum of 5 pharmacies were sampled within each jurisdiction to reduce the risk of sampling bias. Because of this, we deliberately sampled a larger proportion of pharmacies in less populous jurisdictions such as Prince Edward Island (n=5) and the territories (n=5). Consequently, our ~~final~~ initial sample ~~size~~ included 506 pharmacies. (continue next para without break)

Shortly after the survey began, we opted to exclude Alberta (n=59) and Manitoba (n=18)~~,~~ because these provinces released online information specifying which pharmacies offered naloxone to the public. (See Discussion.) Therefore, our final sample included 429 pharmacies. To reduce the risk of sampling bias, pharmacies within a jurisdiction were numbered in sequence and a random number generator (with n = the jurisdiction pharmacy population size) was used to select sites.(40) The selection process is illustrated in Appendix 1.

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For simplicity of presentation, we categorized jurisdictions into one of five regions based on population size: British Columbia, central and northern Canada (Saskatchewan, Yukon Territories, Nunavut, Northwest Territories), Ontario, Quebec, and the Maritimes (Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador) (Table 1).

Data acquisition

We surveyed pharmacies between December 2016 and March 2017. Pharmacies were contacted by telephone between 9:00 a.m. and 5:00 p.m (local time), Monday to Friday, masking the area code of surveyors using standard caller ID blocking technology. During each interaction, we requested to speak with a pharmacist. Using a standardized questionnaire (Appendix 2), we enquired about the on-site availability of naloxone on the date of the call, the cost to patients and the need for a prescription. If the pharmacist indicated that naloxone was not available, we ascertained the basis for this and whether the pharmacist anticipated being able to provide naloxone within one week. Because most pharmacies can obtain drugs from their distributors within 1 to 2 business days, we chose a 1-week metric ~~to avoid~~so as not to overstate ~~exaggerating~~ the extent of non-availability. Pharmacies in Quebec were contacted by a team member (W.J.) fluent in French.

The study received an exemption from the Research Ethics Board of Sunnybrook Health Sciences Centre because as it was a quality improvement initiative not involving human subjects. The authors declare no potential conflicts of interest relating to the contents or results of the study. The reporting of our study is in keeping with the Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) guidelines.(41) We have completed the SQUIRE 2.0 Reviewer Checklist where applicable (Appendix 3).

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Comment [AC1]: Since our study wasn't technically a QI project (no intervention) – some of the Reviewer Checklist cannot be completed. See Appendix 3

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RESULTS

After excluding 59 pharmacies in Alberta and 18 in Manitoba, we contacted 429 of 8,773 pharmacies in the remaining jurisdictions (Table 1). Of these, 103 (24.0%) had naloxone available on the date of contact. Naloxone availability was highest in British Columbia (33 of 65; 50.8%), followed by The Maritimes (12 of 35; 34.3%), Ontario (52 of 193; 26.9%) and Central and Northern Canada (5 of 21; 23.8%). In Quebec, only 1 of 115 (0.8%) pharmacies surveyed had naloxone on hand. Overall, nearly 1 in 7 pharmacists (n=57; 13.3%) incorrectly indicated the need for a prescription or were uncertain about whether one was required.

Across all jurisdictions, the median cost for naloxone was $50 (interquartile range, $40 to $75). However, the quoted costs varied from a minimum of $25 to more than $200 in some jurisdictions. Of the 103 sites with naloxone available on the survey date, nearly half (n=46; 44.7%) charged a fee for the antidote (Table 2), including 1.9% of ~~pharmacies~~ thosein Ontario, 20% in central and northern Canada, 97% in British Columbia and all pharmacies in The Maritimes and Quebec.

Of sites without naloxone on the date of sampling, more than half (165 of 326; 50.6%) cited a perceived lack of demand as the reason for not stocking the antidote. Fewer than 1 in 5 (63 of 326; 19.3%) anticipated the ability to procure naloxone within one week. Other less common reasons for not carrying the antidote included that the pharmacy or parent company simply did not prioritize carrying the product, a perceived lack of availability from distributors, and that pharmacists had not yet received training to provide the drug.

