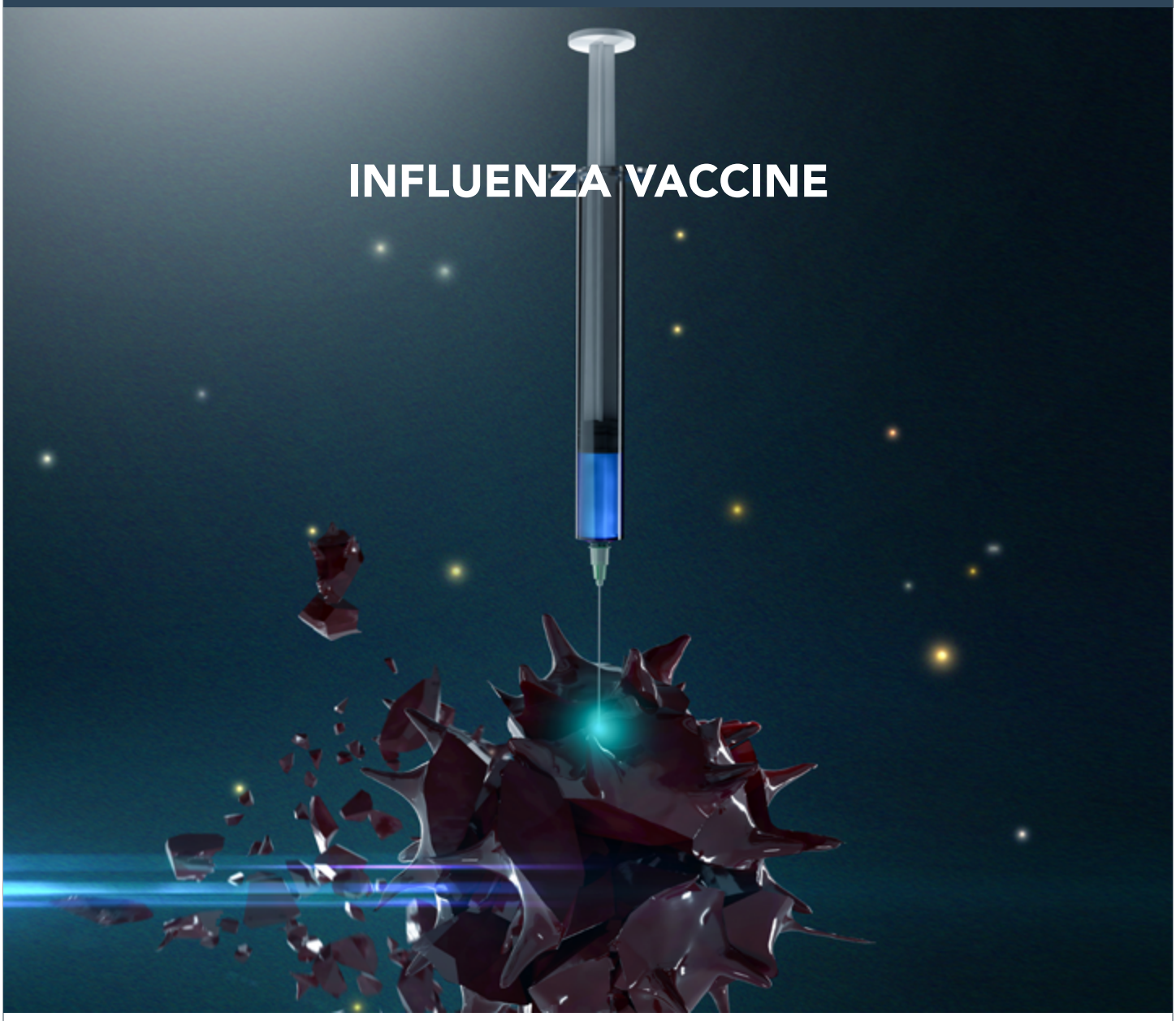
CCDR | CANADA COMMUNICABLE DISEASE REPORT

canada.ca/ccdr

October 2021 - Volume 47-10



Public Health Agency of Canada | Agence de la santé publique du Canada

Canada

CCDR
CANADA COMMUNICABLE DISEASE REPORT

The *Canada Communicable Disease Report* (CCDR) is a bilingual, peer-reviewed, open-access, online scientific journal published by the Public Health Agency of Canada (PHAC). It provides timely, authoritative and practical information on infectious diseases to clinicians, public health professionals, and policy-makers to inform policy, program development and practice.

The CCDR Editorial Board is composed of members based in Canada, United States of America, European Union and Australia. Board members are internationally renowned and active experts in the fields of infectious disease, public health and clinical research. They meet four times a year, and provide advice and guidance to the Editor-in-Chief.

Editorial Team

Indexed
in PubMed, Directory of Open Access (DOAJ)/Medicus

Available
in PubMed Central (full text)

Contact the Editorial Office

ccdr-rmtc@phac-aspc.gc.ca
613.301.9930

Photo credit

The cover image illustrates a vaccine killing the influenza in the digital world. Image from Adobe Stock (https://stock.adobe.com/ca/images/blue-vaccine-destroying-virus-3d-rendering/334615878?prev_url=detail).

CCDR Editorial Board Members

ISSN SN 1481-8531 / Cat. HP3-1E-PDF / Pub. 200434

CCDR
CANADA COMMUNICABLE DISEASE REPORT

INFLUENZA VACCINE

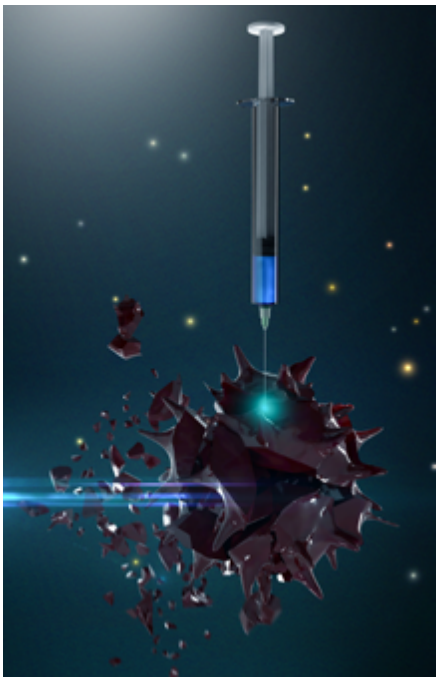


TABLE OF CONTENTS

Epidemiology of norovirus and viral gastroenteritis in Ontario, Canada, 2009–2014

Stephanie L Hughes[1]*, Amy L Greer[1], Alex J Elliot[2], Scott A McEwen[1], Ian Young[3], Andrew Papadopoulos[1]

Abstract

Background: Norovirus is the most common cause of acute gastroenteritis in Canada. The illness causes great morbidity and high societal costs. The objective of this article is to describe the epidemiology of norovirus in the province of Ontario, Canada from 2009 to 2014.

Methods: To assess activity of norovirus and viral gastroenteritis (VGE) in Ontario, three datasets were acquired from the provincial government: two traditional surveillance datasets (outbreak and laboratory) and syndromic surveillance data (telehealth), all spanning 2009–2014. All outbreaks, laboratory submissions and telehealth calls were first assessed for total VGE. Norovirus and norovirus-like illness totals were calculated as a proportion of VGE to estimate agent-specific activity levels. Affected institution types, sexes and age groups were also analyzed.

Results: Between 2009 and 2014, 41.5% of VGE outbreaks, 63.4% of VGE laboratory submissions and 36.6% of all acute gastroenteritis-related (not restricted to viral causes) telehealth calls were attributed to norovirus and norovirus-like illness in Ontario. The most commonly affected institution type was long-term care homes and the most commonly affected age groups were younger (younger than five years) and older (older than 65 years) individuals. Females were slightly more frequently affected than males.

Conclusion: Norovirus and norovirus-like illnesses were the leading cause of VGE in Ontario between 2009 and 2014. They comprised the greatest percentage of VGE when compared with all other VGE-associated viruses. Additional work is needed to determine all component costs and necessary public health actions to reduce the burden of disease.

Affiliations

[1] Department of Population Medicine, University of Guelph, Guelph, ON

[2] Real-time Syndromic Surveillance Team, Field Service, National Infection Service, Public Health England, Birmingham, UK

[3] School of Occupational and Public Health, Ryerson University, Toronto, ON

***Correspondence:**
shughes@alumni.uoguelph.ca

Suggested citation: Hughes SL, Greer AL, Elliot AJ, McEwen SA, Young I, Papadopoulos, A. Epidemiology of norovirus and viral gastroenteritis in Ontario, Canada, 2009–2014. Can Commun Dis Rep 2021;47(10):397–404. https://doi.org/10.14745/ccdr.v47i10a01

Keywords: norovirus, viral gastroenteritis, acute gastroenteritis, surveillance, Ontario, Canada

Introduction

Norovirus is the most common cause of infectious gastroenteritis in Ontario, Canada (1–3). It comprises roughly 50% of acute gastroenteritis (AGE) (all aetiologies) (4). Its high morbidity rate is due to its low infectious dose (approximately 18–1,000 viral particles), various transmission routes, extended viral shedding, short-lasting immunity and persistence in the environment (5,6). Its efficient transmission allows it to thrive in areas of concentrated populations, such as cruise ships and nursing homes (1,7). The burden of disease is high, with an estimated 3.4 million cases and hospital expenditures of 21 million CAD per year in Canada (2,8). It has also been estimated that, in the United States, the average person will experience five episodes of norovirus during their lifetime (9).

The disease is characterized by the sudden onset of nausea, vomiting, diarrhea, abdominal cramps and malaise and is transmitted via the fecal-oral route and aerosolized vomitus (1,5). The incubation period is short (approximately 10–48 h) and symptoms typically clear in 1–3 days; however, this is often longer in high-risk individuals, such as the very young and elderly (1,5). The illness is typically treated with outpatient care (10), although sequelae and serious side-effects, such as irritable bowel syndrome, necrotizing enterocolitis or death can occur (1,11).

Children are particularly susceptible to the disease, requiring medical attention more frequently than any other age group (10,12). This underscores the need for surveillance to

inform public health, plan appropriate intervention measures and develop vaccines (13). A lack of formal reporting mechanisms for norovirus (and AGE in general) leads to knowledge gaps. Approximately 15% of individuals suffering from AGE seek medical care and, of those, diagnostic samples are requested from only 13% (14).

In this study, we describe the epidemiology of norovirus in the province of Ontario, Canada using confirmed outbreak data, laboratory testing data, and telemedicine calls with vomiting calls as a proxy.

Methods

This study was conducted using data from the Canadian province of Ontario, which had a population of approximately 14.3 million residents at the time of this study (15).

Datasets

All data acquired and used in this study were anonymized (no personal identifiers). For further information, see **Appendix**.

Outbreaks: The integrated Public Health Information System (iPHIS) dataset represents confirmed outbreaks of viral gastroenteritis (VGE) in institutions in Ontario reported to local public health units.

Laboratory reports: The Public Health Ontario Laboratories (PHOL) dataset represents all samples submitted to Public Health Ontario (PHO) with suspected VGE for confirmatory testing; more specifically, this dataset contains all samples sent to PHO with suspected norovirus or rotavirus infection.

Telehealth calls: The Telehealth Ontario (THO) dataset represents all calls made to the provincial telehealth service with gastrointestinal chief complaints. These gastrointestinal calls represent a collection of AGE symptoms, encompassing a broader scope than just VGE calls, captured by the nurses at THO. Callers may be ill with these gastrointestinal symptoms for a range of reasons including norovirus. Therefore, telehealth calls with the selected chief complaints "vomiting" and "vomiting with diarrhea" were selected as the "vomiting chief complaints" and used as a proxy for norovirus activity in this study. The vomiting chief complaint was chosen due to its compliance with the main presenting symptoms of norovirus illness and evidence from prior studies demonstrating its role as an indicator of the disease (1,5,16).

Data analyses

All three datasets in this study were analyzed for total VGE outbreaks and the proportion attributed to norovirus (or in the case of THO data, gastroenteritis illness due to the inability to confirm presence of norovirus). These percentages were used to assess norovirus activity levels in Ontario. Ontario census data, as well as the total number of institution type (child care centre, long-term care home, retirement home, correctional facility) were used as denominator data to standardize select analyses (17–20).

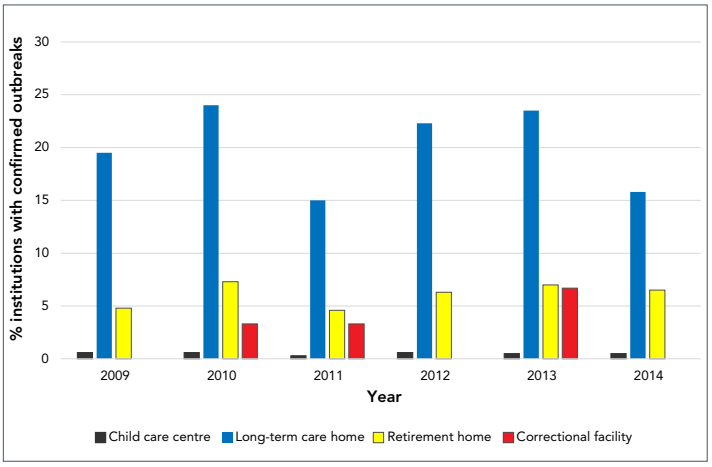
Descriptive analyses were performed on using SAS v.9.4 (Cary, North Carolina, United States) and Microsoft Office (Excel) 2010 (Redmond, Washington, United States).

Results

Outbreaks: There were 3,100 VGE outbreaks in Ontario during the years 2009–2014; 41.6% were caused by norovirus, either by case definition and/or laboratory confirmation. The remaining 58.4% were attributed to adenoviruses, astroviruses, enteroviruses/echoviruses, rotavirus, other caliciviruses and gastroenteritis unspecified/other.

During 2009–2014, 45.1% of VGE outbreaks were in long-term care homes, 30.9% in child care facilities, 22.6% in retirement homes, 0.3% in correctional facilities and 1.2% in other settings. This distribution remained relatively consistent when the analysis was restricted to norovirus outbreaks, in which case retirement homes replaced child care facilities as the second most frequently affected institution type. Of those VGE outbreaks in long-term care homes, more than half (57.2%) were attributed to norovirus. An institutional breakdown for norovirus outbreaks is shown in **Figure 1**.

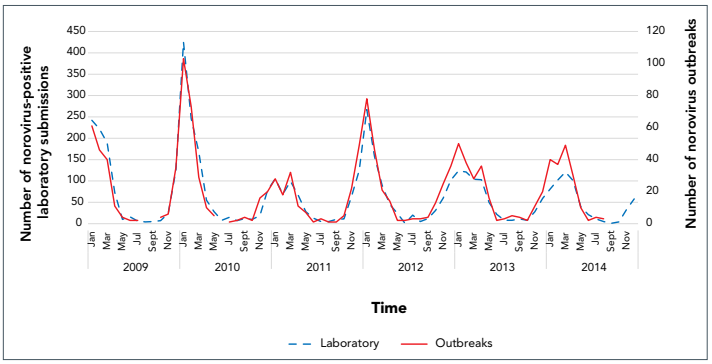
Figure 1: Percent of institutions affected by norovirus outbreaks in Ontario, 2009–2014



The number of norovirus outbreaks per year was relatively stable across the six years; 211 in 2009, 265 in 2010, 178 in 2011, 247 in 2012, 215 in 2013 and 175 in 2014. This is comparable to the stability of VGE outbreaks across the same period.

The seasonal distribution of norovirus outbreaks by month and year is shown in **Figure 2**. The average duration of VGE outbreaks was 12.6 days (range 1–78 days), and for norovirus outbreaks was 14.1 days (range 1–52 days).

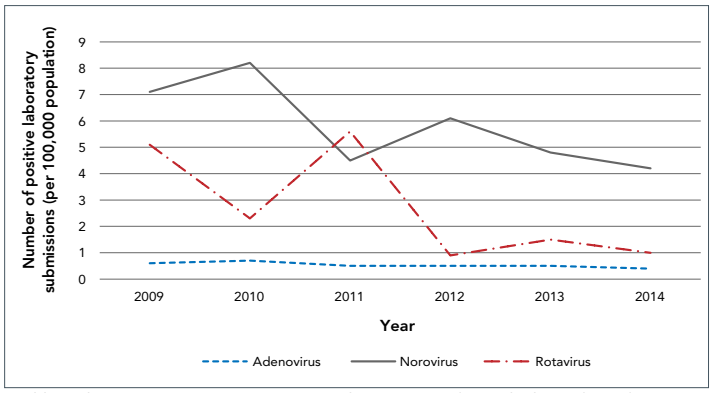
Figure 2: Seasonality of norovirus laboratory submissions[a] and outbreaks[b] in Ontario by month and year, 2009–2014



[a] Laboratory submissions were confirmed using Public Health Ontario Laboratories (PHOL) data
[b] Outbreaks were confirmed using integrated Public Health Information System (iPHIS) data

Laboratory reports: There were 29,459 submitted samples for rotavirus and norovirus-like VGE to PHO between 2009 and 2014, inclusive. The majority (n=22,147; 75.2%) were negative. Among positive samples (n=7,312), 63.4% were attributed to norovirus, with the remaining 36.6% composed of various other VGE aetiologies including adenovirus (16.5%), astrovirus (1.1%), other caliciviruses (0.3%), picornaviruses (0.3%), rotavirus (81.0%) and/or sapovirus (0.5%) (**Figure 3**).

Figure 3: Number of positive specimens submitted to Public Health Ontario Laboratories by virus type and year, 2009–2014 (per 100,000 population)[a]

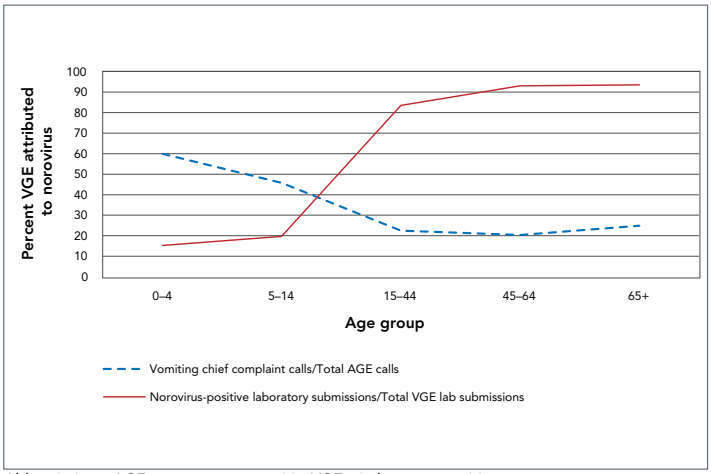


[a] Additional virus types (astrovirus, sapovirus, other *Picornaviridae*, and other *Caliciviridae*) removed due to rates less than 0.10 positive specimens per 100,000 population
Note: The rotavirus vaccine (Rotarix®) was added to the Ontario routine vaccination schedule in 2011

Female patients (40.0%) accounted for more positive VGE submissions (n=7,312) than males (32.4%); however, a large percentage of samples had incomplete sex information (27.6%). When restricting this analysis to norovirus-positive samples (n=4,633), this pattern was repeated.

The 65+ years age group had the highest number of VGE-positive submissions, followed by the 0–4 years age group; 93.5% and 15.3% of these VGE-positive submissions were positive for norovirus, respectively (**Figure 4**). Of all VGE positive submissions, 19% had missing age information

Figure 4: Viral gastroenteritis activity attributed to norovirus by age group 2019–2014[a]



Abbreviations: AGE, acute gastroenteritis; VGE, viral gastroenteritis
[a] Norovirus-positive laboratory submissions presented as a percent of VGE-positive specimens submitted to Public Health Ontario; vomiting chief complaint (vomiting, diarrhea, vomiting+diarrhea) calls to Telehealth Ontario as a percent of all AGE-related calls

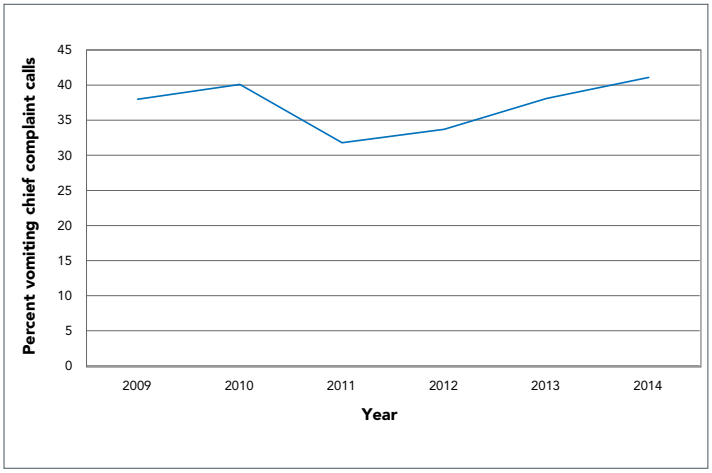
A total of 62.3% (n=4,559/7,312) of the VGE-positive samples were linked to outbreaks. Of the outbreak samples, long-term care homes were the most commonly affected location type, followed by hospitals, retirement homes, day cares and restaurants. The seasonality of norovirus-positive laboratory submissions broken down by month and year was closely associated with the seasonality of norovirus outbreaks (Figure 2).

Telehealth calls: A total of 320,834 telehealth calls was recorded for AGE illness in the period 2009–2014. Of these calls, 36.6% were due to vomiting as the chief complaint. The percentage of AGE calls attributed to the vomiting chief complaints fluctuated between 31% and 41% during 2009–2014 (**Figure 5**).

Telehealth calls were more frequently made by females (62.6% of AGE calls); with male calls comprising 35.9% and 1.5% from unknown/blank. When analyzing the vomiting chief complaints, this pattern was repeated.

The 15–44 age group comprised the highest number of AGE telehealth calls with 131,271 (40.9%) calls between 2009 and 2014. However, for vomiting chief complaint calls the highest call volumes (n=60,058 calls) were recorded for the 0–4 years age group. The 65+ years group consistently had the lowest number of calls. The youngest age groups (0–4, 5–14 years) displayed higher percentages of AGE calls attributed to the vomiting chief complaints in comparison to the older age groups (15–44, 45–64, 65+ years) (Figure 4). Less than 1% of AGE and vomiting chief complaint calls had missing age information.

Figure 5: Percentage of acute gastroenteritis calls to Telehealth Ontario attributed to vomiting chief complaints[a] by year, 2009–2014



[a] Complains involved vomiting, diarrhea and vomiting+diarrhea calls

Discussion

Norovirus was the most common cause of VGE cases and outbreaks in Ontario during the years 2009–2014. This work confirms previous research that has identified norovirus as the most common cause of VGE and intestinal infections in the community (1,14,21,22). The outbreak dataset showed that norovirus comprised 41.6% of all VGE outbreaks during the study period, the laboratory dataset showed that norovirus comprised 63.4% of all VGE submissions, and the telehealth dataset showed 36.6% of all AGE calls had vomiting as the chief complaint.

The 2009–2014 outbreak data demonstrated that long-term care homes were the most commonly implicated institution type for both VGE and norovirus (Figure 1). This was not unexpected due to the higher incidence of VGE in older adults; the virus disproportionately causes more severe illness in vulnerable populations, such the elderly, young children and those with compromised immune systems (1). The number of VGE outbreaks per year in child care facilities decreased after 2011 (Figure 1). This finding is likely due to the introduction of the Rotarix® vaccine administered at the ages of two and four months in the Ontario childhood vaccination schedule in August 2011; this primarily impacted outbreaks occurring in child care centres (23). Rotavirus is a common illness of children younger than five years of age, its primary symptom being diarrhea. Therefore, the presence of rotavirus infection in these data likely impacts the number of VGE outbreaks in young age groups. Other studies, both in Ontario and in countries worldwide, have also reported using surveillance to identify decreases in in rotavirus activity following the introduction of the vaccine (23–25).

Both the outbreak and laboratory data illustrated a rise in norovirus activity above normal seasonal activity during the winter of 2009/2010 (Figure 2). A rise above normal seasonal levels of norovirus activity typically occurs with the introduction of a new strain, mostly due to the quick mutation rate of the virus and lack of herd immunity in the population (22,26). The introduction of new strains can cause shifts in seasonality and/or increases in the number of outbreaks (27). This is likely a result of the emergence of two novel strains: the GII.4 New Orleans strain which affected countries globally; and a GII.12 strain (28,29). The GII.4 New Orleans strain caused many outbreaks and was so widespread that it was still detected in high numbers up until 2013; this may also explain the higher peak seen in Figure 2 for the 2011/2012 season (30).

The two most commonly reported pathogens were norovirus and rotavirus. Norovirus tends to disproportionately affect very young (younger than five years) and older (65+ years) individuals when compared with middle-aged healthy people. Outbreaks are very common in high-density areas, such as daycares, retirement homes and long-term care homes (4,31). Rotavirus has a similar outcome in that it disproportionately affects young children (younger than five years), also resulting in outbreaks in daycares, preschools, etc. (1,23). Older individuals (65+ years) and those living in long-term care homes may be privy to more acute medical care and a higher likelihood of samples being collected and submitted to public health authorities, which might explain these findings. It should be noted that the difference in norovirus and rotavirus-positive samples was present even before the introduction of Rotarix into the Ontario childhood vaccination schedule. Further, our analyses clearly demonstrated the acute decrease in rotavirus cases following the introduction of Rotarix in 2011. From 2012 onwards, the laboratory-positive specimens were almost entirely norovirus.

