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EARLY WARNING IN PUBLIC HEALTH

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Contact the Editorial Office

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

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OVERVIEW

Event-based surveillance: Providing early warning for communicable disease threats

Tenzin Norzin[1], Homeira Ghiasbeglou[1], Marcia Patricio[1], Svetlana Romanova[1], Abdelhamid Zaghlool[1], Florence Tanguay[1], Linlu Zhao[1]* on behalf of the Global Public Health Intelligence Network (GPHIN)

Abstract

The coronavirus disease 2019 pandemic served as a compelling modern-day reminder of the value of early warning against communicable disease threats in public health. As countries exit the acute phase of the pandemic, there remains a continued need to be vigilant for potential communicable disease threats, particularly as the risk of animal-to-human spillover events is increasing due to climate and land use change. Early warning of emerging threats facilitates earlier public health response, which affords more time to implement public health measures that can help minimize the impact of a particular health threat and protect the health and well-being of the population. One approach to providing early warning for communicable disease and other threats is through event-based surveillance (EBS). However, EBS is not often discussed in the context of public health surveillance. This overview introduces EBS and how it might contribute to providing early warning for communicable disease threats.

Affiliation

[1] Global Public Health Intelligence Network (GPHIN), Centre for Emergency Preparedness, Emergency Management Branch, Public Health Agency of Canada

***Correspondence:**
gphin-rmisp@phac-aspc.gc.ca

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Introduction

The value of early warning about potential threats to public health, such as communicable disease outbreaks, has been known for a long time. An early documented example dates back to the 17th century, during the second plague pandemic (1). As modern disease surveillance systems were not yet in existence, the health authorities of Northern Italy of this era customarily informed each other by letter of news they gathered on health conditions in Europe, North Africa, and the Middle East. In 1652, a letter from the Genoa Health Magistracy notified their counterparts in Northern Italy of several deaths due to the plague on the island of Sardinia. The alarming news from Genoa resulted in swift proclamations by Italian governments to suspend trade and travel with Sardinia to prevent the spread of the plague to their jurisdictions.

Several centuries later, borders would again close, but on a global scale in an attempt to limit the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the novel pathogen that caused the coronavirus disease 2019 (COVID-19) pandemic (2). In this contemporary pandemic context, the value of early warning in public health was again demonstrated with surveillance systems detecting and warning of new SARS-CoV-2 variants, some of which caused new pandemic waves (3,4). These early warnings afforded public health authorities and health systems more time to anticipate and prepare for potential spikes in disease burden by implementing measures to enhance prevention, control the spread of disease, and improve disease outcomes.

As countries exit the acute phase of the COVID-19 pandemic, an important question is when the next pathogen of pandemic potential might emerge, particularly in the 21st century context of increasing animal-human interface as a result of climate and land use change (5). The next pandemic will likely arise in a "hotspot" region of the world (6,7), where public health and surveillance capacity, as well as open, transparent and timely sharing of public health intelligence may be challenges (8). Furthermore, the exact timing and nature of the next pandemic would not be

possible to predict; however, public health tools like event-based surveillance (EBS) are expected to play an important role in identifying and alerting potential pandemic signals.

This article provides an overview of EBS, including how it differs from traditional surveillance—also known as indicator-based surveillance (IBS). The Public Health Agency of Canada's Global Public Health Intelligence Network (GPHIN) is highlighted in this article as an example of an EBS system. GPHIN was prototyped in 1997 by the Government of Canada in collaboration with the World Health Organization (WHO) as the world's first EBS system (9). GPHIN has undergone many changes over the years (10,11) and at the time of writing, remains the only state-owned and operated EBS system in the world.

What is event-based surveillance and how is it different from indicator-based surveillance?

Event-based surveillance and IBS are both approaches used to monitor and detect public health threats. However, there are some key differences between the two surveillance systems (see **Table 1** for a summary of these differences). The goal of EBS is to provide early warning signals by identifying and reporting on meaningful signals, while filtering out noise, from open (i.e. publicly accessible) sources. This filtering can be achieved through various methods, including artificial intelligence and human analysis. To identify potential signals, EBS involves the rapid and structured collection, assessment, and reporting of unstructured information (e.g. information that is not organized in a pre-defined manner) about health events that can potentially pose a serious risk to public health (12,13). This information is communicated in a timely fashion to stakeholders (e.g. individual experts, public health authorities, other governmental and non-governmental organizations) for their further assessment and action.

Event-based surveillance systems like GPHIN take advantage of the Internet by web-scraping information from multi-lingual sources, including official sources (e.g. health notices/alerts, press releases/statements, reports), news media, publicly accessible social media and a wide variety of other online media sources (e.g. blog posts, forum posts, scientific publishing). The types of information detected by EBS can be verified (e.g. information from experts, governments, and reputable organizations) and unverified (e.g. rumours, claims, stories) reporting that suggests unusual or heightened disease activity with a potential of public health concern. While GPHIN relies on the Internet to gather information, EBS systems can also leverage other communication technologies, such as telephone, radio, fax and email (12).

Table 1: Differences between event-based surveillance and indicator-based surveillance

Characteristic	Event-based surveillance	Indicator-based surveillance
Objective	To detect health events that can potentially pose a serious risk to public health	To detect disease outbreaks and characterize disease trends and patterns
Scope	Usually takes an all-hazards approach and can report on both known and unknown diseases	Usually focuses on known diseases
Information types	Unstructured information (i.e. information that is not organized in a pre-defined manner), including both verified (e.g. information from experts, governments, and reputable organizations) and unverified (e.g. rumours, claims, stories) reporting	Structured information (i.e. information that meets specific criteria, such as case definitions, and is organized in a pre-defined manner)
Data sources	Official sources, news media, publicly accessible social media, and other online media sources	Health system infrastructure, such as clinical records from the community, hospitals, or laboratories
Outputs	Early warning signals of new, emerging, and re-emerging threats to public health	Indicators or measures related to a particular health issue

Although EBS systems like GPHIN use a set of criteria to determine whether a potential signal is meaningful, signals reported by EBS systems can result in what can be considered "false alarms" or "false positives". Although all public health threats are causes for concern, some signals can result in no, minimal or comparably less public health response due to factors including but not limited to the geographic location of the event, severity of the health threat, availability of resources and countermeasures and potential impact of response. Such events can be considered false positives, but they are not necessarily failures in early warning. These situations may arise because of the need for EBS systems to balance timeliness in providing early warning and waiting for more information to become available.

As an example of a false positive signal, a July 23, 2022 news media report of a cluster of deaths in Tanzania due to an undiagnosed disease involving patients presenting with viral hemorrhagic fever-like symptoms (fever, bleeding, headache and fatigue) was alerted by GPHIN to stakeholders (14). This report raised concern among GPHIN analysts because an outbreak of Ebola virus disease—a severe, often fatal viral hemorrhagic disease that caused an epidemic in West Africa from 2013 to 2016—occurred between April 23 and July 3, 2022 in the neighbouring country of the Democratic Republic of the Congo (15). The cause of the deaths in Tanzania was later verified to be due to leptospirosis, which is endemic in the region (16).

In contrast, IBS involves the collection and reporting of structured information, which is pre-determined indicators or measures that are related to a particular health issue, such as the prevalence of a particular disease or the incidence of certain risk factors. Structured information is usually reported only if specific criteria (e.g. case definitions) have been met and are often presented as counts and/or rates, grouped by important categories for analysis, such as age or sex. Sources of information for IBS rely heavily on data coming from existing health system infrastructure, such as clinical records originating from the community, hospitals, or laboratories. Under IBS, event verification, such as laboratory confirmation, may be a lengthy and required process before the event is communicated to stakeholders.

How does event-based surveillance identify signals of potential communicable disease threats?

For EBS to identify a potential signal, a health event has to be communicated in some way, which is usually through the Internet for EBS systems like GPHIN (13,17). Web-based sources reporting health events have typically been news media or official sources, but social media reporting is becoming increasingly common, due to its ability to facilitate rapid communication and its broad reach (18). A wide range of sources covering multiple languages need to be systematically scanned in order to ensure the detection of potential signals. Given its characteristics, the volume of unstructured information is expectedly large. For example, GPHIN collects thousands of pieces of open-source information on a daily basis as data inputs into the signal identification process (17).

Reported events around the world collected by an EBS system like GPHIN are filtered using automated (e.g. deduplication, categorization by topic) and manual (e.g. assessments of relevancy, public health risk, credibility) approaches to reduce noise and identify potential signals that could be public health threats (13,19). Automation helps organize this large volume of information. To filter all of this information for potential signals, GPHIN's team of multi-lingual and multi-disciplinary analysts rapidly assesses the public health risk of the reported events against the *Annex 2 of the International Health Regulations (2005)* (20) and other considerations (e.g. credibility of the event and source). The International Health Regulations criteria are used to assess whether the event has serious public health impact, is unusual or unexpected, or has a significant risk of international spread or international travel or trade restrictions. Events that are identified as signals are communicated in a timely fashion by GPHIN to stakeholders for follow up, such as further verification, risk assessment and response.

As a hypothetical scenario to demonstrate how an EBS system like GPHIN might pick up a signal, a novel pathogen may emerge in a community as a cluster of illnesses with shared symptoms, somewhat unusual for the region that is noticed by healthcare workers. Local media may pick up the story, describing it as an unknown illness, in the local language. It may take some time for the local public health system to investigate and report on the cluster of illness. It may take even more time for reporting on the event to percolate upwards regionally, nationally and then internationally, through formal or informal channels. By the time an outbreak is recognized by authorities and IBS monitoring is set up, the disease might have already spread internationally. The role of EBS remains the same in this hypothetical scenario as in the real world: to identify a signal from this continuum of information sharing and reporting as early as possible, in order to provide as much lead-time as possible for appropriate public health response.

Why is event-based surveillance a necessary part of the public health toolkit?

Despite their differences, EBS and IBS are complementary components of public health surveillance. Together, EBS and IBS can provide a more complete picture of a particular health issue, by combining information from unstructured and structured sources.

Because of the differences in approach and information sources, EBS reporting can occur earlier than IBS, as well as in populations and geographic regions that are not adequately covered by IBS. Event-based surveillance does not directly rely on healthcare systems, thereby increasing the timeliness and comprehensiveness of public health surveillance. The trade-off for this timeliness is that the events identified by EBS as signals often require further verification by reliable sources (e.g. experts on the ground, formal/informal communications with responsible public health authorities, laboratory testing) in what can be a time and resource-intensive process and could result in false positives.

Thematically, EBS can take an all-hazards approach, in that health events of interest are not limited to known communicable diseases, but extend to unknown, emerging, and re-emerging diseases, and other chemical, biological, radiological and nuclear events. In comparison, IBS usually focuses on known diseases and modes of transmission, as specific case definitions are intrinsic to this type of surveillance. While EBS detects acute events or occurrences reactively, IBS allows for the monitoring of diseases over longer time periods and can provide more detailed information on trends and patterns.

Is event-based surveillance successful in providing early warning about public health threats?

Not all signals identified by EBS are indications of major outbreaks, epidemics or pandemics. Due to the nature of EBS, signals identified by EBS are often based on reporting that is preliminary, incomplete or unverified. The vast majority of these signals end up being assessed as non-events or posing low risk to public health after further verification, as new information emerges, or as a result of public health intervention. Sporadically, however, there are signals that are linked to serious threats to public health. **Table 2** provides a snapshot of such early warning signals for outbreaks of emerging communicable diseases identified by GPHIN in the past two decades, including the COVID-19 pandemic. The specific impacts of these signals on the outcomes of public health response, such as morbidity and mortality, have not been investigated.

As a source for all-hazards intelligence, signals identified by GPHIN are not limited to communicable diseases. The GPHIN identified early signals of the outbreak of renal disease in China in 2008 that was associated with the consumption of melamine-adulterated; powdered infant formula; the nuclear accident at the Fukushima Daiichi nuclear power plant in Japan in 2011 that was triggered by a tsunami; the multi-state outbreak of fungal meningitis in the United States in 2012 that was caused by injections with contaminated medication; and the emerging evidence of severe pulmonary illness associated with vaping in the United States in 2019. These early warning signals provided lead time for risk assessment and response by relevant authorities. For example, after GPHIN reported on vaping-associated severe pulmonary illness in the United States on August 2, 2019, the Public Health Agency of Canada mobilized resources to monitor the emerging disease pattern and support case finding activities, with the first confirmed Canadian case detected in September 2019 (17).

Table 2: Examples of Global Public Health Intelligence Network's successes in providing early warning signals for emerging communicable diseases

Disease	Date of first signal detected by GPHIN	Country where signal was detected	Type of source (Language of source)	Description of signal	Date of first report in the WHO Disease Outbreak News	Date of WHO declaration as a PHEIC	Date of first case confirmed in Canada
2002—2004 SARS outbreak	November 27, 2002	China	International media report (Chinese)	Cases of pneumonia-like illness in Guangdong, China	February 11, 2003	Not applicable (PHEIC declaration developed after the SARS outbreak)	February 23, 2003
2009 H1N1 pandemic	April 1, 2009	Mexico	Local media report (Spanish)	Outbreak of respiratory illness in La Gloria, Mexico	April 24, 2009	April 26, 2009	April 26, 2009
2012 MERS-CoV outbreak	April 19, 2012	Jordan	Local media reports (Arabic)	Outbreak of an unknown disease in Zarqa, Jordan	February 11, 2013	Not declared	Not applicable
2014 Ebola virus disease outbreak in West Africa	March 19, 2014	Guinea	International media report (English)	Outbreak of hemorrhagic fever in southeast Guinea	March 23, 2014	August 8, 2014	Not applicable
2015—2016 Zika virus disease outbreak in the Americas	March 24, 2015	Brazil	Local media reports (Portuguese)	Cases of unidentified mosquito-borne illness in Recife, Brazil	October 21, 2015	February 1, 2016	December 2015
COVID-19 pandemic	December 31, 2019	China	International media reports (English)	Cases of viral pneumonia of unknown origin in Wuhan, China	January 5, 2020	January 30, 2020	January 25, 2020
2022 mpox outbreak	May 7, 2022	United Kingdom	Government health notice (English)	Confirmed case of mpox in London, England	May 16, 2022	July 23, 2022	May 19, 2022

Abbreviations: COVID-19, coronavirus disease 2019; GPHIN, Global Public Health Intelligence Network; MERS-CoV, Middle East respiratory syndrome coronavirus; PHEIC, Public Health Emergency of International Concern; SARS, severe acute respiratory syndrome; WHO, World Health Organization

Conclusion

Finding the signal for the next significant public health threat as early as possible is a challenge for public health surveillance. Although public health has a robust suite of IBS tools available, the signal might be missed or delayed due to inherent limitations behind existing surveillance systems that range from active to passive forms of surveillance and laboratory or syndromic-based reporting styles (21). There are also multitudes of barriers, such as a lack of expertise, data management systems and laboratory capacity, in implementing these surveillance tools in many countries, particularly in low and middle-income countries (22) and in preventing vigilance atrophy (i.e. the relaxation of vigilance over time in the absence of manifestations of further incidents) (23).

As the risk of animal-to-human spillover events increases due to climate and land use changes, it will be increasingly important to remain vigilant of these communicable diseases and other emerging threats to provide timely early warning for public health response. Although it is impossible to predict when the next threat to public health will occur, EBS systems like GPHIN will play a vital role in public health surveillance by complementing IBS systems. To best fulfil its unique role in providing early warning, EBS systems will need to continue to evolve and increase in sophistication, as advances in technology will change the way humans share information and how meaningful signals can be identified from this information.

Authors' statement

TN — Conceptualization, writing–original draft, writing–review and editing
HG — Conceptualization, writing–review and editing
MP — Conceptualization, writing–review and editing
SR — Conceptualization, writing–review and editing
AZ — Conceptualization, writing–review and editing
FT — Conceptualization, writing–review and editing
LZ — Conceptualization, writing–original draft, writing–review and editing

Competing interests

None.