Our study was conducted between January and March 2017 when provincial and federal initiatives to address the opioid crisis were evolving, as they ~~still are~~continue to do. In response to the launch of online

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naloxone repositories in British Columbia, we once again contacted the 32 pharmacies in British Columbia that originally had naloxone and indicated a fee was required to receive it. These calls, made between July 10th and July 20th, 2017, ~~Of these, all~~ reaffirmed the need for a fee, which in some instances was higher than previously stated. Morerover, some pharmacies no longer had the antidote on hand. This finding directly contradicts postings on the federal government's website (https://www.canada.ca/en/health-canada/services/substance-abuse/prescription-drug-abuse/opioids/naloxone.html) regarding both naloxone availability and cost ~~(https://www.canada.ca/en/health-canada/services/substance-abuse/prescription-drug-abuse/opioids/naloxone.html).~~

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INTERPRETATION

In this population-based survey of community pharmacies in Canada, we found that most did not have naloxone on hand despite its nonprescription status. Availability varied dramatically by jurisdiction, with access being highest in British Columbia and particularly poor in Quebec. Nearly all pharmacies in Ontario that had naloxone on hand provided it at no cost to patients, while the majority of pharmacies in jurisdictions such as British Columbia and The Maritimes required a fee. The price of naloxone varied considerably, with a median cost of $50. Of pharmacies without naloxone on hand, fewer than 1 in 5 anticipated the ability to procure it within 1 week. These findings emphasize the need to increase the availability of naloxone in pharmacies across Canada to address an actionable item in the Canadian Government's comprehensive Federal Action on Opioids strategy aimed at reducing the risk of opioid-related harm.

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We were surprised to find that many pharmacies perceived a lack of demand ~~Our finding of a perceived lack of demand~~ for naloxone given ~~was surprising given~~ the high frequency of high-dose opioid

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prescribing across Canada and North America along with increased use of clandestinely manufactured products containing fentanyl and other high-potency opioids fueling the opioid crisis.(7,14,18,42) ~~We speculate several possible~~ This perception may relate to perceptions of stigma ~~reasons for this perception. The etiology of this finding is likely multifactorial.~~among people with ~~Patients with~~ an opioid use disorder~~ may feel uncomfortable or stigmatized when seeking naloxone in a community pharmacy~~, of the perception that ~~while~~ patients ~~with~~ receiving high-dose opioids for chronic pain ~~may perceive themselves to be~~are not at risk of ~~at low risk of~~ overdose. The cost of naloxone may also be a limiting factor. Although nearly all pharmacies in jurisdictions where cost was reimbursed by the provincial government (Ontario and Northern Canada) offered naloxone free of charge, other jurisdictions cited costs varying from $25 to more than $200. This is likely to represent a significant barrier for some patients, particularly those ~~with an opioid use disorder and financial constraints who are~~ likely to prioritize acquisition of opioids over naloxone. The reason for variability in price may be driven by government-decision making, pharmaceutical manufacturers, wholesale supply-demand matching or other considerations at the pharmacy level.

~~A more user-friendly formulation (such as naloxone spray) could improve uptake and demand, reduce the need for intensive training, reduce the risk of needlestick injury, and increase the efficiency by which the drug could be administered.[43,44] However, the cost of intranasal naloxone is much higher and likely prohibitive for many opioid users.[45]~~

In addition to perceived lack of demand, p~~P~~harmacies not offering naloxone ~~that did not offer naloxone~~ may perceive training for overdose recognition and drug administration to be ~~prohibitively time-intensive and challenging~~ onerous. ~~during daytime hours at a busy community pharmacy~~. For example, to become a naloxone distributor in Ontario, pharmacists complete a short online training course that improves understanding of the Take-Home Naloxone program. Participants in this program learn about principles

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of harm reduction, how to identify at-risk individuals, the contents of a Take-Home Naloxone kit, and counseling about proper administration of naloxone.