The difference in telehealth call volumes for AGE and vomiting chief complaints for the 15–44 and 0–4-years age groups, respectively, is likely influenced by rotavirus. Because the illness disproportionately affects young populations, it would lead to a higher call volume for the 0–4 age group. It is likely that many callers phoning telehealth are parents concerned about their children. The 15–44 age group likely had the highest number of callers for AGE because of the various of illnesses affecting this population and their preference for virtual care.

While the datasets provided insight into activity of VGE and norovirus in Ontario, there was one clear disadvantage: a lack of community data (i.e. data from people suffering from illness at-home). Both the laboratory and outbreak datasets are biased towards institutional settings primarily because, outside of institutional settings, it is not mandatory for norovirus and other VGE to be reported to Ontario public health authorities. In addition, many VGE cases (norovirus specifically) suffer from underreporting (32). The inclusion of telehealth data in this study helps to bridge this gap in that it primarily collects community-based data that is not well-represented by the outbreak or laboratory data. Syndromic data are known for their ability to reduce underreporting and represent a higher percentage of the

population (33). Therefore, including telehealth data provides a greater understanding of VGE activity in Ontario and reduces bias.

Syndromic data are becoming increasingly more common and frequently utilized in public health practice due to their array of advantages. They are timely, can detect new/emerging threats, supplement data from traditional surveillance systems and are non-specific (34). Telehealth data are particularly beneficial as they represent one of the timeliest syndromic data options available; telemedicine helplines are one of the first points of medical care for symptomatic patients (34). These data are also known for their availability in real-time and ease of access. However, telehealth data are not as specific as other sources and cannot necessarily be used to detect specific or severe outbreaks (34). In this study, telehealth data do not need to be specific because non-specific gastrointestinal calls provide the early warning of illness required for the system designed, and will be the most effective at observing norovirus and gastrointestinal illness in Ontario when combined with laboratory and outbreak data.

Limitations

There are a few notable limitations to this study. In the outbreak dataset, there was no age-related data. Rather, the institution type was used as an age proxy. In addition, there were many "gastroenteritis unspecified" and "gastroenteritis other" entries in the dataset, which likely contained additional norovirus cases, but were unusable. Furthermore, there was a lack of standardized reporting for norovirus and VGE in Ontario. Only institutional cases of norovirus are required to be reported to Ontario public health authorities (which also suffers from underreporting and time lags). As a result, analyses of norovirus and VGE activity are challenging due to the data gaps, as well as biases in age group reporting across the province. It is also important to note there is likely overrepresentation in the laboratory dataset. This dataset includes both outbreak samples as well as sporadic; when an outbreak occurs, one or more samples may be submitted. This study is, therefore, unable to describe specifically the burden of sporadic norovirus in Ontario, and there is likely a heavier focus on outbreak-related data. Finally, the telehealth calls may have included non-viral causes and may have contained some duplicate callers; however, it was not possible to stratify this in the dataset. As well, it was assumed vomiting was the main symptom of norovirus for telehealth analyses, which likely excluded additional norovirus-related calls from our results. Each dataset had limitations in terms of representative population; however, when combined, an overall summary of norovirus epidemiology in Ontario during the period 2009–2014 was generated.

Conclusion

This study describes the epidemiology of VGE and, specifically, norovirus in the province of Ontario, Canada between 2009 and 2014.Our study demonstrates that norovirus is a highly prevalent illness and the most dominant cause of VGE in the province. Our findings are in line with those of similar international studies, demonstrating norovirus as the leading cause of VGE (1–3). While a vaccine has been introduced in Ontario and countries worldwide to mitigate rotavirus infection, there is no vaccine for norovirus. Introducing preventative interventions, such as a vaccine, is ideal; however, other public health actions, such as novel surveillance techniques, are also necessary to inform public health interventions A combination of traditional and novel surveillance techniques will best capture data representative of Ontarians and reduce bias in surveillance. Additional techniques to help estimate norovirus disease burden knowledge gaps, such as sporadic norovirus, should be considered (35).

Authors' statement

SLH — Conceptualized, obtained datasets, methodology, analyzed and interpreted data, drafted and revised the manuscript
AP — Participated in study designed, methodology, revision

All authors contributed to methodology and manuscript revisions and read and approved the final draft of the manuscript.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

Acknowledgements

We are grateful for the assistance provided by Public Health England throughout this study. In addition, many thanks are necessary to W Sears at the University of Guelph for his assistance with the analyses in this study.

Funding

This work was supported by the University of Guelph.

References

1. Patel MM, Hall AJ, Vinjé J, Parashar UD. Noroviruses: a comprehensive review. J Clin Virol 2009;44(1):1–8. DOI PubMed

2. Morton VK, Thomas MK, McEwen SA. Estimated hospitalizations attributed to norovirus and rotavirus infection in Canada, 2006-2010. Epidemiol Infect 2015;143(16):3528–37. DOI PubMed

3. Yen C, Hall AJ. Challenges to estimating norovirus disease burden. J Pediatric Infect Dis Soc 2013;2(1):61–2. DOI PubMed

4. Karst SM. Pathogenesis of noroviruses, emerging RNA viruses. Viruses 2010;2(3):748–81. DOI PubMed

5. Glass RI, Parashar UD, Estes MK. Norovirus gastroenteritis. N Engl J Med 2009;361(18):1776–85. DOI PubMed

6. Teunis PF, Moe CL, Liu P, Miller SE, Lindesmith L, Baric RS, Le Pendu J, Calderon RL. Norwalk virus: how infectious is it? J Med Virol 2008;80(8):1468–76. DOI PubMed

7. Kaplan JE, Gary GW, Baron RC, Singh N, Schonberger LB, Feldman R, Greenberg HB. Epidemiology of Norwalk gastroenteritis and the role of Norwalk virus in outbreaks of acute nonbacterial gastroenteritis. Ann Intern Med 1982;96(6 Pt 1):756–61. DOI PubMed

8. Thomas MK, Murray R, Flockhart L, Pintar K, Pollari F, Fazil A, Nesbitt A, Marshall B. Estimates of the burden of foodborne illness in Canada for 30 specified pathogens and unspecified agents, circa 2006. Foodborne Pathog Dis 2013;10(7):639–48. DOI PubMed

9. Hall AJ, Lopman BA, Payne DC, Patel MM, Gastañaduy PA, Vinjé J, Parashar UD. Norovirus disease in the United States. Emerg Infect Dis 2013;19(8):1198–205. DOI PubMed

10. Burke RM, Mattison C, Marsh Z, Shioda K, Donald J, Salas SB, Naleway AL, Biggs C, Schmidt MA, Hall AJ. Norovirus and other viral causes of medically attended acute gastroenteritis across the age spectrum: Results from the Medically Attended Acute Gastroenteritis Study in the United States. Clin Infect Dis. 2021;73(6):e913-20. DOI

11. Cremon C, De Giorgio R, Giovanni B. Norovirus gastroenteritis. N Engl J Med 2010l362(6):577-8. DOI PubMed

12. Tarr GA, Pang XL, Zhuo R, Lee BE, Chui L, Ali S, Vanderkooi OG, Michaels-Igbokwe C, Tarr PI, MacDonald SE, Currie G, MacDonald J, Kim K, Freedman SB. Attribution of pediatric acute gastroenteritis episodes and emergency department visits to norovirus genogroups I and II. J Infect Dis 2021;223(3):452–61. DOI PubMed

13. Esposito S, Principi N. Norovirus vaccine: priorities for future research and development. Front Immunol 2020;11:1383. DOI PubMed

14. Hall AJ, Rosenthal M, Gregoricus N, Greene SA, Ferguson J, Henao OL, Vinjé J, Lopman BA, Parashar UD, Widdowson MA. Incidence of acute gastroenteritis and role of norovirus, Georgia, USA, 2004-2005. Emerg Infect Dis 2011;17(8):1381–8. DOI PubMed

15. Statistics Canada. Population estimates on July 1st, by age and sex. Ottawa (ON): Government of Canada; 2021 (accessed 2021-04-10). https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501&pickMembers%5B0%5D=1.7&pickMembers%5B1%5D=2.1

16. Freedman SB, Xie J, Lee BE, Ali S, Pang X-L, Chui L, Zhuo R, Vankerkooi OG, Tellier R, Funk AL, Tarr PI, Alberta Provincial Pediatric EnTeric Infection Team (APPETITE). Microbial etiologies and clinical characteristics of children seeking emergency department care due to vomiting in the absence of diarrhea. Clin Infect Dis 2021:ciab451. (Epub ahead of print). DOI

17. Ministry of Education. Find Licensed Child Care. Toronto (ON): Government of Ontario; 2019 (accessed 2021-04-10). https://www.iaccess.gov.on.ca/LCCWWeb/childcare/search.xhtml

18. Ministry of the Solicitor General. Corrections: Facilities - locations and visiting hours. Toronto (ON): Government of Ontario; 2020 (accessed 2021-04-10). https://www.mcscs.jus.gov.on.ca/english/corr_serv/facilitieslocationsandvisitinghours/facilities.html

19. Ontario Long Term Care Association. About long-term care in Ontario: Facts and figures. Toronto (ON): OLTCA; 2019 (accessed 2021-04-10). http://www.oltca.com/oltca/OLTCA/LongTermCare/OLTCA/Public/LongTermCare/FactsFigures.aspx

20. Statistics Canada. Annual demographic estimates by economic region, age and sex, based on the Standard Geographical Classification (SGC) 2011, inactive. Ottawa (ON): Government of Canada; 2021 (accessed 2021-04-10). https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1710008101#timeframe

21. Loveridge P, Cooper D, Elliot AJ, Harris J, Gray J, Large S, Regan M, Smith GE, Lopman B. Vomiting calls to NHS Direct provide an early warning of norovirus outbreaks in hospitals. J Hosp Infect 2010;74(4):385–93. DOI PubMed

22. Gastañaduy PA, Hall AJ, Curns AT, Parashar UD, Lopman BA. Burden of norovirus gastroenteritis in the ambulatory setting--United States, 2001-2009. J Infect Dis 2013;207(7):1058–65. DOI PubMed

23. Wilson SE, Rosella LC, Wang J, Le Saux N, Crowcroft NS, Harris T, Bolotin S, Deeks SL. Population-level impact of Ontario's infant rotavirus immunization program: evidence of direct and indirect effects. PLoS One 2016;11(5):e0154340. DOI PubMed

24. Thomas SL, Walker JL, Fenty J, Atkins KE, Elliot AJ, Hughes HE, Stowe J, Ladhani S, Andrews NJ. Impact of the national rotavirus vaccination programme on acute gastroenteritis in England and associated costs averted. Vaccine 2017;35(4):680–6. DOI PubMed

25. Bawa Z, Elliot AJ, Morbey RA, Ladhani S, Cunliffe NA, O'Brien SJ, Regan M, Smith GE. Assessing the likely impact of a rotavirus vaccination program in England: the contribution of syndromic surveillance. Clin Infect Dis 2015;61(1):77–85. DOI PubMed

26. Karst SM, Baric RS. What is the reservoir of emergent human norovirus strains? J Virol 2015;89(11):5756–9. DOI PubMed

27. Allen DJ, Adams NL, Aladin F, Harris JP, Brown DW. Emergence of the GII-4 Norovirus Sydney2012 strain in England, winter 2012-2013. PLoS One 2014;9(2):e88978. DOI PubMed

28. Vega E, Vinjé J. Novel GII.12 norovirus strain, United States, 2009-2010. Emerg Infect Dis 2011;17(8):1516–8. DOI PubMed

29. Yen C, Wikswo ME, Lopman BA, Vinjé J, Parashar UD, Hall AJ. Impact of an emergent norovirus variant in 2009 on norovirus outbreak activity in the United States. Clin Infect Dis 2011;53(6):568–71. DOI PubMed

30. Medici MC, Tummolo F, Grazia S, Calderaro A, Conto F, Terio V, Chironna M, Bonura F, Pucci M, Bányai K, Martella V, Giammanco GM. Epidemiological dynamics of norovirus GII.4 variant New Orleans 2009. J Gen Virol 2015;96(9):2919–27. DOI PubMed

31. Said MA, Perl TM, Sears CL. Healthcare epidemiology: gastrointestinal flu: norovirus in health care and long-term care facilities. Clin Infect Dis 2008;47(9):1202–8. DOI PubMed

32. Tam CC, Rodrigues LC, Viviani L, Dodds JP, Evans MR, Hunter PR, Gray JJ, Letley LH, Rait G, Tompkins DS, O'Brien SJ; IID2 Study Executive Committee. Longitudinal study of infectious intestinal disease in the UK (IID2 study): incidence in the community and presenting to general practice. Gut 2012;61(1):69–77. DOI PubMed

33. Silva AD, Evangelista MS. Syndromic surveillance: etiologic study of acute febrile illness in dengue suspicious cases with negative serology. Brazil, Federal District, 2008. Rev Inst Med Trop São Paulo 2010;52(5):237–42. DOI PubMed

34. French Institute for Public Health Surveillance. Triple-S Project (Syndromic Surveillance System in Europe). Guidelines for designing and implementing a syndromic surveillance system. InVS; 2013. https://webgate.ec.europa.eu/chafea_pdb/assets/files/pdb/20091112/20091112_d08_giss_en_ps.pdf

35. Vanderkooi OG, Xie J, Lee BE, Pang XL, Chui L, Payne DC, MacDonald J, Ali S, MacDonald S, Drews S, Osterreicher L, Kim K, Freedman SB; Alberta Provincial Pediatric EnTeric Infection TEam (APPETITE) and Pediatric Emergency Research Canada (PERC). A prospective comparative study of children with gastroenteritis: emergency department compared with symptomatic care at home. Eur J Clin Microbiol Infect Dis 2019;38(12):2371–9. DOI PubMed

Appendix

integrated Public Health Information System

The integrated Public Health Information System (iPHIS) dataset contains information on confirmed outbreaks of viral gastroenteritis (VGE) in Ontario reported to public health between January 1, 2009 and December 13, 2014. It is mandated in Ontario that all Reportable Diseases (as of 2018, these are now called "Diseases of Public Health Significance") be submitted to the database (1,2). Local public health units are responsible for collecting case information on all reportable diseases and entering them into iPHIS, as part of provincial and federal surveillance.

All outbreaks in the dataset are institutional (i.e. occurred at long-term care homes, retirement homes, child care facilities, correctional facilities, etc.).Additional information found in iPHIS includes the method of exposure (if determined), aetiologic agent (if determined), public health unit, disease confirmed status, date the outbreak was declared by the medical officer of health, date the outbreak was declared over by the medical officer of health, the initial onset date (time of index case) and final onset date (time of last case). The onset dates (time of index case) were used for analyses were used for this study, and the range between the onset date (time of index case) and onset date (time of last case) was used to calculate average VGE and norovirus outbreak duration.

While iPHIS data are continuously updated, public health authorities are required to enter all outbreaks from the past year by each August; therefore, incurring time delays. It should be noted laboratory confirmation is not required for an outbreak to be entered into the dataset, and when laboratory confirmation is present not all cases associated with an outbreak are laboratory tested.

Public Health Ontario Laboratories

The Public Health Ontario Laboratories (PHOL) dataset represents all the samples submitted to Public Health Ontario (PHO) between January 1, 2009 and December 31, 2014 for testing in Ontario. The data represent samples which were submitted to PHO from patients ill with suspected norovirus and/or rotavirus (i.e. symptoms of vomiting and/or diarrhea). Samples are submitted by medical professionals in the form of stool samples and are either tested by polymerase chain reaction, electron microscopy or immunochromatographic test. The dataset provides age, gender and public health unit information, as well as the dates the samples were collected and subsequently entered into the dataset. For analyses, the sample collection dates were used (i.e. the results represent the date the samples were collected from the ill person by the healthcare practitioner for testing). It should be noted not all VGE test requisitions from institutions and physicians are tested by PHO in Ontario; samples may also be sent to other private labs in Ontario, or in duplicates to multiple labs. As a result, not all laboratory-confirmed samples of VGE from Ontario are captured in this dataset.

Telehealth Ontario

The Telehealth Ontario (THO) dataset represents all phone calls made by residents of Ontario between January 1, 2009 and December 31, 2014 with gastrointestinal symptoms as chief complaints. Telehealth Ontario is a 24-hour, 7-days-a-week, confidential telephone hotline service which has been in service since 2001 and is available to anyone (providing a health card number is optional). The service is operated by Sykes Assistance Services Corporation, who are contracted by the Ontario Ministry of Health and Long-Term Care. An individual may call the hotline for any reason, where a responding nurse provides basic medical advice and directs the caller to an appropriate next course of action (i.e. visit an emergency room immediately, see a family physician very soon or within the next day, or self-care). The hotline helps alleviate the pressure on emergency departments and doctor's offices, while simultaneously providing free medical advice to millions of Ontarians. The THO dataset provides information on the date and time of call, the caller's chief complaint (primary reason for calling), the nurse's suggested next steps, age, gender, and location (city) of call.

The calls made to THO are referred to as acute gastroenteritis (AGE) in this study rather than VGE as in the iPHIS and PHOL datasets due to the fact they are less specific and encompass all causes of AGE, not strictly viral aetiologies. In addition, the calls made to THO for norovirus-like illness has not been confirmed as norovirus. Therefore, the "vomiting chief complaints" are used as a proxy for norovirus and norovirus-like illness and the burden of AGE calls cannot be attributed strictly to norovirus, but rather norovirus and norovirus-like illness.

National Influenza Annual Report, Canada, 2020–2021, in the global context

Andrea Nwosu[1]*, Liza Lee[1], Kara Schmidt[1], Steven Buckrell[1], Claire Sevenhuysen[1], Christina Bancej[1]

Abstract

During the 2020–2021 Canadian influenza season, no community circulation of influenza occurred. Only 69 positive detections of influenza were reported, and influenza percent positivity did not exceed 0.1%. Influenza indicators were at historical lows compared with the previous six seasons, with no laboratory-confirmed influenza outbreaks or severe outcomes being reported by any of the provinces and territories. Globally, influenza circulation was at historically low levels in both the Northern and the Southern Hemispheres. The decreased influenza activity seen in Canada and globally is concurrent with the implementation of non-pharmaceutical public health measures to mitigate the spread of the coronavirus disease 2019 (COVID-19). Although it is difficult to predict when influenza will begin to re-circulate, given the increased COVID-19 vaccination and the relaxation of public health measures, an influenza resurgence can be expected and may be more severe or intense than recent seasons. Influenza vaccination, along with non-pharmaceutical public health measures, continues to remain the best method to prevent the spread and impact of influenza. Public health authorities need to remain vigilant, maintain surveillance and continue to plan for heightened seasonal influenza circulation.

Affiliation

[1] Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
fluwatch-epigrippe@phac-aspc.gc.ca

Suggested citation: Nwosu A, Lee L, Schmidt K, Buckrell S, Sevenhuysen C, Bancej C. National Influenza Annual Report, Canada, 2020–2021, in the global context. Can Commun Dis Rep 2021;47(10):405–13. https://doi.org/10.14745/ccdr.v47i10a02

Keywords: influenza, influenza-like illness, surveillance, pandemic preparedness, outbreaks, COVID-19

Introduction

Public health measures implemented to reduce the spread of coronavirus disease 2019 (COVID-19) have impacted the transmission of influenza in every country around the world, including Canada (1–4). By the middle of Canada's 2020–2021 influenza season (week 50, ending December 12, 2020), seasonal influenza circulation in Canada was at unprecedented lows and had not approached the seasonal threshold (5). The following surveillance report provides a summary of Canada's 2020–2021 annual influenza season (August 23, 2020 to August 28, 2021) as well as the 2020–2021 Southern Hemisphere and 2020–2021 Northern Hemisphere influenza surveillance seasons.

FluWatch is a national influenza surveillance program that monitors the transmission of influenza and influenza-like illness (ILI) in Canada. Established in 1996, it is a pan-Canadian surveillance network of laboratories, hospitals, healthcare practitioners, individual Canadians and provincial and territorial ministries of health. The objectives of this program are as follows: 1) to identify signals for timely detection of, and coordinated assessment and response to, epidemics and other events of public health concern; 2) to contribute to the evidence base necessary for planning, development and implementation of health programs and healthy public policies for the control of influenza; and 3) to enable a robust surveillance infrastructure for the timely and relevant response and research necessary to mitigate the impacts of influenza (6).

Method

Design

The FluWatch program conducts prospective surveillance on influenza and ILI. Annually, influenza surveillance occurs from epidemiological week 35 to 34 of the following year. The FluWatch program is a composite surveillance system consisting of virologic surveillance, syndromic surveillance, influenza activity level surveillance, outbreak surveillance, severe outcome surveillance and vaccine monitoring.

Indicator definitions

Standardized definitions of the core indicators that are monitored through the FluWatch program and presented in this report are defined in **Table 1**.

Table 1: FluWatch core indicators used to summarize the 2020–2021 influenza season in Canada

Indicator	Definition	Calculation	Data source
Influenza percent positivity	The weekly proportion of diagnostic tests positive for influenza relative to all diagnostic tests conducted.	Numerator: The number of influenza detections. Denominator: The total number of influenza diagnostic tests processed.	Respiratory Virus Detection Surveillance System and FluNet
Influenza strain characterization	The number of influenza isolates characterized by the National Microbiology Laboratory compared to recent Canadian and global isolates and World Health Organization recommended vaccine strain viruses.	Counts and proportions antigenically similar/dissimilar to the vaccine strains.	National Microbiology Laboratory
Proportion of visits for ILI	The weekly proportion of patient-visits to sentinel practitioners due to ILI relative to all patient-visits.	Numerator: The number of patient visits for ILI seen at sentinel sites. Denominator: The total number of patients seen at sentinel sites for any reason.	Sentinel Practitioner ILI Reporting system
Proportion of FluWatcher participants with ILI	The weekly proportion of FluWatcher participants self-reporting cough and fever, relative to all FluWatcher participants.	Numerator: The number of FluWatchers participants reporting cough and fever. Denominator: The total number of participants reporting to FluWatchers.	FluWatchers
Influenza outbreaks	The number of influenza or ILI outbreaks by setting and influenza type.	Counts and proportions of outbreaks by setting and influenza/ILI type.	Provincial and territorial public health authorities
Influenza-associated hospitalizations	The number and rate of hospitalizations that are associated with influenza.	Counts and rates per 100,000 population.	Provincial and territorial public health authorities, Immunization Monitoring Program Active and Canadian Immunization Research Network
Vaccine effectiveness against medically-attended influenza	The proportionate reduction in influenza among those vaccinated, relative to those unvaccinated among medically attended ILI.	Vaccine effectiveness estimates are based on the results of a modified case control study (test negative design) and derived using the following equation: $VE = 100\% * \left(1 - \frac{O_{pos}}{O_{neg}}\right)$ where O_{pos} is the odds of vaccination among those testing positive for influenza and O_{neg} is the odds of vaccination among those testing negative.	Canadian Sentinel Practitioners Surveillance Network
Vaccine effectiveness against influenza associated hospitalization	The proportionate reduction in influenza among those vaccinated, relative to those unvaccinated among adults hospitalized for acute respiratory illness.	Vaccine effectiveness estimates are based on the results of a modified case control study (test negative design) and derived using the following equation: $VE = 100\% * \left(1 - \frac{O_{pos}}{O_{neg}}\right)$ where O_{pos} is the odds of vaccination among those testing positive for influenza and O_{neg} is the odds of vaccination among those testing negative.	Canadian Immunization Research Network
Influenza vaccination coverage	The percentage of Canadians aged six months and older who received one dose of seasonal influenza vaccine during the current influenza season.	Numerator: number of people who received the influenza vaccine for that season. Denominator: the number of people eligible for the vaccine that season.	Public Health Agency of Canada's National Influenza Immunization Coverage Survey

Abbreviation: ILI, influenza-like illness

Data sources

Canadian virologic data: Aggregate and case-level data on influenza detections are reported to FluWatch through the Respiratory Virus Detection Surveillance System (7). The Respiratory Virus Detection Surveillance System is a sentinel laboratory-based system that monitors the temporal circulation of respiratory viruses in Canada at a national and regional level. This surveillance system consists of 34 laboratories reporting on the number of tests conducted and number of positive specimens for influenza and other respiratory viruses. Specimens from every province and territory are represented in the virologic data. Provincial laboratories provide individual case-level data.

Genetic and antigenic characterization data and antiviral susceptibility data: A proportion of laboratory-confirmed influenza detections undergo genetic and antigenic characterization and antiviral susceptibility testing. Results are provided by the Public Health Agency of Canada's National Microbiology Laboratory.

Global virologic data: FluNet is a global web-based tool for influenza virological surveillance (8). Virologic data from national influenza centres and laboratories in 75 countries are reported through this platform. Aggregate data on influenza testing and detections from countries/continents in the Northern (United States, Europe) and Southern Hemisphere (Australia, Chile, South Africa) were extracted from the World Health Organization's FluNet platform on September 11, 2021. Updated numbers of detections from Chile were unavailable in the September 11, 2021, extract from the FluNet database; therefore, a previous data extraction from July 27, 2021, was used.