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RAPID COMMUNICATION

Wastewater surveillance for earlier detection of seniors congregate living COVID-19 outbreaks in Peterborough, Ontario

Thomas Piggott[1,2,3]*, Mohamed Kharbouch[3], Michael Donaldson[4,5], Carolyn Pigeau[3], Donna Churipuy[3], Gillian Pacey[3], Christopher Kyle[4,5]

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has disproportionately affected seniors living in congregate living settings. The evolving surveillance context has led to novel use of wastewater surveillance to monitor levels of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in these settings. This study presents a pilot of upstream congregate living wastewater surveillance of SARS-CoV-2 for the detection of COVID-19 outbreaks and the effects of early public health interventions. We monitored localized wastewater SARS-CoV-2 levels from four congregate living settings March 15, 2021 to October 1, 2022 and correlated these levels with suspected and confirmed COVID-19 outbreaks determined by other methods. We identified five wastewater signals that correlated with confirmed outbreaks and three wastewater signals that did not correlate with subsequent outbreaks. In the five confirmed outbreaks, the wastewater signal was detected 2–10 days (median, five days) prior to confirmation of the outbreak by case testing. This pilot demonstrates upstream sampling for SARS-CoV-2 in wastewater may effectively detect outbreaks prior to their detection through symptomatic case testing and could support a balanced approach to outbreak response in congregate living settings, leading to increased wellbeing of these residents.

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Affiliations

[1] Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON

[2] Department of Family Medicine, Queen's University, Kingston, ON

[3] Peterborough Public Health, Peterborough, ON

[4] Department of Forensic Science, Trent University, Peterborough, ON

[5] Environmental and Life Sciences Graduate Program, Trent University, Peterborough, ON

***Correspondence:**

piggott@mcmaster.ca

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has disproportionately affected seniors—particularly those living in congregate care homes (1,2). Congregate care settings, such as retirement and long-term care homes, carry a greater risk of spread of communicable diseases such as COVID-19, due to the close contact proximity of residents, and a greater risk of burden of outbreaks due to a higher proportion of residents with risk factors for severe disease, including medical comorbidities and age (2).

Wastewater surveillance for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has become a mainstay of surveillance and has proven to be tremendously important in informing the continued COVID-19 pandemic response as the pandemic has evolved and availability of individual level testing has decreased. Wastewater surveillance has informed policy decisions on public health measures and public health risk communication pertaining to current transmission levels. Congregate living settings continue to be a high-risk location for outbreaks of COVID-19, even after the advent of COVID-19 vaccinations (3). Detection and early intervention, with other outbreak control measures, continue to be important to decrease morbidity and mortality of COVID-19 outbreaks in congregate living settings. Wastewater surveillance in congregate living settings for seniors has been proposed in both published protocols and articles (4–8); however, no research to date has evaluated wastewater surveillance at an institution level in congregate living settings for seniors and compared these data with available COVID-19 case and outbreak information.

In the Peterborough Public Health region, wastewater surveillance for SARS-CoV-2 has been conducted in collaboration

with Peterborough Public Health and Trent University through the Ministry of the Environment, Conservation and Parks funding program (9). Wastewater surveillance began in the region in January 2021 at nine sampling sites and progressed to include 18 sampling sites.

Peterborough Public Health follows provincial (Ontario) COVID-19 outbreak guidance. At the time of the outbreaks included in this article (March 15, 2021–October 1, 2022), the definition of a probable case was one with both compatible symptoms and an epi-link, and a confirmed case required laboratory testing confirmation (10). In congregate living settings, including in the retirement homes as we discuss here, the suspect outbreak definition for this period was one positive molecular test or rapid antigen test (RAT) in a resident (11). A confirmed outbreak was defined as two or more residents and/or staff/visitors with positive polymerase chain reaction (PCR) test or RAT in a 10 day period (11).

Due to the burden experienced by congregate living facilities, a pilot of upstream wastewater collection for congregate living settings was initiated in collaboration with the homes. The purpose of this study was to assess the utility of upstream wastewater sampling at congregate living settings to detect and track outbreaks of COVID-19. As these data were collected as part of routine surveillance and all facilities have been anonymized. The study did not require research ethics board approval.

This article presents an outbreak summary and rapid communication on the experience of Peterborough Public Health and the use of congregate living facility wastewater data for COVID-19 surveillance.

Current situation

The four congregate living settings were selected among the various such sites in the region on a convenience basis due to willingness to participate, facility size and logistical feasibility. The total number of sites included was driven by budgetary constraints. Logistical considerations included ease of sampling a unique wastewater site (e.g. one site was deemed not feasible due to an inability to isolate a sampling location independent of other effluent sources). Sampling location was chosen in such a way that the sewage system was confirmed to be unique to the facility. Sites were selected in collaboration between Peterborough Public health, Trent University and local congregate living setting operators.

Sampling was initiated on March 15, 2021, at three congregate living sites, and a fourth site was added on May 14, 2021. The wastewater sampling frequency was at least three times per week during the pilot period, but often increased to five times per week when SARS-CoV-2 levels were elevated.

The public health unit epidemiological team worked with Trent University researchers to identify key case studies that constituted all wastewater signals and/or confirmed outbreaks that had occurred at any of the congregate living settings included in the pilot from the period of March 15, 2021 until October 1, 2022. Each case study was plotted in a traditional epi curve bar chart denoting confirmed and probable cases, and both normalized and non-normalized N1 N2 copies per millimetres were plotted by line graph. In keeping with provincial case definitions in Ontario, confirmed cases were diagnosed by nasopharyngeal swab PCR test for COVID-19 and probable cases were defined as RAT positive and symptomatic (not all cases elected to undergo PCR after a positive RAT). The date of wastewater signal detection was defined as any increase above one copy per millimetres by PCR testing.

We assessed case-level data, including the date of symptom onset and date of diagnosis, in relation to the facility's wastewater signal, to assess temporality of a wastewater signal for early detection and monitoring progression of COVID-19 outbreaks in congregate living facilities. We assessed the dominant community variant from the simple majority of samples in the corresponding period of the outbreak from Public Health Ontario SARS-CoV-2 Genomic Surveillance in Ontario Reports (12). The primary outcome measure was defined as the "date delta", which is the difference (in days) between the date of wastewater signal detection and the date of a confirmed outbreak. A negative date delta signifies that the wastewater signal preceded the confirmation of the outbreak in that facility.

"Preventive" outbreak guidance was developed by the Peterborough Public Health Infectious Diseases team and Medical Officer of Health drawing from current outbreak control guidance in Ontario and in consultation with Public Health Ontario. The preventive outbreak guidance is available in **Appendix**. This guidance was elective for congregate care settings and was intended to be less burdensome on residents than traditional outbreak measures; however, it was hoped that these measures would decrease early transmission and thus lessen or avert the outbreaks. Public health nurses/inspectors from the infectious disease team began issuing preventive outbreak guidance to congregate living setting operators participating in the pilot beginning in September 2022.

Assessment

There were five confirmed outbreaks at these four congregate living settings during the pilot period. Additionally, there were three instances of detection wastewater signals that did not ultimately lead to confirmed outbreaks. **Table 1** presents all wastewater detections/confirmed outbreaks during the pilot period.

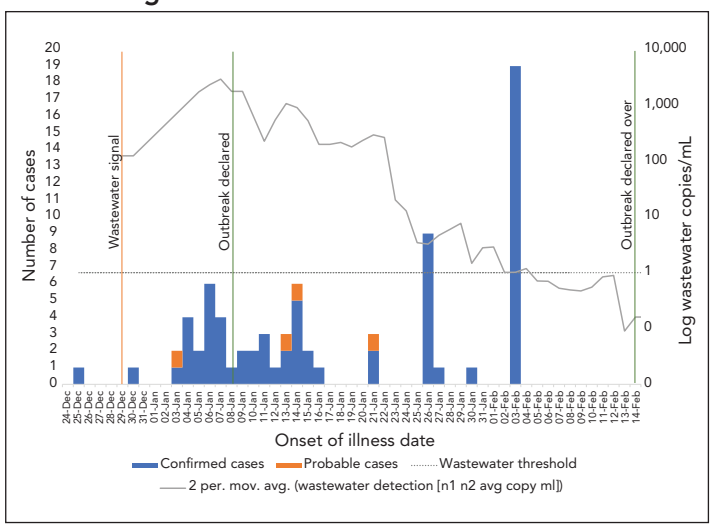
Table 1: List of COVID-19 wastewater signal detections and outbreaks in Peterborough pilot congregate living settings

Congregate living setting number and outbreak letter	Dominant community variant	Confirmed outbreak detection date	Wastewater surveillance date	Date preventive guidance issued	Date delta	Number of confirmed cases	Number of probable cases
1a (Figure 1)	Omicron BA.1	Jan 8, 2022	Dec 29, 2021	N/A	-10	70	4
1b (Figure 2)	Omicron BA.5	N/A	Aug 24, 2022	Aug 31, 2022	N/A	0	0
2a (Figure 3)	Omicron BA.5	N/A	Aug 5, 2022	Aug 16, 2022	N/A	0	0
2b (Figure 4)	Omicron BA.5	Sept 12, 2022	Sept 7, 2022	Sept 12, 2022	-5	17	9
3a (Figure 5)	Omicron BA.5	Sept 6, 2022	Sept 4, 2022	Sept 6, 2022	-2	6	22
4a (Figure 6)	Omicron BA.1	N/A	Feb 7, 2022	N/A	N/A	0	0
4b (Figure 7)	Omicron BA.2	Mar 31, 2022	Mar 25, 2022	N/A	-6	8	1
4c (Figure 8)	Omicron BA.5	Sept 21, 2022	Sept 18, 2022	Sept 21, 2022	-3	44	5

Abbreviations: COVID-19, coronavirus disease 2019; N/A, not applicable

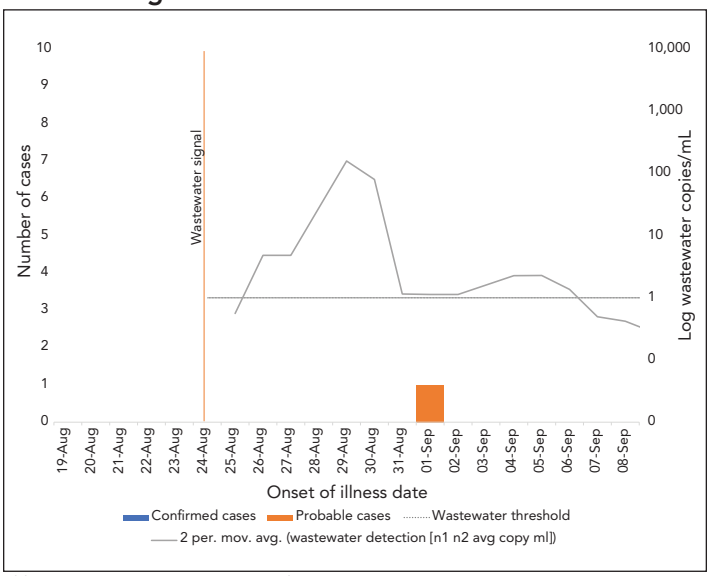
Figures 1 to 8 present epi curves for all wastewater detections and confirmed outbreaks. We present the data from two outbreaks, where evidence from the wastewater did or may have influenced early detection and public health action. We report a negative date delta for all five confirmed outbreaks ranging from -10 to -2 (median, -5). Notably, the date delta decreased with the progression of Omicron sub-variants implicated in community transmission at the time of outbreak detection. Outbreaks during BA.1/2 transmission had a longer date delta (-6, -10, respectively) than outbreaks during BA.4/5 transmission (-2, -3, respectively).

Figure 1: Event 1a in Retirement Home #1 in Peterborough[a]



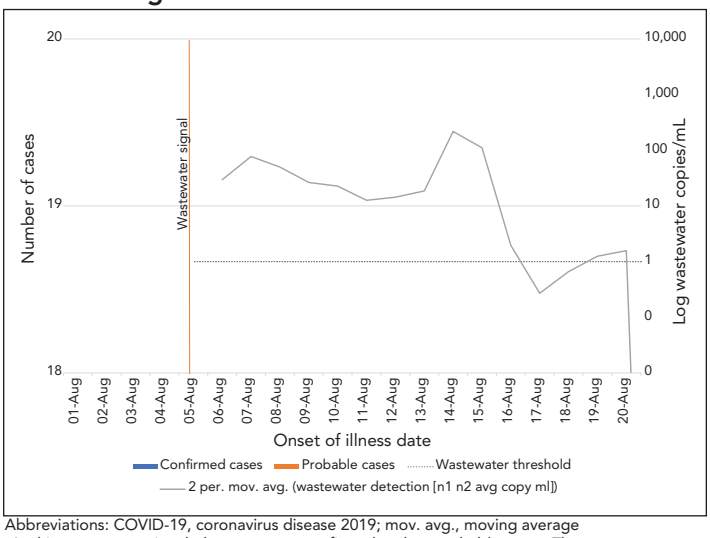
Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this outbreak, there were a total of 70 confirmed cases and four probable cases. This outbreak was analyzed in relation to wastewater levels in retrospect and no preventive guidance was issued. The wastewater surveillance signal was detected December 29, 2021, and the outbreak ultimately declared based on confirmed cases on January 2, 2022. The date delta for wastewater signal was -10 days for this outbreak

Figure 2: Event 1b in Retirement Home #1 in Peterborough[a,b]



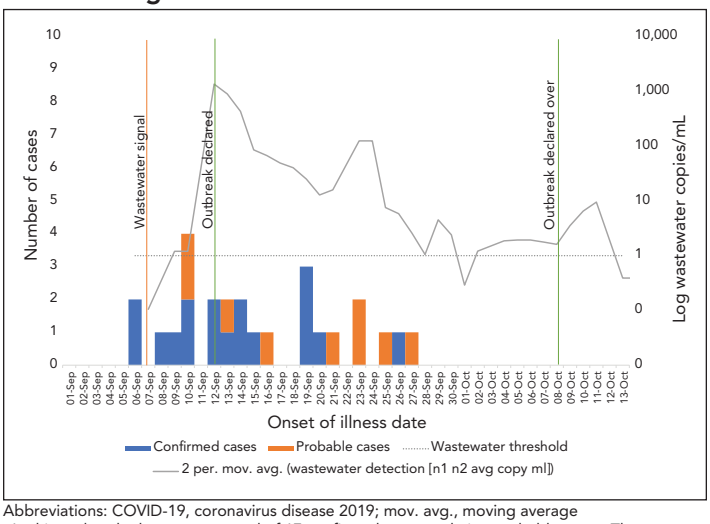
Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] Even there was no outbreak declared in Retirement Home #1 for this period, there was a probable case on September 1, 2022
[b] In this wastewater signal, there was one probable case and no outbreak was declared. The wastewater surveillance signal was detected August 24, 2022

Figure 3: Event 2a in Retirement Home #2 in Peterborough[a]



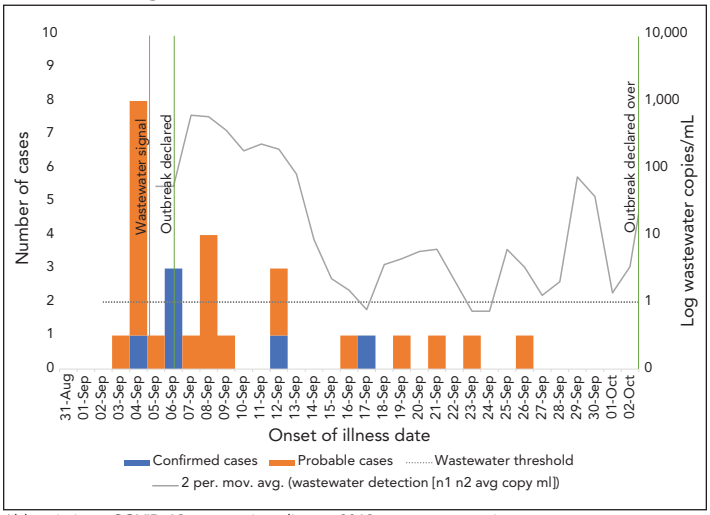
Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this wastewater signal, there were no confirmed and no probable cases. The wastewater surveillance signal was detected August 5, 2022, and preventive guidance was shared with the facility August 16, 2022. No outbreak was ultimately confirmed

Figure 4: Outbreak 2b in Retirement Home #2 in Peterborough[a]



