

Availability of naloxone in Canadian pharmacies: a population-based survey

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Abstract

Background: Naloxone is life-saving when administered after opioid overdose. In March 2016, the Canadian government made the antidote available without prescription, but anecdotal reports suggest members of the public have difficulty in procuring it. We examined the availability of naloxone in community pharmacies across Canada.

Methods: We identified community pharmacies in Canada ($n = 10\,296$) and randomly selected 506, stratified using proportionate allocation by population size. We excluded pharmacies in Alberta and Manitoba because these provinces released data indicating which pharmacies made naloxone available to the public during the data collection phase of the study. We contacted pharmacies by telephone during working hours and used a standardized survey 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 if it could be procured within 7 days.

Results: We contacted 429 community pharmacies. Of these, 103 (24.0%) had naloxone available. 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, 1 of 115 (0.9%) pharmacies had naloxone available. Of pharmacies without naloxone, fewer than 1 in 5 anticipated being able to provide it within 1 week (63 of 326; 19.3%).

Interpretation: Most community pharmacies in Canada did not have naloxone on hand and in those without naloxone available, fewer than 1 in 5 anticipated being able to provide it within 1 week. Our findings emphasize the need for increased availability of naloxone in pharmacies across Canada.

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 being advocated to counter the opioid crisis, including efforts to increase the use of opioid agonist therapies, provide greater access to addiction care, establish supervised consumption sites and ensure 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 opioids through illicit means and those receiving high-dose prescription opioids for pain. Both groups are at an increased risk of opioid-related death.^{18,19} The 2016 Centers for Disease Control and Prevention Guideline for Prescribing Opioids for Chronic Pain suggests that as a harm

reduction strategy, opioid doses of greater than 50 mg 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 Increasing naloxone availability 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

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introduction of community-based opioid education and naloxone distribution programs.^{27–33} Moreover, take-home naloxone is acceptable to patients receiving opioids for chronic pain,^{34,35} with recipients stating 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 if 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 services is not uniform across Canada. 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 high 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 supporting widespread access to naloxone as a means of reducing the toll of the opioid crisis, Health Canada reclassified the antidote's status in March 2016, making it available without prescription.³⁶ 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 health care 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 aimed to characterize the availability of naloxone in Canadian pharmacies using a telephone-based cross-sectional survey of community pharmacies.

Methods

Setting and design

This study was conducted in Ontario, Canada, with data collected via telephone from across the country. We used publicly available regional pharmacy association data and online repositories to identify the contact information of community pharmacies in Canada ($n = 10\,296$). Jurisdictions were defined using Canadian federal census data and included the 13 Canadian provinces and territories (British Columbia, Alberta, Saskatchewan, Manitoba, Yukon, 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 on the basis of the most recent federal census. We chose this sample size on the basis of 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 because of 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 ($n = 5$). Shortly after the survey began, we opted to exclude Alberta and Manitoba because these provinces released online information specifying which pharmacies offered naloxone to the public. 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 (Research Randomizer, version 4.0). The selection process is illustrated in Appendix 1 (available at www.cmajopen.ca/content/5/4/E779/suppl/DC1).

Sources of data

This was an investigator-driven quality improvement cross-sectional survey study in which all study coauthors administered surveys to selected pharmacies between December 2016 and March 2017. The survey was designed and developed in accordance with the *CMaJ* guide for design and conduct of self-administered surveys of clinicians³⁷ using an iterative process with a goal of maintaining brevity while identifying access to naloxone in Canadian community pharmacies. Pharmacies were contacted by telephone between 900 and 1700 (local time), Monday to Friday; the area code of the surveyor was masked using standard caller ID blocking technology. During each interaction, we asked to speak with a pharmacist and using a standardized questionnaire (Appendix 2, available at www.cmajopen.ca/content/5/4/E779/suppl/DC1), 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. To reduce response bias, participants were not informed that they were participating in a survey.

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 1 week. Because most pharmacies can obtain drugs from their distributors within 1 to 2 business days, we chose a 1-week metric so as not to overstate the extent of nonavailability. Pharmacies in Quebec were contacted by a team member (W.J.) who is fluent in both French and English. If no response was obtained on initial contact, the site was contacted again until the survey could be administered. Consequently, all pharmacies we contacted participated in the survey.

We chose not to present pharmacy-level demographic data (such as location, pharmacy characteristics and regional opioid overdose rates) to maintain anonymity. The reporting of our study is in keeping with the Revised Standards for Quality Improvement Reporting Excellence (SQUIRE 2.0) and the Strengthening of Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional observational studies.^{38,39}

Statistical analysis

For simplicity of presentation, we categorized jurisdictions into 5 regions on the basis of population size: BC, central and northern Canada (Saskatchewan, Yukon, Nunavut, Northwest Territories), Ontario, Quebec and the Maritimes (Nova Scotia, New Brunswick, Prince Edward Island, Newfoundland and Labrador) (Table 1). We present data on naloxone availability, ability

to procure naloxone within 1 week and cost to participants as a dichotomous variable and proportions (%) in Table 2.

Ethics approval

The study received an exemption from the Research Ethics Board of Sunnybrook Health Sciences Centre because it was a quality improvement initiative that did not directly involve human participants.

Results

Our initial sample included 506 pharmacies. After we excluded Alberta ($n = 59$) and Manitoba ($n = 18$) (see Methods), our final sample included 429 of 8663 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 BC (33 of 65; 50.8%), followed by the

Table 1: Population, total number of pharmacies and number of pharmacies in the study sample for each jurisdiction

Jurisdiction	Population	Pharmacies	
		No. in jurisdiction	No. in study sample*
British Columbia	4 751 612	1296	65
Maritimes			
Newfoundland and 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	1785	115
Ontario	13 982 984	4360	193
Central and northern Canada			
Saskatchewan	1 150 632	366	16
Territories	119 043	18	5
Yukon	37 492	4	
Northwest Territories	44 469	11	
Nunavut	37 082	3	
Manitoba	1 318 128	417	18
Alberta	4 252 879	1216	59
Total	36 286 425	10 296	506

*To maintain anonymity, the number of pharmacies in the study sample in the individual territories is not included in this table.