Activity level and outbreak data: All provincial and territorial public health departments provide a categorical assessment (no activity, sporadic, localized or widespread) of the intensity and geographic spread of influenza (activity level) as well as the number of influenza and ILI outbreaks by setting and type and subtype for surveillance regions within their jurisdictions.

Syndromic data: Syndromic data are reported from two systems: the Sentinel Practitioner ILI Reporting system; and FluWatchers. The Sentinel Practitioner ILI Reporting system consists of healthcare practitioners across Canada who report the number of patients seen with ILI and the total number of patients seen by age group. FluWatchers consists of volunteers across Canada who report whether they had any influenza-like symptoms each week using an online questionnaire.

Severe outcome surveillance data: Data on influenza-associated severe outcomes (i.e. hospitalization, intensive care unit [ICU] admissions and deaths) are reported through three sources: 1) Provincial and territorial ministries of health—severe outcomes surveillance; 2) Canadian Immunization Monitoring Program ACTive; and 3) Canadian Immunization Research Network's Serious Outcomes Surveillance Network.

Provincial/territorial severe outcome surveillance: Nine provincial and territorial ministries of health across Canada (Alberta, Manitoba, Saskatchewan, Nova Scotia, New Brunswick, Newfoundland and Labrador, Prince Edward Island, Yukon and Northwest Territories) participate and report case-level information (age, associated influenza type/subtype) for influenza-associated hospitalizations, ICU admissions and deaths.

Paediatric (16 years of age and younger) influenza-associated severe outcomes data: The Canadian Immunization Monitoring Program ACTive is a sentinel paediatric hospital network that consists of 12 paediatric hospitals across eight provinces in Canada. Detailed case-level information such as age, influenza type/subtype, gender, underlying medical conditions, vaccination status and treatment for influenza-associated hospitalizations, ICU admissions and in-patient deaths are reported on a weekly basis.

Adult (16 years of age and older) influenza-associated severe outcome data: The Canadian Immunization Research Network is a sentinel adult hospital network that consists of ten hospitals across four provinces. This network provides detailed case-level information for influenza-associated hospitalizations, ICU admission and in-patient deaths.

Vaccine monitoring data: Data on influenza vaccine coverage are provided by the Public Health Agency of Canada's National Influenza Immunization Coverage Survey. Vaccine effectiveness data are provided through two networks, the Canadian Sentinel Practitioners Surveillance Network and Canadian Immunization Research Network's Severe Outcome Surveillance. The Canadian Sentinel Practitioners Surveillance Network provides estimates of how well the influenza vaccine prevents primary care visits for influenza. The Canadian Immunization Research Network's Severe Outcome Surveillance estimates how effective the seasonal influenza vaccine is in preventing hospitalization in adults. During a typical influenza surveillance season both interim and final estimates are provided.

Statistical analysis

Temporal and geographic trends in the core surveillance indicators (Table 1) were monitored throughout the season. Case counts and proportions are presented and compared, where available, with historical data from the 2014–2015 to 2019–2020 season. All analyses were performed using SAS PC 9.4 for Windows.

Results

Laboratory-confirmed influenza detections

There was no community circulation of influenza in Canada during the 2020–2021 season. A total of 69 laboratory-confirmed influenza virus detections were reported during the 2020–2021 influenza season, all representing sporadic activity; 31 of these detections were associated with receipt of live attenuated influenza vaccine (9,10). Influenza A accounted for 67% (n=46) of reported detections. Only 20 influenza A viruses were subtyped; thus, subtype characteristics of the sporadic detections could not be ascertained.

Despite few reported detections, high levels of influenza testing that were above seasonal averages were maintained throughout the 2020–2021 influenza season, with a total of 632,580 tests reported. Historically, during the non-pandemic surveillance seasons 2014–2015 to 2018–2019, the total number of tests conducted ranged from 237,777 to 391,862. The percentage of laboratory tests positive for influenza remained at exceptionally low levels throughout the 2020–2021 influenza season. The reported percent positivity ranged from 0.0% to 0.1% this season compared to a historical average range of 0.8% to 25.1% while testing through the season was roughly twice the historical average (**Figure 1**).

Figure 1: Number of influenza tests and percentage of tests positive, in Canada, United States and Europe, by surveillance week

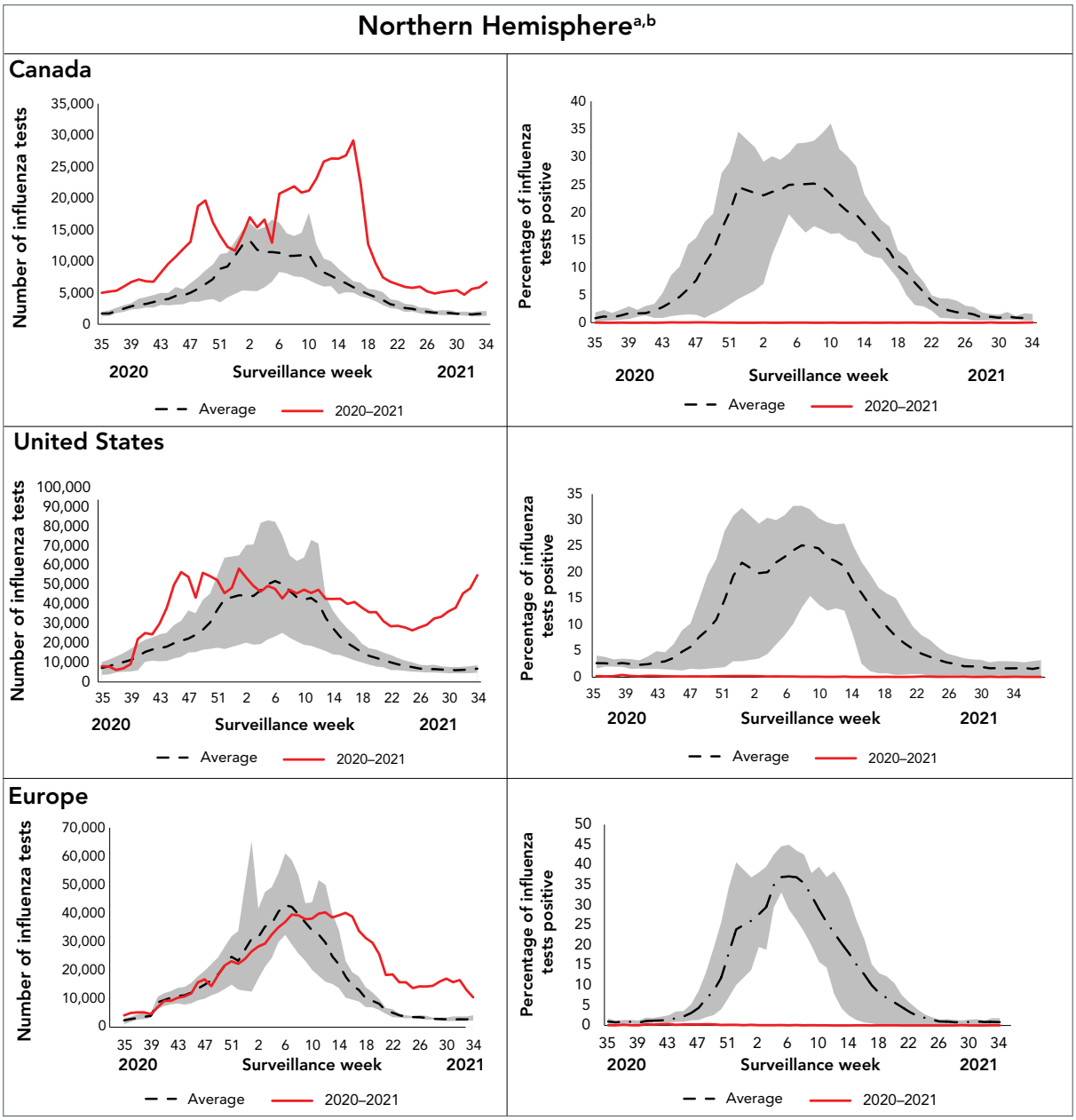
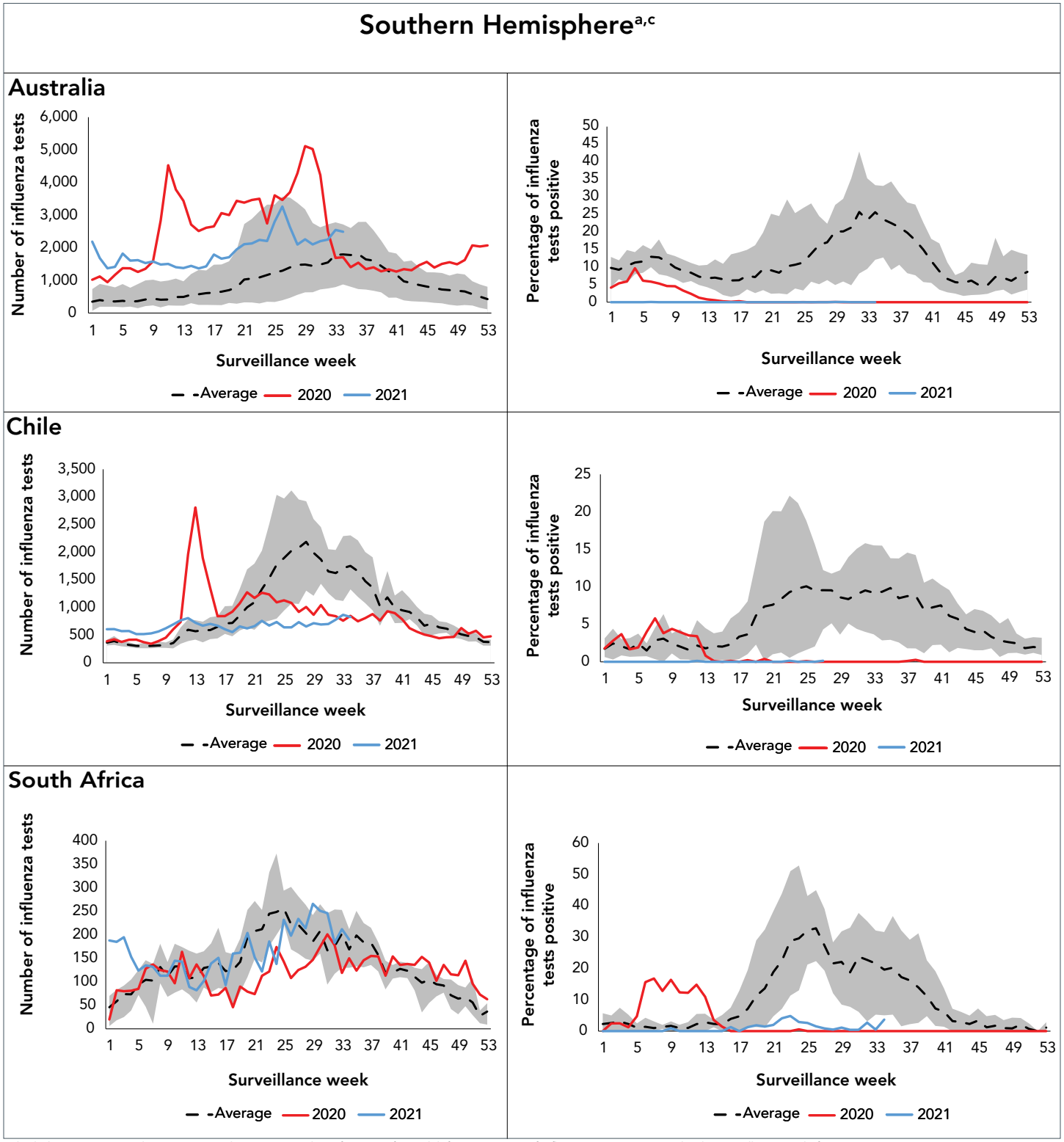


Figure 1: Number of influenza tests and percentage of tests positive, in Canada, United States and Europe, by surveillance week (*continued*)



[a] Shaded area represents the maximum and minimum number of tests performed (left), percentage of influenza tests positive (right), by surveillance week, from seasons 2014–2015 to 2019–2020 (Northern Hemisphere) and seasons 2014–2019 (Southern Hemisphere). Data from week 11 of the 2019–2020 season onwards is excluded from the historical comparison due to the COVID-19 pandemic

[b] 2020–2021 Northern Hemisphere influenza season in Canada, United States and Europe compared to historical average (seasons 2014–2015 to 2019–2020)

[c] 2020–2021 Southern Hemisphere influenza seasons in Australia, Chile and South Africa compared to historical average (seasons 2014 to 2019)

Internationally, a similar trend of decreased circulation of influenza was seen during the 2020 Southern Hemisphere, the 2020–2021 Northern Hemisphere and the 2021 Southern Hemisphere influenza seasons (Figure 1). In the Southern Hemisphere, influenza activity occurred in the first part of the 2020 surveillance season, then decreased and remained at exceptionally low levels as of week 14 of 2020. The reported percent positivity in Australia (range: 0.0%–9.7%), Chile (range: 0.0%–5.8%) and South Africa (range: 0.0%–16.8%) were lower when compared to their respective historical range 4.8%–25.7%, 1.5%–10.1% and 0.0%–32.8%. Similarly, in both the United States and Europe, the percentage of laboratory tests positive for influenza has remained at exceptionally low levels (Figure 1). During the 2020–2021 season, the percent positivity in the United States and Europe did not exceed 0.4% and 0.4%, respectively. Whereas respective historical average percent positivity ranged from 1.6%–25.2% and 0.7%–37.1%. As of week 34 (week 27 for Chile), influenza activity has remained at exceptionally low levels during the 2021 Southern Hemisphere with influenza percent positivity not exceeding 3.9% in Australia, Chile and South Africa (Figure 1).

Strain characterization and antiviral resistance testing

Due to low influenza circulation in Canada, only five influenza viruses were characterized this season, which was significantly lower than what is typically characterized by the National Microbiology Laboratory during an influenza surveillance season (n=1,171 to 3,857 from 2014–2015 to 2019–2020). Of these five viruses, one was a seasonal influenza B virus and the other four were zoonotic infections. All submitted viruses were from Alberta and Manitoba.

The influenza B virus that was characterized was antigenically related to B/Washington/02/2019 (Victoria). The four zoonotic infections were swine influenza variants H1N2v (n=2), H3N2v (n=1) and H1N1v (n=1) (11–14).

Syndromic

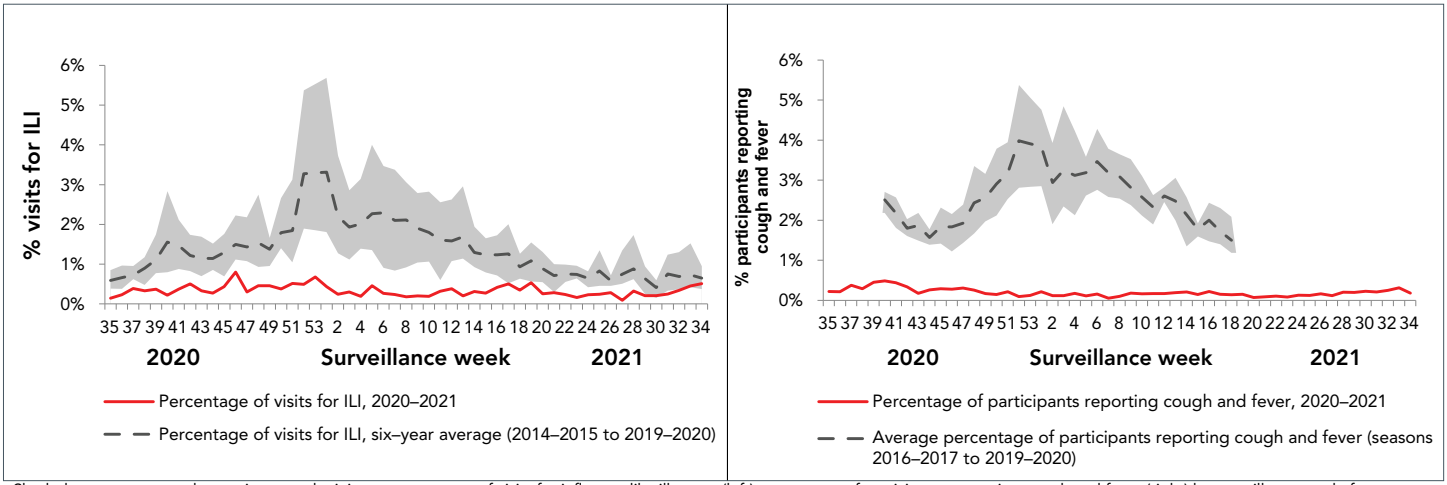
Both syndromic surveillance programs within FluWatch showed lower than usual activity, which is not unexpected given the lack of community circulation of influenza. Throughout the season, there were small fluctuations in ILI activity (**Figure 2**). These fluctuations in activity were likely signals of other respiratory virus activity such as enterovirus/rhinovirus, respiratory syncytial virus, adenovirus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Healthcare practitioners sentinel syndromic surveillance

The healthcare practitioners sentinel ILI surveillance system reported below average percentages of visits due to ILI compared with previous seasons. Weekly percentages of visits due to ILI have ranged from 0.06%–0.49% (compared to the six-year average range of 0.41%–3.32%). This is not unexpected given the changes in healthcare seeking behaviour, the additional healthcare options for individuals with ILI symptoms, a reduction in the number of sentinels reporting and the average number of weekly patients seen. In the previous season, a weekly average of 94 sentinels reported and an average of 8,775 patients were seen compared with the current season's weekly average of 62 sentinels reporting and an average of 5,503 patients seen.

For the majority of the season, the highest weekly percentage of visits for ILI was reported among those younger than 20 years of age. The lowest percentage of visits for ILI was reported

Figure 2: Percentage of visits for influenza-like illnesses reported by healthcare practitioners sentinel syndromic surveillance and FluWatchers participants reporting fever and cough[a], by surveillance week, Canada, season 2020–2021, compared to historical average



[a] Shaded area represents the maximum and minimum percentage of visits for influenza-like illnesses (left) percentage of participants reporting cough and fever (right) by surveillance week, from seasons 2014–2015 to 2019–2020)
Note: Data from week 11 of the 2019–2020 season onwards is excluded from the historical comparison due to the COVID-19 pandemic

among adults 65 years of age and older. This trend was similar to that seen in previous seasons, despite the reduced number of patients and the lower percentages of visits due to ILI.

FluWatchers

The FluWatchers program reported below average percentages of participants reporting fever and cough compared with previous seasons. Weekly percentage of reports of fever and cough have ranged from 0.1%–0.5%, compared to the four-year average range of 1.5%–4.0%. On average 12,048 participants reported weekly (range 9,290–12,831), which is approximately 3.5 times higher than the previous season. FluWatchers reporting is not impacted by changes in health services or health seeking behaviour; however, these low reports of cough and fever may be a direct effect of individual and/or public health measures enacted to reduce the spread of COVID-19.

Similar to the healthcare practitioners sentinel syndromic surveillance, for the majority of the season, the highest weekly percentages of participants reporting cough and fever were among those younger than 20 years of age. The lowest weekly percentages of participants reporting cough and fever were among adults 65 years of age and older. This trend is similar to that seen in previous seasons.

Outbreaks

All outbreaks reported during the season (n=138) were ILI outbreaks in schools and/or daycares. The number of ILI outbreaks in schools and/or daycares was higher compared with the previous two seasons. This is not unexpected given changes to outbreak surveillance, specifically the increased vigilance in schools to monitor and report absenteeism due to ILI, and the increased restrictions on attendance for children with symptoms of viral respiratory illness.

No laboratory-confirmed influenza outbreaks were reported this season.

Severe outcomes

No influenza-associated hospitalizations were reported by participating provinces and territories (Alberta, Manitoba, New Brunswick, Newfoundland and Labrador, Northwest Territories, Nova Scotia, Prince Edward Island and Yukon).

No influenza-associated hospitalizations were reported by the adult sentinel influenza hospitalization network (Canadian Immunization Research Network) and fewer than five influenza-associated hospitalizations were reported by the paediatric sentinel influenza hospitalization network (Canadian Immunization Monitoring Program ACTive).

Vaccine monitoring

The World Health Organization recommended that the 2020–21 Northern Hemisphere egg-based influenza vaccine contain the following strains (15):

- A/Guangdong-Maonan/SWL1536/2019 (H1N1)pdm09-like virus
- A/Hong Kong/2671/2019 (H3N2)-like virus
- B/Washington/02/2019 (B/Victoria lineage)-like virus
- B/Phuket/3073/2013 (B/Yamagata lineage)-like virus (quadrivalent vaccine only)

Vaccine coverage

Vaccine coverage for the 2020–2021 influenza season was similar to the previous season. Thirty-two percent of adults 18 to 64 years of age received their influenza vaccine (10). Vaccine coverage was higher among seniors aged 65 years and older (70%) and adults with chronic medical conditions (40%). Overall vaccine coverage was higher amongst females compared to males.

Vaccine effectiveness

Due to an absence of seasonal influenza circulation no estimates of influenza vaccine effectiveness could be produced for Canada nor any Northern or Southern Hemisphere country since the 2019–2020 Northern Hemisphere influenza season.

Discussion

The 2020–2021 Canadian influenza season was characterized by sporadic influenza detection and the absence of sustained circulation of the virus within the community. In Canada, non-pharmaceutical public health measures (i.e. school closures, travel restrictions, mandatory masking and increased handwashing) were implemented in March 2020 and maintained throughout the 2020–2021 flu season to reduce the transmission of COVID-19. Epidemiological analysis of laboratory influenza data have shown that these measures were effective in reducing the incidence and impact of influenza in Canada (3,4). Despite elevated respiratory virus testing this season, only 69 influenza viruses were detected, and influenza percent positivity did not exceed 0.1%. Historically, on average, 52,169 influenza viruses were detected within a season with the percent positivity ranging from 0.8%–25.1%. Decreased influenza circulation was also observed in other countries around the world. Laboratory data submitted to the World Health Organization's FluNet program showed that during the 2020 Southern Hemisphere, 2020–2021 Northern Hemisphere and 2021 Southern Hemisphere influenza seasons, Australia, Chile, South Africa, the United States and countries in Europe also experienced decreased influenza activity for the majority of their surveillance season. As of week 34 of 2021 (week 27 for Chile), laboratory data from the 2021 Southern Hemisphere influenza season showed

that influenza activity continued to remain low as public health measures to mitigate COVID-19 remained in place or were reinstated when COVID-19 cases rebounded.

The lack of influenza epidemics has implications that will require increased vigilance. Because of decreased circulation of influenza over the previous two seasons, a lower level of immunity amongst the population, particularly infants and younger children, could lead to higher infection rates once influenza re-circulates (15,16). As well, given the decreased influenza circulation, there may be an increased possibility for influenza vaccine mismatch (15). Recommendations for the composition of the influenza vaccine virus each year are made by predicting which viruses will circulate in the upcoming surveillance season (17). These predictions are based on laboratory surveillance data indicating which viruses are currently circulating (17). Given the paucity of surveillance data due to reduced influenza surveillance and circulation, the ability to accurately predict which viruses will circulate may be diminished (15). Furthermore, as COVID-19 vaccination coverage increases and countries start to ease public health measures, influenza strains similar to pre-pandemic years or novel strains may emerge, resulting in larger than normal influenza epidemics (15). Although it is currently difficult to predict whether influenza circulation will remain low in Canada and globally for the 2021–2022 influenza season, public health authorities need to remain vigilant and continue to plan for seasonal influenza circulation and maintain laboratory diagnostics and surveillance capacity. Influenza vaccination together with non-pharmaceutical public health measures continue to remain the best methods to prevent the spread and impact of influenza, especially given the uncertainty of the severity and intensity of respiratory virus circulation in the upcoming seasons.

Authors' statement

The FluWatch team in the Centre for Immunization and Respiratory Infectious Diseases developed the first draft collaboratively; all authors contributed to the conceptualization, writing and revision of the manuscript.

Competing interests

None.

Acknowledgements

Many thanks to all those across Canada who contribute to influenza surveillance. The FluWatch program consists of a volunteer network of labs, hospitals, doctor's offices, provincial and territorial ministries of health and individual Canadians who contribute as FluWatchers. We also acknowledge the following surveillance and research networks who contribute enhanced surveillance and knowledge exchange on influenza vaccine effectiveness to FluWatch: Canada's Immunization Monitoring Program ACTive, Canadian Immunization Research Network Serious Outcomes Surveillance Network, and the Canadian Influenza Sentinel Practitioner Surveillance Network. Finally, we wish to acknowledge the National Microbiology Laboratory's Influenza and Respiratory Virus section for the strain characterization and antiviral resistance testing data and the Centre for Immunization and Respiratory Infectious Diseases' Vaccination Coverage Section for their analysis of the annual national Seasonal Influenza Vaccination Coverage Surveys.

Funding

FluWatch surveillance is funded by the Public Health Agency of Canada.