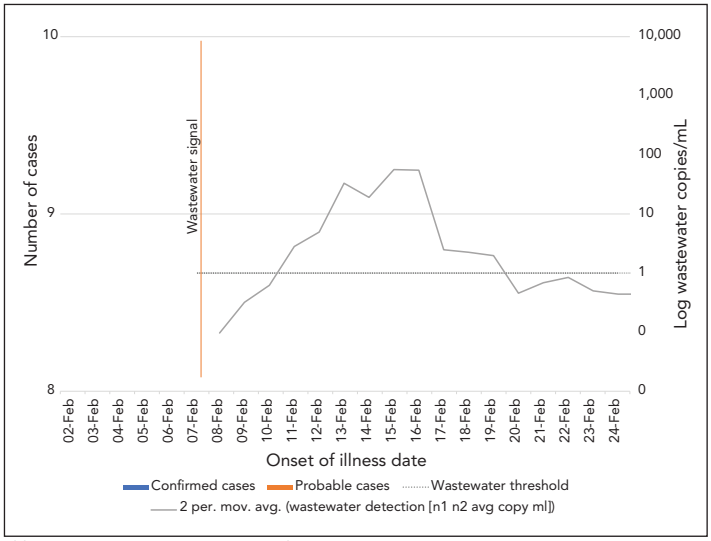
Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this outbreak, there were a total of 17 confirmed cases and nine probable cases. The wastewater surveillance signal was detected September 7, 2022, and the outbreak ultimately declared based on confirmed cases on September 12, 2022. Preventive measure guidance was shared with the facility on September 12, 2022. The date delta for wastewater signal was -5 days for this outbreak

Figure 5: Event 3a in Retirement Home #3 in Peterborough[a]



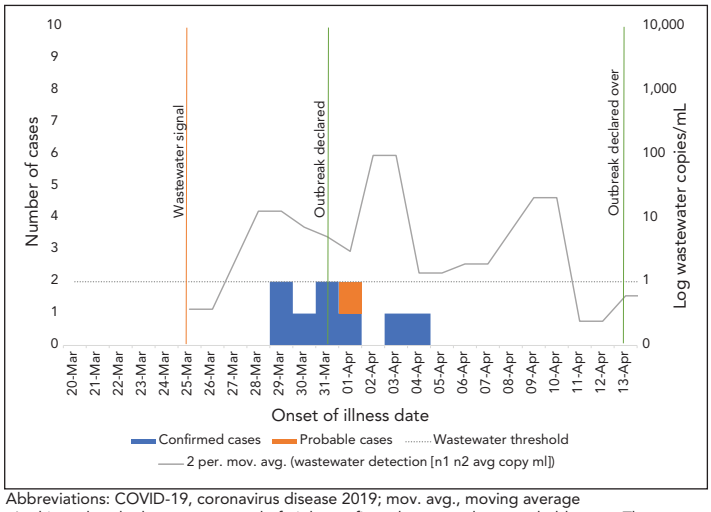
Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this outbreak, there were a total of six confirmed cases and 22 probable cases. The wastewater surveillance signal was detected September 4, 2022, and the outbreak declared based on confirmed cases on September 6, 2022. The date delta for wastewater signal was -2 days for this outbreak

Figure 6: Event 4a in Retirement Home #4 in Peterborough[a]



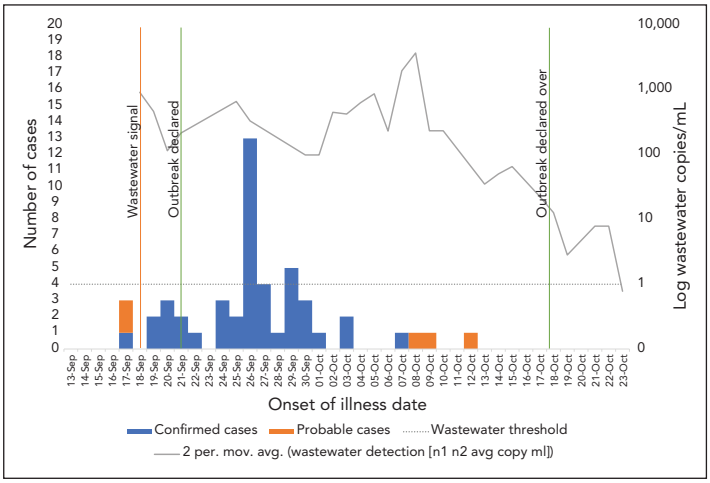
Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this wastewater signal, there were no confirmed and no probable cases. The wastewater surveillance signal was detected February 7, 2022. No outbreak was ultimately confirmed

Figure 7: Event 4b in Retirement Home #4 in Peterborough[a]



Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this outbreak, there were a total of eight confirmed cases and one probable case. The wastewater surveillance signal was detected March 25, 2022, and the outbreak ultimately declared based on confirmed cases on March 31, 2022. The date delta for wastewater signal was -6 days for this outbreak

Figure 8: Event 4c in Retirement Home #4 in Peterborough[a]



Abbreviations: COVID-19, coronavirus disease 2019; mov. avg., moving average
[a] In this outbreak, there were a total of 44 confirmed cases and five probable cases. The wastewater surveillance signal was detected September 18, 2022, and the outbreak ultimately declared based on confirmed cases on September 21, 2022. The date delta for wastewater signal was -3 days for this outbreak

Retirement Home Outbreak #1a (see Figure 1) experienced an outbreak of relatively long duration, lasting 37 days, from January 8 to February 14, 2022. As the outbreak progressed, the wastewater surveillance proved useful in identifying when transmission had lessened and the outbreak was over, though cohort testing detected asymptomatic cases who were likely infected and not detected earlier in the outbreak. On January 26, 2022 and February 3, 2022, facility-wide testing was completed as part of an intensive case finding surveillance exercise. On January 26, nine new individuals were identified as COVID-19 positive without a history of symptoms, and on February 3, nineteen new individuals were identified as positive. These cases presented a challenge in interpretation to the outbreak team—were these previously asymptomatic cases or early infections? However, in contextualizing with symptoms (most were asymptomatic) and the wastewater signal (which had lessened substantially), we were able to place greater confidence that these cases were previously undetected and not continued outbreak transmission. Relying on the wastewater signal, Peterborough Public Health was, therefore, able to declare the outbreak over earlier than we otherwise may have, based solely on the number of PCR-test confirmed cases. This resulted in a return to socialization, resident services and thus a better quality of life for the residents.

Figures 2, 3, 6 demonstrate instances where a wastewater signal was detected, but no confirmed outbreak was ultimately declared; this could have been due to a lack of testing conducted or asymptomatic or pauci-symptomatic cases in residents, staff or visitors who were never diagnosed.

Figure 4 demonstrates an outbreak where a wastewater signal was identified in retrospect five days before a confirmed case and an outbreak was declared, however, due to delays in lab reporting the preventive guidance and checklist (**Supplemental material**) was shared the same date as an outbreak was subsequently declared.

Figure 5 demonstrates an outbreak in the period of Omicron BA.5 transmission, where the confirmation was just two days after, in retrospect a wastewater signal was detected. This is similar to Figure 8, which also demonstrates a BA.5 outbreak with only three days between a wastewater signal and a declared outbreak.

In contrast, Figure 7 demonstrates an outbreak where the wastewater signal was detected eight days prior to the confirmation of an outbreak.

Implications

This pilot study presents compelling evidence that wastewater sampling in congregate living settings could support early identification of SARS-CoV-2 and mitigation of COVID-19 outbreak spread. The possible utility of early wastewater SARS-CoV-2 detection and intervention was demonstrated in this pilot. This is the first study to comprehensively assess person-level testing and outbreak data in relation to wastewater surveillance in the congregate living setting for seniors.

The utility of early detection and intervention may have decreased with the advent of more rapidly transmissible variants because these variants may also demonstrate different viral kinetics, which would impact gastrointestinal shedding and thus wastewater detection. We did track variants of concern within a subset of the processed samples, which demonstrated differing

variants than dominant when analyzed at the provincial-level. This may be useful where variants have different transmissibility or immune-escape characteristics to direct local public health action.

Given the decreases in individual testing efforts, wastewater surveillance initiatives such as this continue to hold importance for tracking the continued COVID-19 pandemic and emerging variants. Wastewater surveillance has garnered significant interest during the COVID-19 pandemic. This activity is relatively cost-effective in relation to individual-level testing for monitoring of transmission levels of COVID-19 at the community level (13,14).

Much of the modifiable non-pharmacological interventions recommended to reduce transmission through the COVID-19 pandemic (e.g. masking, cessation of social activities or isolation of infectious individuals) can be linked to reductions in community transmission levels. In addition, social isolation in congregate living settings due to outbreak response measures has been significant (15). Therefore, a balanced approach in responding to outbreaks, advocating for structural improvements such as ventilation improvements is important, and to date has been inadequate (16).

The use of upstream wastewater sampling of congregate living settings—and the resultant targeted early interventions to mitigate or arrest the transmission of COVID-19—warrants further consideration as part of the ongoing response to the COVID-19 pandemic. Further research should also assess the possible implications of "false positive" signal detection: the signals that do not result in a declared outbreak in this setting likely represent asymptomatic or pauci-symptomatic cases in staff/visitors/residents, which do not result in further transmission. Preventive actions in scenarios where transmission does not ultimately occur may lead to potential unintended consequences. Additionally, further research is required to assess whether the signal detection and implementation of preventive outbreak guidance is able to change the trajectory of outbreak transmission.

Conclusion

The potential for upstream wastewater sampling in congregate settings can be expanded beyond SARS-CoV-2 detection to a spectrum of other respiratory pathogens (11), which are experiencing a resurgence that threatens these populations. We have recently incorporated screening for influenza and respiratory syncytial virus into wastewater testing to explore the utility of this technique beyond COVID-19.

Authors' statement

TP — Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, supervision, software, validation, visualization, roles/writing original draft, writing–review and editing
MK — Formal analysis, investigation, methodology, software, validation, roles/writing original draft, writing–review and editing
MED — Lab data analysis, lab methodology, data mining, lab quality control
CP — Formal analysis, investigation, methodology, software, validation, writing–review and editing
DC — Formal analysis, investigation, methodology, writing–review and editing
GP — Formal analysis, investigation, methodology, writing–review and editing
CJK — Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, supervision, software, validation, visualization, roles/writing original draft, writing–review and editing

Competing interests

TP, MK, CP, DC, GP are employed by Peterborough Public Health, and have no other interests to declare.

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Funding

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Supplemental material

These documents can be accessed on the Supplemental material file.

Wastewater COVID-19 Early Detection Control Measures Checklist for Institutions

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Appendix: Peterborough Public Health Wastewater Surveillance Guidance for Retirement Homes

Wastewater Surveillance Guidance for Congregate Living Settings

This guidance document is meant to provide participating congregate living settings (CLS), including retirement homes or other CLS, with the rationale and benefits of wastewater surveillance (especially in high-risk settings), the importance of implementing control measures to mitigate outbreaks and the role of both Peterborough Public Health and the CLS participating in this program.

Background

Wastewater (also known as sewage) surveillance involves the sampling and analysis of wastewater to monitor the prevalence of certain viruses and diseases within communities. The use of wastewater surveillance for coronavirus disease 2019 (COVID-19) has the potential to provide an early warning system of the presence of COVID-19 in a source population, with some studies observing a signal 2–14 days prior to clinical detection (Public Health Ontario, 2021). COVID-19 is detected in wastewater because severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (the virus that causes COVID-19) is shed in the feces of some infected individuals, who are either asymptomatic, pre-symptomatic, symptomatic, or recovering from COVID-19 (it is known that peak viral shedding occurs before the onset of symptoms). Wastewater surveillance involves the collection of untreated wastewater samples which are then processed to detect the virus (Public Health Ontario, 2021).

Rationale and benefits of wastewater surveillance

Wastewater surveillance is a non-invasive, anonymous method of obtaining samples within a specific geographic area (Public Health Ontario, 2021). Wastewater surveillance is an important detection method to monitor trends in COVID-19 in Ontario and in our local community. Locally, we use the Peterborough Public Health Local COVID-19 Risk Index to assess current risk based on a number of factors including COVID-19 detection in wastewater. Using wastewater data can provide a 'signal' of community spread in an area, and with a standard and timely response using control measures, this data may help prevent or mitigate outbreaks and the subsequent risk of infection for residents in retirement homes.

How the program works

1. Local wastewater is monitored by the research team at Trent University, under the direction of Dr. Christopher Kyle. When two subsequent detections of COVID-19 occur at a CLS, it is reported to Peterborough Public Health and directly to the affected facility.

2. **Low, moderate and high detections** in the wastewater will initiate a response by an Infectious Disease Program Public Health Nurse (PHN) at Peterborough Public Health.

    a Quantifying these detections depends on a number of factors; however, as a general guide the following ranges are used:
    - Low <5 cp/ml
    - Moderate 5–15 cp/ml
    - High >15 cp/ml
    - Very High >100 cp/ml

3. If a facility is already in outbreak when the detection is observed, the wastewater detection levels may be used to support decision-making regarding control measures.

4. The assigned PHN will connect with the home to confirm they are aware of the detection.

5. **Control measures** (please see control measures checklist in Supplemental material) will be reviewed with the facility and implemented as appropriate.

6. If, upon further testing, cases are identified and an outbreak is declared additional control measures may be recommended.

7. Control measures will continue until the wastewater signal has returned to no detection, outbreak has been declared over and/or at the discretion of Peterborough Public Health in the case of ongoing detection without evidence of cases.

Role of the congregate living setting

This program involves a strong collaboration between Peterborough Public Health and the CLS. The role of the CLS in this surveillance program is to receive and monitor wastewater surveillance reports and implement all necessary control measures at the first indication of the virus being detected in the facility. Peterborough Public Health will support the facility by connecting with the home and providing guidance on implementing the control measures as well as outbreak management if necessary. By working together to implement control measures in the facility as quickly as possible, we can better protect residents and mitigate facility outbreaks.

We thank you for your continued efforts and dedication to keeping our communities safe.

Further reading

- Wastewater Surveillance of COVID-19 (publichealthontario.ca)
- PHO Rounds: Wastewater Surveillance of COVID-19: Potential Applications, Challenges, and Experiences in Ontario (publichealthontario.ca)
- Interim Infection Prevention and Control Measures based on COVID-19 Transmission Risks in Health Care Settings (publichealthontario.ca)
- Trent University and Peterborough Public Heath Join Provincial COVID-19 Wastewater Surveillance Initiative - News - Trent University
- Wastewater Signal - Peterborough Region COVID-19 Tracker

Utility of the Peterborough Public Health COVID-19 rapid antigen test self-report tool: Implications for COVID-19 surveillance

Erin Smith[1,2], Carolyn Pigeau[2], Jamal Ahmadian-Yazdi[2,3], Mohamed Kharbouch[2], Jane Hoffmeyer[2], Thomas Piggott[1,2,4]*

Abstract

Background: The ongoing coronavirus disease 2019 (COVID-19) pandemic has necessitated novel testing strategies, including the use of rapid antigen tests (RATs). The widespread distribution of RATs to the public prompted Peterborough Public Health to launch a pilot RAT self-report tool to assess its utility in COVID-19 surveillance. The objective of this study is to investigate the utility of RAT using correlations between RAT self-report results and other indicators of COVID-19.

Methods: We investigated the association between RAT results, PCR test results and wastewater levels of nmN1N2 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) genes (to infer COVID-19 levels) using Pearson's correlation coefficient. Percent positivity and count of positive tests for RATs and polymerase chain reaction (PCR) tests were analyzed.

Results: The PCR percent positivity and wastewater were weakly correlated (r=0.33, p=0.022), as were RAT percent positivity and wastewater nmN1N2 levels (r=0.33, p=0.002). The RAT percent positivity and PCR percent positivity were not significantly correlated (r=-0.035, p=0.75). Count of positive RATs and count of positive PCR tests were moderately correlated (r=0.59, p<0.001). Wastewater nmN1N2 levels were not significantly correlated with either count of positive RATs (r=0.019, p=0.864) or count of positive PCR tests (r=0.004, p=0.971).

Conclusion: Our results support the use of RAT self-reporting as a low-cost simple adjunctive COVID-19 surveillance tool, and suggest that its utility is greatest when considering an absolute count of positive RATs rather than percent positivity due to reporting bias towards positive tests. These results can help inform COVID-19 surveillance strategies of local public health units and encourage the use of a RAT self-report tool.