Table 2: Availability of naloxone and requirement for payment in community pharmacies in Canada

Jurisdiction	Naloxone immediately available, no. (%)	Naloxone available in 1 week,* no. (%)	Payment required,† no. (%)
British Columbia ($n = 65$)	33 (50.8)	7 (21.9)	32 (97.0)
Central and northern Canada ($n = 21$)	5 (23.8)	4 (25.0)	1 (20.0)
Ontario ($n = 193$)	52 (26.9)	16 (11.3)	1 (1.9)
Quebec ($n = 115$)	1 (0.9)	33 (28.9)	1 (100.0)
Maritimes ($n = 35$)	12 (34.3)	3 (12.5)	12 (100.0)
Total ($n = 429$)	103 (24.0)	63 (19.3)	46 (44.7)

*Applies to sites without naloxone available on initial contact by surveyor.

†Applies to sites with naloxone available on initial contact by surveyor.

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 (0.9%) 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.

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 those in Ontario, 20.0% in central and northern Canada, 97.0% in BC and all pharmacies in the Maritimes and Quebec. Across all jurisdictions, the median cost for naloxone was \$50 (interquartile range \$40 to \$75). Among pharmacies requiring payment, the quoted costs varied from a minimum of \$25 to more than \$200.

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 being able to procure naloxone within 1 week. Other less common reasons for not carrying the antidote were that the pharmacy or parent company simply did not prioritize carrying the product, that there was a perceived lack of availability from distributors, and that pharmacists had not yet received training to provide the drug.

Our study was conducted between December 2016 and March 2017, when provincial and federal initiatives to address the opioid crisis were evolving, as they continue to do. After the launch of online naloxone repositories in BC, we once again contacted the 32 pharmacies in BC that had naloxone at the time of the initial survey and required payment to receive it. These calls were made between July 10 and 20, 2017; the pharmacists we contacted reaffirmed the need for payment of a fee, which in some instances was higher than previously stated. Moreover, many 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.

Interpretation

In this population-based cross-sectional 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 BC and particularly poor in Quebec. Nearly all pharmacies in Ontario that had naloxone on hand provided it at no cost to patients, while most pharmacies in jurisdictions such as BC and the Maritimes required payment of 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 being able 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 to reduce the risk of opioid-related harm.

We were surprised to find that many pharmacies perceived a lack of demand for naloxone, given the high frequency of high-dose opioid prescribing across Canada along with increased use of clandestinely manufactured products containing fentanyl and other high-potency opioids fuelling the opioid crisis.^{7,14,18,40} This may relate to a perceived stigma among people with an opioid use disorder or the perception that patients receiving high-dose opioids for chronic pain are not at 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 offered naloxone free of charge (such as Ontario and parts of central and northern Canada), other jurisdictions cited costs varying from \$25 to more than \$200 per kit. This is likely to represent a substantial barrier for most patients, particularly those who prioritize the acquisition of opioids over naloxone. The variability in price may be driven by government decision-making, pharmaceutical manufacturers, wholesale supply-demand matching or other considerations at the pharmacy level. In addition to the perceived lack of demand, pharmacies not offering naloxone may perceive training for overdose recognition and drug administration to be onerous. For example, to become a naloxone distributor in Ontario, pharmacists must complete a short online training course that improves their understanding of the Take-Home Naloxone program. Participants in this program learn about principles of harm reduction, how to identify at-risk individuals, the contents of a Take-Home Naloxone kit and how to counsel clients 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 mg 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 care professionals with regular, direct patient contact, pharmacists are uniquely positioned to facilitate access to an extremely safe and potentially life-saving antidote for patients receiving prescription opioids, particularly at high doses. 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 offering naloxone more broadly within the community. These programs have been effective in the United States and the United Kingdom.^{27–32} Similar programs exist in Canada and aim to provide education 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 cost-effective strategy with high acceptance rates.^{41,42} Moreover, a more user-friendly formulation (such as naloxone spray) could improve uptake and demand, reduce the need for intensive training and the risk of needlestick injury, and increase the efficiency with which the drug could be administered.^{43,44} However, the cost of intranasal naloxone is much higher than that of injectable naloxone and is likely to be prohibitive for many opioid users.⁴⁵

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 100% response rate, which is atypical for survey-based research.³⁷

Limitations

Limitations of our study include the exclusion of pharmacies from Alberta and Manitoba; these provinces released online information specifying which pharmacies offered naloxone to the public. Although we did not sample sites in 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.^{46,47} We collected data over a 3-month interval, during which time the availability of naloxone may have evolved. Finally, our sample size was relatively small in relation to the number of pharmacies across Canada (more than 10 000). Although some jurisdictions now provide online data using geospatial mapping to identify access points for naloxone, our secondary analysis of pharmacies in BC identified inaccuracies in these databases. All of the 32 sampled pharmacies in BC reaffirmed the need for payment of 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 or communities where rates of opioid prescribing, opioid-related overdose, visits to the emergency department and death are disproportionately higher than in others.^{7,14,40,48}

Conclusion

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 being able to provide it within 1 week. Enhancing community access to naloxone through community pharmacies represents an actionable component of a broader federal opioid strategy aimed at providing education about the benefits and harms of opioids, offering training for 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 care 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.

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