References

1. Olsen SJ, Azziz-Baumgartner E, Budd AP, Brammer L, Sullivan S, Pineda RF, Cohen C, Fry AM. Decreased Influenza Activity During the COVID-19 Pandemic — United States, Australia, Chile, and South Africa, 2020. MMWR Morb Mort Wkly Rep. 2020;69:1305-9. https://www.cdc.gov/mmwr/volumes/69/wr/mm6937a6.htm

2. World Health Organization. Global Influenza Programme. Influenza Update No 398. Geneva, Switzerland: WHO; 2021 (accessed 2021-07-28). https://cdn.who.int/media/docs/default-source/influenza/influenza-updates/2021/2021_07_19_surveillance_update_398.pdf?sfvrsn=cc48538f_5&download=true

3. Groves HE, Piché-Renaud PP, Peci A, Farrar DS, Buckrell S, Bancej C, Sevenhuysen C, Campigotto A, Gubbay JB, Morris SK. The impact of the COVID-19 pandemic on influenza, respiratory syncytial virus, and other seasonal respiratory virus circulation in Canada: A population-based study. Lancet Reg Health Am 2021;1:100015. DOI PubMed

4. Lagacé-Wiens P, Sevenhuysen C, Lee L, Nwosu A, Smith T. Impact of nonpharmaceutical interventions on laboratory detections of influenza A and B in Canada. Can Commun Dis Rep 2021;47(3):142–8. DOI PubMed

5. Lee L, Butt K, Buckrell S, Nwosu A, Sevenhuysen C, Bancej C. National influenza mid-season report, 2020-2021. Can Commun Dis Rep 2021;47(1):1–4. DOI PubMed

6. Public Health Agency of Canada. Flu (influenza): FluWatch surveillance. Overview of Influenza monitoring in Canada. Ottawa (ON): PHAC; 2021 (accessed 2021-07-28). https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance/about-fluwatch.html

7. Public Health Agency of Canada. Flu (influenza): FluWatch surveillance. Respiratory Virus Detections in Canada. Ottawa (ON): PHAC; 2021 (accessed 2021-07-28). https://www.canada.ca/en/public-health/services/surveillance/respiratory-virus-detections-canada.html

8. World Health Organization. Global Influenza Programme. FluNet. Geneva, Switzerland: WHO; 2021 (accessed 2021-07-27). https://www.who.int/tools/flunet

9. Public Health Agency of Canada. National Advisory Committee on Immunization (NACI). Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2020-2021. Ottawa (ON): PHAC; 2020 (accessed 2021-07-28). https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2020-2021.html#IV2

10. Public Health Agency of Canada. Flu (influenza): FluWatch surveillance. FluWatch report: July 25, 2021 to August 28, 2021 (weeks 30-34). Ottawa (ON): PHAC; 2021 (accessed 2021-09-03). https://www.canada.ca/en/public-health/services/publications/diseases-conditions/fluwatch/2020-2021/weeks-21-24-may-23-june-19-2021.html

11. Public Health Agency of Canada. Human Emerging Respiratory Pathogens Bulletin: Issue 47, November 2020. Ottawa (ON): PHAC; 2020 (accessed 2021-07-28). https://www.canada.ca/en/public-health/services/surveillance/human-emerging-respiratory-pathogens-bulletin/2020/november.html

12. Public Health Agency of Canada. Human Emerging Respiratory Pathogens Bulletin: Issue 52, April 2021. Ottawa (ON): PHAC; 2020 (accessed 2021-07-28). https://www.canada.ca/en/public-health/services/surveillance/human-emerging-respiratory-pathogens-bulletin/2021/april.html

13. Public Health Agency of Canada. Human Emerging Respiratory Pathogens Bulletin: Issue 54, June 2021. Ottawa (ON): PHAC; 2020 (accessed 2021-07-28). https://www.canada.ca/en/public-health/services/surveillance/human-emerging-respiratory-pathogens-bulletin/2021/june.html

14. World Health Organization. Global Influenza Programme. Recommended composition of influenza virus vaccines for use in the 2020-2021 northern hemisphere influenza season. Geneva, Switzerland: WHO; 2020 (accessed 2021-07-28). https://www.who.int/publications/m/item/recommended-composition-of-influenza-virus-vaccines-for-use-in-the-2021-2022-northern-hemisphere-influenza-season

15. The Academy of Medical Sciences. COVID-19: Preparing for the future. London, UK: AMS; 2021(accessed 2021-07-30). https://acmedsci.ac.uk/file-download/4747802

16. Baker RE, Park SW, Yang W, Vecchi GA, Metcalf CJ, Grenfell BT. The impact of COVID-19 nonpharmaceutical interventions on the future dynamics of endemic infections. Proc Natl Acad Sci USA 2020;117(48):30547–53. DOI PubMed

17. Centers for Disease Control and Prevention. Selecting Viruses for the Seasonal Influenza Vaccine. Atlanta (GA): CDC; (updated 2021-08-31; accessed 2021-08-30). https://www.cdc.gov/flu/prevent/vaccine-selection.htm

Describing the burden of diphtheria in Canada from 2006 to 2017, using hospital administrative data and reportable disease data

Dolly Lin[1], Brigitte Ho Mi Fane[2], Susan G Squires[2], Catherine Dickson[2]

Abstract

Background: Canada has maintained a low incidence of toxigenic diphtheria since the 1990s, supported by continued commitment to publicly funded vaccination programs.

Objective: To determine whether hospitalization data, complemented with notifiable disease data, can describe the toxigenic respiratory and cutaneous diphtheria burden in Canada, and to assess if Canada is meeting its diphtheria vaccine–preventable disease-reduction target of zero annual cases of locally transmitted respiratory diphtheria.

Methods: Diphtheria-related hospital discharge data from 2006 to 2017 were extracted from the Discharge Abstract Database (DAD), and diphtheria case counts for the same period were retrieved from the Canadian Notifiable Disease Surveillance System (CNDSS), for descriptive analyses. As data from the province of Québec are not included in the DAD, CNDSS cases from Québec were excluded.

Results: A total of 233 diphtheria-related hospitalizations were recorded in the DAD. Of these, diphtheria was the most responsible diagnosis in 23. Half the patients were male (52%), and 57% were 60 years and older. Central region (Ontario) accounted for the most discharge records (61%), followed by Prairie region (Alberta, Manitoba and Saskatchewan; 23%). Cutaneous diphtheria accounted for 43% of records, and respiratory diphtheria accounted for 3%, with the remainder being other diphtheria complications or site unspecified. Two records with diphtheria as the most responsible diagnosis resulted in inpatient deaths. Eighteen cases of diphtheria were reported through CNDSS. Cases occurred in all age groups, with the largest proportions among those aged 20 to 59 years (39%) and those aged 19 years and younger (33%). Cases were only reported in the Prairie (89%) and West Coast (British Columbia; 11%) regions.

Conclusion: Hospital administrative data are consistent with the low incidence of diphtheria reported in CNDSS, and a low burden of respiratory diphtheria in Canada. Although Canada appears to be on track to meet its disease-reduction target, information on endemic transmission is not available.

Affiliations

[1] School of Epidemiology and Public Health, University of Ottawa, Ottawa, ON

[2] Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, Ottawa, ON

Correspondence:

vpd-mev@phac-aspc.gc.ca

Suggested citation: Lin D, Ho Mi Fane B, Squires SG, Dickson C. Describing the burden of diphtheria in Canada from 2006 to 2017, using hospital administrative data and reportable disease data. Can Commun Dis Rep 2021;47(10):414–21. https://doi.org/10.14745/ccdr.v47i10a03

Keywords: discharge data, notifiable disease, Discharge Abstract Database, DAD, Canadian Notifiable Disease Surveillance System, CNDSS, surveillance, incidence rate, *Corynebacterium diphtheriae*, vaccine-preventable disease, VPD

Introduction

Diphtheria is a now-rare vaccine-preventable disease (VPD) associated with a wide range of clinical illnesses, depending on the infection site and the toxigenicity of the bacteria.

Classic respiratory diphtheria describes toxin-mediated pseudomembranous respiratory disease associated with inflammation in the throat, high fatality rates and severe

complications affecting the heart and nervous system (1). Case series from Canada, consistent with global surveillance, have found that the disease burden is increasingly attributed to cutaneous, non-pseudomembranous respiratory and systemic disease from toxigenic and non-toxigenic strains of *Corynebacterium diphtheriae* and *C. ulcerans* (2–8). In addition to disease burden, other toxigenic Corynebacteria (*C. ulcerans* or *C. pseudotuberculosis*) and non-toxigenic *C. diphtheriae* may serve to maintain a reservoir for toxigenic respiratory diphtheria (2,4,8).

Countries with diphtheria vaccine coverage similar to Canada's report sporadic toxigenic respiratory diphtheria mostly associated with travel to endemic countries (2,5,9,10). The last known fatal case of diphtheria in Canada, described in a case report published in 2021, occurred in a traveller who was not up to date with relevant vaccines (10).

Canada has maintained a low incidence of toxigenic diphtheria, both respiratory and cutaneous, since the 1990s, with 0–5 cases of toxigenic respiratory or cutaneous diphtheria reported annually from 1991 to 2017 (11). The low burden of diphtheria is likely sustained by universal immunization programming; 76% of Canadian two-year-olds and 81% of seven-year-olds were fully immunized for diphtheria toxoid in 2017 (12). Consistent with its commitment to World Health Organization disease elimination goals, Canada's VPD-reduction targets aim to achieve zero annual cases of respiratory diphtheria resulting from exposure in Canada by 2025 (13). However, infection site and travel history are not reportable with current nationally notifiable disease data. This makes it difficult to determine if Canada has achieved its target for reducing the number of cases of respiratory diphtheria.

This study aims to determine whether hospital administrative data, with information on site of infection, can add to the data in the Canadian Notifiable Disease Surveillance System (CNDSS) in order to better understand the burden of toxigenic respiratory and cutaneous diphtheria in Canada. Doing so could more effectively enable us to assess if Canada is meeting its diphtheria VPD-reduction target.

Methods

Data sources

Hospitalizations

Hospital discharge records for all patients admitted for diphtheria to any Canadian acute care hospital, between 1 January 2006 and 31 December 2017, were extracted in January 2020 from the Canadian Institute for Health Information (CIHI) patient-specific Discharge Abstract Database (DAD). These dates were selected to cover the period from when all provinces and territories had fully implemented International Classification of Diseases version 10 (ICD-10-CA) codes up to 2017, to correspond with the time period for which reportable disease data are currently available. The DAD records approximately 75% of all acute care hospital discharges in Canada as data from Québec are not included (14).

Diphtheria hospitalizations were defined as those with ICD-10-CA discharge diagnoses corresponding to diphtheria (A36.0, A36.1, A36.2, A36.3, A36.8 or A36.9). All levels of diagnoses were used in this study, including most responsible diagnosis (the diagnosis that contributes the most to the length of hospital stay) and other diagnoses (secondary diagnoses, pre-admission or post-admission comorbidities). Respiratory diphtheria was identified by codes A36.0 through A36.2, and diphtheria not otherwise specified A36.9 concurrently with an upper respiratory disease code (J00–J06, J30–J39). Cutaneous diphtheria was identified by code A36.3. Other diphtheria complications were identified by code A36.8; complications include diphtheric cardiomyopathy, radiculomyelitis, polyneuritis, tubulo-interstitial nephropathy, cystitis, conjunctivitis and other diphtheritic complications.

The ICD-10-CA codes were assigned by trained medical coders based on hospital discharge notes and do not differentiate between toxigenic and non-toxigenic disease.

Health card numbers were used to identify repeat hospitalization events.

National case counts

The CNDSS collects nationally notifiable disease reports from provincial and territorial public health authorities, which obtain data from local and regional public health authorities (15). Confirmed cases of diphtheria from 2006 to 2017 were extracted from the CNDSS database in December 2019 (11), with cases from Québec excluded.

Before 2008, the national diphtheria case definition was limited to the isolation of the species *C. diphtheriae* from an appropriate clinical specimen (16). In May 2008, the national case definition was revised to limit laboratory confirmation to toxigenic *C. diphtheriae* or other *Corynebacterium* species (*C. ulcerans* or *C. pseudotuberculosis*) isolated from an appropriate clinical specimen, which now includes wounds and other cutaneous sites (17,18). See **Appendix A** for the two versions of the confirmed case definitions.

Record level data from the DAD and the CNDSS do not include information on results of case investigation to identify the source of exposure.

Analysis

Records were aggregated by year of admission in the DAD and year of reporting in the CNDSS. We conducted descriptive analyses of hospitalization records and case reports by year, age group, sex and region. Data were grouped by region: West Coast (British Columbia), Prairie (Alberta, Manitoba and Saskatchewan), Central (Ontario), Atlantic (Nova Scotia, New Brunswick,

Newfoundland and Labrador, and Prince Edward Island) and Northern (Yukon, Northwest Territories and Nunavut). Due to low counts, age groups in years were limited to 0 to 19, 20 to 59 and 60 and older.

We obtained denominators for rate calculations from census and intercensal projections published by Statistics Canada, excluding the population of Québec (19). Average annual crude hospitalization rate and average annual crude case incidence rate were used to compare diphtheria-related hospitalization and cases by age, sex and region. We used annual hospitalization rate and case incidence rate to compare rates by data source over time. Discharge status (discharged alive or dead) and admittance to a special care unit (such as a high dependency unit, intensive care unit or critical care unit) were used to describe the severity of the disease for discharges where diphtheria was the most responsible diagnosis. Readmissions were defined as hospitalizations that occurred more than once for the same patient from 2006 to 2017. Analysis was performed using Microsoft Excel. Small numbers are more susceptible to change and so corresponding rates should be interpreted with caution.

Results

Case distribution

A total of 233 diphtheria hospitalizations for 230 individual patients were recorded in the DAD from 2006 to 2017. Approximately half of the records were male (52%), and 57% were patients 60 years old and older. During the study period, Central region (which excludes Québec) represented 61% (n=141) of all discharge records, followed by Prairie region (23%, n=54), West Coast (8%, n=19), and Atlantic (7%, n=16) (**Table 1**).

Table 1: Diphtheria-related hospitalizations and reported cases by data source, 2006–2017

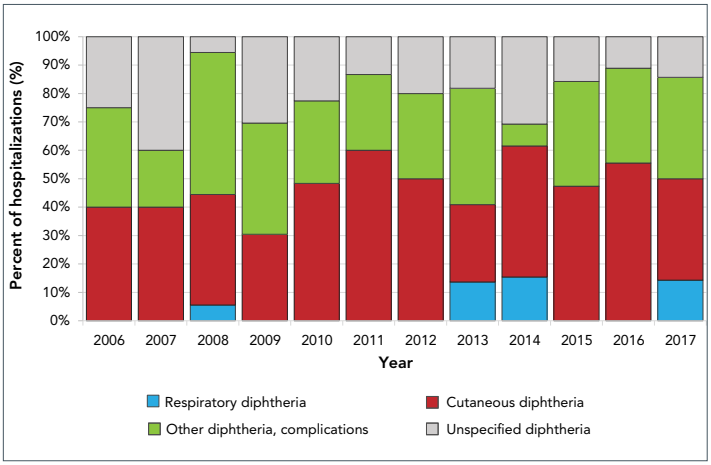
Characteristics		Diphtheria-related hospitalizations						CNDSS (n=18)		
		All diagnoses (n=233)			Most responsible diagnosis (n=23)					
		n	%	Average annual crude hospitalization rate per 100,000 population	n	%	Average annual crude hospitalization rate per 100,000 population	n	%	Average annual crude incidence rate per 100,000 population
Median age (range)		64 (<1–97)			47 (1–92)			16.5 (<1–42)[a]		
Age groups in years	0–19	18	8	0.019	–		–[b]	6	33	0.006
	20–59	82	35	0.035	11	48	0.005	7	39	0.003
	≥60	133	57	0.157	9	39	0.010	5	28	0.006
Sex	Female	112	48	0.054	11	48	0.010	7	39	0.005
	Male	121	52	0.059	12	52	0.011	11	61	0.003
Region	West Coast	19	8	0.035	–		–[b]	2	11	0.004
	Prairie	54	23	0.073	7	30	0.009	16	89	0.022
	Central	141	61	0.089	12	52	0.008	0	0	0
	Atlantic	16	7	0.056	–		–[b]	0	0	0
	Northern	–	–[b]	–[b]	0	0	0	0	0	0
Diphtheria type	Respiratory	8	3	N/A	–		–[b]	N/A		N/A
	Cutaneous	100	43	N/A	5	22	N/A	N/A		N/A
	Other (with complications)	76	33	N/A	6	26	N/A	N/A		N/A
	Unspecified	49	21	N/A	9	39	N/A	N/A		N/A

Abbreviations: CNDSS, Canadian Notifiable Disease Surveillance System; N/A, not applicable
[a] Detailed age information used to calculate the median age and range was available only for eight cases out of the 18 reported cases. Age group information was available for all 18 cases
[b] Suppressed because of small cell sizes (n<5)

The annual number of hospitalizations were between 13 and 31, with an average of 19 records (Table 1).

Cutaneous diphtheria accounted for the largest proportion of hospitalization records (43%; annual average of eight hospitalizations), followed by other diphtheria with complications (33%; annual average of six hospitalizations) and unspecified diphtheria (21%; annual average of four hospitalizations). None of the other diphtheria or unspecified diphtheria was concurrent with an upper respiratory disease code. Respiratory diphtheria accounted for 3% of all diphtheria-related hospitalizations, with an annual average of one hospitalization (**Figure 1**).

Figure 1: Distribution of diphtheria hospitalizations for all levels of diagnosis, by site of infection and year, 2006–2017



Three patients had two diphtheria-related discharge records during the study period. Of these three patients, two had a diagnosis of cutaneous diphtheria and one of unspecified diphtheria; the diagnostic codes for each of these cases did not change their classification of diphtheria type between hospital discharges.

Between 2006 and 2017, 18 cases of diphtheria were reported through CNDSS, and 61% were male (Table 1). The annual number of cases were between 0–4, with an average of 1.5. The highest proportion of CNDSS cases occurred among 20 to 59-year-olds (39%) followed by those aged 19 years and younger (33%). While the lowest proportion of cases occurred among CNDSS cases aged 60 years and older (28%), this group represented the highest (57%) and second highest (39%) of diphtheria-related hospitalizations for all diagnosis and most responsible diagnosis respectively. In contrast with hospitalization data, cases occurred mostly in the Prairie region, with 89% of all cases reported from 2006 to 2017. The remaining cases (11%) were reported in the West Coast region.

Indicators of severity

Of the 233 diphtheria-related hospitalizations, 23 (10%) had diphtheria as the most responsible diagnosis. Of the 23 hospitalization records, unspecified diphtheria and other diphtheria accounted for the majority (65%, n=15) (Table 1). All respiratory and cutaneous diphtheria hospitalizations were reported in adults aged 20 years and older.

The median length of stay in an acute care facility was three days (range: 1–24 days) for hospitalizations with respiratory diphtheria and six days (range: 2–39 days) for hospitalizations with cutaneous diphtheria as the most responsible diagnosis (**Table 2**). Of the 23 hospitalizations with diphtheria as the most responsible diagnosis, five were admitted to special care units and two resulted in inpatient deaths. Both fatalities were in adults with a diagnosis of either diphtheria with complications or unspecified diphtheria.

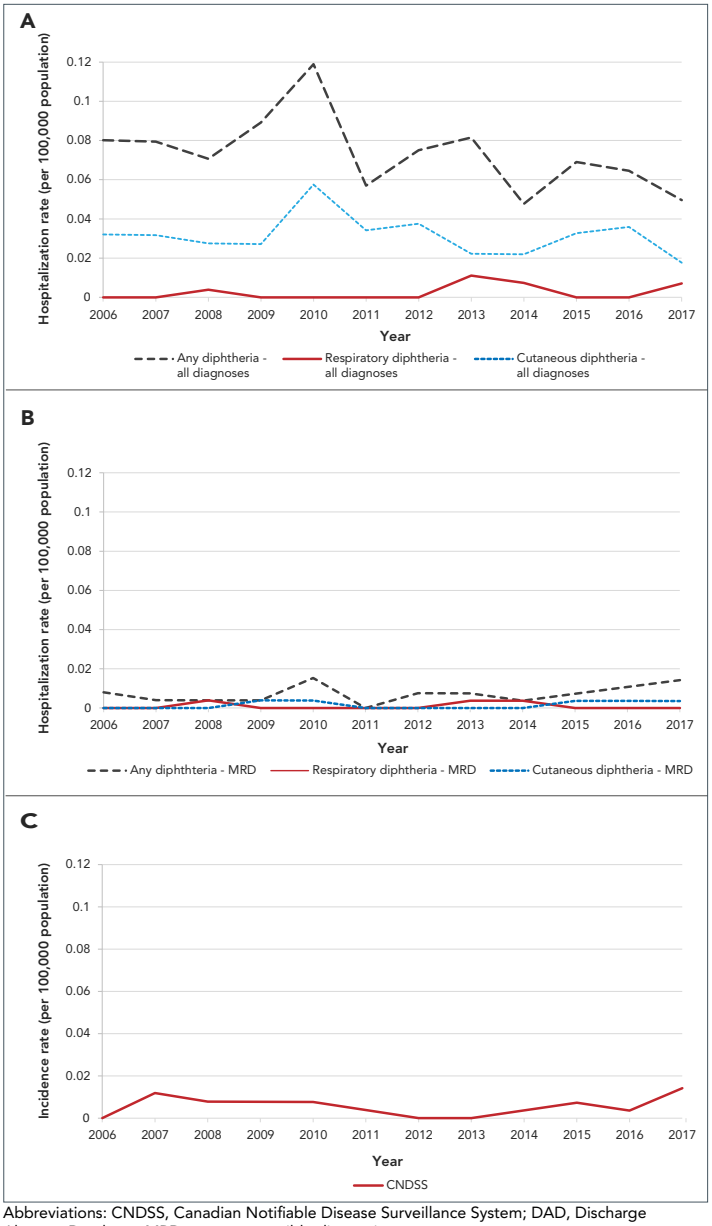
Table 2: Median length of hospital stay and number of special care unit admissions for hospital discharges with diphtheria as the most responsible diagnosis, by age group and diphtheria type, 2006–2017

Characteristics (number of cases)		Median length of hospital stay in days		Number of special care unit admissions
		Number	Range	
Age group in years	0–19 (n=3)	3	3–5	–[a]
	20–59 (n=11)	3	1–24	–[a]
	>60 (n=9)	14	5–39	–[a]
	Overall (n=23)	6	1–39	5
Diphtheria type	Respiratory diphtheria[a]	3	1–24	–[a]
	Cutaneous diphtheria (n=5)	6	2–39	0
	Other (with complications) (n=6)	5.5	1–35	–[a]
	Diphtheria unspecified (n=9)	8	2–37	–[a]

[a] Suppressed because of small cell sizes (n<5)

From 2006 to 2017, the number of hospitalizations with diphtheria as the most responsible diagnosis was within the same range (annual average of 1.9 cases, range 0–4) as the number of diphtheria cases reported through CNDSS, although age distribution and region differed. Breaking down hospitalization records by diphtheria type, the number of respiratory diphtheria hospitalizations for all levels of diagnosis (0–3 hospitalizations per year) and most responsible diagnosis (0–1 hospitalization per year) do not differ substantially. This results in average incidence rate of less than 0.01 hospitalizations per 100,000 population for respiratory diphtheria. The average incidence rate for reported diphtheria cases in CNDSS during the same period was less than 0.01 cases per 100,000 population **(Figure 2)**.

Figure 2: Diphtheria-related hospitalization rates for all levels of diagnosis (A) and most responsible diagnosis (B) reported in the DAD, and incidence rate of diphtheria cases in the CNDSS (C), by year, 2006–2017



Abbreviations: CNDSS, Canadian Notifiable Disease Surveillance System; DAD, Discharge Abstract Database; MRD, most responsible diagnosis

Discussion

With this study, we attempted to describe the burden of toxigenic respiratory and cutaneous diphtheria in Canada. We also tried, using a combination of hospital administrative and notifiable disease data, to examine whether we are meeting Canada's diphtheria VPD target. Overall, rates of diphtheria remained consistently low in Canada, at less than 0.06 per 100,000 per year. The DAD recorded 233 diphtheria-related hospitalizations. Of these, 23 had diphtheria as the most responsible diagnosis. Half the patients were male (52%), and most (57%) were 60 years old and older. Central region accounted for the most discharge records (61%), followed by the Prairie region (23%). Cutaneous diphtheria accounted for 43% of records, and respiratory diphtheria accounted for 3%, with the remainder being other diphtheria with complications or site unspecified. Eighteen cases of toxigenic diphtheria were reported through CNDSS over the same period. Cases occurred in all age groups, with the largest proportions among 20 to 59-year-olds (39%) and those aged 19 years old and younger (33%). Cases were only reported in the Prairie (89%) and West Coast (11%) regions.

The number of diphtheria-related hospitalizations is much higher than the number of cases reported through CNDSS, and the age and geographic distribution also differ. This suggests that these datasets do not necessarily capture the same individuals, although a comparison of the geographic breakdown of cases suggests that up to 50% of CNDSS cases may be represented in DAD cases with diphtheria as most responsible diagnosis. For context, Savage *et al.* found health administrative data in Ontario to have 69% to 86% sensitivity and 0.3% to 41.3% positive predictive value for hepatitis A, enteric fever and malaria (20). The DAD counts diphtheria cases based on clinical information in the medical chart and can include nonreportable non-toxigenic disease requiring hospitalization or diagnosed prior to or during hospitalization (6,7). In contrast, the CNDSS focuses on toxigenic *Corynebacterium* species with confirmed toxin production by specialized assays in order to capture possible diphtheria toxoid VPDs. As a result, DAD hospitalizations may be less specific for toxigenic diphtheria and capture more individuals with non-toxigenic diphtheria, such as the elderly and people with comorbidities (14,18). This is supported by the overrepresentation of those aged over 60, those with cutaneous diphtheria and other diphtheria complications (myocarditis, neuritis) classified as conditions not most responsible for hospitalization (secondary diagnoses, pre-admission or post-admission comorbidities), without concurrent respiratory diagnostic codes (75.5%; Table 1). The much higher diphtheria case counts recorded in the DAD than in the CNDSS suggest that this system is picking up on non-toxigenic cases in addition to the toxigenic cases the CNDSS captures.