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Keywords: COVID-19, rapid antigen test, PCR test, wastewater, evaluation, surveillance, Peterborough Public Health

Affiliations

[1] Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, ON

[2] Peterborough Public Health, Peterborough, ON

[3] Public Health and Preventive Medicine Residency Program, University of Ottawa, Ottawa, ON

[4] Department of Family Medicine, Queen's University, Kingston, ON

***Correspondence:**

piggott@mcmaster.ca

Introduction

The ongoing resource pressures in the coronavirus disease 2019 (COVID-19) pandemic have warranted the implementation of novel testing strategies. For example, limits to polymerase chain reaction (PCR) testing (i.e. available only for only high-risk individuals in late 2021) posed a new challenge for accurately monitoring COVID-19 case counts (1). Wastewater surveillance has proven useful in addressing surveillance gaps (2–4); however, limitations exist in the interpretation of wastewater data.

Self-administered rapid antigen tests (RATs) can detect the viral proteins that cause COVID-19 in as little as 15 minutes (5), and is an alternative method employed by the Government of Ontario

to monitor the virus' spread. In December 2021, the Ontario government announced the distribution of RATs for elementary and secondary school students and staff (6), followed by the expansion of the RAT rollout to pharmacies and grocery stores in February 2022 (7). This program continues until present, with publicly funded and privately purchased RATs widely available. The provincial distribution of RATs prompted Peterborough Public Health (PPH) to launch a pilot surveillance project asking local residents to voluntarily and confidentially report their RAT results via an online self-report tool. The objective was to monitor an approximate percent positivity among those who reported their results using the online self-report tool to contribute to community COVID-19 surveillance.

Peterborough Public Health is the only public health unit globally that has launched a RAT self-report tool. The objective of this study is to investigate the utility of this tool using correlations between RAT self-report results and other indicators of COVID-19, specifically PCR test results and wastewater levels of COVID-19. This is the first study to investigate the utility of a RAT self-report tool, and the results will contribute robust evidence towards the role of RAT self-report results in COVID-19 surveillance.

Methods

Wastewater samples were collected and analyzed by Trent University in Peterborough. Wastewater levels of COVID-19 were measured in the region's primary municipal wastewater source, the City of Peterborough, using a normalized average of viral genes N1 and N2 (nmN1N2) (8).

The PCR test results were obtained from the Ontario Ministry of Health and Long-Term Care COVID-19 Testing Dashboard (9). The RAT results were obtained from the PPH online RAT self-report tool (10). The PCR and RAT results from Peterborough City and County were included in the analysis while only the wastewater data from the City of Peterborough were included.

This study did not require ethics approval as the data we analyzed is routinely collected by PPH for COVID-19 surveillance and is not reported on an individually identifiable basis.

Analysis

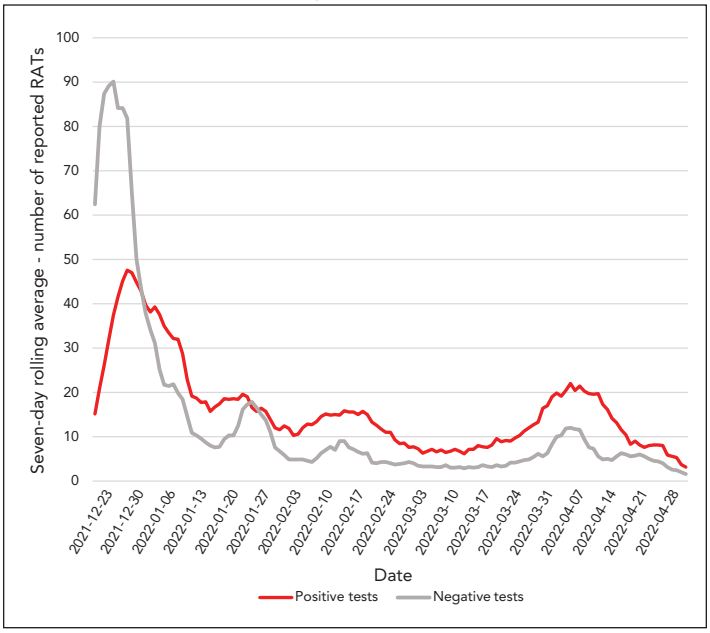
The relationship between RAT results, PCR results, and wastewater levels of COVID-19 was analyzed using Pearson's correlation. Both percent positivity as well as count of positive tests for RATs and PCR tests were analyzed. The data obtained for all three indicators were collected from December 17, 2021 to April 30, 2022; dates with missing data were excluded. All data were analyzed using R statistical software (11). The RAT, PCR test and wastewater data were screened for outliers and log-transformed to meet the assumption of a normal distribution for Pearson's correlation. A weak correlation was defined as a value between 0.2 and 0.39, while a moderate correlation was defined as between 0.4 and 0.59 (12).

Results

Descriptive results

From December 17, 2021 to April 30, 2022, 4,571 RAT self-report results were recorded and 2,138 responses were reported as positive. **Figure 1** summarizes the count of positive and negative RATs, **Figure 2** summarizes the percent positivity of PCR tests, RATs and wastewater nmN1N2 levels and **Figure 3** summarizes the count of PCR tests, RATs and wastewater nmN1N2 levels.

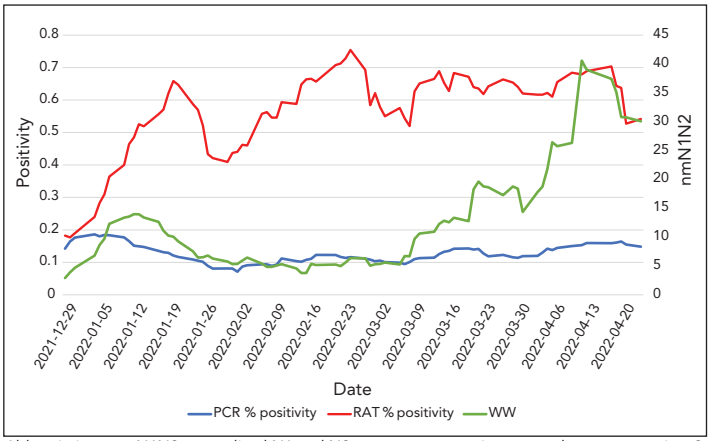
Figure 1: Seven-day rolling average of reported positive and negative rapid antigen test results, by date, in the Peterborough Public Health region, from December 17, 2021 to April 30, 2022



Analytical results

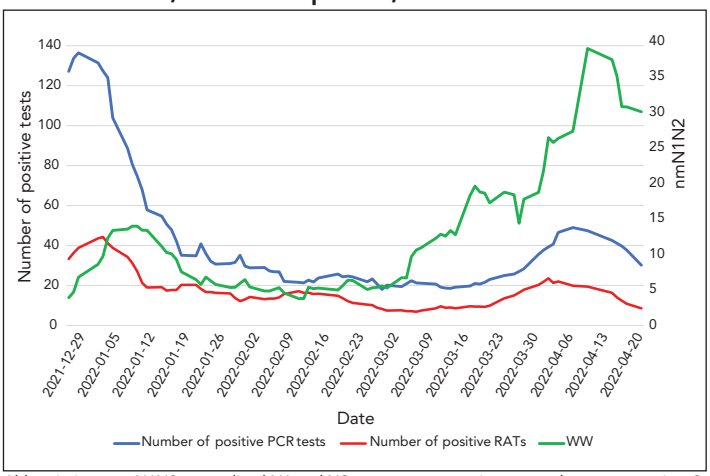
The PCR percent positivity and wastewater levels were weakly correlated (r=0.33, p=0.022), as were RAT percent positivity and wastewater (r=0.33, p=0.002); these results were statistically significant. The RAT percent positivity and PCR percent positivity were not significantly correlated to each other (**Table 1**).

Figure 2: Percent positivity of the polymerase chain reaction and rapid antigen tests and wastewater nmN1N2 levels by date, in the Peterborough Public Health region, from December 17, 2021 to April 30, 2022



Abbreviations: nmN1N2, normalized N1 and N2 severe acute respiratory syndrome coronavirus 2 genes; PCR, polymerase chain reaction; RAT, rapid antigen test; WW, wastewater

Figure 3: Count of positive polymerase chain reaction and rapid antigen tests and wastewater nmN1N2 levels by date, in the Peterborough Public Health region, from December 17, 2021 to April 30, 2022



Abbreviations: nmN1N2, normalized N1 and N2 severe acute respiratory syndrome coronavirus 2 genes; PCR, polymerase chain reaction; RAT, rapid antigen test; WW, wastewater

Table 1: Correlation matrix of rapid antigen and polymerase chain reaction test percent positivity and wastewater nmN1N2 levels from December 17, 2021 to April 30, 2022[a]

Indicators of COVID-19	RAT % positivity	PCR % positivity	Wastewater (nmN1N2)
RAT % positivity	1.0	N/A	N/A
PCR % positivity	-0.035 (p=0.75)	1.0	N/A
Wastewater (nmN1N2)	0.33 (p=0.002)	0.33 (p=0.022)	1.0

Abbreviations: COVID-19, coronavirus disease 2019; nmN1N2, normalized average of viral genes N1 and N2; N/A, not applicable; PCR, polymerase chain reaction; RAT, rapid antigen test
[a] Pearson correlation, r

Count of positive RATs and count of positive PCR tests were moderately correlated (r=0.59, p<0.001); this result was statistically significant. Wastewater was not significantly correlated to count of positive RATs or count of positive PCR tests (**Table 2**).

Table 2: Correlation matrix of count of positive RAT, count of positive PCR, and wastewater nmN1N2 levels from December 17, 2021 to April 30, 2022[a]

Indicators of COVID-19	Count of positive RAT	Count of positive PCR	Wastewater (nmN1N2)
Count of positive RAT	1.0	N/A	N/A
Count of positive PCR	0.59 (p<0.001)	1.0	N/A
Wastewater (nmN1N2)	0.019 (p=0.864)	0.004 (p=0.971)	1.0

Abbreviations: COVID-19, coronavirus disease 2019; nmN1N2, normalized average of viral genes N1 and N2; N/A, not applicable; PCR, polymerase chain reaction; RAT, rapid antigen test
[a] Pearson correlation, r

Discussion

Our study is the first to investigate the utility of a RAT self-report tool for COVID-19 surveillance. We found that both PCR percent positivity and RAT percent positivity were weakly correlated with wastewater levels of COVID-19, and that the count of positive RAT and count of positive PCR tests were moderately correlated. We did not find a significant correlation between PCR percent positivity and RAT percent positivity or the count of positive RATs and count of positive PCR tests with wastewater levels. A possible explanation for these results is that not everyone who contracts COVID-19 obtained a RAT or PCR test, as many cases were asymptomatic or testing access criteria had changed. In addition, a significant proportion of people with active COVID-19 infections shed the virus in their feces, sometimes before their symptoms start; this contrasts with the time lag associated with RAT and PCR testing (13). Previous studies have also indicated the incidence and persistence of viral shedding through feces even after a negative nasopharyngeal swab (14). These temporal differences, along with a lack of testing in some active cases, may offer explanation for why there was no significant correlation observed between the counts of positive PCR tests or RATs with wastewater levels.

Strengths and limitations

A key strength of our study is that we used data collected during the peak in cases during the Omicron wave in Ontario. Heightened public awareness of COVID-19 transmission as well as the launch of the PPH RAT self-report tool contributed to a high number of RAT self-report submissions and an overall robust dataset. An additional strength was our investigation of the utility of this RAT self-report tool compared with multiple indicators of COVID-19. This quantified the relative utility of the RAT self-report tool using correlations and suggested that, in a

complex landscape of COVID-19 surveillance, RAT self-reporting may present a helpful adjunctive surveillance tool at a minimal cost and administrative burden to public health organizations.

The main limitations in our study are the biases in reporting COVID-19 cases through both PCR testing and the RAT self-report tool. As mentioned, the restrictions on PCR testing to only high-risk individuals in late 2021 likely resulted in a significant under-representation of actual COVID-19 cases in the PCR data that we analyzed. In addition, the voluntary nature of self-reporting a RAT result introduces inaccuracies, as the PPH self-report tool likely only captured a fraction of actual positive and negative RAT results. Intermittent efforts to raise awareness of RAT self-reporting may result in fluctuations when the baseline reporting rates we observed were fairly low. A second limitation relates to availability of RATs. The RATs will continue to be distributed free of charge for the foreseeable future. If free tests are no longer readily available, the likely respondents would be further restricted to those who could afford or choose to purchase RATs. The role of differential positive reporting bias in the RAT self-report data necessitated the analysis of absolute numbers of positive RATs and trends over time as opposed to traditional measures such as percent positivity. This ultimately informed the decision to base the PPH COVID-19 Risk Index indicator on RAT based on the number of positive reports and continues to be assessed for utility over time.

The use of Pearson's correlation coefficient in our analysis also presents limitations; for example, the exclusion of potential confounding variables (15). In the future, a more robust statistical analysis could be conducted that would account for extraneous variables.

A final limitation in our study is that although the RAT and PCR test results were collected from the entire county, the wastewater data we analyzed was collected only from the City of Peterborough. Although these samples may have differed from other areas in the county, the City of Peterborough represents the majority of the PPH population and can, therefore, be used as a proxy for the PPH region in a geographically small region such as ours.

Implications for policy

The weak correlation that we found between RAT percent positivity and wastewater, as well as PCR percent positivity and wastewater nmN1N2 levels, suggests that RAT percent positivity can be used in COVID-19 surveillance; however, the limitations of this surveillance method must be explored. Further assessment through additional waves of COVID-19 is needed to understand temporality in RAT self-reporting signals. For instance, corroborative information of RAT percent positivity, PCR percent positivity and increasing wastewater nmN1N2 levels may be useful in reporting on changes in community transmission risk. Indeed, this is the reason that PPH has incorporated RAT testing into its COVID-19 Community Risk Index (16).

The moderate correlation between count of positive RAT and count of positive PCR tests suggests that the utility of RAT self-report results is greatest when using the count of positive RATs compared to percent positivity as a tool for COVID-19. In the event of further changes to PCR testing eligibility continuing to decrease, maintaining access to RATs and RAT self-reporting could be a complementary surveillance tool. These results could provide evidence in favour of the use of RAT self-report results in COVID-19 surveillance and support the potential for public health units across Canada to develop local RAT self-report tools.

With this being said, multiple surveillance tools are required to obtain the most accurate picture of pandemic risk. For example, PPH has developed a COVID-19 Risk Index to inform community members about the current risk for COVID-19 transmission (16). Six indicators (case rate, hospitalizations, deaths, PCR test positivity, positive RAT count, wastewater surveillance) are weighted to present an overall risk level with accompanying risk guidance. A key consideration in the use of COVID-19 surveillance tools such as the PPH COVID-19 Risk Index is to ensure public awareness of the complexities of COVID-19 surveillance; for example, adequate communication around limitations to interpreting each indicator is necessary.

In addition, some limitations surrounding reporting bias might be effectively addressed through collaboration between the public funder of RATs and local public health agencies; for example, exploring the potential for linking RAT promotion, distribution and surveillance through a coordinated mechanism, such as including a QR code on the test package linking to a survey.

Implications for research

We identified reporting biases as a risk to the use of data from RAT self-reports, yet further research is required to determine how public health units can encourage community members to report their RAT results. Additionally, further research on alternative surveillance tools is important as we progress through the pandemic given decreased access to PCR testing and reliability of their results to measure COVID-19 infections in the community. Finally, additional research is warranted to investigate which indicators are the most sensitive to change. From a visual analysis of our data (Figure 3), wastewater was the most sensitive COVID-19 indicator as it was the first to increase—coinciding with the start of wave 6 (March–April 2022). The RAT results have the next greatest sensitivity, with PCR being the least sensitive as it was the last indicator to show an increase. Further research evaluation is required to assess the sensitivity of each indicator to enable the earliest detection of an increase in COVID-19.

Conclusion

The ongoing COVID-19 pandemic has necessitated the use of numerous indicators and testing strategies to approximate levels of COVID-19 infections. Our results provide evidence that may support the use of RAT self-reports in COVID-19 surveillance.

The utility of RAT self-reports is likely greatest when considering count of positive RAT tests (when public availability of RATs is constant over time) rather than percent positivity due to reporting biases. The results from our study may inform the COVID-19 surveillance strategies of local public health units and encourage the use of a RAT self-reports as an adjunctive surveillance tool.