While the time involved in training for naloxone distribution and patient education is not trivial, it is unquestionably important. There is a clear dose-dependent risk of opioid-related death,(1,3,22) with 3.8% of men and 2.2% of women receiving greater than 200 milligrams of morphine (or equivalent) per day eventually dying of opioid-related causes.(18) There are tens of thousands of such patients in Canada. As health professionals with regular, direct patient contact, pharmacists are uniquely positioned to facilitate access to an extremely safe and potentially life-saving antidote to patients receiving prescription opioids, particularly at high doses.

~~A more user-friendly formulation (such as naloxone spray) could improve uptake, reduce the need for intensive training, reduce the risk of needlestick injury, and increase the efficiency by which the drug could be administered. However, the cost of intranasal naloxone is much higher and likely prohibitive for many opioid users. Alternative s~~Strategies to increase the availability of naloxone, independent of pharmacy involvement, may include increasing funding to community programs that provide training and education on recognizing opioid overdose and to offer naloxone more broadly within community. These programs have been effective in the United States and United Kingdom.(28,32-36) Similar programs also exist in Canada and aim to educate about prevention, recognition and treatment of opioid overdose. Providing take-home naloxone through emergency departments or supervised consumption sites to high-risk individuals is another strategy that has shown to be cost-effective and with high acceptance rates.(30,43) Moreover, a more user-friendly formulation (such as naloxone spray) could improve uptake and demand, reduce the need for intensive training and the risk ~~, reduce the risk~~ of needlestick injury, and increase the efficiency by which the drug could be administered.(44,45) However, the cost of intranasal naloxone is much higher and likely prohibitive for many opioid users.(46)

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Limitations of our study include the exclusion of Alberta and Manitoba, which released online information specifying which pharmacies offered naloxone to the public. Although we did not sample sites in ~~Alberta or Manitoba~~those provinces, online data suggest that more than half of the community pharmacies in Alberta (732 of 1216; 60.2%) offer the antidote while 1 in 6 in Manitoba (60 of 417; 14.4%) do.(47,48) We collected data over a 3-month interval, during which time the availability of naloxone may have evolved. Finally, ~~, and~~ our sample size was relatively small in relation to the more than 10,000 pharmacies across Canada. Although some jurisdictions now provide online data using geospatial mapping to identify access points for naloxone, our secondary analysis of pharmacies in British Columbia identified inaccuracies in these databases~~-~~. All of the 32 sampled pharmacies reaffirmed the need for a fee, which in some instances was higher than previously stated, but several indicated they no longer had naloxone on hand. These data indicate that the Government of Canada's website may sometimes be inaccurate with regard to both naloxone availability and cost. A future study might purposively sample pharmacies in areas where rates of opioid prescribing, opioid-related overdose, emergency-department visits, and death are disproportionately higher compared to others.(7,14,42,49)

In contrast, our study has several strengths that merit emphasis. We used a population proportionate sampling strategy that yielded a representative sample of pharmacies across Canada and used a standardized approach to query pharmacists anonymously. Given the nature of our data collection method, we had a nearly 100% response rate, which is atypical for survey-based research.(50)

CONCLUSIONS

Most community pharmacies in Canada do not have naloxone on hand despite its nonprescription status. Naloxone availability varies dramatically, and of sites without naloxone on hand, fewer than 1 in 5

anticipated the ability to provide it within 1 week. Enhancing community access to naloxone through community pharmacies represents one core actionable component of a broader federal opioid strategy aimed at providing education about the benefits and harms of opioids, training bystanders about overdose recognition and prevention, enrolling high-risk individuals in naloxone take-home programs and improving access to addiction treatment and services. As health professionals with regular, direct patient contact, pharmacists are uniquely positioned to promote the broad availability of naloxone for patients receiving prescription opioids and have an opportunity to facilitate broader access to this safe, relatively inexpensive and potentially life-saving antidote.