Most diphtheria cases recorded in the DAD and the CNDSS are adults (67%–92%; see Table 1), which is consistent with high national childhood immunization coverage. Further investigation with individual-level immunization data for cases could examine whether waning immunity in adults is a concern (21,22).

Geographic distribution differed between hospitalization and reportable disease data: all regions (except Northern) reported at least one hospitalization with a most responsible diagnosis of diphtheria, but the Prairie and West Coast regions accounted for all diphtheria cases in the CNDSS. There may also be differences in how the ICD-10-CA codes for diphtheria are applied between provinces or between institutions (23). The National Microbiology Laboratory documented that the

majority of *C. diphtheriae* and *C. ulcerans* isolates received from 2006 to 2019 for toxigenicity testing were from British Columbia, Alberta, Saskatchewan and Manitoba (4), consistent with CNDSS case reports. Somewhat surprising was the high proportion of diphtheria-related hospitalizations reported in Ontario, despite the very small number of isolates sent from Ontario to the National Microbiology Laboratory for toxigenicity testing (4). Colleagues from Public Health Ontario confirmed that, to their knowledge, their laboratory conducted most, if not all, diphtheria testing in the province and that they had not received the number of samples positive for *C. diphtheriae* and *C. ulcerans* that the hospital discharge data from Ontario suggest (*Personal communication, J.V. Kus and S.E. Wilson, January and March 2021*). This discrepancy suggests that the DAD may be overcounting cases. It is possible that a past history of diphtheria infection or a case being worked up with a differential diagnosis that included diphtheria, even if cultures turned out to be negative, might have still been coded as diphtheria in the DAD.

This study is the first to describe health administrative data for diphtheria in Canada. Given that the CNDSS does not differentiate between respiratory and cutaneous diphtheria, examining patterns in hospitalizations with diphtheria ICD-10-CA codes over time in the DAD is useful for describing the severity of disease and frequency at which respiratory diphtheria cases are seen in hospital, even if it cannot identify the respiratory cases that are toxigenic. The inclusion of the DAD in this analysis also characterizes the burden of non-toxigenic disease, providing a broader picture than what the CNDSS reports.

Strengths and limitations

This study was limited by several factors. Firstly, the small counts of diphtheria limited the ability to conduct analyses adjusting for all of age, sex, geographic distributions and time, concurrently. Secondly, the DAD and the CNDSS use different case definitions, leading to different estimates of the burden of disease. Third, the representativeness of this study on the national burden of diphtheria could be improved by including data from Québec. During the study period, from 2006 to 2017, one case was reported from Québec through CNDSS. The case was a cutaneous diphtheria caused by *C. ulcerans* (9).

Our study was also limited by the lack of individual-level linkage between datasets. As a result, we could not apply diphtheria source attribution or quantification of disease burden through capture–recapture (20).

Surveillance of diphtheria by both the DAD and the CNDSS show temporally stable low rates, robust to changes in CNDSS case definition in 2008–2009, changes in DAD ICD-10-CA coding system in 2001–2005, and changes in laboratory detection methods for Corynebacteriae (4,15,16,23). Zero to one hospitalization per year were reported with a most responsible diagnosis of respiratory diphtheria, which suggests that Canada is on track to meet the VPD target of zero annual cases of respiratory diphtheria resulting from exposure in Canada. However, as neither the CNDSS nor the DAD capture exposure data, further work is needed to capture information on site of exposure in order to fully demonstrate that Canada is meeting its disease-reduction target for diphtheria. While cases attributed to travel have not been thoroughly studied, many countries without endemic diphtheria report sporadic cases associated with travel to endemic countries (3,5,8). We would expect similar patterns in Canada despite reports of small localized clusters of cutaneous diphtheria in vulnerable populations with comorbidities such as hepatitis C infection, diabetes, alcoholism, intravenous drug use, poverty and housing insecurity (6–8).

Conclusion

A brief investigation of hospital administrative and notifiable disease data confirms stable low incidence of diphtheria reported in CNDSS and low burden of respiratory diphtheria in Canada. Although this study indicates that Canada is on track to meet its disease-reduction target of zero annual cases of respiratory diphtheria as a result of exposure in Canada, information on endemic transmission of diphtheria cases is limited.

Further study of recent *C. diphtheriae* strains as well as enhancing reporting to include travel history and site of infection could improve our understanding of the current situation in Canada and provide a better tool to ensure that Canada is meeting its VPD-reduction targets by 2025.

Authors' statement

DL — Conceptualization, writing–original draft, writing–review & editing
BHMF — Formal analysis, writing–review & editing
SGS — Conceptualization, writing–review & editing
CD — Conceptualization, writing–review & editing

Competing interests

None.

Acknowledgements

The authors would like to thank KA Bernard, SE Wilson, JV Kus and T Harris for their valuable feedback and assistance with data interpretation.

Funding

This work was supported by the Public Health Agency of Canada.

References

1. Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases. 13th ed. Washington (DC): Public Health Foundation; 2015.

2. Wagner KS, White JM, Neal S, Crowcroft NS, Kuprevičiene N, Paberza R, Lucenko I, Jõks U, Akbaş E, Alexandrou-Athanassoulis H, Detcheva A, Vuopio J, von Hunolstein C, Murphy PG, Andrews N, Efstratiou A; Members of the Diphtheria Surveillance Network. Screening for Corynebacterium diphtheriae and Corynebacterium ulcerans in patients with upper respiratory tract infections 2007-2008: a multicentre European study. Clin Microbiol Infect 2011;17(4):519–25. DOI PubMed

3. Wagner KS, Zakikhany K, White JM, Amirthalingam G, Crowcroft NS, Efstratiou A. Diphtheria surveillance. Corynebacterium diphtheriae and related toxigenic species. Bayern (DE): Springer; 2014. p. 207–24. DOI

4. Bernard KA, Pacheco AL, Burdz T, Wiebe D. Increase in detection of Corynebacterium diphtheriae in Canada: 2006-2019. Can Commun Dis Rep 2019;45(11):296–301. DOI PubMed

5. Wagner KS, White JM, Lucenko I, Mercer D, Crowcroft NS, Neal S, Efstratiou A; Diphtheria Surveillance Network. Diphtheria in the postepidemic period, Europe, 2000-2009. Emerg Infect Dis 2012;18(2):217–25. DOI PubMed

6. Dewinter LM, Bernard KA, Romney MG. Human clinical isolates of Corynebacterium diphtheriae and Corynebacterium ulcerans collected in Canada from 1999 to 2003 but not fitting reporting criteria for cases of diphtheria. J Clin Microbiol 2005;43(7):3447–9. DOI PubMed

7. Romney MG, Roscoe DL, Bernard K, Lai S, Efstratiou A, Clarke AM. Emergence of an invasive clone of nontoxigenic Corynebacterium diphtheriae in the urban poor population of Vancouver, Canada. J Clin Microbiol 2006;44(5):1625–9. DOI PubMed

8. Lowe CF, Bernard KA, Romney MG. Cutaneous diphtheria in the urban poor population of Vancouver, British Columbia, Canada: a 10-year review. J Clin Microbiol 2011 Jul;49(7):2664–6. DOI PubMed

9. Brousseau N, Amini R. Direction des risques biologiques et de la santé au travail. Maladies évitables par la vaccination à déclaration obligatoire au Québec: rapport de surveillance 2018. Québec (QC): Gouvernement du Québec; 2019. p. 1–38. https://www.inspq.qc.ca/sites/default/files/publications/2588_maladies_evitables_vaccination_declaration_obligatoire_quebec.pdf

10. Cholewa S, Karachiwalla F, Wilson SE, Nadarajah J, Kus JV. Fatal respiratory diphtheria in a visitor to Canada. CMAJ 2021;193(1):E19–22. DOI PubMed

11. Public Health Agency of Canada. Notifiable diseases online: notifiable disease charts. Ottawa (ON): Government of Canada; 2020 (accessed 2021-06-26). https://diseases.canada.ca/notifiable/charts-list

12. Public Health Agency of Canada. Vaccine coverage in Canadian children: results from the 2017 Childhood National Immunization Coverage Survey (cNICS). Ottawa (ON): Government of Canada; 2020 (accessed 2020-06-06). https://www.canada.ca/en/public-health/services/publications/healthy-living/2017-vaccine-uptake-canadian-children-survey.html

13. Public Health Agency of Canada. Vaccination coverage goals and vaccine preventable disease reduction targets by 2025. Ottawa (ON): Government of Canada; 2020 (accessed 2020-06-05). https://www.canada.ca/en/public-health/services/immunization-vaccine-priorities/national-immunization-strategy/vaccination-coverage-goals-vaccine-preventable-diseases-reduction-targets-2025.html

14. Canadian Institute for Health Information. Data quality documentation, discharge abstract database. Current-year information, 2017–2018. Ottawa (ON): CIHI; 2018 (accessed 2020-06-05). https://www.cihi.ca/sites/default/files/document/current-year-information-dad-2017-2018-en-web.pdf

15. Public Health Agency of Canada. Canadian notifiable disease surveillance national report: 2005-2008. Ottawa (ON): Government of Canada; 2012. https://publications.gc.ca/collections/collection_2012/aspc-phac/HP40-75-2012-eng.pdf

16. Health Canada. Case definitions for diseases under national surveillance. Can Commun Dis Rep 2000;26S3:i-iv 1–122. https://publications.gc.ca/collections/collection_2016/aspc-phac/HP3-1-26-S3-eng.pdf

17. Public Health Agency of Canada. Case definitions for communicable diseases under national surveillance. Results of provincial/territorial (P/T) consultation process. Can Commun Dis Rep 2009;35S2:1–123. https://www.canada.ca/content/dam/phac-aspc/migration/phac-aspc/publicat/ccdr-rmtc/09pdf/35s2-eng.pdf

18. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Appendix: Factors affecting case definition changes in Ontario: 1991-2016. Toronto (ON): Queen's Printer for Ontario; 2018. https://www.publichealthontario.ca/-/media/documents/A/2018/appendix-factors-reportable-diseases-ontario-1991-2016.pdf

19. Statistics Canada. Population estimates on July 1st, by age and sex. Table 17-10-0005-01 (formerly CANSIM 051-0001). Ottawa (ON): Government of Canada (updated 2020-09-29; accessed 2020-06-05). https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501

20. Savage RD, Rosella LC, Crowcroft NS, Horn M, Khan K, Varia M. Accuracy of health administrative data to identify cases of reportable travel or migration-related infectious diseases in Ontario, Canada. PLoS One 2018;13(11):e0207030. DOI PubMed

21. Clarke KE, MacNeil A, Hadler S, Scott C, Tiwari TS, Cherian T. Global epidemiology of diphtheria, 2000-2017(1). Emerg Infect Dis 2019;25(10):1834–42. DOI PubMed

22. Truelove SA, Keegan LT, Moss WJ, Chaisson LH, Macher E, Azman AS, Lessler J. Clinical and epidemiological aspects of diphtheria: a systematic review and pooled analysis. Clin Infect Dis 2020 Jun;71(1):89–97. DOI PubMed

23. Walker RL, Hennessy DA, Johansen H, Sambell C, Lix L, Quan H. Implementation of ICD-10 in Canada: how has it impacted coded hospital discharge data? BMC Health Serv Res 2012 Jun;12(1):149. DOI PubMed

Appendix A

National case definition for diphtheria prior to May 2008 (11)

Confirmed case

Laboratory confirmation of infection:

- Isolation of *Corynebacterium diphtheriae* from an appropriate clinical specimen

OR

- Histopathologic diagnosis of diphtheria

OR

Epidemiologic link (contact within two weeks prior to onset of symptoms) to a laboratory-confirmed case PLUS at least one of the following:

- Upper respiratory tract infection (nasopharyngitis, laryngitis or tonsillitis) with or without an adherent nasal, tonsillar, pharyngeal and/or laryngeal membrane, plus at least one of the following:
  - o Gradually increasing stridor
  - o Cardiac (myocarditis) and/or neurologic involvement (motor and/or sensory palsies) 1–6 weeks after onset
  - o Death, with no known cause
- Systemic manifestations compatible with diphtheria in a person with an upper respiratory tract infection or infection at another site

National case definition for diphtheria as of May 2008 (12)

Confirmed case

Clinical illness (see "Clinical evidence" section) or systemic manifestations compatible with diphtheria in a person with an upper respiratory tract infection or infection at another site (e.g. wound, cutaneous) PLUS at least one of the following:

- Laboratory confirmation of infection:
  - o Isolation of *Corynebacterium diphtheriae* with confirmation of toxin from an appropriate clinical specimen, including the exudative membrane
    OR
  - o Isolation of other toxigenic Corynebacterium species (*C. ulcerans* or *C. pseudotuberculosis*) from an appropriate clinical specimen, including the exudative membrane
    OR
  - o Histopathologic diagnosis of diphtheria

OR

- Epidemiologic link (contact within two weeks prior to onset of symptoms) to a laboratory-confirmed case

Laboratory comments

Isolation of Corynebacterium species capable of producing diphtheria toxin (*C. diphtheriae, C. ulcerans* or *C. pseudotuberculosis*) should be tested using the modified Elek assay OR assay for the presence of the diphtheria tox gene, which, if detected, should be tested for expression of diphtheria toxin using the modified Elek assay.

Clinical evidence

Clinical illness is characterized as an upper respiratory tract infection (nasopharyngitis, laryngitis or tonsillitis) with or without an adherent nasal, tonsillar, pharyngeal and/or laryngeal membrane, plus at least one of the following:

- Gradually increasing stridor
- Cardiac (myocarditis) and/or neurologic involvement (motor and/or sensory palsies) one to six weeks after onset
- Death, with no known cause

Surveillance of laboratory exposures to human pathogens and toxins, Canada 2020

Nicole Atchessi[1], Megan Striha[1], Rojiemiahd Edjoc[1]*, Emily Thompson[1], Maryem El Jaouhari[1], Marianne Heisz[1]

Affiliation

[1] Centre for Biosecurity, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
rojiemiahd.edjoc@phac-aspc.gc.ca

Abstract

Background: The Laboratory Incident Notification Canada surveillance system monitors laboratory incidents reported under the *Human Pathogens and Toxins Act* and the *Human Pathogens and Toxins Regulations*. The objective of this report is to describe laboratory exposures that were reported in Canada in 2020 and the individuals who were affected.

Methods: Laboratory incident exposures occurring in licensed Canadian laboratories in 2020 were analyzed. The exposure incident rate was calculated and the descriptive statistics were performed. Exposure incidents were analyzed by sector, activity type, occurrence type, root cause and pathogen/toxin. Affected persons were analyzed by education, route of exposure sector, role and laboratory experience. The time between the incident and the reporting date was also analyzed.

Results: Forty-two incidents involving 57 individuals were reported to Laboratory Incident Notification Canada in 2020. There were no suspected or confirmed laboratory acquired infections. The annual incident exposure rate was 4.2 incidents per 100 active licenses. Most exposure incidents occurred during microbiology activities (n=22, 52.4%) and/or were reported by the hospital sector (n=19, 45.2%). Procedural issues (n=16, 27.1%) and sharps-related incidents (n=13, 22.0%) were the most common occurrences. Most affected individuals were exposed via inhalation (n=28, 49.1%) and worked as technicians or technologists (n=36, 63.2%). Issues with standard operating procedures was the most common root cause (n=24, 27.0%), followed by human interactions (n=21, 23.6%). The median number of days between the incident and the reporting date was six days.

Conclusion: The rate of laboratory incidents were lower in 2020 than 2019, although the ongoing pandemic may have contributed to this decrease because of the closure of non-essential workplaces, including laboratories, for a portion of the year. The most common occurrence type was procedural while issues with not complying to standard operating procedures and human interactions as the most cited root causes.

Suggested citation: Atchessi N, Striha M, Edjoc R, Thompson E, El Jaouhari M, Heisz M. Surveillance of laboratory exposures to human pathogens and toxins, Canada 2020. Can Commun Dis Rep 2021;47(10):422–9. https://doi.org/10.14745/ccdr.v47i10a04

Keywords: laboratory exposures, laboratory incidents, laboratory-acquired infections, human pathogens and toxins, surveillance, Laboratory Incident Notification Canada, Centre for Biosecurity

Introduction

Laboratory work with human pathogens and toxins (HPTs) poses an inherent risk to the security of laboratory personnel. While safety practices and regulations of HPTs have evolved considerably over the years, accidental or deliberate exposure to human pathogens and toxins in laboratory settings remain a biosafety and biosecurity concern, both within Canada and abroad.

In response to the reporting requirements for incidents involving HPTs outlined by the 2009 *Human Pathogens and Toxins Act* (HPTA) (1), the Laboratory Incident Notification Canada (LINC)

surveillance system was launched in December 2015. The LINC system is unique in that it is one of the first comprehensive national surveillance systems to provide a systematic framework for reporting HPT exposures and laboratory-acquired infections (LAIs) across various settings. A total of 247 exposure incidents have been reported between 2016 and 2019, involving a total of 539 individuals among private, public, hospital, and academic sector laboratories (2–5). In contrast, national reporting requirements for LAIs among other countries is often voluntary or conducted via retrospective survey (6–9).

The Public Health Agency of Canada's Centre for Biosecurity is mandated to protect the health and safety of the public against risks posed by HPTs through the administration and enforcement of the HPTA and the *Human Pathogen and Toxins Regulations* (HPTR). Under the HPTA, all Canadian laboratory facilities conducting controlled activities with HPTs are required to obtain a license, unless otherwise exempted. Under the HPTA, all licensed facilities are required to report laboratory incidents involving risk group 2 (RG2) pathogens or above in the following instances:

- Exposures and laboratory-acquired infections/intoxication
- Inadvertent release, production, or possession of an HPT
- Missing, stolen or lost HPT, including security sensitive biological agents (SSBA) not received within 24 hours of the expected date and time of receipt
- Changes in biocontainment

Canadian Biosafety Standard (*CBS*) *Second Edition* categorizes pathogens among four RGs, dependent upon a pathogen's risk to the individual and to the community (10). The RG2 pathogens pose a low risk to public health, but a moderate risk to an individual's health. These pathogens can cause serious disease in humans but are unlikely to do so. The RG3 pathogens pose a low risk to public health, but a high risk to an individual's health, and are likely to cause serious disease in humans. Finally, RG4 pathogens pose a high risk to both public and individual health and are likely to cause serious disease in humans that often leads to death.

The 2020 Annual Report marks the fifth year of the program and would normally be the year at which a baseline on incident reporting is established. However, due to the unprecedented response to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic by the Public Health Agency of Canada and the associated resource re-allocation, the development of a baseline will occur in the 2022 annual report, to be released in 2023.

As with previous years, this annual report aims to describe the distribution of laboratory incidents reported to LINC across years with special attention to exposures, LAIs and factors associated with these exposures at the license (by sector of exposures, HPT, occurrence type) and person (number of affected persons, education, main role, type of activity, years of experience, route of exposure, root causes) level.

Methods

Data sources

The Biosecurity Portal, LINC's external interface, receives notification and follow-up report(s) of laboratory incidents, which are then captured by the internal Customer Relationship Management system. For this report, exposure incidents that took place from January 1, 2020 to December 31, 2020 were extracted from the Customer Relationship Management system. Incidents that did not have a known occurrence date were also included if they were reported during this period. Data of the most recent follow-up reports were used for analysis, while the data of initial reports were used where corresponding follow-up reports and/or data were not present as of the data extraction date, February 8, 2021. Extracted data were cleaned by investigation of any outliers and removal of duplicate entries. It should be noted that while licensed facilities are obligated to report laboratory incidents, the rate of non-reporting is currently unknown and a confounder in this analysis.

Within the scope of the HPTA/HPTR, an exposure incident was defined as a laboratory incident that may have resulted in intoxication/infection or had resulted in suspected or confirmed LAI (1,10). A non-exposure incident referred to inadvertent possession or production of an HPT that is a higher RG than the lab is licensed to work with, release of a pathogen or toxin (to which no laboratory personnel are exposed), or a missing, lost or stolen pathogen or toxin or a security-sensitive biological agent not being received within 24 hours of expected arrival.

Analysis

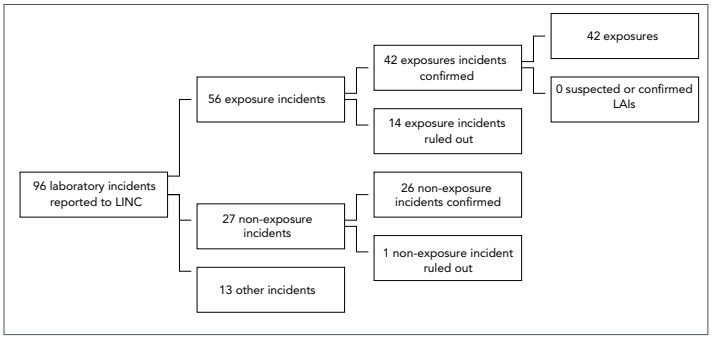
Data from reports submitted to the LINC surveillance system were extracted to Microsoft Excel 2016 for analysis and R 4.0.2 was used to perform descriptive statistics with cross-validation using SAS EG 7.1. All exposure incidents were first subdivided into ruled out incidents and confirmed incidents, with confirmed and suspected LAIs included in the latter. Reports can be ruled out for a variety of reasons, including if no exposure was found to have occurred, if the exposure involved an RG1 HPT or an HPT in its natural environment such as a primary specimen (neither are mandated by the HPTA and these reports are considered voluntary) or if duplicate reports are received. Affected persons in confirmed incidents were also subdivided into confirmed or ruled out individuals. Among confirmed exposure incidents, the numbers of incidents were analyzed against parameters obtained at two levels of reporting. At the level of the active license holder, the distributions of incidents by sector, main activity, root cause, occurrence type, and implicated pathogen/toxin reported were examined as well as reporting delays. At the level of persons affected in these incidents, the distributions of their highest level of education, years of experience, route of exposure, sector and regular role were examined. Particular attention was given to exposures involving SARS-COV-2 because of its status as an emerging pathogen and its role in the ongoing coronavirus disease 2019 (COVID-19) pandemic.

A comparison of exposure incidents and a measure of the exposure incident rate per 100 active licenses from 2016 to 2020 were also performed. The incident rate was described in greater detail in a previous report (5). Active licenses are licenses that were considered active during 2020 and were able to report an incident. Given the unavailability of the number of active licenses for December 31, 2020 owing to the impact of the pandemic on normal operations, and given the low fluctuation over the year (25–50 licenses each year), the number of active licenses on April 2020 was used for the calculation of the exposure incidence rate. The median time between the date of occurrence and the date of submission of the exposure incidents was also calculated. Median values were chosen compared to mean values owing to the presence of extreme outliers.

Results

Between January 1, 2020 and December 31, 2020, LINC received 96 laboratory incident reports: 56 exposure reports, 27 non-exposure reports and 13 other reports (**Figure 1**). All 13 other reports described changes within the laboratory that could affect biocontainment. There were 14 exposure reports and one non-exposure report ruled out, leaving 42 exposure incidents and 26 non-exposure incidents (**Figure 2**). There were no suspected or confirmed LAIs in 2020. From the exposure reports, 79 people were identified as having been exposed in laboratory incidents. Upon further investigation, 22 of those people were ruled out, leaving a total of 57 exposed people in 2020.

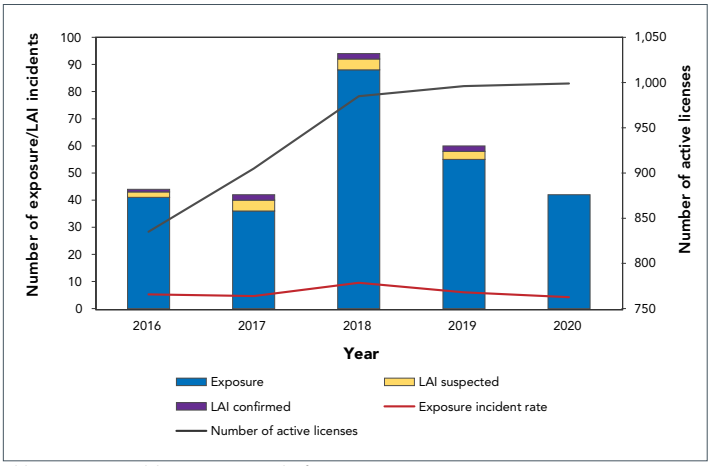
Figure 1: Types of incidents reported to Laboratory Incident Notification Canada and exposure incidents included in analysis, Canada 2020



Abbreviations: LAIs, laboratory-acquired infections; LINC, Laboratory Incident Notification Canada

There were 999 active licenses held in Canada permitting the use of HPTs in 2020. The exposure incident rate was 4.2 incidents per 100 active licenses in 2020. The total number of incidents and the rate of incidents per 100 active licenses was lower in 2020 than in 2019 (60 exposure incidents and 6.0 per 100 active licenses) (Figure 2).