Authors' statement

ES — Analysis, writing, original draft, review, editing
CP — Analysis, review, editing, supervision
JAY — Analysis, review, editing
MK — Analysis, review, editing
JH — Study design and conception, review, editing, supervision
TP — Study design and conception, review, editing, supervision, funding

Competing interests

None declared.

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Quality over quantity in active tick surveillance: Sentinel surveillance outperforms risk-based surveillance for tracking tick-borne disease emergence in southern Canada

Camille Guillot[1,2,3]*, Catherine Bouchard[4], Kayla Buhler[5], Roxane Pelletier[6], François Milord[2,7], Patrick Leighton[1,3]

Abstract

Background: Lyme disease (LD) emerged in southern Québec at the start of the century, with many municipalities now endemic. A coordinated active surveillance programme has been in place in the province of Québec since 2014, including a limited number of sentinel field sites resampled each year and a larger set of accessory field sites that change yearly according to the LD surveillance signal. We aimed to evaluate whether a sentinel approach to active surveillance was more representative of LD risk to human populations, compared to risk-based surveillance.

Methods: We compared enzootic hazard measures (average nymph densities) from sentinel and accessory sites with LD risk (number of human LD cases) across the study area between 2015 and 2019 using local bivariate Moran's I analysis.

Results: Hazard measures from sentinel sites captured spatial risk significantly better than data from accessory sites (x^2=20.473, p<0.001). In addition, sentinel sites successfully tracked the interannual trend in LD case numbers, whereas accessory sites showed no association despite the larger sample size.

Conclusion: Where surveillance aims to document changes in tick-borne disease risk over time and space, we suggest that repeated sampling of carefully selected field sites may be most effective, while risk-based surveillance may be more usefully applied to confirm the presence of emerging disease risk in a specific region of interest or to identify suitable sites for long-term monitoring as LD and other tick-borne diseases continue to emerge.

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Keywords: tick surveillance, sentinel surveillance, tick-borne diseases

Affiliations

[1] Groupe de recherche en épidémiologie des zoonoses et santé publique (GREZOSP), Faculté de médecine vétérinaire, Université de Montréal, Montréal, QC

[2] Faculté de médecine et des sciences de la santé, Université de Sherbrooke,QC

[3] Centre de recherche en santé publique de l'Université de Montréal et du CIUSSS du Centre-Sud-de-l'Île-de-Montréal, Université de Montréal, Montréal, QC

[4] Public Health Risk Sciences Divisions, National Microbiology Laboratory, Public Health Agency of Canada, Saint-Hyacinthe, QC

[5] Department of Veterinary Microbiology, Western College of Veterinary Medicine, University of Saskatchewan, Saskatoon, SK

[6] Direction des risques biologiques, Institut national de santé publique du Québec (INSPQ), Montréal, QC

[7] Direction de santé publique, Centre intégré de santé et de services sociaux (CISSS) de Montérégie-Centre, Longueuil, QC

***Correspondence:**
camille.guillot@umontreal.ca

Introduction

Lyme disease (LD) is a tick-borne disease that has been emerging in southern Canada over the past three decades. *Ixodes scapularis* is the vector of *Borrelia burgdorferi*, the primary agent of LD in Canada, east of the Rocky Mountains (1,2). Populations of *I. scapularis* ticks, first established in the north-eastern and midwestern United States, have expanded their geographic distribution northward via migratory birds to invade southern Canada (3) with the first established populations appearing in Manitoba, Ontario, Québec and Nova Scotia (4). In response to this emerging health threat, public health authorities require effective surveillance systems to monitor the emerging risk of LD.

Active acarological surveillance, whereby forested field sites are sampled to collect questing ticks in the environment, is commonly used to assess enzootic hazard for LD (5). Active surveillance usually consists of drag sampling, where a piece of white flannel cloth is dragged across the forest floor such that questing ticks cling to the passing fabric, allowing them to be collected and analyzed. From such field studies, enzootic hazard is calculated as the density of nymphal ticks (DON) or density of infected nymphs (6,7). Density of nymphal ticks and density of infected nymphs have both been associated with LD risk in different studies in North America (8–11). Although some studies have evaluated the association between enzootic hazard and LD risk in southern Canada where LD is emerging, it is worth re-evaluating this link as the epidemiological portrait continues to evolve (10,12). In addition, because increasingly large regions of southern Canada need to be surveyed as *Ixodes* spp. continue to increase their geographic range, there is a growing need to adapt active surveillance approaches to ensure their sustainability and relevance within the evolving epidemiological context (13).

Due to complex ecological requirements, tick populations tend to expand their geographical range heterogeneously in space (14,15). To reflect this, active surveillance systems must be able to capture the spatially heterogenous LD risk pattern across a region. Some provincial public health authorities have developed risk-based criteria to decide which sites to target for surveillance whilst others visit the same sites repeatedly over time (16–18). Currently, it is not known which of these approaches best represents LD risk in space and time.

Among the ten provinces in Canada, Québec has the third-highest number of reported LD cases (19,20). Québec is the largest and second most populated province in Canada, with a total population of nearly 8.5 million (21). Most of the population resides in the south of the province, where the highest *I. scapularis* tick densities occur. In the past five years, the number of human LD cases has more than tripled, an increase that is consistent with the expanding geographic distribution of *I. scapularis* in southern Canada (22).

Active tick surveillance has been carried out in southern Québec since 2007, with the first coordinated provincial surveillance system established in 2014 by the *Institut national de santé publique du Québec* in collaboration with the Université de Montréal (18,23). From 2015 to 2019, active surveillance was carried out at two types of field sites: sentinel sites, which are kept constant through time and are visited every year, and accessory sites, which change every field season and are selected through a risk-based algorithm (24). These two types of sites were intended to serve different objectives within the surveillance program, with sentinel sites designed to provide a geographically representative surveillance signal allowing risk to be compared between regions and over time, and accessory sites selected each year to confirm the risk status of areas where LD was thought to be emerging. Sentinel surveillance was initiated in 2015 based on the hypothesis that repeated sampling of a small number of carefully selected sites could provide a more representative portrait of evolving LD risk at the provincial scale than annual risk-based surveillance. In addition, sentinel surveillance has several important logistical advantages, including reduced annual effort for site selection and lower overall sampling effort. However, the spatial and temporal representativeness of sentinel vs. risk-based surveillance have yet to be formally compared.

In this study, we analyzed LD surveillance data collected over a five-year period (2015–2019) to test the hypothesis that sentinel surveillance provides a more representative signal of LD risk in space and time than a risk-based approach, in the epidemiological context of pre-emerging/emerging LD risk in southern Québec.

Methods

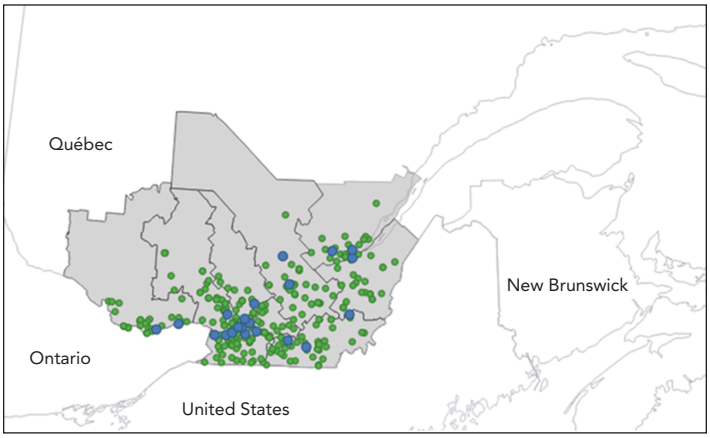
Study site

The province of Québec is in eastern Canada, located between the provinces of Ontario and New Brunswick. The ten most southern administrative regions of the province encompass the emergence zone for *I. scapularis* and are targeted annually by the *Institut national de santé publique du Québec* for active surveillance (**Figure 1**). This study analyzed data collected from 2015 to 2019 by active surveillance within this study zone.

Active surveillance in Québec

A network of 21 sentinel sites for the active surveillance of LD risk in the environment was designed by the Québec Tick-Borne Disease Expert Panel (*Groupe d'expert sur les maladies transmises par les tiques*), a panel bringing together public health authorities, laboratory experts, scientific and medical advisors and epidemiologists. Two sentinel sites were chosen per administrative region, except in Montréal where three sites were selected (Figure 1) (25). The sites were placed in provincial or

Figure 1: The ten most southern administrative regions in the province of Québec, constituting the active surveillance zone targeted[a] by the provincial Lyme disease surveillance program



[a] Blue dots represent sentinel site locations, with two sites per region, except the Montréal region with three sites. Green dots represent accessory sites sampled during the study period from 2015 to 2019

regional parks, which are readily accessible to the public, contain suitable habitat for the establishment of tick populations and are located in geographically distinct areas of the administrative region. These sentinel sites have remained the same throughout the study period (2015–2019) and were usually visited twice during the field season (May–August), the first time in early June, followed by a second visit at least two weeks later. Sites considered endemic for LD (one site in Montérégie and another in Estrie) were only visited once. Occasionally, other sites were only visited once per season due to logistical constraints (e.g. park closure).

In addition to the network of sentinel sites, 60–80 accessory sites were sampled once per field season. Accessory sites were selected according to the LD risk signal, generated from past passive and active acarological surveillance data and reported human cases. A standardized drag sampling protocol was carried out during each site visit, in both sentinel and accessory sites. Two field technicians dragged a 1 m^2 piece of white flannel cloth along two parallel transects: the first in the vegetation along the edge of a public footpath; and the second in the forest 25 m from the path. Each team member sampled 1,000 m^2 for total area sampled of 2,000 m^2 per site. Presence of ticks on the cloth was checked every 25 m and collected ticks were stored in tubes containing 70% ethanol. Subsequently, ticks were classified by species at the Québec Public Health Laboratory (*Laboratoire de santé publique du Québec*).

Human Lyme disease surveillance

Risk was calculated by the number of human LD cases reported at the municipal scale over the five-year study period, divided by the logarithm of human population size. A potential source of error is the misclassification of the municipality in which LD was acquired. As only half of LD cases recall have been bitten by a tick (26), it was sometimes difficult for individuals to identify the precise location where they acquired LD. However, in Québec, each LD case is subject to a public health investigation, which includes a review of the clinical and personal history of the patient to determine the most likely location of acquisition, limiting this source of error.

Statistical analyses

Enzootic hazard from active surveillance: The DON was calculated as a measure of enzootic hazard (24). Due to their small size, nymphs represent a greater hazard to humans as they are likely to be missed during self-examination (27). As tick densities are relatively low in southern Québec, we decided not to use density of infected nymphs, which may not be representative due to the low numbers of collected ticks.

Using seasonality models of *I. scapularis* phenology in southern Québec, we estimated standardized nymph densities for a reference date of June 15 (28). This allowed us to correct for temporal variability in nymph densities due to site visits occurring at different periods of the tick life cycle. We used these estimated nymph densities to compute the mean density per site across the study period. The data were georeferenced using the start location of the surveillance transect.

Densities of nymphs measured annually at both sentinel sites and accessory sites were interpolated across the study zone to generate a hazard map based on each type of surveillance. Interpolation was done using a Kernel density estimation (QGIS version 3.18; Zurich, Switzerland). A distance of 80 kilometres was used as the radius of interpolation, as correlogram-revealed spatial dependency of active surveillance data up to this distance (24,29). The resulting hazard maps were used to assign an estimated value of DON based on sentinel surveillance and risk-based surveillance to each municipality across the study zone.

Temporal association between enzootic hazard and LD risk

To assess the association between enzootic hazard (average nymph density) and LD risk (number of human LD cases) across the study period. Pearson correlations between these two variables were tested using R version 4.0.4 (30). The estimated DON was calculated at sentinel and accessory sites as described in the previous section. The resulting average nymph density derived from all sentinel or accessory sites in the same year was then correlated with total human cases reported that year.

Spatial association between enzootic hazard and LD risk

Bivariate local Moran's I analyses were performed using GeoDa 1.18.0 to determine the spatial association between enzootic hazard and LD risk. Bivariate local Moran's I can capture the relationship between a value of one variable in space, and the average neighbouring values for another variable (31). GeoDa creates cluster maps that determine if the spatial association between the variables is significant or not across municipalities. If significant, the maps indicate if 1) both

variables represent high values, 2) both represent low values or 3) one variable is a high value and the second is a low value. Furthermore, some municipalities may remain "undefined" if they do not have an attributed value of either one of the variables or be "neighbourless" if adjacent polygons are missing data.

The results from the Moran's I analyses were transcribed into a contingency table. From the contingency table, we were able to calculate if hazard measures were positively associated with risk as predicted (i.e. both risk and hazard are low or high), or if they diverged (i.e. risk is high whilst that hazard is low, or vice versa), for sentinel and accessory site hazard measures. Chi-square tests were performed to evaluate significant statistical differences in hazard-risk associations between site types.

Results

Active surveillance

A total of 197 site visits were conducted at sentinel sites between 2015 and 2019: 28 in 2015; 45 in 2016; 43 in 2017; 39 in 2018; and 42 in 2019. A total of 346 accessory site visits were carried out over the same period: 47 in 2015; 104 in 2016; 55 in 2017, 65 in 2018; and 75 in 2019. Average nymph density across the study period was 0.13 (0.10–0.16) nymphs/100 m^2 at sentinel sites and 0.08 (0.07–0.11) nymphs/100 m^2 at accessory sites. Sentinel sites identified the regions of Montérégie, Estrie and Outaouais as having the highest DON (**Table 1**), whereas for accessory sites, the highest DON were found in Outaouais followed by Montérégie. It is worth noting that for accessory sites in Mauricie-et-Centre-du-Québec, high average nymph density in 2016 was due to a single site where 2.17 nymphs/100 m^2 was recorded.