Table 1. Jurisdictions and study population

Jurisdiction	Population	Pharmacies	Sample
British Columbia	4 751 612	1 296	65
Maritimes			
Newfoundland & Labrador	530 128	210	7
Prince Edward Island	148 649	49	5
Nova Scotia	949 501	354	13
New Brunswick	756 780	225	10
Quebec	8 326 089	1 785	115
Ontario	13 982 984	4 360	193
Central/northern Canada			
Saskatchewan	1 150 632	366	16
Territories	119 043	18	5
Yukon	37 492		
Northwest Territories	44 469		
Nunavut	37 082		
Manitoba	1 318 128	417	18
Alberta	4 252 879	1 216	59
TOTAL	36 286 425	10 295	506

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Table 2. Availability of naloxone in community pharmacies in Canada

Jurisdiction	Naloxone Available n (%)	Naloxone in 1 week* n (%)	Cost+ n (%)
British Columbia (n=65)	33 (50.8)	7 (21.9)	32 (97)
Central/northern Canada (n=21)	5 (23.8)	4 (25.0)	1 (20)
Ontario (n=193)	52 (26.9)	16 (11.3)	1 (1.9)
Quebec (n=115)	1 (0.8)	33 (28.9)	1 (100)
Maritimes (n=35)	12 (31.4)	3 (12.5)	12 (100)
TOTAL (n=429)	103 (24.0)	63 (19.3)	46 (44.7)

*applies to those sites without naloxone available on initial contact; +applies to those sites with naloxone available on initial contact

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AUTHOR CONTRIBUTIONS

Study concept and design: Cressman, Mazereeuw, Guan, Gomes, Juurlink

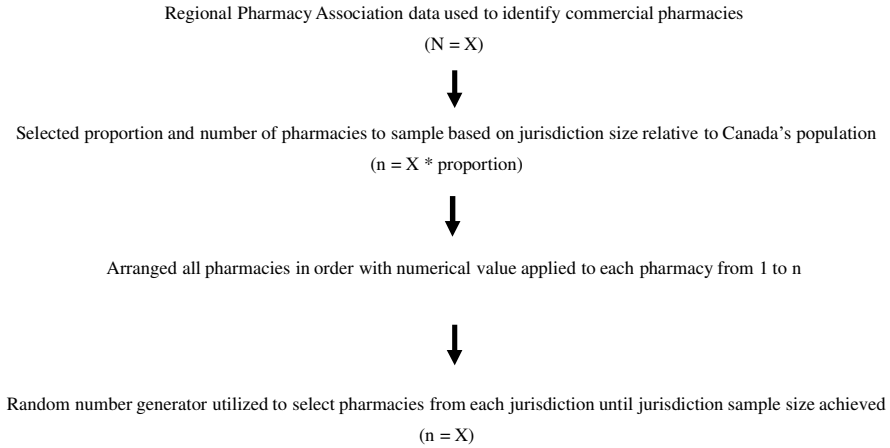
Analysis and interpretation of data: Cressman, Mazereeuw, Guan, Gomes, Juurlink

Acquisition of data: Cressman, Mazereeuw, Guan, Jia, Gomes

Drafting of the manuscript: Cressman, Mazereeuw, Guan, Gomes, Juurlink

Critical revision of manuscript: Cressman, Mazereeuw, Guan, Gomes, Juurlink

APPENDIX 1:



APPENDIX 2: Survey Structure

"Hi, I was wondering if I could speak with a pharmacist. I'm calling to ask if you have any naloxone available for pick up today?"

YES

Is there an associated cost? (Y/N)

NO

1. What is the reason?

Need prescription?

Not trained?

Not available yet?

No demand?

We simply do not carry it?

FREE TEXT

2. Would you be able to get it within the next week?

3. If yes, is there an associated cost?

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