Figure 2: Confirmed exposure incidents, suspected and confirmed laboratory acquired infections and active licenses, Canada 2016–2020



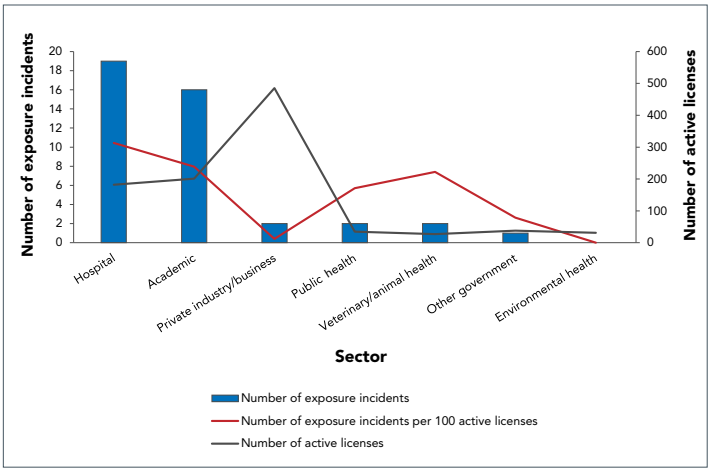
Abbreviation: LAIs, laboratory-acquired infections

Exposure incidents by main activity and sector

Microbiology was the most common activity being performed during exposure incidents (n=22, 52.4%), followed by *in vivo* animal research (n=5, 11.9%). Other activities include cell culture, autopsy/necropsy, maintenance, animal care, molecular investigation, microscopy or other (n=15, 35.7%). Definitions of activities are available in **Appendix A1**.

Most exposure incidents occurred in the hospital sector (n=19, 45.2%) followed by the academic sector (n=16, 38.1%) (**Figure 3**). The hospital sector had the highest number of exposure incidents per 100 active licenses (10.4 per 100), while the environmental health sector had the lowest with no incidents reported in 2020.

Figure 3: Confirmed exposures incidents and active licenses by sector reported to Laboratory Incident Notification Canada, Canada 2020



Implicated human pathogens and toxins

Among the 42 implicated biological agents, most were non-SSBA (n=37, 88.1%) and human risk group 2 (n=23, 54.8%) (**Table 1**). Bacteria were the most commonly implicated agent (n=17, 40.5%), while parasites and prions were the least frequently implicated (n=1, 2.3% each). *Neisseria meningitidis* was the most common RG2 agent (n=6, 14.3%), followed by lentiviral vectors (n=3, 7.1%). *Blastomyces* (*Ajellomyces*) *dermatitidis* was the most common RG3 agent (n=7, 16.7%), followed by SARS-CoV-2 (n=4, 9.5%) (data not shown).

Table 1: Human pathogens or toxins involved in reported exposure incidents by risk group level and security sensitive status, Canada 2020 (N=42)

Biological agent type by risk group	Non-SSBA		SSBA		Total	
	n	%	n	%	n	%
RG2	**23**	**55**	**0**	**0**	**23**	**55**
Bacteria	12	29	0	0	12	29
Fungus	0	0	0	0	0	0
Parasite	1	2	0	0	1	2
Prion	1	2	0	0	1	2
Toxin	3	7	0	0	3	7
Virus	6	14	0	0	6	14
Unknown	0	0	0	0	0	0
RG3	**14**	**33**	**4**	**10**	**18**	**43**
Bacteria	2	5	3	7	5	12
Fungus	7	17	1	2	8	19
Parasite	0	0	0	0	0	0
Prion	0	0	0	0	0	0
Toxin	0	0	0	0	0	0
Virus	5	12	0	0	5	12
Unknown	0	0	0	0	0	0
Unknown	**0**	**0**	**0**	**0**	**1**	**2**
Bacteria	0	0	0	0	0	0
Fungus	0	0	0	0	0	0
Parasite	0	0	0	0	0	0
Prion	0	0	0	0	0	0
Toxin	0	0	0	0	0	0
Virus	0	0	0	0	0	0
Unknown	0	0	0	0	1	2
Total	37	88	4	10	42	100

Abbreviations: RG2, risk group 2; RG3, risk group 3; SSBA, security sensitive biological agents

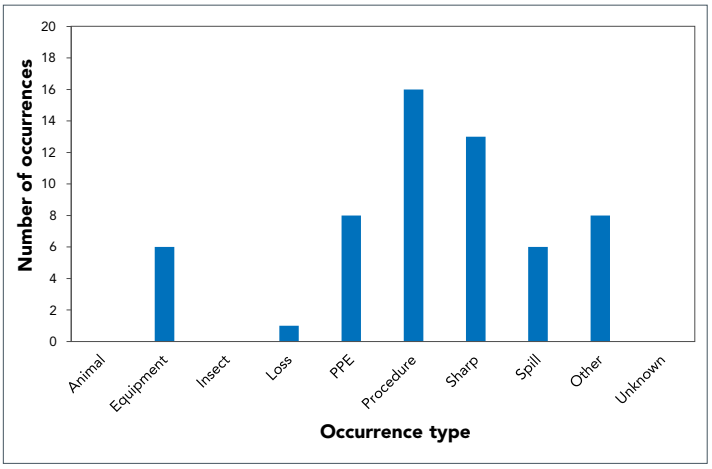
Occurrence types

The 42 exposure reports cited 58 incident occurrence types. Procedural (n=16, 27.1%) and sharps-related incidents (n=13, 22.0%) were the most common (**Figure 4**). Definitions are given in **Appendix B1**.

Exposed individuals

In total, 57 individuals were exposed through the 42 confirmed exposure reports. Most exposed individuals had a technical or trades college diploma as their highest level of education (n=24, 42.1%), followed by a Bachelor's degree (n=12, 21.1%)

Figure 4: Reported occurrence types involved in reported exposure incidents, Canada 2020 (N=58)

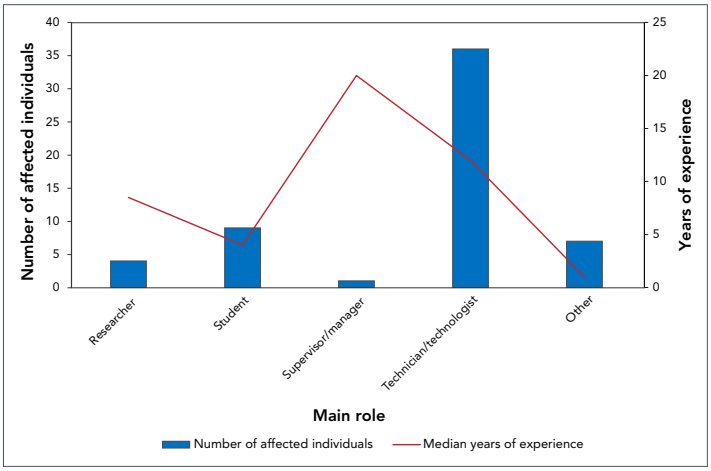


Abbreviation: PPE, personal protective equipment

or a Master's degree (n=11, 19.3%). Other highest levels include high school (n=2, 3.5%), a MD/PhD (n=1, 1.8%) and a postdoctoral fellow (n=1, 1.8%). The remaining six individuals had other (n=3, 5.3%) or unknown (n=3, 5.3%) highest level of education (data not shown).

Consequently, most of the exposed individuals worked as technicians or technologists (n=36, 63.2%), students (n=9, 15.8%) and researchers (n=4, 7.0%). One exposed person was a supervisor or manager (1.8%), and the rest had other roles (n=7, 12.3%) (**Figure 5**).

Figure 5: Individuals affected in exposure incidents reported by number of years of laboratory experience and main role[a], Canada 2020 (N=57)



[a] Other roles included clinical veterinarians, service helpers, and a laboratory equipment service worker

Among the 57 exposed individuals (not shown), most were exposed through inhalation (n=32, 56.1%) or sharps (n=9, 15.8%). Other routes of exposure include absorption (n=3, 5.3%) and ingestion (n=2, 3.5%). The rest were other (n=11, 19.3%) routes of exposure (data not shown).

Root causes and areas for laboratory safety improvement

In total, there were 89 root causes identified in the 42 exposure reports (**Table 2**). Issues with standard operating procedures (SOP) was the most common root cause (n=24, 27.0%), followed by human interactions (n=21, 23.6%) and equipment issues (n=12, 13.5%).

Time between the incident and the reporting date

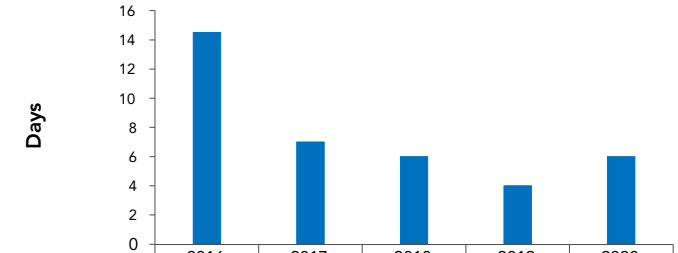
Table 2: Root causes reported in follow-up reports of exposure incidents, Canada 2020 (N=89)

Root cause	Examples of areas of concern	Citations	
		n	%[a]
Communication	Communication did not occur but should have	8	9
	Communication was unclear, ambiguous, etc.		
Equipment	Equipment quality control needed improvement	12	13
	Equipment failed		
	Equipment was not appropriate for purpose		
Human interaction	A violation (cutting a corner, not follow correct procedure, deviating from standard operating procedure)	21	24
	An error (a mistake, lapse of concentration, or slip of any kind)		
Management and oversight	Supervision needed improvement	10	11
	Lack of auditing of standards, policies and procedures		
	Risk assessment needed improvement		
Training	Training not in place but should have been in place	9	10
	Training not appropriate for task/activity		
	Staff were not qualified or proficient in performing task		
Standard operating procedure	Documents were followed as written but not correct for activity/task	24	27
	Procedures that should have been in place were not in place		
	Documents were not followed correctly		
Other	Not applicable	5	6

[a] Percentages rounded to the nearest whole number

Exposure incident reports are to be submitted to LINC without delay. In 2020, of the 41 incident exposure reports that included the incident date, 23 (56.1%) were submitted to LINC within one week of the incident. The median number of days between the incident and the reporting date was six days in 2020, up slightly from a median of four days in 2019 (**Figure 6**).

Figure 6: Time between the date of the incident and the date report was submitted to Laboratory Incident Notification Canada, Canada 2016–2020



	2016	2017	2018	2019	2020
25th percentile	3.75	3	2	2	2
Median	14.5	7	6	4	6
75th percentile	42.75	18.5	20.5	9	15

Median time between incident date and reporting date

Discussion

In 2020, 42 laboratory exposures to HPTs had been reported to LINC, a decrease from the 60 reported in 2019. The reports did not include any LAI and were submitted within a median delay of six days. Reports on RG2, non-SSBA agents as well as bacteria were the most common types of HPTs involved in exposure incidents. *Neisseria meningitides* and lentiviral vector exposures were more common among RG2 HPTs, whereas *Blastomyces* (*Ajellomyces*) *dermatitidis* and SARS-CoV-2 exposures were more common among RG3.

Similar to 2019, exposures were mainly due to procedure breaches and sharps, and occurred mostly in academic and hospital sectors while performing microbiology activities. In total, 57 individuals, predominantly technicians or technologists, were exposed to an HPT. Lack of awareness or compliance with standard operating procedures and human interactions were the main root causes identified.

Number of exposures and exposure incident rate have followed the same trend over the past five years

At the onset of the LINC program in 2016, the number of exposure incidents reported had increased, with a peak reached in 2018. The increase was concomitant to the rise of the number of licenses granted to laboratories over the same period. After 2018, despite the number of licenses remaining stable, the number of incidents started to decrease. The exposure incident rate followed a trend similar to the number of licenses, meaning that the increase from 2016 to 2018 and the decrease from 2018 to 2020 were not due to a change in the number of licenses granted to laboratories. The initial rise of the exposure incident rate from 2016 to 2018 was likely the result of the actions engaged by the LINC surveillance system to facilitate reporting and enhance clarity on regulatory requirements (5). Regarding the decrease from 2018 to 2020, when an exposure incident

occurs in a licensed laboratory, an incident response is actioned by the Centre for Biosecurity with the final goal of identifying root causes and encouraging corrective actions. This feedback may have raised the awareness of licensed parties and may be partially responsible for the decline in reports in recent years. Further information on incident reporting specifics can be found in the incident reporting guidelines published in 2017 (11). In addition, stay at home orders and other pandemic responses likely led to a reduction in laboratory activities for a portion of 2020, possibly leading to fewer reports.

Exposure incidents involving SARS-CoV-2 reported to Laboratory Incident Notification Canada did not include exposure incidents occurring during diagnostic activities

The reporting of exposure incidents in a laboratory setting through activities involving HPTs in their natural environment is not mandatory under the HPTA. Pathogens and toxins are considered to be in their natural environment if they are collected directly from humans or animals (e.g. blood, serum, tissue, urine, feces, saliva, milk, etc.) or from the environment (e.g. water, soil). Consequently, exposure incidents occurring during diagnostic activities involving SARS-CoV-2 were not systematically reported to LINC and were not included in this report. Four of the 42 exposure incidents reported to LINC involved SARS-CoV-2. These incidents occurred during research activities and were therefore mandatory. Although such reporting was voluntary, laboratory workers are encouraged to report exposure incidents involving HPTs in the HPTs' natural environment. This reporting enables the collection of data at the national level that can be used to detect real-time trends and potential patterns of concern, and to facilitate early responses in order to prevent and/or mitigate biosafety risks.

Delay of notification of exposure incidents has improved over the past five years

According to the Notification and Reporting under the HPTA and HPTR Guidelines and the HPTA, notification reports of exposure incidents have to be submitted to LINC without delay (11). From 2016 to 2019, the median time of submission of exposure incidents decreased from two weeks to four days. Such a decrease maybe explained by the LINC surveillance system actions to facilitate reporting and inform laboratories regarding submission timeliness recommendations. However, in the past year (2020), the median time of report submission increased slightly, from four to six days. This change was possibly attributable to an increase of the workload of laboratories and to disruptions of work caused by the ongoing pandemic. A comparison of time of submission was not done internationally, since exposure reports in other countries were done on a voluntary basis or through surveys (8,12,13).

Strengths and limitations

The main strength of this study is the centralized and mandatory reporting process of laboratory incidents in laboratories across Canada. Further, the LINC allows for an almost real-time identification of causes of incidents and potential areas of improvement that could be addressed in conjunction with laboratories to ensure risks are mitigated in a timely manner. For example, the most exposed individuals were found to be technicians, due to lack of compliance to SOPs. This information could be used by licensed facilities to examine current protocols that are related to SOP compliance to reduce the risk of exposures of laboratory workers in the future. Newsletters (14) and e-blasts prepared by the LINC team discuss common safety issues and areas for improvement as they arise, which are shared with stakeholders. In addition, there is constant communication between the Centre for Biosecurity and regulated parties. Further follow-up with regulated parties are planned to communicate these results to ensure incidents involving SOP compliance are addressed and adhered to.

There are several limitations of this study. First, non-reporting is a possible confounder in this analysis. The magnitude and significance of non-reporting is currently unmeasured; however, we continually encourage license holders to report laboratory exposure incidents without delay. Second, the exclusion of reports with missing dates from the analysis of the "time to reporting" calculation is another limitation. Given that the proportion of missing values was lower than 10%, the estimation of the median time to reporting likely had only a minor impact. Another limitation is that the number of licenses was used as a proxy of the laboratory workforce for the calculation of the exposure incidence rate (5). Further, the number of active licenses from December 2020 was unavailable due to the effects of the pandemic. Instead, the number of active licenses for April 2020 was used, as the number of licenses usually fluctuates minimally throughout the year. We will continue to address these limitations through constant communication with stakeholders, by ways of newsletters and e-blasts and biosafety advisories.

Conclusion

The rate of laboratory exposure incidents was lower in 2020 than 2019. The ongoing pandemic may have contributed to this decrease because of the closure of laboratories (and other non-essential workplaces) for a portion of the year. The most common occurrence type was procedural, while issues with non-compliance with SOP and human interactions were the most cited root causes.

Authors' statement

NA — Methodology, investigation, writing: original draft, review and editing
MS — Methodology, investigation, writing: original draft, review and editing
RE — Conceptualization, methodology, investigation, writing: original draft, review and editing, supervision
ET — Writing–original draft, review and editing
MEJ — Writing–original draft, review and editing
MH — Writing–review and editing

Competing interests

None.

Acknowledgements

We would like to express our gratitude to our regulated parties for their continued support and contribution regarding incident reporting across Canada. We would also like to say a special thanks to the staff of the Centre of Biosecurity for their continued input, support and expertise.

Funding

None.

References

1. Government of Canada. Human Pathogens and Toxins Act. Ottawa (ON): Government of Canada; (updated 2021-06). https://laws.justice.gc.ca/eng/acts/H-5.67/page-2.htm

2. Bienek A, Heisz M, Su M. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2016. Can Commun Dis Rep 2017;43(11):228–35. DOI PubMed

3. Pomerleau-Normandin D, Heisz M, Tanguay F. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2017. Can Commun Dis Rep 2018;44(11):297–304. DOI PubMed

4. Choucrallah D, Sarmiento L, Ettles S, Tanguay F, Heisz M, Falardeau E. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2018. Can Commun Dis Rep 2019;45(9):244–51. DOI PubMed

5. Lien A, Abalos C, Atchessi N, Edjoc R, Heisz M. Surveillance of laboratory exposures to human pathogens and toxins, Canada 2019. Can Commun Dis Rep 2020;46(09):292–8. DOI

6. Chamberlain AT, Burnett LC, King JP, Whitney ES, Kaufman SG, Berkelman RL. Biosafety Training and Incident-reporting Practices in the United States: A 2008 Survey of Biosafety Professionals. Appl Biosaf 2009;14(3):135–43. DOI PubMed

7. Siengsanan-Lamont J, Blacksell SD. A Review of Laboratory-Acquired Infections in the Asia-Pacific: Understanding Risk and the Need for Improved Biosafety for Veterinary and Zoonotic Diseases. Trop Med Infect Dis 2018;3(2):36. DOI PubMed

8. Singh K. Laboratory-acquired infections. Clin Infect Dis 2009;49(1):142–7. DOI PubMed

9. Health Protection Agency Centre for Infections, National Public Health Service for Wales, CDSC Northern Ireland, Health Protection Scotland. Eye of the Needle: United Kingdom Surveillance of Significant Occupational Exposures to Bloodborne Viruses in Healthcare Workers. Oxford (UK): HCVAction; 2008 (accessed 2021-02-25). http://www.hcvaction.org.uk/resource/eye-needle-united-kingdom-surveillance-significant-occupational-exposures-bloodborne-0

10. Public Health Agency of Canada. Canadian Biosafety Standard (CBS) Second Edition. Ottawa (ON): PHAC; (updated 2015-12; accessed 2021-02-25). https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/second-edition.html

11. Government of Canada. Canadian Biosafety Standards and Guidelines. Notification and Reporting Under the HPTA and HPTR. Ottawa (ON): Government of Canada; 2017 (accessed 2021-03-10). https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/guidance/notification-reporting-human-pathogens-toxins-act-regulations-overview.html

12. Willemarck N, Van Vaerenbergh B, Descamps E, Brosius B, Thi CD, Leunda A, Baldo A. Laboratory-Acquired Infections in Belgium (2007-2012). An online survey. Brussels (Belgium): ISP/WIV; Feb 2015 (accessed 2021-02-25). https://www.bioveiligheid.be/sites/default/files/2015_willemarck_lai_report_belgium_2007_2012_final.pdf

13. Wurtz N, Papa A, Hukic M, Di Caro A, Leparc-Goffart I, Leroy E, Landini MP, Sekeyova Z, Dumler JS, Bădescu D, Busquets N, Calistri A, Parolin C, Palù G, Christova I, Maurin M, La Scola B, Raoult D. Survey of laboratory-acquired infections around the world in biosafety level 3 and 4 laboratories. Eur J Clin Microbiol Infect Dis 2016;35(8):1247–58. DOI PubMed

14. Government of Canada. Biosafety and biosecurity for pathogens and toxins news. Ottawa (ON): Government of Canada; (updated 2021-06-30; accessed 2021-06-25). https://www.canada.ca/en/services/health/biosafety-biosecurity/newsletter.html

Appendices

Appendix A1: Definitions of main activity

Main activity	Definition
Animal care	Activities such as attending to the daily care of animals and providing animals with treatment
Autopsy or necropsy	Post-mortem surgical examinations for purposes such as determining cause of death or to evaluate disease or injury for research or educational purposes
Cell culture	The process of growing cells under controlled conditions; it can also involve the removal of cells from an animal or plant
Education or training	Education or training of students and/or personnel on laboratory techniques and procedures
In vivo animal research	Experimentation with live, non-human animals
Maintenance	The upkeep, repair, and/or routine and general cleaning of equipment and facilities
Microbiology	Activities involving the manipulation, isolation, or analysis of microorganisms in their viable or infectious state
Molecular investigations	Activities involving the manipulation of genetic material from microorganisms or other infectious material for further analysis
Serology	Diagnostic examination and/or scientific study of immunological reactions and properties of blood serum
Hematology	Scientific study of the physiology of blood

Appendix B1: Definitions of occurrence type

Occurrence type	Definition
Spill	Any unintended release of an agent from its container
Loss of containment	Includes malfunction or misuse of containment devices or equipment and other type of failures that results in the agent being spilled outside of, or released from containment
Sharps-related	Needle stick, cut with scalpel, blade or other sharps injury (i.e. broken glass)
Animal-related	Includes animal bites or scratches, as well as other exposure incidents resulting from animal behavior (i.e. animal movement resulting in a needle stick)
Insect-related	Includes insect bites
PPE-related	Includes either inadequate PPE for the activity or failure of the PPE in some way
Equipment-related	Includes failure of equipment, incorrect equipment for the activity, or misuse of equipment
Procedure-related	Includes instances when written procedures were not followed, were inadequate or absent, or were incorrect for the activity

Abbreviation: PPE, personal protective equipment

Influenza vaccine during the 2019–2020 season and COVID-19 risk: A case-control study in Québec

Jacques Pépin[1]*, Philippe De Wals[2], Annie-Claude Labbé[3,4], Alex Carignan[1], Marie-Elise Parent[5], Jennifer Yu[5], Louis Valiquette[1], Marie-Claude Rousseau[5]

Abstract

Background: We carried out a case-control study that examined whether receipt of the inactivated influenza vaccine during the 2019–2020 season impacted on the risk of coronavirus disease 2019 (COVID-19), as there was a concern that the vaccine could be detrimental through viral interference.

Methods: A total of 920 cases with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (diagnosed between March and October 2020) and 2,123 uninfected controls were recruited from those who were born in Québec between 1956 and 1976 and who had received diagnostic services at two hospitals (Montréal and Sherbrooke, Québec). After obtaining consent, a questionnaire was administered by phone. Data were analyzed by logistic regression.

Results: Among healthcare workers, inactivated influenza vaccine received during the previous influenza season was not associated with increased COVID-19 risk (AOR: 0.99, 95% CI: 0.69–1.41). Among participants who were not healthcare workers, influenza vaccination was associated with lower odds of COVID-19 (AOR: 0.73, 95% CI 0.56–0.96).

Conclusion: We found no evidence that seasonal influenza vaccine increased the risk of developing COVID-19.

Affiliations

[1] Université de Sherbrooke, Sherbrooke, QC

[2] Université Laval, Québec, QC

[3] CIUSSS de l'Est-de-l'Ile-de-Montréal, Montréal, QC

[4] Université de Montréal, Montréal, QC

[5] Institut national de la recherche scientifique, Laval, QC

***Correspondence:**

jacques.pepin@usherbrooke.ca

Suggested citation: Pépin J, De Wals P, Labbé A-C, Carignan A, Parent M-E, Yu J, Valiquette L, Rousseau M-C. Influenza vaccine during the 2019–2020 season and COVID-19 risk: A case-control study in Québec. Can Commun Dis Rep 2021;47(10):430–4. https://doi.org/10.14745/ccdr.v47i10a05

Keywords: SARS-CoV-2, COVID-19, seasonal influenza, influenza vaccine

Introduction

During the early stage of the coronavirus disease 2019 (COVID-19) pandemic, a hypothesis was raised that inactivated influenza vaccine could paradoxically enhance the risk of developing COVID-19, and this suggestion was picked up by some anti-vaccine advocates on the internet. Such viral interference has been described between the influenza vaccine and coronaviruses (other than severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) although the validity of these findings has been questioned (1,2). This interference was reported more frequently among persons who had received the influenza vaccine during the 2017–2018 season. A further concern was that one sentinel surveillance and three other observational studies showed that receipt of the trivalent influenza vaccine during the 2008–2009 season increased the risk of medically attended pandemic H1N1 illness 1.4-fold to 2.5-fold during the spring-summer 2009. The authors offered several potential mechanisms for their findings (3).