Table 1: Average nymph densities[a] for sentinel and accessory sites in the ten administrative regions included in the active surveillance system for Lyme disease in Québec, Canada, from 2015 to 2019

Admin region	Density of nymphs (nymphs/100 m^2)[b]					
	Year					Average
	2015	2016	2017	2018	2019	
Sentinel sites						
CN	0	0	0	0	0	0
MC	0.02 (0–0.05)	0.01 (0–0.03)	0	0	0	0.01 (0–0.01)
ES	0.74 (0–1.47)[c]	0.22 (0–0.43)[c]	0.27 (0–0.53)[c]	0.05 (0–0.1)	0.05 (0–0.1)	0.23 (0.11–0.35)[c]
MT	0.02 (0–0.05)	0.05 (0–0.1)	0.25 (0.09–0.41)[c]	0	0.1 (0.02–0.18)	0.09 (0.05–0.14)
OU	0.13 (0.09–0.17)	0.06 (0.02–0.1)	0.20 (0.15–0.25)[c]	0.03 (0.01–0.04)	0.85 (0.3–1.4)[c]	0.20 (0.10–0.30)[c]
CA	0	0	0	0	0	0
LV	0.02 (0–0.05)	0.01 (0–0.03)	0.01 (0–0.03)	0.03 (0–0.05)	0.05 (0.01–0.09)	0.02 (0.01–0.04)
LN	0	0	0.02 (0–0.03)	0	0	0.005 (0–0.01)
LA	0.04 (0–0.08)	0.04 (0.01–0.06)	0.11 (0.05–0.18)	0	0.02 (0–0.03)	0.05 (0.03–0.06)
MR	0.45 (0.02–0.88)[c]	0.38 (0.14–0.62)[c]	1.23 (0.55–1.90)[c]	0.47(0–0.93)[c]	0.05 (0–0.1)	0.57 (0.36–0.77)[c]
Accessory sites						
CN	0	0	0	0.05 (0–0.1)	0.01 (0–0.02)	0.01 (0–0.02)
MC	0	0.54 (0–1.09)[c]	0	0.01 (0–0.01)	0	0.06 (0–0.13)
ES	0.01 (0–0.02)	0	0.2 (0.05–0.35)	0	0.02 (0.01–0.04)	0.02 (0.01–0.04)
MT	0	0	0.06 (0–0.13)	0	0	0.02 (0–0.03)
OU	0	0.35 (0.13–0.57)[c]	0.81 (0.28–1.36)[c]	0	0	0.31 (0.31–0.49)[c]
CA	0	0	0	0	0.01 (0–0.01)	0.002 (0–0.004)
LV	0.01 (0–0.02)	0	0.06 (0–0.12)	0	0	0.02 (0–0.04)
LN	0	0	0.12 (0.01–0.23)	0	0.12 (0.001–0.25)	0.05 (0.02–0.09)
LA	0	0.002 (0–0.003)	0	0	0.03 (0.01–0.05)	0.005 (0–0.008)
MR	0.02 (0–0.04)	0.37 (0.28–0.46)[c]	0.05 (0.01–0.08)	0.01 (0–0.01)	0.01 (0.01–0.02)	0.19 (0.14–0.24)

Abbreviations: CA, Chaudière-Appalaches; CN, Capitale-Nationale; ES, Estrie; LA, Laurentides; LN, Lanaudière; LV, Laval; MC, Mauricie-et-Centre-du-Québec; MR, Montérégie; MT, Montréal; OU, Outaouais

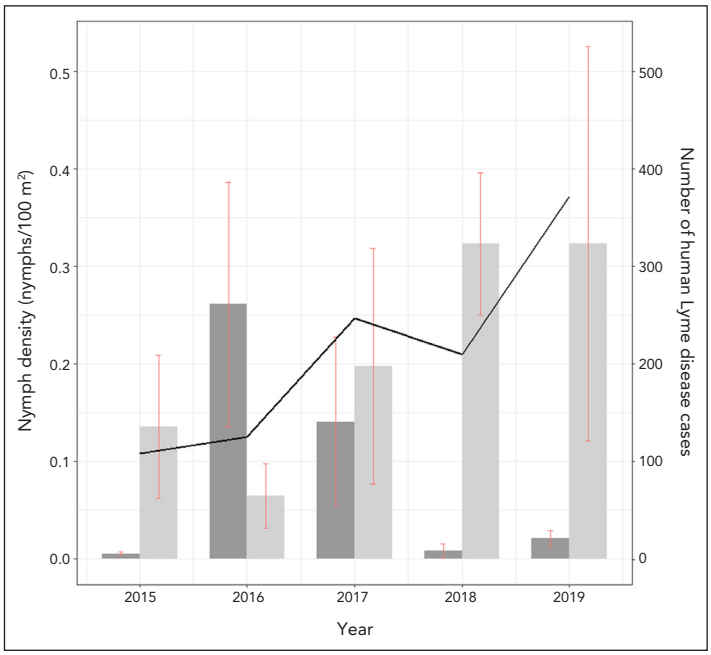
[a] 95% confidence intervals across the study period

[b] No colour: <0.20 nymphs/100 m^2

[c] Red: >0.20 nymphs/100 m^2

These densities were subsequently adjusted using the seasonality model to account for tick phenology prior to using the data for further analysis (**Figure 2**).

Figure 2: Average nymph density (nymphs/100 m²)[a] with standard errors at the provincial level in Québec, Canada, from 2015 to 2019[b]



[a] Adjusted using seasonality models for estimated densities on June 15
[b] Annual nymph densities measured at sentinel sites (light grey bars) and accessory sites (dark grey bars) are compared with the number of human Lyme disease cases in Québec (black line)

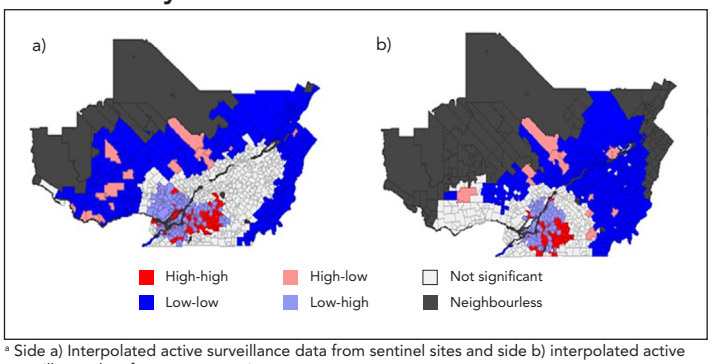
Statistical analyses

Correlation between enzootic hazard (average DON) and LD risk (number of human cases) showed a positive association (r=0.88; 95% CI, -0.02–0.99) for data obtained from sentinel sites. This association was weakly significant by Pearson's correlation test (p=0.05). In contrast, for data collected from accessory sites, the correlation between enzootic hazard and LD risk was negative (r=-0.32; 95% CI, -0.937–0.784) and not significant (p=0.60).

Interpolated data at the municipal level across Québec were used in local bivariate Moran's I to see if nymph densities collected during active surveillance methods were associated with the degree of LD risk (number of human cases/logarithm of the population (**Figure 3**). The cluster maps show whether there is significant spatial association between these two variables. Accessory site data had a greater proportion of non-significant classifications (n=490, 46.4%) compared to sentinel site data (n=348, 33.0%) (**Table 2**). Limited number of sampling sites during active surveillance meant that some of the study zone was undefined or neighbourless in the analyses, as no data was collected in these areas to incorporated within the analysis.

Within significant associations, some showed positive associations (both variables either "high" or "low") whilst others showed negative associations (one variable was "high" whilst the other was "low"). In the context of surveillance, positive associations between active surveillance and LD risk suggest reliability of active surveillance sites. In this analysis, sentinel sites showed positive association with LD risk for 388 municipalities (36.8%), whereas accessory sites showed positive association with LD risk for 302 (28.6%). The proportion of positive vs. negative association was significantly higher for sentinel vs. accessory sites (x^2=20.473, p<0.001).

Figure 3: Cluster maps derived from local bivariate Moran's I comparing human Lyme disease incidence with interpolated active surveillance data from sentinel and accessory sites[a]



[a] Side a) Interpolated active surveillance data from sentinel sites and side b) interpolated active surveillance data from accessory sites

Table 2: Outcome of local bivariate Moran's I for human cases data compared with active surveillance data from sentinel and accessory sites

Local bivariate Moran's I outcome	Sentinel	Accessory
Not significant	348	490
High-high	44	53
Low-low	344	249
Low-high	124	181
High-low	13	15
Neighbourless	17	22
Undefined	165	45
Totals		
Positive association	388	302
Negative association	137	196

Discussion

This paper demonstrates the ability of active surveillance at a limited number of high-quality sentinel sites to capture spatiotemporal LD risk trends in a context of emerging disease over a five-year period. In contrast, roughly twice the number of site visits carried out at accessory sites during this same period using a risk-based approach provided a less accurate geographic portrait of emerging risk and failed to capture the steep increase in human cases over time, even suggesting that risk had decreased rather than increased over the study period. Sentinel

and risk-based surveillance provide complementary information and serve different purposes within a surveillance system; this study demonstrates that the analysis and interpretation of the resulting surveillance data should take these differences into account. Specifically, where surveillance aims to document changes in tick-borne disease risk over time and space, we suggest that repeated sampling of carefully selected field sites may be most effective, while risk-based surveillance may be more usefully applied to confirm the presence of emerging disease risk in a specific region of interest or to identify suitable sites for long-term monitoring as LD and other tick-borne diseases continue to emerge.

In our analyses, we used enzootic hazard measures, in the form of nymph density collected at sentinel and accessory sites, to track the temporal trend in LD risk between 2015 and 2019. A Pearson correlation test at the provincial level demonstrated that average nymph density calculated from sentinel sites was positivity correlated with LD risk (number of human LD cases) (r=0.88), compared with average nymph density calculated from accessory sites where no significant correlation was found. As accessory sites change yearly, average nymph densities will not only account for interannual variation, but also for the heterogeneous spatial distribution of tick populations which make the yearly variation more difficult to interpret. However, as our study period was limited to five years, this result should be interpreted with caution. Furthermore, in previous research we noted that a positive association between nymph densities from sentinel sites and annual human cases was not always evident at the regional scale (e.g. in the Estrie region) (24). It would be interesting to explore the reasons for regional variation in this relationship; for instance, it is possible that the sentinel sites chosen in Estrie were not optimal to represent the epidemiological portrait at this scale. In the meantime, we suggest that average nymph density calculated from sentinel sites at a broader scale may be more robust and informative for evaluating interannual variation in LD risk.

The spatial relationship between enzootic hazard and LD risk was more reliably represented by sentinel sites compared to accessory sites. For both analyses, interpolation was used to permit representation of enzootic hazard across the full extent of the study zone; hence, the interpolation will not capture fine-scale heterogeneity in tick population establishment across space, which could subsequently lead to information bias. It is thus important to consider that sentinel surveillance provides a general risk indicator to follow spatiotemporal trends, whereas the targeted information derived from risk-based surveillance strategies may be more appropriate for confirming the establishment of endemic LD risk at the municipal scale (13). Areas where risk was not well captured by sentinel surveillance (e.g. the North Shore of Montréal) (see Figure 3) could subsequently be surveyed using an exploratory approach; risk-based surveillance (accessory sites) could be added to the surveillance strategy and the most informative sites retained as part of the sentinel system. While we show that two sentinel sites per administrative region were able to capture broad-scale trends in LD risk, increasing the number of sentinel sites per region would be useful in allowing better geographic representativeness and higher-resolution risk estimates. Another source of information bias could come from underreporting of LD cases, for instance in lower-risk areas due to reduced awareness of the public and clinicians. Previous studies suggest that this may not be a significant issue in Canada (32); however, this reiterates the advantage of having a longer time series or repeating a similar study to determine if the relationship between enzootic hazard and LD risk holds, especially as awareness of LD may change with time.

Sentinel surveillance for tick-borne disease in not a novel concept. Many studies, including some in southern Canada, have sampled sites repeatedly to determine geographic or ecological risk of LD associated with presence of ticks (33–35). In the United States, data from repeated field sampling have shown a positive correlation between density of infected nymphs and human cases (11); however, these sites were not part of a coordinated surveillance system. In Canada, field data from repeated site visits have been used to develop and evaluate indicators to determine the likelihood of establishment of *I. scapularis*, thus contributing to knowledge of hazard distribution (34, 36). A national sentinel surveillance system for tick-borne disease was launched in 2019 by the Canadian Lyme Disease Research Network (CLyDRN); however, the data generated from this new surveillance initiative remain to be analyzed (37). The surveillance system put in place in Québec, which uses both sentinel and risk-based surveillance, permitted the first comparative evaluation of these surveillance approaches in the southern Canada—an area where LD is emerging. As the epidemiological portrait of LD is fast evolving, the relationship between enzootic hazard measured at sentinel sites and LD risk may have to be re-evaluated regularly to determine if this relationship holds. Clow *et al.* (13) proposed a framework for surveillance of tick-borne diseases where surveillance is described as an adaptive process, with surveillance goals modified over time as the epidemiological context continues to evolve.

Strength and limitation

According to this framework, active surveillance at sentinel field sites is considered suitable for both the emergence and endemic phases of the disease process. Although we have shown the ability of sentinel sites to track spatiotemporal risk more reliably than accessory sites, this remains to be demonstrated for endemic regions. Furthermore, an important limitation of sentinel surveillance is its inefficiency in pre-emergence context; as sentinel sites are a small subset of possible surveillance locations, they have limited sensitivity for capturing early emergence signals. This highlights the complementary role of sentinel surveillance within larger surveillance network that includes other surveillance methods such as passive acarological surveillance (e.g. eTick) (10,38).

Conclusion

Our study demonstrated the capacity of sentinel surveillance to track spatiotemporal risk of LD in a region where the risk is spreading. In Canada, where tick-borne diseases continue to emerge, this study can support the planning of active surveillance strategies. Active surveillance at sentinel sites allows for comparable hazard measures through space and time, whilst limiting sampling effort to a restricted number of sites. A careful decision-making process must support site selection, to ensure that these are representative of the underlying epidemiological context and that the resulting data provide a robust portrait of emerging disease trends in space and time.

Authors' statement

CG — Conceptualization, methodology, analysis, interpretation, writing original draft, review and editing
PAL — Supervision, conceptualization, methodology, interpretation, review and editing
CB — Supervision, methodology, interpretation, review and editing
FM — Supervision, review and editing
KB — Review and editing
RP — Review and editing

Competing interests

None.

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RAPID COMMUNICATION

Community-based COVID-19 outbreak of the B.1.1.7 (Alpha) variant of concern in Newfoundland, February to March 2021

Alexandra Nunn[1]*, Andrea Morrissey[2], Ashley Crocker[2], Kaitlin Patterson[3], Joanne Stares[4], Kerri Smith[2], Laura Gilbert[5], Krista Wilkinson[6]

Abstract

Background: From March 2020 to January 2021, Newfoundland and Labrador experienced 408 coronavirus disease 2019 (COVID-19) cases (incidence 78 per 100,000). In February and March 2021, a community outbreak of the B.1.1.7 (Alpha) variant occurred in the Eastern Regional Health Authority. This article describes the epidemiology of this variant of concern outbreak, identifies settings that likely contributed to spread and informs recommendations for public health measures (PHMs).

Methods: Provincial surveillance data were linked with case interview data and a school class roster. Descriptive epidemiological methods were used to characterize the outbreak. Secondary attack rates (SAR) were calculated for households and classrooms.

Results: This outbreak involved 577 laboratory-confirmed and 38 probable cases. Whole genome sequencing determined cases were B.1.1.7. The median age was 31 years and the highest proportion of cases were in the 15 to 19-year age group (29%); 293 (51%) were female and 140 (24%) were asymptomatic upon identification. Early cases were linked to a high school, sports activities, a restaurant and social gatherings. As the outbreak progressed, cases were associated with household transmission, a daycare, healthcare settings and a workplace. The unadjusted SAR estimate among laboratory-confirmed cases was 24.4% for households and 19.3% for classroom exposures. When adjusted for other potential exposures, SAR estimates were 19.9% for households and 11.3% for classrooms.

Conclusion: This outbreak demonstrated how B.1.1.7 spread rapidly through a community with previously low COVID-19 transmission and few preventative PHMs in place. Implementation and compliance with school and community-based PHMs is critical for preventing transmission during outbreaks.

Affiliations

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

[2] Eastern Health, St. John's, NL

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

[4] Centre for Emergency Preparedness, Public Health Agency of Canada, St. John's, NL

[5] Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, St. John's, NL

[6] Vaccine Rollout Task Force, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
alexandra.nunn@phac-aspc.gc.ca

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Keywords: COVID-19, Canada, variant of concern, outbreak, emerging infectious diseases, household transmission, school transmission, secondary attack rates, public health measures

Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by severe acute respiratory coronavirus 2 (SARS-CoV-2). Variant of concern (VOC) refers to a SARS-CoV-2 lineage characterized by significant genetic mutations that affect its spread, severity, detection, prevention or treatment (1).

The B.1.1.7 (Alpha) VOC was first identified in England in September 2020. The first cases in Canada (Ontario) were identified in December 2020 (2). The B.1.1.7 variant was associated with significantly increased rates of transmission (3,4)

and increased disease severity (5,6) compared to non-VOC SARS-CoV-2.

One of the first community outbreaks of B.1.1.7 in Canada occurred in February 2021 among residents of Newfoundland and Labrador (NL)'s largest health authority, Eastern Regional Health Authority (Eastern Health), when Canadian health authorities had little experience with the prevention and control of VOCs. Evidence was accumulating about the effectiveness of personal public health measures (PHMs) such as handwashing, mask wearing and physical distancing, and societal PHMs such as quarantine (7).

Newfoundland and Labrador had observed only 408 cases of COVID-19 across the province from March 2020 to January 2021 (incidence: 78 per 100,000) (1). The outbreak of 577 laboratory-confirmed cases in the Eastern Health region occurred primarily in a census metropolitan area of 206,000 population (8) and did not extend into other parts of the province.

The outbreak was identified when a restaurant worker, with no known exposures, became symptomatic on February 4, 2021, and tested positive the following day. On February 6, patrons were advised to seek testing if they had attended the restaurant during the index case's incubation period (9). Mass testing within surrounding communities identified cases and clusters linked to other potential transmission settings.

This outbreak investigation aimed to describe the epidemiology, identify settings that likely contributed to spread and inform recommendations for PHMs. Evaluating the effectiveness of PHMs in various settings was out of scope.