The objective of the present study was to determine whether there was any detrimental viral interference between influenza vaccine and SARS-CoV-2 infection such that the former increased the risk of the latter. If so, this would need to be taken into consideration in the planning of upcoming seasonal influenza vaccine campaigns.

Methods

In mid and late 2020, we carried out a large case-control study to determine whether the Bacillus Calmette-Guérin (BCG) vaccine (against tuberculosis) administered during infancy or childhood, through its non-specific effect on innate immunity, provided long-term protection against infection with SARS-CoV-2 (the results of this study will be published elsewhere). We also included in our questionnaire an exploratory question regarding influenza vaccination in the 2019–2020 season. Such self-reports are thought to be reliable for the most recent season (4). A total of 920 cases with polymerase chain reaction-confirmed SARS-CoV-2 infection (diagnosed between March and October 2020) and 2,123 uninfected controls (individuals who never had a SARS-CoV-2 polymerase chain reaction assay, either positive or negative) were recruited among persons born in Québec between 1956 and 1976. Identification of potential participants was made through the databases of the microbiology laboratories of the Hôpital Maisonneuve-Rosemont (HMR) in Montréal and the Centre Hospitalier Universitaire de Sherbrooke (CHUS). The institutional review boards of these two hospitals authorized this study.

For controls only, exclusion criteria were used to ensure that they were relatively representative of the overall catchment population of the two hospitals rather than its sickest fraction. For this, we excluded as potential controls individuals who had been hospitalized (for any reason) or had attended the emergency room during the study period, as well as those who were attending clinics where immunocompromised patients are often seen (hematology, oncology, rheumatology, HIV, renal transplants, dialysis, etc.). Persons living in long-term care facilities were also excluded as cases or controls, as most would have been unable to give an informed consent. We used frequency matching on sex and year of birth, aiming for two controls per case at HMR and three at CHUS.

Consenting individuals were administered a questionnaire over the phone which, after verifying eligibility, gathered sociodemographic data and information about occupation—healthcare worker (HCW) or not. We also verified the six-digit postal code that was used to obtain a census-based material deprivation index as per an application developed by the Institut national de santé publique du Québec (5). Other collected variables were not germane to the current paper (e.g. self-reported BCG/smallpox scar, age at BCG, etc).

Univariable and multivariable analyses were carried out by unconditional logistic regression, using R version 4.0.2 (6). Potential confounders, which could have been linked to both SARS-CoV-2 and influenza vaccination, included age (as a continuous variable), sex, recruitment hospital, census-based material deprivation quintile and HCW status. We elected to adjust for all these *a priori* confounders regardless of their contribution to the fit of the models. Effect modification by HCW status, sex and age was evaluated by including an interaction term in three separate regression models including all potential confounders (HCW status*influenza vaccination, sex*influenza vaccination, age group*influenza vaccination) to obtain a *p*-value for each interaction term. Stratified analyses according the HCW status, sex and age group were also conducted to estimate odds ratios (OR) and 95% confidence intervals for the association between influenza vaccination and SARS-CoV-2 in these subgroups.

Data on influenza vaccination was missing for 42 cases and 16 controls. The analytical sample thus consisted in 878 cases and 2,107 controls for whom this information was available.

There were some missing data for the deprivation index (unavailable for recent residential developments and postal codes where more than 15% of the population lived in an institution) for 6.3% of the participants (56 cases and 132 controls). To address this issue and to avoid excluding subjects with known influenza vaccination status, multiple imputation by chained equations was performed for this variable (20 imputed datasets).

Results

Characteristics of cases and controls are shown in **Table 1**. As expected, given that the study was carried out before the availability of SARS-CoV-2 vaccines, there were more HCW among cases than controls.

Table 1: Characteristics of cases and controls

Characteristics	Cases n=878		Controls n=2,107	
	n	%	n	%
Sex				
Men	333	37.9	814	38.6
Women	545	62.1	1,293	61.4
Age (years)				
44–49	213	24.3	525	24.9
50–54	213	24.3	465	22.1
55–59	250	28.5	579	27.5
60–64	202	23.0	538	25.5
Hospital				
Maisonneuve-Rosemont	591	67.3	1,226	58.2
CHUS	287	32.7	881	41.8
Material deprivation				
Lowest	149	17.0	292	13.9
Low	159	18.1	386	18.3
Middle	163	18.6	442	21.0
High	202	23.0	460	21.8

Table 1: Characteristics of cases and controls (*continued*)

Characteristics	Cases n=878		Controls n=2,107	
	n	%	n	%
Material deprivation (*continued*)				
Highest	149	17.0	395	18.7
Missing	56	6.4	132	6.3
Work				
Healthcare settings	425	48.4	231	11.0
All others	453	51.6	1,876	89.0

Abbreviation: CHUS, Centre hospitalier universitaire de Sherbrooke

One third of healthcare workers and one fifth of other workers had been vaccinated against influenza. Results of univariable and multivariable logistic regression are shown in **Table 2**.

Inactivated influenza vaccine during the 2019–2020 season was not associated with COVID-19 among HCW. Among participants who were not HCW, it was associated with lower odds of COVID-19. However, there was no indication of interaction when considering the interaction term. The association between influenza vaccination and COVID-19 did not differ by sex or age group based on the estimates of association or the *p*-values or interaction terms (Table 2).

Discussion

We found that in non-HCW, seasonal influenza vaccine was associated with lower odds of SARS-CoV-2 infection and not with an enhanced risk as initially hypothesized. No effect of seasonal influenza vaccine on odds of SARS-CoV-2 infection was seen among HCW. There is no reason to believe that influenza vaccine could offer cross-protection against SARS-CoV-2 through adaptive immune mechanisms, given the dissimilarity in the surface proteins of these two viruses. A possible hypothesis to explain this apparent protective effect in non-HCW is that vaccine-derived protection against influenza during the 2020 spring (its efficacy in Canada was estimated at 58%) (7) may have lowered the chances of consulting for influenza-related upper

Table 2: Influenza vaccine during the 2019–2020 season among cases of COVID-19 and uninfected controls

Characteristics	Cases n=878		Controls n=2,107		Crude		Adjusted		*p*-value for interaction[a]
	N	%	N	%	OR	95% CI	OR	95% CI	
All participants									
Not vaccinated	649	73.9	1,626	77.2	1.00	N/A	1.00	N/A	N/A
Vaccinated	229	26.1	481	22.8	1.19	0.99–1.43	0.81	0.66–1.00[b]	
Healthcare workers									
Not vaccinated	273	64.2	149	64.5	1.00	N/A	1.00	N/A	0.14
Vaccinated	152	35.8	82	35.5	1.01	0.72–1.42	0.99	0.69–1.41[c]	
Not healthcare workers									
Not vaccinated	376	83.0	1,477	78.7	1.00	N/A	1.00	N/A	0.14
Vaccinated	77	17.0	399	21.3	0.76[c]	0.58–0.99[c]	0.73	0.56–0.96[c,d]	
Men									
Not vaccinated	252	75.7	645	79.2	1.00	N/A	1.00	N/A	0.73
Vaccinated	81	24.3	169	20.8	1.23	0.90–1.66	0.87	0.62–1.23[e]	
Women									
Not vaccinated	397	72.8	981	75.9	1.00	N/A	1.00	N/A	0.73
Vaccinated	148	27.2	312	24.1	1.17	0.93–1.47	0.78	0.60–1.01[e]	
Age 44–54 years									
Not vaccinated	321	75.4	812	82.0	1.00	N/A	1.00	N/A	0.86
Vaccinated	105	24.6	178	18.0	1.49[c]	1.13–1.96[c]	0.85	0.62–1.17[f]	
Age 55–64 year									
Not vaccinated	328	72.6	814	72.9	1.00	N/A	1.00	N/A	0.86
Vaccinated	124	27.4	303	27.1	1.02	0.79–1.30	0.82	0.62–1.08[f]	

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; N/A, not applicable; OR, odds ratio

[a] *p*-value for the interaction term between influenza vaccination status and each of the three stratification variable (healthcare worker status, sex or age group) obtained from models including the stratification variable, influenza vaccination status, the interaction term and potential confounders

[b] Adjusted for age as a continuous variable, sex, recruitment hospital, census-based material deprivation quintile and healthcare worker status

[c] $p<0.05$

[d] Adjusted for age as a continuous variable, sex, recruitment hospital and census-based material deprivation quintile

[e] Adjusted for age as a continuous variable, recruitment hospital, census-based material deprivation quintile and healthcare worker status

[f] Adjusted for sex, recruitment hospital, census-based material deprivation quintile and healthcare worker status

respiratory tract symptoms when a concomitant SARS-CoV-2 infection could be diagnosed or may have reduced the risk of a more severe (thus better detected) SARS-CoV-2 episode in the presence of a dual infection. Such co-infections are, however, quite uncommon. In the United Kingdom during the first wave of COVID-19 (January–April 2020), out of 19,256 individuals tested, only 58 had a dual infection, while 992 had only an influenza and 4,442 had only a SARS-CoV-2 infection (8). Similar finding were reported from California (9). Furthermore, in Canada, circulation of the influenza virus came to an end in March 2020, and the overwhelming majority of our COVID-19 cases were reported after this date (10).

It is more plausible that non-HCW individuals who get the seasonal influenza vaccine, some of whom have chronic diseases, were more concerned with their health in general such that they may have been more compliant with social distancing and the use of masks, or reduced their potential exposures by staying at home. These public health measures would have reduced their risk of SARS-CoV-2 infection; a variation of the phenomenon known as the healthy vaccinee bias (11). This may not have been the case in HCW, who knew they were at high-risk for occupational COVID-19, and thus may have been consistently very prudent in decreasing exposure to SARS-CoV2.

In a systematic review dating back to October 2020, Del Riccio identified seven methodologically sound studies that had examined this association, and individuals vaccinated against influenza were less likely to have COVID-19 in five (12). More recent publications have also shown influenza vaccine associated with lower odds of SARS-CoV-2 infection in the United States (13–15) and Israel (16), while a smaller American study failed to document any effect (17). The largest study, comprising 137,037 individuals from the Mayo Clinic electronic health record database, showed a lower likelihood of developing COVID-19 not only among individuals vaccinated against influenza, but also in those who had received polio, *Haemophilus influenzae* type B, measles-mumps-rubella, varicella, hepatitis B, hepatitis A or pneumococcal conjugate vaccines (15). Such associations with multiple and unrelated vaccine products suggests a "healthy user" or "healthy vaccinee" effect.

A study limitation was that we did not collect data on co-morbidities since this could not confound the association between BCG and COVID-19, the primary objective of this study (this would have required these diseases to be associated with the administration of BCG four to six decades earlier—a very unlikely scenario). However, among participants who were not HCW, indications for the influenza vaccine include some conditions (diabetes, obesity, cardiac or pulmonary diseases, etc.) that are themselves associated with severe forms of COVID-19, and thus with the likelihood of getting tested. Adjustment for these unmeasured confounders could have slightly altered the measure of association between influenza vaccine and COVID-19 towards the null value if risk mitigation among vaccinees was more marked in patients with co-morbidities.

Another limitation of our study is that we studied individuals aged 44–64 years, whilst the main target of seasonal influenza vaccination is the age group 65 years or older. It seems unlikely, however, that a viral interference between SARS-CoV-2 and the seasonal influenza vaccine would vary with age.

Finally, compared to the controls, a much higher proportion of cases (48%) were HCWs. This reflected the overall epidemiological portrait of COVID-19 in Québec during the first wave, when HCW were at great risk of occupational infection and represented 41% of cases among persons aged 18–59 (18). In this context, a selection bias seems unlikely, but we cannot rule out the possibility that HCWs differed from the other participants in their recollection of influenza vaccination during the previous season due to a social desirability bias. However, such a bias seems unlikely given that only 36% of HCW alleged to have been vaccinated, which is comparable to routine surveillance data of influenza vaccination in healthcare institutions of Québec.

Conclusion

We found no evidence that seasonal influenza vaccine increased the risk of developing COVID-19 and the usual vaccination strategy does not need to be altered for the 2021–2022 season.

Authors' statement

ACL, JP, PDW, MCR, MEP — Conceived the study, analyzed and interpreted the data, drafted and edited the manuscript
MCR, JY — Data analysis
AC, LV — Contributed to data interpretation and writing the manuscript

All authors approved the final version of the manuscript.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

Acknowledgements

The following persons contributed to data collection (alphabetical order): KA Baki, D Ag Bazet, M-A Binette, J Boisvert, M-P Boisvert, J Bourget, V Choinière, A Delimi, A Deneault, V Dumont, L Duquette-Laplante, R Escobar Careaga, K Farag, L Foudil, S Gélin, K Gendron, L-A Gervais, O Grimard, R Harti, R Lachance, A Marcil-Héguy, N Métayer, S Payeur, J-C Pellerin, C Simard, R Thibeault, A-S Thiffault, and K Vettese. We are also grateful to M Malachy, J-H Lee, and N Frappier for their assistance with hospital databases, to N Gagnon for his

help in setting up the data entry interface, and to G Deceuninck for helpful suggestions.

Funding

This work was supported by the Centre de recherche du centre hospitalier universitaire de Sherbrooke through a special COVID-19 emergency funding provided by the Fondation du centre hospitalier universitaire de Sherbrooke. The funder had no role in study design, in collection, analysis and interpretation of data, in the writing of the report nor in the decision to submit.

References

1. Wolff GG. Influenza vaccination and respiratory virus interference among Department of Defense personnel during the 2017-2018 influenza season. Vaccine 2020;38(2):350–4. DOI PubMed

2. Skowronski DM, Zou M, Clarke Q, Chambers C, Dickinson JA, Sabaiduc S, Olsha R, Gubbay JB, Drews SJ, Charest H, Winter AL, Jassem A, Murti M, Krajden M, De Serres G. Influenza vaccine does not increase the risk of coronavirus or other noninfluenza respiratory viruses: retrospective analysis from Canada, 2010-11 to 2016-17. Clin Infect Dis 2020;71(16):2285–8. DOI PubMed

3. Skowronski DM, De Serres G, Crowcroft NS, Janjua NZ, Boulianne N, Hottes TS, Rosella LC, Dickinson JA, Gilca R, Sethi P, Ouhoummane N, Willison DJ, Rouleau I, Petric M, Fonseca K, Drews SJ, Rebbapragada A, Charest H, Hamelin ME, Boivin G, Gardy JL, Li Y, Kwindt TL, Patrick DM, Brunham RC; Canadian SAVOIR Team. Association between the 2008-09 seasonal influenza vaccine and pandemic H1N1 illness during Spring-Summer 2009: four observational studies from Canada. PLoS Med 2010;7(4):e1000258. DOI PubMed

4. King JP, McLean HQ, Belongia EA. Validation of self-reported influenza vaccination in the current and prior season. Influenza Other Respir Viruses 2018;12(6):808–13. DOI PubMed

5. Institut National de Santé Publique du Québec. Indice de défavorisation matérielle et sociale (accessed 2021-07-21). https://www.inspq.qc.ca/defavorisation/indice-de-defavorisation-materielle-et-sociale

6. The R Foundation. The R Project for Statistical Computing. Vienna (Austria): R Foundation; 2020. https://www.R-project.org/

7. Skowronski DM, Zou M, Sabaiduc S, Murti M, Olsha R, Dickinson JA, Gubbay JB, Croxen MA, Charest H, Jassem A, Krajden M, Bastien N, Li Y, De Serres G. Interim estimates of 2019/20 vaccine effectiveness during early-season co-circulation of influenza A and B viruses, Canada, February 2020. Euro Surveill 2020;25(7):2000103. DOI PubMed

8. Stowe J, Tessier E, Zhao H, Guy R, Mulller-Pebody B, Zambon M, Andrews N, Ramsay M, Lopez Bernal J. Interactions between SARS-CoV-2 and influenza and the impact of coinfection on disease severity: a test negative design. Int J Epidemiol 2021;dya081. DOI

9. Kim D, Quinn J, Pinsky B, Shah NH, Brown I. Rates of co-infection between SARS-CoV-2 and other respiratory pathogens. JAMA 2020 May;323(20):2085–6. DOI PubMed

10. Public Health Agency of Canada. FluWatch. April 5 to May 9, 2020 (weeks 15 to 19). https://www.canada.ca/en/public-health/services/publications/diseases-conditions/fluwatch/2019-2020/weeks-15-19-april-5-may-9-2020.html

11. Remschmidt C, Wichmann O, Harder T. Frequency and impact of confounding by indication and healthy vaccinee bias in observational studies assessing influenza vaccine effectiveness: a systematic review. BMC Infect Dis 2015;15:429. DOI PubMed

12. Del Riccio M, Lorini C, Bonaccorsi G, Paget J, Caini S. The association between influenza vaccination and the risk of SARS-CoV-2 infection, severe illness, and death: a systematic review of the literature. Int J Environ Res Public Health 2020;17(21):7870. DOI PubMed

13. Huang K, Lin SW, Sheng WH, Wang CC. Influenza vaccination and the risk of COVID-19 infection and severe illness in older adults in the United States. Sci Rep 2021;11(1):11025. DOI PubMed

14. Zein JG, Whelan G, Erzurum SC. Safety of influenza vaccine during COVID-19. J Clin Transl Sci 2020;5 e49:1–3. DOI

15. Pawlowski C, Puranik A, Bandi H, Venkatakrishnan AJ, Agarwal V, Kennedy R, O'Horo JC, Gores GJ, Williams AW, Halamka J, Badley AD, Soundararajan V. Exploratory analysis of immunization records highlights decreased SARS-CoV-2 rates in individuals with recent non-COVID-19 vaccinations. Sci Rep 2021;11(1):4741. DOI PubMed

16. Green I, Ashkenazi S, Merzon E, Vinker S, Golan-Cohen A. The association of previous influenza vaccination and coronavirus disease-2019. Hum Vaccin Immunother 2021;17(7):2169–75. DOI PubMed

17. King JP, McLean HQ, Belongia EA. Risk of symptomatic severe acute respiratory syndrome coronavirus 2 infection not associated with influenza vaccination in the 2019-2020 season. Influenza Other Respir Viruses 2021. DOI PubMed

18. Institut National d'Excellence en Santé et Services Sociaux. Première vague de la pandémie de COVID-19 au Québec: regard sur les facteurs associés aux hospitalisations et aux décès. https://www.inesss.qc.ca/fileadmin/doc/INESSS/COVID-19/COVID-19_INESSS_EP_Portrait_cohorte_COVID.pdfINESSS/COVID-19/COVID-19_INESSS_EP_Portrait_cohorte_COVID.pdf

OBSERVATIONAL STUDY

HIV self-testing in Ottawa, Canada used by persons at risk for HIV: The GetaKit study

Patrick O'Byrne[1]*, Alexandra Musten[2], Amanda Vandyk[1], Nikki Ho[1], Lauren Orser[1], Marlene Haines[1], Vickie Paulin[3]

Abstract

Background: The Public Health Agency of Canada estimates that about 87% of persons living with human immunodeficiency virus (HIV) in Canada have been diagnosed, which is well below the Joint United Nations Programme on HIV/AIDS target to have 95% of HIV-positive persons diagnosed. Research has shown that HIV self-testing may help increase such diagnoses, especially among the populations who are most affected by HIV. The objective of the study was to determine the uptake and diagnosis outcomes associated with free HIV self-testing.

Methods: We developed the first online mailout free HIV self-testing program in Canada and implemented it in Ottawa. This project ran through the website, www.GetaKit.ca. We intended to recruit 150–400 participants over a 6–12-month period, estimating that this number would yield between 0–1 positive test results (expected positivity rate of 0.08%).

Results: Between July 20, 2020 and April 1, 2021, 1,268 people accessed the GetaKit website and verified their eligibility. In total, 600 persons were eligible and 405 ordered an HIV kit. Of those who ordered a kit, 399 completed a baseline survey. Overall, 71% of these participants were members of HIV priority groups. For test results, 228 persons reported test results, with one being positive, for a positivity rate of 0.24% overall and 0.44% of reported results. These rates exceed that normally observed in Ottawa.

Conclusion: Self-testing of HIV can be effectively delivered through a website. Such an intervention will also be used by persons with undiagnosed infections and appears to do so at a rate higher than that observed by other means of testing. Self-testing of HIV may therefore help Canada achieve the United Nations 95-95-95 targets.

Affiliations

[1] School of Nursing, University of Ottawa, Ottawa, ON

[2] Ontario HIV Treatment Network, Toronto, ON

[3] Ottawa Public Health, Ottawa, ON

***Correspondence:**
patrick.obyrne@uottawa.ca

Suggested citation: O'Byrne P, Musten A, Vandyk A, Ho N, Orser L, Haines M, Paulin V. HIV self-testing in Ottawa, Canada used by persons at risk for HIV: The GetaKit study. Can Commun Dis Rep 2021;47(10):435–41. https://doi.org/10.14745/ccdr.v47i10a06

Keywords: HIV, self-test, Ottawa, Canada, priority group, GetaKit

Introduction

The Joint United Nations Programme on HIV/AIDS 95-95-95 targets aim to have 95% of persons living with human immunodeficiency virus (HIV) diagnosed, 95% of those diagnosed engaged in care and 95% of those in care achieving and maintaining a suppressed HIV viral load by 2030 (1). However, the Public Health Agency of Canada (2) estimates that in 2018 only 87% of HIV-positive persons in Canada were diagnosed. Moreover, PHAC data highlight that in addition to approximately 13% of persons remaining undiagnosed, HIV continues to unequally affect the same priority groups: gay, bisexual and other men who have sex with men (gbMSM); persons who are transgender; individuals of African, Caribbean or Black ethnicities; members of Indigenous communities; and persons who use drugs (3,4). One factor that likely contributes to this ongoing transmission and to why persons remain unaware of their HIV-positive status is persistent barriers to current methods of HIV testing, including at the individual level (fear of results, concerns about confidentiality, etc.), at the healthcare provider level (stigma, reluctance to test, etc.), and at the institutional/policy level (criminalization of behaviour, limited resources, etc.) (5).

Because HIV self-testing, compared to peer and clinic-based testing, often corresponds to increased testing, diagnosis and reported user satisfaction among members of HIV priority groups (6–9), we studied the outcomes associated with free

at-home HIV self-testing in Ottawa. To accomplish this, we launched GetaKit (www.GetaKit.ca), which was the first online mailout program in Canada through which individuals could order an INSTI® HIV self-test and have it delivered to their home or other designated pick-up location. While other studies have observed patients completing self-testing in controlled clinical settings, in implementing GetaKit, our goals were to: 1) evaluate HIV self-testing in real-world settings, 2) facilitate HIV testing, 3) identify persons with undiagnosed HIV infection and 4) link persons to care or prevention services depending on their HIV test result. While we have detailed GetaKit implementation elsewhere, herein we report findings from July 20, 2020 to April 1, 2021 and describe our participants, including details about the number who belonged to a priority group or who identified as women; we also report on the correlates of first-time testers and persons who reported their results.

Methods

Design

GetaKit is an open-cohort prospective observational study with three phases. Phase 1 piloted free at-home HIV self-tests in Ottawa. Because test positivity for HIV was 0.1% in Ontario and 0.08% in Ottawa (unpublished data—available upon request), a 6–12-month period was deemed sufficient to enroll 150–400 adults who could test up to three times each; we expected 0–1 positive result from this sample. Phase 2 involved self-test delivery in additional sites in Ontario. Phase 3 involved the addition of full sexually transmitted infection testing. This article reports on Phase 1.

Data collection

To be eligible, persons had to be HIV-negative or of unknown HIV-status, 18 years of age or older, live in or around Ottawa and have a cellular phone. Exclusion criteria included being on pre-exposure prophylaxis (PrEP), being in an HIV vaccine trial and having a diagnosed bleeding disorder.

For recruitment, we created GetaKit.ca and engaged in public awareness through posters in public places and healthcare centres and via social media. We worked with local acquired immunodeficiency syndrome service organizations to promote to priority groups.

Data collection occurred via GetaKit.ca. Stepwise, potential participants had to first complete an anonymous eligibility screening test, for which all questions were obligatory. Ineligible persons were referred to other resources for testing and support. Eligible persons could register, which involved providing a name, date of birth and cellular phone number (for two-factor authentication). Once registered, participants were asked to complete a survey, which collected information about country of birth, ethnicity, sex, gender, sexual orientation, sex and drug use practices and HIV testing history; "prefer not to answer" was an option in the survey. Once completed, participants could order an HIV self-test, which would be delivered in 1–3 business days. The self-test and shipping were free. We asked, but did not require, participants to report their HIV self-test results via GetaKit.ca.

The Ontario HIV Treatment Network funded GetaKit and the University of Ottawa Research Ethics Board approved the project (H-12-20-6450).

Data analysis

Data were extracted from Getakit.ca into an Excel file. Participant characteristics were reported for the total sample using frequencies and percentages. We stratified by gender, described the participants who identified as women using frequencies and percentages, and used bivariate X^2 to determine which characteristics differed significantly between groups. For outcomes of interest, we sought to understand which participants: 1) had previously completed HIV testing, 2) reported their HIV self-test results and 3) completed the HIV self-test appropriately (i.e. received a valid result). Each outcome was dichotomous, and independent variables (i.e. participant characteristics) were categorized to ensure adequate cell size. Relationships among independent variables and outcomes were first explored using bivariate binary logistic regression. If a significant relationship (in any direction) was identified at $p<0.1$, the variable was retained for multivariable analysis using hierarchical binary logistic regression. Each outcome was explored separately, and only variables significant at $p<0.05$ were included in the final models. Goodness of fit was assessed using the Hosmer-Lemeshow test. Cases with missing data were deleted listwise. SPSS v.26 was used for analysis.