Methods

Eastern Health led data collection and case finding via case interviews and contact tracing. Data sources included case and contact data from the provincial COVID-19 surveillance system, detailed case interview information, a school class roster and documentation of PHMs (e.g. web pages, press releases, and internal government documents).

The provincial definition of a laboratory-confirmed case (9) was a person with confirmation of infection with SARS-CoV-2 documented by:

- Detection of at least one specific gene target by a validated laboratory-based nucleic acid amplification test-based assay (e.g. real-time polymerase chain reaction or nucleic acid sequencing) performed at a community, hospital or reference laboratory (National Microbiology Laboratory or a provincial public health laboratory)

OR

- The detection of at least one specific gene target by a validated point-of-care nucleic acid amplification test that has been deemed acceptable to provide a final result (i.e. does not require confirmatory testing)

OR

- Seroconversion or diagnostic rise (at least fourfold or greater from baseline) in viral-specific antibody titre in serum or plasma using a validated laboratory-based serological assay for SARS-CoV-2

Outbreak cases resided in the Eastern Health region, met the provincial definition of a laboratory-confirmed case (9), had an episode date of February 1, 2021, to March 31, 2021 (inclusive), did not have an out-of-province travel history in the 14 days prior to the episode date, were not linked to a travel-associated case, and whose viral lineage was B.1.1.7 or not typed. Lineage assignments were determined in a subset of cases with sufficient viral load using pangolin v.2.2.2 (10), following whole genome sequencing on the Oxford Nanopore Technology GridION platform using a 1,200-base pair tiled amplicon scheme (11).

Cases with a positive lab test were interviewed by a public health nurse using a standardized form to identify potential exposures and contacts. The episode date for each case was the date of symptom onset or of specimen collection (if asymptomatic). Contacts were identified through case interviews as individuals who had close interactions with cases during the communicability period, starting 72 hours before the episode date.

Social network diagrams were used to explore connections between cases and identify clusters, defined as four or more cases epidemiologically linked to a setting where there was reasonable evidence of transmission (i.e. likely exposure to a case during their period of communicability).

Secondary attack rates (SAR) were calculated for households and school classrooms. The first laboratory-confirmed case in each household or classroom was considered the primary case, and any subsequent case was secondary if their onset occurred one to 14 days after the episode date of the primary case (or the last classroom exposure). Co-primary cases whose onset dates were the same as other primary cases were not considered secondary cases and were excluded from the SAR analysis. Household contacts of cases were identified in the provincial surveillance system. Classroom contacts were identified by the class roster, assuming perfect attendance. The SARs were calculated as the number of secondary cases divided by the number of contacts and represent the proportion of contacts who became cases. The unadjusted classroom SAR was calculated for all secondary cases in a classroom, and adjusted classroom SARs excluded school-associated cases who were secondary within their household or linked to other clusters.

An acquisition setting was assigned for each case, based on a hierarchy. Secondary cases in households were assumed to have acquired COVID-19 in their home, due to high proximity and duration of household contact compared to other settings. All other cases were categorized by their linkage to a cluster and its setting. No attempt was made to further distinguish the acquisition setting of cases linked to multiple clusters.

Public health measures were immediately implemented for containment, with incremental school closures and subsequently a province-wide lockdown beginning on February 12, including closure of all nonessential businesses and facilities, restrictions on gathering in groups over five, and restricted visitation to long-term care homes and assisted living facilities (12,13).

Analyses were completed in R/R Studio, using data accessed April 18, 2021 (14).

Results

There were 577 laboratory-confirmed and 38 probable cases in this outbreak. Of the confirmed cases, 183 (32%) were identified as B.1.1.7; the remainder were locally acquired and assumed B.1.1.7 as there had been no known community transmission prior to the outbreak. The median age was 31 years and the highest proportion of cases were in the 15 to 19-year age group (29%); 293 (51%) were female and 140 (24%) were asymptomatic upon identification (**Table 1**). The last episode date was March 28, 2021 (**Figure 1**).

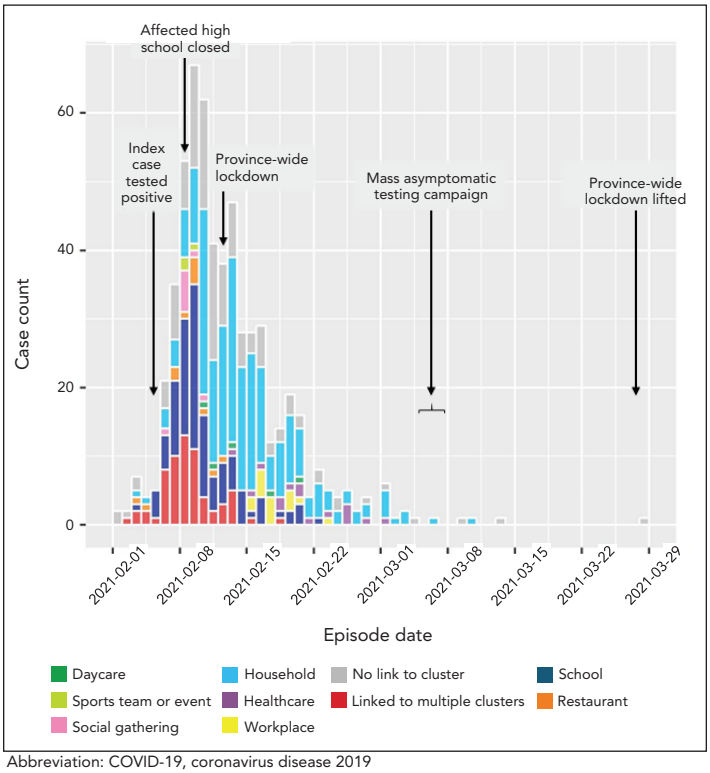
Table 1: Percent positivity by age group for COVID-19 testing performed from February 1 to March 31, 2021, during a COVID-19 B.1.1.7 variant of concern community outbreak in Newfoundland, Canada

Population tested, age (years)	Percent positivity (%)
Younger than 10	1.1
10–14	2.1
15–19	4.1
20–29	0.6
30–39	0.7
40–49	1.6
50–59	1.0
60 and older	0.7
All	1.2

Abbreviation: COVID-19, coronavirus disease 2019

There were 15 hospitalizations, seven intensive care unit admissions and two deaths associated with this outbreak. Most hospitalized cases were females (67%); none were younger than 40 years (**Table 2**). The two deaths occurred in males who were 75 years or older. One breakthrough case was identified following two doses of a messenger ribonucleic acid (mRNA) vaccine.

Figure 1: Epidemiologic curve for a COVID-19 B.1.1.7 variant of concern community outbreak in Newfoundland, Canada, 2021[a]



Abbreviation: COVID-19, coronavirus disease 2019
[a] By acquisition setting

Table 2: Demographics, symptoms and outcomes of laboratory-confirmed cases for a COVID-19 B.1.1.7 variant of concern community outbreak in Newfoundland, Canada, February 1 to March 31, 2021, (n=577)

Case characteristic		Count	Percent (%)
Age group (years)	Younger than 10	35	6
	10–14	51	9
	15–19	166	29
	20–29	30	5
	30–39	51	9
	40–49	125	22
	50–59	63	11
	60 and older	56	10
Sex	Female	293	51
Symptom status at time of identification	Asymptomatic	63	11
	Presymptomatic	77	13
	Symptomatic	437	76
Severe outcome(s)	Hospitalized	15	3
	Admitted to intensive care unit	7	1
	Death linked to COVID-19	2	Fewer than 1
	Not reported	561	97
Total		577	100

Abbreviation: COVID-19, coronavirus disease 2019

Provincially, the cumulative number of COVID-19 tests increased by 55% from February 1 (n=142,398) to March 31 (n=221,205), as contacts and community members were encouraged to be tested following exposure, sometimes multiple times during the incubation period. The maximum daily percent positivity was 5.3%. Youth aged 15 to 19 years had the highest percent positivity (4.1%) during the outbreak period (Table 1).

The index case was likely not the primary case, given that they had no history of travel or contact with travellers. The suspected primary case was a rotational worker who returned on January 14, followed all applicable provincial guidance, and tested negative on day seven. The rotational worker isolated at home—but not from their household contacts (per public health direction), who were among the earliest outbreak cases according to episode dates and had multiple potential community exposures. The rotational worker was identified as a symptomatic case after their household contacts tested positive, with symptom onset more than 14 days after travelling.

The number of contacts per laboratory-confirmed outbreak case ranged from zero to 189. The median number of contacts was eight prior to implementation of the province-wide lockdown order on February 12; thereafter, cases had a median of three contacts. Among the eight cases who had more than 100 contacts, their ages ranged from five to 17 years.

Twenty-five clusters of four or more confirmed cases were associated with settings, events or locations where transmission may have occurred. Households were the most common acquisition setting (39%), followed by a senior high school (18%) (**Table 3** and Figure 1). Approximately 21% of cases were not linked to a known cluster.

Table 3: Acquisition setting for laboratory-confirmed cases of a COVID-19 B.1.1.7 variant of concern community outbreak in Newfoundland, Canada, 2021 (n=577)

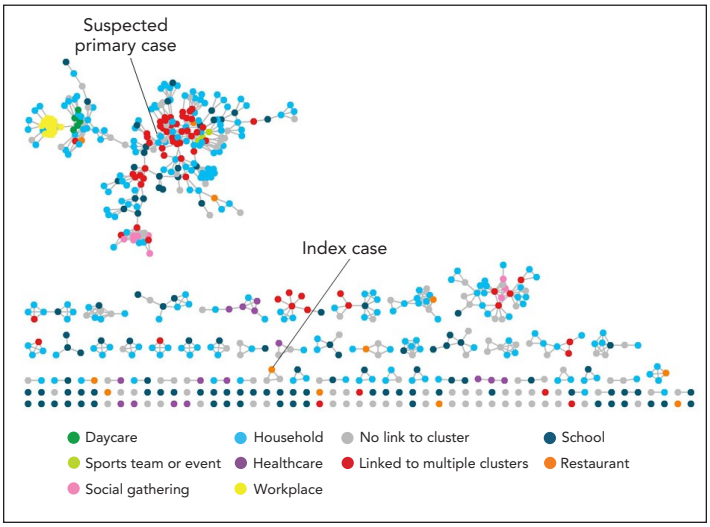
Acquisition setting	Count	%
Household	226	39
No link to cluster	122	21
School	106	18
Linked to multiple clusters	64	11
Healthcare	15	3
Workplace	15	3
Restaurant	12	2
Social gathering	9	2
Daycare	5	1
Sports team or event	3	1
Total laboratory-confirmed cases	577	100

Abbreviation: COVID-19, coronavirus disease 2019

Early cases in the outbreak were linked to school, sports activities/events, a restaurant and social gathering settings. As the outbreak progressed, cases were associated with household transmission, daycare, healthcare settings and a workplace (Figure 1).

A social network diagram (**Figure 2**) identified one large cluster and 25 smaller clusters of four or more cases. Figure 2 shows the connectivity of cases from contact tracing data and does not incorporate directionality or timing. Cases linked to multiple clusters (n=73) were centrally located among the largest clusters in the social network diagram; 68 (93%) were linked to the school, 44 (60%) to sports-related cluster(s), 36 (49%) to social gathering cluster(s) and 15 (21%) to the restaurant.

Figure 2: Social network diagram of laboratory-confirmed cases (n=577) for a COVID-19 B.1.1.7 variant of concern community outbreak in Newfoundland, Canada, 2021[a]



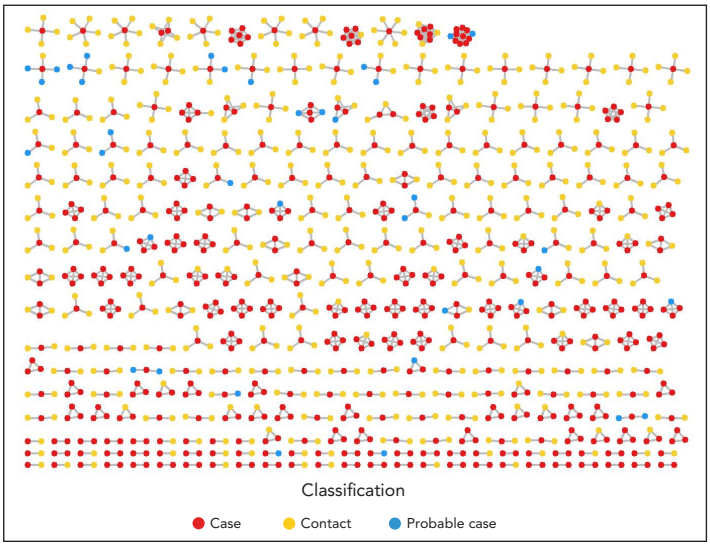
Abbreviation: COVID-19, coronavirus disease 2019
[a] By acquisition setting

The largest cluster of cases (n=183) was among individuals attending a senior high school, of which 167 (91%) were students and 16 (9%) were teachers or coaches. The number of COVID-19 cases per classroom ranged from zero to 19 (mean: 4.4).

Of all classroom groups in the school (n=298), 161 (54%) were exposed to a student or teacher case during their infectious period. Of the 945 students and teachers on the class list, 845 (89%) were exposed to an infectious student or teacher in their classroom, 17 (2%) were the primary cases in their classes and 163 (17%) became a confirmed case within 14 days following the last date of exposure in the classroom. Including all secondary classroom cases, the unadjusted classroom SAR was 19.3%. The adjusted classroom SAR was 17.8% when excluding those who were secondary cases within their household, and 11.6% when further excluding those linked to other clusters.

There were 308 households of two or more individuals that had at least one laboratory-confirmed outbreak case. Confirmed cases, probable cases and contacts were clustered by household in a social network diagram (**Figure 3**). The number of close household contacts per laboratory-confirmed outbreak case ranged from zero to 10 (median: 3). Transmission from a laboratory-confirmed primary household case to a laboratory-confirmed secondary household case appeared to have occurred in 119/308 (38.6%) households. The estimated household SAR was 24.4%. The adjusted household SAR was 28.5% when including probable cases and 19.9% when excluding secondary cases who were linked to other cluster types/settings.

Figure 3: Social network diagram of 308 household clusters for a COVID-19 B.1.1.7 variant of concern community outbreak in Newfoundland, Canada, 2021[a]



Abbreviation: COVID-19, coronavirus disease 2019
[a] By classification

Discussion

Introduction of B.1.1.7 into Newfoundland (the island portion of one of Canada's least populous provinces) likely occurred through travel, given its relative geographic isolation, border quarantine measures and absence of prior evidence of community transmission. It is hypothesized that a rotational worker who returned from work and followed all applicable provincial guidance may have had a false-negative screening test on day seven, and/or may have had a longer incubation period (more than 14 days). Alternatively, it is possible that B.1.1.7 was circulating undetected within the community from an earlier introduction, and was identified upon reaching a susceptible population, resulting in rapid spread (15).

Major contributors to spread were identified as 1) the vulnerability of a highly connected, unvaccinated population including school-aged youth, 2) household transmission within the community and 3) asymptomatic or presymptomatic transmission.

At the time of B.1.1.7 introduction, most adults and all youth were unvaccinated. Less than 2% of the province's population had received one dose at the beginning of the outbreak period (16), while a phased approach to vaccine rollout was underway (17). Although PHMs were in place (e.g. mandatory masking and restrictions on occupancy of indoor settings) (18,19), there were opportunities for community transmission in indoor settings such as restaurants, workplaces and private social gatherings.

Attendees of the senior high school had a high degree of connectedness due to in-person learning, no student or staff cohorting (i.e. students attended multiple classrooms with different teachers and students) and in-person extracurricular activities (e.g. sports tournaments). Non-medical masks (i.e. cloth masks or face coverings) were required in common areas but were not required in classrooms if students were distanced by at least one metre, and no requirements regarding ventilation and indoor air quality were in place for schools.

Evidence is conflicted regarding school-based transmission's contribution to community transmission (20–23). Data and modelling show that without robust mitigation measures, school settings with an effective reproduction number above one can contribute to growth of an outbreak (24). The school setting was likely a driver of community transmission; however, the unadjusted classroom SAR of 19.3% decreased to 11.6% when excluding those linked to household exposure or other clusters, suggesting uncertainty about how directly school-associated cases can be linked with classroom transmission given other potential exposures.