Results

Phase 1 of our study lasted from July 20, 2020 to April 1, 2021. During this time, 1,268 persons submitted the eligibility screening test, averaging 160 accesses per month; 47.3% (n=600) were eligible to register for a self-test. Notably, 59.1% (n=395) of persons were ineligible after submitting incomplete data. Among the 273 persons with complete data, 14.3% (n=39) were ineligible for multiple reasons and the rest for single reasons. As summarized in **Table 1**, residing outside Ottawa was the most common reason for ineligibility, followed by pre-exposure prophylaxis use.

Of 600 eligible participants, 67.5% (n=405) completed a survey and ordered an HIV self-test. Six participants selected "prefer not to report" for all answers and were removed from the analysis. The remaining 399 participants were on average 32 years old, with 66% (n=264) reporting they were white, 68% (n=270) identifying as male, 57.4% (n=229) indicating they were gbMSM. As well, 57.1% (n=228) reported an income more than $40,000 and 77% reported having College or University level education

Table 1: Reasons for participant ineligibility for HIV self-testing for Getakit.ca program

Reason for ineligibility	Number of individuals (non-exclusive)[a]	% of individuals (non-exclusive)[a]	Number of individuals (exclusive)	% of individuals (exclusive)
Live outside Ottawa	150	49	125	51
On PrEP	85	28	67	27
No cell phone	32	10	26	11
Younger than 18 years of age	17	6	10	4
HIV test result (indeterminate[b]/ positive)	10	3	7	3
Bleeding disorder	9	3	7	3
In an HIV vaccine trial	4	1	2	1

Abbreviations: HIV, human immunodeficiency virus; PrEP, pre-exposure prophylaxis
[a] Non-exclusive denotes that this was one of many reasons why a participant was excluded; exclusive denotes that this was the only reason why this person was deemed ineligible
[b] Persons with indeterminate and positive results should undergo serology as follow-up

(ongoing or completed). In total, 70.9% (n=283) of participants had one or more characteristic of an HIV priority group, which rose to 76.4% (n=305) when all racialized persons were included in this analysis (**Table 2**).

Table 2: Characteristics of eligible participants for Getakit.ca program

Characteristic	Description	n	%
Member of a priority population (n=399)	Yes	283	71
	No	116	29
Age (years) (n=395)	25 years or younger	110	28
	26–49 years old	257	65
	50 years and older	28	7
Ethnicity (n=399)	Arab	16	4
	Black	23	6
	Indigenous	16	4
	Latin	13	3
	Mixed	22	6
	South Asian	13	3
	Southeast Asian	25	6
	White	264	66
Gender (n=395)	Men (includes transgender men)	270	68
	Women (includes transgender women)	115	29
	Gender non-conforming	10	3
Sexual orientation (n=390)	Gay (all genders)	287	74
	gbMSM	229	59
	Straight	103	26
Income (n=348)	Less than $20K per year	60	17
	$20K–$75K per year	176	51
	$75K+ per year	112	32
Education (n=391)	High school of less	89	23
	College or bachelor's degree	219	56
	Advanced university degree	83	21
Has a primary care provider (n=392)	Yes	264	67
	No	128	33
Has completed prior HIV testing (n=398)	Yes	290	73
	No	108	27
Location of prior HIV testing (n=281)	General practitioner's office	98	35
	Public health clinic	154	55
	Emergency Department or other hospital setting	6	2
	Other	29	10
Number of sexual partners (n=382)	0 or 1	191	50
	2–5	165	43
	6 or more	26	7
Partners' HIV status (n=389)	HIV negative (or no partners)	280	72
	HIV positive	16	4
	Unknown	93	24
Has a history of substance use (n=364)	Yes	194	53
	No	170	47

Abbreviations: gbMSM, gay bisexual and men who have sex with men; HIV, human immunodeficiency virus

One hundred fifteen participants identified as women, with 24% (n=28) belonging to a priority group, which increased to 39% (n=45) when including women of any racial minority. When comparing participants who identified as men or women, there were significant (bivariate) associations between gender and eight characteristics. Women and men differed based on the following: 1) whether they were members of a priority group ($p<0.001$); 2) whether they identified as straight or gay ($p<0.001$); 3) whether they had a primary care provider ($p=0.005$); 4) whether they had prior HIV testing ($p<0.001$); 5) whether they were tested in a public health clinic ($p<0.001$); 6) whether they reported substance use ($p=0.002$); 7) whether they had more than one sexual partner ($p<0.001$); or 8) their age ($p=0.029$). When all significant characteristics were entered into a binary logistic regression model, only priority group status and number of sexual partners remained significant, with women being less likely to belong to racialized groups, use injection drugs and/or be a sexual minority (OR=0.04; 95% CI=0.02–0.08). Women were also more likely to report having fewer sexual partners than men (OR=0.47; 95% CI=0.25–0.92) (**Table 3**).

For HIV testing history, among all participants, 23.9% (n=95) reported no prior testing and an additional 3.3% (n=13/398) were uncertain if they had ever previously undergone HIV

Table 3: Characteristics of eligible participants who had previously been tested for HIV

Characteristics	Men		Women		Bivariate		Multivariable[a] [ref = first]		
	n	%	n	%	X^2	*p*	OR	95% CI	
								Lower	Upper
Priority population									
Member of a priority population	244	90	28	24	167.404	<0.001	0.04	0.02	0.08
Ethnicity									
White	177	65	79	69	3.977	NS	N/A	N/A	N/A
Black or Indigenous	23	9	15	13					
Other	71	26	21	18					
Sexual orientation									
Gay	229	85	53	47	58.970	<0.001	NS	N/A	N/A
Straight	41	15	60	53					
Income									
Less than $20K per year	38	16	20	20	0.757	NS	N/A	N/A	N/A
$20K to <$75K per year	120	51	48	48					
$75K+ per year	78	33	32	32					
Education									
High school	54	20	34	30	4.262	NS	N/A	N/A	N/A
College or university	153	58	57	50					
Advanced degree	59	22	22	20					
Healthcare provider									
Has a primary healthcare provider	168	63	88	78	7.837	0.005	NS	N/A	N/A
HIV testing									
Has history of prior HIV testing	216	80	63	55	25.705	<0.001	NS	N/A	N/A
Location of testing									
Public health clinic	131	63	16	26	28.076	<0.001	N/A[b]	N/A	N/A
General Practitioner's office	57	27	38	62					
Other	21	10	7	12					
Number of sexual partners									
0 or 1	102	39	80	72	34.334	<0.001	0.47	0.25	0.88
2 to 5	133	51	29	26					
6 or more	24	7	2	<1					
Partner HIV status									
Negative or no partner	187	71	84	75	4.435	NS	N/A	N/A	N/A
Positive	15	6	1	<1					
Unknown	63	24	27	24					
Substance use									
Reported substance use	146	59	44	42	9.244	0.002	NS	N/A	N/A
Age									
Younger than 25 years	63	24	42	37	7.097	0.029	NS	N/A	N/A
26 to 49 years	182	68	67	58					
50+ years	22	8	6	2					

Abbreviations: HIV, human immunodeficiency virus, N/A, not applicable; NS, non-significant
[a] Hosmer-Lemeshow test *p*=0.104
[b] Not entered, insufficient cell size after listwise deletion of case

testing. Among the 290 participants who reported prior HIV testing, 59.6% (n=174) did so fewer than 12 months ago. For testing site (n=281 reported), 54.8% (n=154) indicated they were last tested in a public health or sexually transmitted infection clinic, 33.6% (n=98) tested with a primary care provider and 2.1% (n=6) tested in an emergency department or other hospital setting (Table 2).

Participants who have previously been tested for HIV were more likely to be older ($p<0.005$), identify as men ($p<0.005$), have 2–5 sexual partners ($p<0.005$) and know their sexual partners' HIV-status (**Table 4**). While 46% (n=50) of first-time testers were members of a priority population, 82% of all members of priority populations reported having previously completed HIV testing. Further, participants who were not members of a priority population were nearly five times more likely to be tested for HIV at a primary care provider clinic compared to a public health clinic ($p<0.001$; OR 4.71; 95% CI=2.39–9.27). These results identified differences in healthcare access for women versus men.

Overall, 57.1% (n=228) of participants reported their HIV self-test results back through GetaKit.ca, with 77.6% (n=177) being negative, 20.6% (n=47) being invalid, 1.3% (n=3) being "prefer not to report" and 0.4% (n=1) being positive. The positivity rate was 0.24% for all tests (n=1) and 0.44% for reported results (n=1). There were no significant relationships between participant characteristics and HIV test results. Participants who identified as straight were less likely to report their HIV test result compared to participants who identified as gbMSM ($p<0.05$; OR .58; 95% CI=0.37–0.91).

Table 4: Characteristics of eligible GetaKit participants who have previously been tested for HIV

Characteristic	Interpretation	Bivariate				Multivariable[a] [ref = first]			
		p	OR	95% CI		*p*	OR	95% CI	
				Lower	Upper			Lower	Upper
Priority population	Members of priority populations more likely	<0.05	4.74	2.95	6.64	NS	N/A	N/A	N/A
Age	26–49 years old	<0.05	4.85	2.96	7.93	<0.005	4.58	2.63	8.00
	50+ years old more likely		4.86	1.72	13.71		9.13	2.64	31.49
Race	No difference	NS	NS	NS	NS	NS	NS	NS	NS
Gender	Women less likely	<0.05	0.30	0.19	0.49	NS	N/A	N/A	N/A
Sexual orientation	Persons who identify as straight less likely	<0.05	0.25	0.15	0.40	<0.005	0.33	0.18	0.58
Income	Persons with a yearly income between $20K and $75K more likely	<0.05	2.07	1.07	3.97	NS	N/A	N/A	N/A
Education	Persons with college/university education	<0.05	2.62	1.56	4.43	NS	N/A	N/A	N/A
	Persons with advanced degrees more likely		3.92	1.93	8.00				
Primary care	No difference	NS	NS	NS	NS	NS	NS	NS	NS
Number of partners	2–5	<0.05	3.16	1.91	5.24	<0.005	2.89	1.57	5.32
	6+ more likely		3.4	1.13	10.27	NS			
Partner HIV status	Persons who do not know partners HIV status are less likely	<0.05	0.39	0.24	0.65	<0.005	0.28	0.15	0.53
Substance use	Persons with a history are more likely	<0.05	2.34	1.45	3.76	NS	N/A	N/A	N/A
Reported result	No difference	NS	NS	NS	NS	NS	NS	NS	NS

Abbreviations: N/A, not applicable; NS, non-significant
[a] Hosmer-Lemeshow test $p=0.387$

Discussion

During Phase 1 of GetaKit, 1,268 persons assessed their eligibility; half were eligible, and one-third ordered a test. The most common ineligibility reason was living outside Ottawa. Nearly three-quarters of eligible participants (about one-quarter of eligible women) belonged to priority groups and nearly half of first-time testers were members of priority groups. Priority group participants were more likely to report results, compared with non-priority participants. About one-quarter of all eligible participants (almost one-half of women participants) reported no prior HIV testing. Over half of the participants reported their HIV self-test result back through the GetaKit website; most results were negative and one was positive, for a positivity rate of 0.24% (0.44% for reported tests) – compared to a baseline HIV positivity rate of 0.08% in Ottawa.

Consistent with previously published studies, our results highlight that an online ordering system for free HIV self-tests can facilitate testing for some persons affected by HIV (10–15). Supporting this assertion is that nearly three-quarters of our participants were members of a priority group and that our positivity rates were 3–5.5 times higher than the baseline rate in Ottawa. Notably, data from the local health unit indicated that, during the study period, there were 32 reported HIV diagnosis, of whom 13 had been previously diagnosed in other jurisdictions and were aware of their HIV-positive status. As such, GetaKit accounted for 5.2% (n=1) of new diagnoses in Ottawa during the Phase 1 study period. This outcome is likely related to the fact that over half of our participants identified as gbMSM, which is the group that accounts for over three-quarters of new HIV infections (defined as having been acquired within the preceding 12 months) in Ottawa (16).

Limitations

Our findings also highlighted facilitated access to testing for women who had not previously been tested for HIV. Indeed, nearly half of participants who identified as women indicated no prior testing. However, no women tested positive for HIV and only one-quarter of women belonged to priority groups—signalling that more efforts are required to target testing at women most at-risk for and affected by HIV. This would include women who are African, Caribbean or Black, Indigenous, use drugs, are transgender, and have other social/economic factors that increase their vulnerability to HIV. One reason why uptake was lower among women may have been the risk of violence associated with receiving an HIV self-test at-home (17). Another reason for lowered participation in GetaKit may have been that women were accessing testing through traditional healthcare venues. That HIV prevention services are often targeted at gbMSM may have also affected uptake among women. Phase 2 of the GetaKit program includes curbside pick-up and ordering at discrete community locations, which will address inadvertent inaccessibly for women who are high-risk for HIV acquisition.

Another important limitation for this study was that it occurred during the coronavirus disease 2019 pandemic (COVID-19), when access to HIV testing services was limited. As such, people may have used GetaKit at a higher rate than would have occurred had healthcare settings been accessible. Conversely, the requirement for access to testing during the study period may have been lower if persons had restricted their sexual practices due to COVID-19 isolation protocols. As well, our findings about women may have been affected by the stepwise deletion process, as this reduced the analytic sample for women due to missing data. To address this, in Phase 2 we added more questions regarding persons who are transgender and gender non-conforming. Next, the proportion of women who belonged to priority groups may have been higher than we identified, as our Phase 1 survey did not inquire about sex work. This has been corrected for Phase 2. Lastly, that GetaKit operated exclusively through a website likely restricted access to persons with lower tech literacy or those who did not have ready access to computers. While COVID-19 restrictions did not allow in-person registration, paper-based surveys have been produced for Phase 2 and will be available at select on-site locations.

Conclusion

The GetaKit study was the first free mail-out HIV self-testing study in Canada. During Phase 1, we had good interest and uptake among member of the groups most affected by HIV in Canada and among persons never previously tested for HIV. While achieving such outcomes, GetaKit nevertheless seemed to have primarily reached more educated, higher income gbMSM, rather than the full spectrum of HIV priority groups. Thus, our findings highlight the importance of providing HIV self-testing in this manner, while also identifying the pressing need both to scale-up GetaKit to more regions and to reduce barriers to access (as will be addressed in Phase 2). Our findings also highlight the need to expand access to women who are most at-risk for HIV. This could occur through direct outreach and by having more discrete mechanisms for ordering and pick-up (Phase 2). Through such improvements, we may decrease the proportion of persons unaware they are HIV-positive and may help Canada move toward the United Nations 95-95-95 goals.

Authors' statement

POB is the principal investigator for GetaKit and was involved in all aspects of the project and article. AM was involved in all aspects of GetaKit and this article. AV was involved in all statistical analyses; she wrote all statistical text and reviewed and approved the final manuscript. NH was a research assistant for GetaKit, and was involved in data collection, article writing, editing, submission, and approval. LO was the HIV clinical lead for GetaKit and a research assistant for GetaKit, and was involved in data collection, article writing, editing, submission, and approval. MH was a research assistant for GetaKit, and was

involved in data collection, article writing, editing, submission, and approval. VP was a clinician involved in GetaKit; she also oversaw all social media during phase 1 of GetaKit; VP was involved in data collection, article writing, editing, submission, and approval.

The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

Acknowledgements

POB would like to thank the Ontario HIV Treatment Network for his research chair in public health and HIV prevention. LO would like to thank the Canadian Institutes of Health Research for her Vanier Scholarship.

Funding

The Ontario HIV Treatment Network funded this project.

References

1. Joint United Nations Programme on HIV/AIDS. Fast-track: Ending the AIDs epidemic by 2030. Geneva (Switzerland): UNAIDS; 2014 (accessed 2021-05-03). https://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report

2. Public Health Agency of Canada. Estimates of HIV incidence, prevalence and Canada's progress on meeting the 90-90-90 HIV targets. Ottawa (ON): PHAC; (updated 2021-06; accessed 2021-05-03). https://www.canada.ca/en/public-health/services/publications/diseases-conditions/summary-estimates-hiv-incidence-prevalence-canadas-progress-90-90-90.html

3. Ontario HIV Treatment Network. Priority populations. Toronto (ON): OHTN (accessed 2021-05-04). https://www.ohtn.on.ca/research-portals/priority-populations/

4. Haddad N, Weeks A, Robert A, Totten S. HIV in Canada-surveillance report, 2019. Can Commun Dis Rep 2021;47(1):77–86. DOI PubMed

5. Laprise C, Bolster-Foucault C. Understanding barriers and facilitators to HIV testing in Canada from 2009-2019: A systematic mixed studies review. Can Commun Dis Rep 2021;47(2):105–25. DOI PubMed

6. Bjørnshagen V, Moseng BU, Ugreninov E. Who do you reach? A Norwegian pilot project on HIV self-testing that targeted men who have sex with men. AIDS Behav 2020;24(2):568–79. DOI PubMed

7. Johnson CC, Kennedy C, Fonner V, Siegfried N, Figueroa C, Dalal S, Sands A, Baggaley R. Examining the effects of HIV self-testing compared to standard HIV testing services: a systematic review and meta-analysis. J Int AIDS Soc 2017;20(1):21594. DOI PubMed

8. Witzel TC, Eshun-Wilson I, Jamil MS, Tilouche N, Figueroa C, Johnson CC, Reid D, Baggaley R, Siegfried N, Burns FM, Rodger AJ, Weatherburn P. Comparing the effects of HIV self-testing to standard HIV testing for key populations: a systematic review and meta-analysis. BMC Med 2020;18(1):381. DOI PubMed

9. Witzel TC, Wright T, McCabe L, Gabriel MM, Wolton A, Gafos M, Ward D, Lampe FC, Phillips AN, Trevelion R, Collaco-Moraes Y, Harbottle J, Speakman A, Bonell C, Dunn DD, McCormack S, Burns FM, Weatherburn P, Rodger AJ. Impact and acceptability of HIV self-testing for trans men and trans women: A mixed-methods subgroup analysis of the SELPHI randomised controlled trial and process evaluation in England and Wales. EClinicalMedicine 2021;32:100700. DOI PubMed

10. Bell SF, Dean JA, Lemoire J, Debattista J, Driver G, Gilks CF, Redmond A, Williams OD. Integrated HIV self-testing (HIVST) service delivery in Queensland for policy and service development: study protocol. AIDS Care 2019;31(2):207–15. DOI PubMed

11. De Boni RB, Veloso VG, Fernandes NM, Lessa F, Corrêa RG, Lima RS, Cruz M, Oliveira J, Nogueira SM, de Jesus B, Reis T, Lentini N, Miranda RL, Bingham T, Johnson CC, Barbosa Junior A, Grinsztejn B. An internet-based HIV self-testing program to increase HIV testing uptake among men who have sex with men in Brazil: descriptive cross-sectional analysis. J Med Internet Res 2019;21(8):e14145. DOI PubMed

12. Dean J, Lui C, Mutch A, Scott M, Howard C, Lemoire J, Crothers A, Fitzgerald L, Williams OD. Knowledge and awareness of HIV self-testing among Australian gay and bisexual men: a comparison of never, sub-optimal and optimal testers willingness to use. AIDS Care 2019;31(2):224–9. DOI PubMed

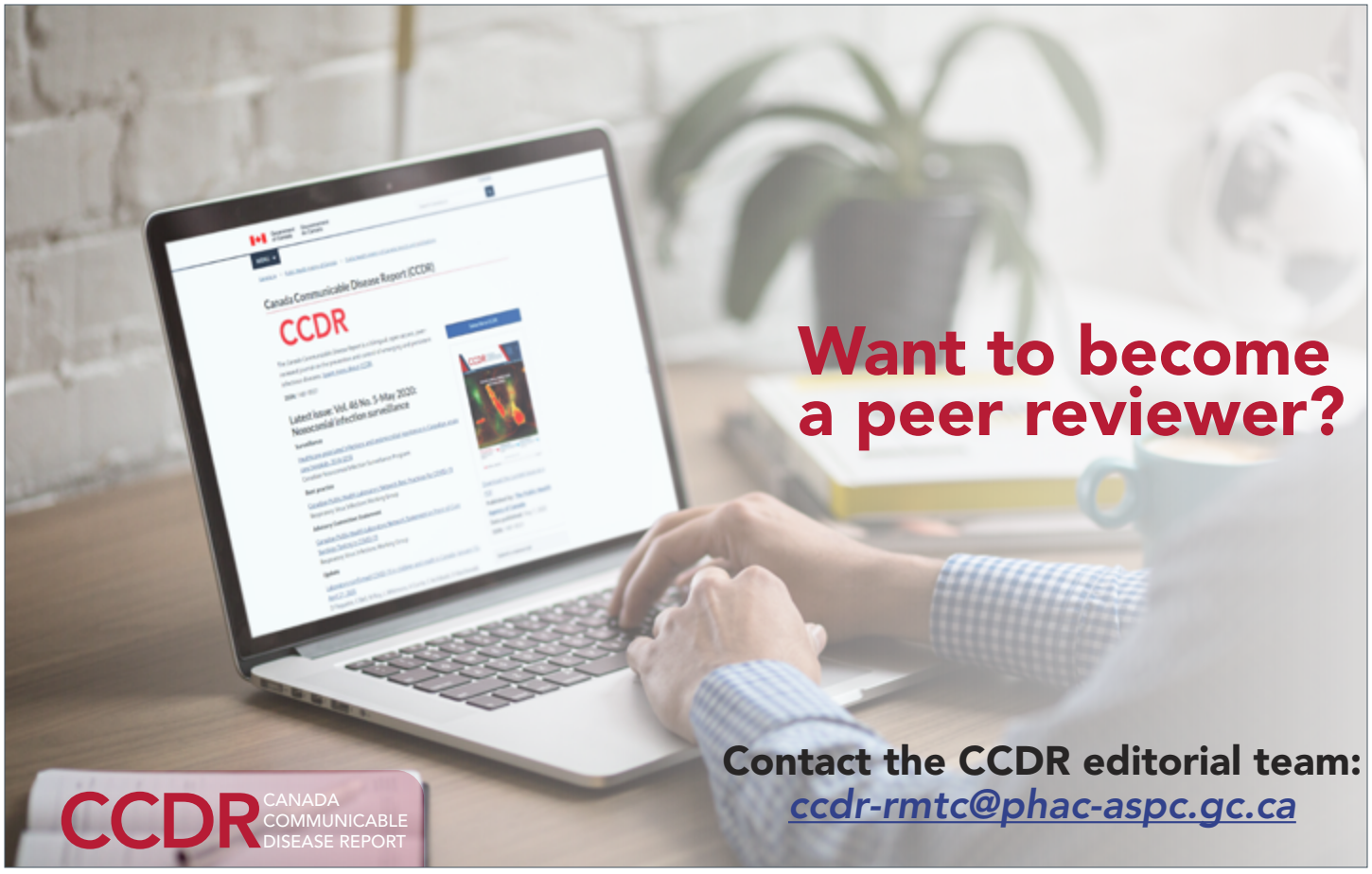
13. Giacomazzo A. HIV self-testing: Learning from international program models to increase testing. Toronto (ON): CATIE; 2020 (accessed 2021-05-04). https://www.catie.ca/en/pif/fall-2020/hiv-self-testing-learning-international-program-models-increase-testing

14. Han L, Bien CH, Wei C, Muessig KE, Yang M, Liu F, Yang L, Meng G, Emch ME, Tucker JD. HIV self-testing among online MSM in China: implications for expanding HIV testing among key populations. J Acquir Immune Defic Syndr 2014;67(2):216–21. DOI PubMed

15. LeGrand S, Muessig KE, Horvath KJ, Rosengren AL, Hightow-Weidman LB. Using technology to support HIV self-testing among MSM. Curr Opin HIV AIDS 2017;12(5):425–31. DOI PubMed

16. Spatz Friedman D, O'Byrne P, Roy M. Comparing those diagnosed early versus late in their HIV infection: implications for public health. Int J STD AIDS 2017;28(7):693–701. DOI PubMed

17. World Health Organization. Guidelines on HIV self-testing and partner notification. Geneva, Switzerland: WHO; 2016 (accessed 2021-05-04). https://apps.who.int/iris/bitstream/handle/10665/251655/9789241549868-eng.pdf


Want to become a peer reviewer?
Contact the CCDR editorial team:
ccdr-rmtc@phac-aspc.gc.ca
CCDR
CANADA COMMUNICABLE DISEASE REPORT

CCDR

CANADA COMMUNICABLE DISEASE REPORT

Public Health Agency of Canada
130 Colonnade Road
Address Locator 6503B
Ottawa, Ontario K1A 0K9
ccdr-rmtc@phac-aspc.gc.ca

To promote and protect the health of Canadians through leadership, partnership, innovation and action in public health.

Public Health Agency of Canada

Published by authority of the Minister of Health.

This publication is also available online at

https://www.canada.ca/ccdr

Également disponible en français sous le titre :
Relevé des maladies transmissibles au Canada