The classroom SAR estimates are comparable to a May 2020 high school outbreak in Israel (25), but higher than in-school SAR estimates reported in meta or regional analyses (26–28), reflecting overdispersion in transmission (29). High school outbreaks of this size were unusual in Canada (30,31); however, they have been documented elsewhere when PHMs were not in place or were not followed (25,32). School sports have also been associated with secondary transmission in high and middle school settings in the United States (33).

Although mask-wearing (and other measures) is associated with reduced transmission in schools (34), the masking requirements in place at the school did not appear to curb transmission. Closing the affected school and implementing community-wide restrictions on indoor gatherings were key interventions in containing this outbreak. Improved ventilation could also have contributed to reducing the risk of transmission (35). Subsequent household transmission from school-associated cases in this outbreak is consistent with survey data from the United States that demonstrated increased odds of COVID-19-like illness within households with children in full-time in-person schooling (36).

Household settings accounted for the highest proportion of exposures among laboratory-confirmed cases (39%). Compared to other Canadian estimates for non-VOC COVID-19 household

SARs (e.g. 20.2% in Ontario (37), and 14.7% in the Winnipeg Health Region (38)), the estimated household SAR of 24.4% in this outbreak appears higher, which may reflect increased transmissibility of B.1.1.7. A similar SAR of 25.1% was observed among B.1.1.7 cases in Ontario (37).

In this outbreak, 24% of cases were asymptomatic or presymptomatic (i.e. developed symptoms after testing positive). The younger age groups (zero to nine and 10 to 19 years) had the highest proportion of asymptomatic or presymptomatic infection, which is consistent with evidence that children and adolescents are more commonly asymptomatic or have mild, non-specific symptoms (22,39). Findings from this outbreak support asymptomatic testing as an important case finding intervention in outbreaks among children and youth.

Strengths and limitations

One strength of this investigation is the detailed analysis of potential transmission settings, possible because the outbreak was well contained in an area of low background transmission. There were several limitations to the study. First, the acquisition setting analysis was dependent on case interviews that may have been incomplete due to case volume, or subject to recall bias. Second, there may have been misclassification of COVID-19 lineage, since only 32% of cases were sequenced due to resource limitations. Similar to other jurisdictions (40), all locally acquired outbreak cases were managed thereafter as B.1.1.7. This potential misclassification means that when comparing attack rates in this outbreak to non-VOC outbreaks, the effect of B.1.1.7's increased transmissibility may be underestimated. Third, the analyses mostly excluded probable cases who tested negative, but clinical data suggests these symptomatic individuals who were contacts to laboratory-confirmed household cases were likely true cases (41). The SARs may have been underestimated due to the exclusion of probable cases. Fourth, although hypothesized, the primary case remains unknown.

Conclusion

This outbreak demonstrated how B.1.1.7 spread through an adolescent population and surrounding community with few preventative PHMs in place. Implementation and compliance with school- and community-based PHMs is critical to reduce the number of contacts and prevent transmission, particularly while vaccination coverage is low.

Authors' statement

AN, AM, AC, KP, JS, and KW contributed to conceptualization, analysis and interpretation of data. All authors contributed to drafting and revising the paper.

Competing interests

LG is a member of study teams that received funding from Roche Diagnostics and Seegene Inc. No other competing interests were declared.

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Integration of hospital with congregate care homes in response to the COVID-19 pandemic

Christina K Chan[1], Mercedes Magaz[1,2], Victoria R Williams[1], Julie Wong[3], Monica Klein-Nouri[3], Sid Feldman[4], Jaclyn O'Brien[1], Natasha Salt[1], Andrew E Simor[1,5], Jocelyn Charles[6,7], Brian M Wong[2,8], Steve Shadowitz[8], Karen Fleming[7], Adrienne K Chan[1,5], Jerome A Leis[1,2,5]*

Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has highlighted the need to improve the safety of the environments where we care for older adults in Canada. After providing assistance during the first wave, many Ontario hospitals formally partnered with local congregate care homes in a "hub and spoke" model during second pandemic wave onward. The objective of this article is to describe the implementation and longitudinal outcomes of residents in one hub and spoke model composed of a hospital partnered with 18 congregate care homes including four long-term care and 14 retirement or other congregate care homes.

Intervention: Homes were provided continuous seven-day per week access to hospital support, including infection prevention and control (IPAC), testing, vaccine delivery and clinical support as needed. Any COVID-19 exposure or transmission triggered a same-day meeting to implement initial control measures. A minimum of weekly on-site visits occurred for long-term care homes and biweekly for other congregate care homes, with up to daily on-site presence during outbreaks.

Outcomes: Case detection among residents increased following implementation in context of increased testing, then decreased post-immunization until the Omicron wave when it peaked. After adjusting for the correlation within homes, COVID-related mortality decreased following implementation (OR=0.51, 95% CI, 0.30–0.88; p=0.01). In secondary analysis, homes without pre-existing IPAC programs had higher baseline COVID-related mortality rate (OR=19.19, 95% CI, 4.66–79.02; p<0.001) and saw a larger overall decrease during implementation (3.76% to 0.37%–0.98%) as compared to homes with pre-existing IPAC programs (0.21% to 0.57%–0.90%).

Conclusion: The outcomes for older adults residing in congregate care homes improved steadily throughout the COVID-19 pandemic. While this finding is multifactorial, integration with a local hospital partner supported key interventions known to protect residents.

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Keywords: COVID-19, SARS-CoV-2, long-term care, infection prevention and control, IPAC, congregate care, retirement homes

Affiliations

[1] Infection Prevention and Control, Sunnybrook Health Sciences Centre, Toronto, ON

[2] Centre for Quality Improvement and Patient Safety, Temerty Faculty of Medicine, University of Toronto, Toronto, ON

[3] Meighen Health Centre, Toronto, ON

[4] Apotex Centre, Jewish Home for the Aged, Baycrest Health Sciences, Toronto, ON

[5] Division of Infectious Diseases, Department of Medicine, Sunnybrook Health Sciences Centre, Toronto, ON

[6] Veterans Centre, Sunnybrook Health Sciences Centre, Toronto, ON

[7] Department of Family and Community Medicine, Sunnybrook Health Sciences Centre, Toronto, ON

[8] Division of General Internal Medicine, Department of Medicine, Sunnybrook Health Sciences Centre, Toronto, ON

***Correspondence:**
jerome.leis@sunnybrook.ca

Introduction

Individuals who reside in congregate care (CC) homes, including long-term care (LTC) and retirement homes (RH), have been disproportionately affected by the coronavirus disease 2019 (COVID-19) pandemic in Canada (1–3). During the first wave of the COVID-19 pandemic, a greater proportion of COVID-19 deaths in Canada occurred in LTCs as compared to other countries in the Organisation for Economic Co-operation and Development (2).

Multiple system gaps were identified as contributing to extensive COVID-19 transmission in these homes, including lack of formal infection prevention and control (IPAC) programs and insufficient human and physical resources for resident care (4–7). A prior description of one of the first outbreaks of COVID-19 in Canada demonstrated how undetected rapid spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) occurred in homes that lacked surveillance and control measures (7).

In October 2020, Ontario Health, a government agency charged with connecting and coordinating the province's healthcare system, established a "hub and spoke" model where some hospitals were formally partnered with their local community CC homes to support IPAC (8). The objective of this study was to describe the implementation and longitudinal outcomes of residents in one hub and spoke program in Toronto, Canada.

Intervention

Sunnybrook Health Sciences Centre is an academic health sciences centre in Toronto that began to support on-site management of COVID-19 outbreaks in local CC homes as early as April 2020. The formalized hub and spoke model was funded by Ontario Health and officially launched on October 6, 2020, across north Toronto following a webinar between all partner organizations outlining expectations and available resources. The north Toronto hub team was composed of a 0.8 full-time equivalent (FTE) IPAC medical director, 1.0 FTE IPAC operations lead, 1.0 FTE IPAC coordinator per 280 LTC beds and 1.0 FTE IPAC coordinator per 600 RH beds. This team was integrated with the existing manager of strategy and integration for the hospital, and physicians from family medicine, general internal medicine and infectious disease as needed. The "spokes" consisted of 18 CC homes including 4 LTC (1,116 beds) and 14 RH or other CC homes (1,543 beds). There were 16 (88.9%) facilities with exclusively private rooms and nine (50.0%) that were for-profit organizations. Each home's leadership and internally appointed IPAC lead worked directly with the hub daily. Three facilities (two LTC, one RH) already had structured IPAC programs at baseline meaning that they had dedicated on-site IPAC personnel before the creation of the hub.

The intervention involved continuous seven-day per week access to the hospital hub to support IPAC, diagnostic testing and vaccine delivery and administration as needed. A secure group email was created to reach the hub, which was monitored continuously by hub members to ensure timely support. On-site visits occurred minimum weekly for LTC and biweekly for other CC homes, with up to daily on-site presence during outbreak periods. Active surveillance was performed minimum daily at each site and access to nasopharyngeal testing for SARS-CoV-2 polymerase chain reaction (PCR) testing was supported by the hospital hub as needed. Any confirmed case of COVID-19 among residents or exposure by staff who worked during their period of infectivity was reported to the hub and triggered a same-day virtual meeting to implement control measures and/or on-site visits as required. Support with collection of SARS-CoV-2 testing and clinical management was deployed as needed, including within-home treatment of residents and/or direct transfer to the hospital ward as appropriate.

Iterative improvements to IPAC were made in partnership with homes during site visits, across the hierarchy of hazard controls. Elimination controls focused on vaccination against COVID-19 for all residents and staff starting in December 2020, including supplying and administering the primary series and booster doses. Engineering controls included assessment and optimization of heating, ventilation and air conditioning systems as needed, installation of portable high-efficiency particulate air filters and limiting occupancy of shared rooms where possible. Administrative controls included deployment of standardized signage, and dedicated training of staff regarding personal protective equipment (PPE) use, hand hygiene, environmental cleaning and disinfection and other IPAC practises. Formal audits were performed by hospital hub using a standard tool adapted from the World Health Organization and Public Health Ontario (9,10). These audits included five IPAC components scored on a five-point scale each including hand hygiene, environmental cleaning, use of PPE, screening and adherence to physical distancing where appropriate (**Supplemental material, Table S1**).

Evaluation

A multicentre prospective quality improvement study was conducted comparing five study periods: baseline (wave one; March 1, 2020, to June 30, 2020), implementation period 1 pre-immunization (wave two; October 1, 2020, to December 31, 2020), implementation period 2 post-immunization (waves two and three; January 1, 2021, to May 31, 2021), implementation period 3 post-immunization (wave four; August 1, 2021, to December 14, 2021) and implementation period 4 post-immunization (wave five; December 15, 2021, to February 28, 2022). **Table 1** describes the broader context of each study period in terms of factors influencing the outcome of residents in CC homes, while **Table 2** provides the baseline characteristics of these homes during each period.

Table 1: Summary of COVID-19 context during the five study periods

Factors influencing outcomes of residents in congregate care settings	Baseline (Wave 1 pre-immunization, original virus)	Implementation period 1 pre-immunization (Wave 2, original virus)	Implementation period 2 post-immunization (Wave 2 and 3, Alpha variant)	Implementation period 3 post-immunization (Wave 4, Delta variant)	Implementation period 4 post-immunization (Wave 5, Omicron variant)
Community rate	Moderate[a]	Moderate[a]	Moderate[a]	Lowest[b]	Highest[c]
IPAC programs	None[c,d]	In place[b]	In place[b]	In place[b]	In place[b]
COVID-19 vaccine	None[c]	None[c]	Implemented (1–2 doses)[b]	2–3 doses[b]	3–4 doses[b]
Vaccine effectiveness	None[c]	None[c]	High (11) (63%–82% with 1 dose and 89%–92% with 2 doses)[b]	High (12) (87%–95% with 2 doses and 97% with 3 doses)[b]	Reduced (12) (61% with 3 doses)[a]
Vaccine protection against severe outcomes	None[c]	None[c]	High (11) (80%–87% with 1 dose and 82%–96% with 2 doses)[b]	High (11,12) (91%–98% with 2 doses and 99% with 3 doses)[b]	High (12) (95% with 3 doses)[b]
Therapeutics available	None[c]	Dexamethasone[b]	Dexamethasone Tocilizumab[b]	Dexamethasone Tocilizumab Remdesivir[b]	Dexamethasone Tocilizumab Remdesivir Sotrovimab Baricitinib[b]

Abbreviations: COVID-19, coronavirus disease 2019; IPAC, infection prevention and control
[a] Factors that conferred some protection of residents in congregate care settings are coloured yellow
[b] Factors that conferred significant protection of residents in congregate care settings are coloured green
[c] Factors that conferred no protection of residents in congregate care settings are coloured red
[d] Three congregate care homes had formal IPAC homes at baseline

Table 2: Characteristics of the 18 congregate care homes before and after implementation of "hub and spoke" program supporting response to the COVID-19 pandemic

Characteristics of congregate care homes	Baseline (Wave 1 pre-immunization, original virus)	Implementation period 1 pre-immunization (Wave 2, original virus)	Implementation period 2 post-immunization (Wave 2 and 3, Alpha variant)	Implementation period 3 post-immunization (Wave 4, Delta variant)	Implementation period 4 post-immunization (Wave 5, Omicron variant)
Staff					
Number of staff	2,389	2,259	2,208	2,454	2,632
Average number of staff in LTC	350	333	325	372	434
Average number of staff in RH	71	66	65	69	64
Staff vaccinated with 1 dose only, n (%)	N/A	N/A	494 (21.9)	418 (17.0)	3 (0.1)
Staff vaccinated with 2 doses only, n (%)	N/A	N/A	1,369 (58.5)	1,908 (77.8)	1,369 (51.7)
Staff vaccinated with 3 doses, n (%)	N/A	N/A	N/A	N/A	1,257 (47.5)
Residents					
Number of residents	2,325	2,134	2,043	2,108	2,231
LTC	1,034	912	852	890	931
RH	1,291	1,222	1,191	1,218	1,300
Age of residents, years, mean (SD)	84.5 (8.4)	85.1 (7.8)	84.9 (7.7)	83.8 (7.9)	86.6 (5.5)
Female residents, n (%)	1,408 (60.8)	1,291 (60.6)	1,274 (57.7)	1,251 (59.3)	1,311 (58.8)
Residents vaccinated with 1 dose only, n (%)	N/A	N/A	31 (1.5)	92 (4.4)	22 (1.1)
Residents vaccinated with 2 doses only, n (%)	N/A	N/A	1,925 (94.2)	1,910 (90.6)	183 (8.2)
Residents vaccinated with 3 doses, n (%)	N/A	N/A	N/A	N/A	1,981 (88.8)

Abbreviations: COVID-19, coronavirus disease 2019; LTC, long-term care; N/A, not applicable; RH, retirement home; SD, standard deviation

Process measures were prospectively tracked to assess implementation of interventions including number of emails received/sent by the hub, number of on-site visits for IPAC or testing or vaccination, number of town halls/webinars and number of virtual meetings.

The primary outcome was the incidence of COVID-19-related mortality among residents defined as the rate of death due to COVID-19 across the entire home. Attribution of death was based on the home's physician review and categorization reported to the local public health unit. Secondary outcomes included proportion of residents who developed laboratory-confirmed COVID-19, resident COVID-19 case fatality rate defined as death within 30 days of start of infection, staff COVID-19 infection rate defined as overall infection rate including community-acquired cases, the number of PCR tests performed per day (including testing of both residents and staff), and adherence to IPAC practises based on site audits by hospital hub IPAC specialists. Infection and mortality rates were calculated based on the number of residents residing in the home and the number of employees at the start of each study period. Dichotomous outcomes between different periods were compared using a logistic regression model that adjusted for correlation within homes. Scatter plot diagrams were used to visually compare IPAC practises across the five study periods.

As a secondary analysis, the primary outcome of the three facilities with pre-existing structured IPAC programs were combined as a control group, to assess for any difference compared to the remaining homes, both at baseline and during implementation. Finally, to partially address potential for survivor bias, a sensitivity analysis was performed where the analysis was repeated with the exclusion of residents with COVID-19 during wave one who survived from implementation period one.

Research ethics review to complete this evaluation was not required because the study met criteria for exemption as the project was deemed quality improvement and not human subject research.

Outcomes

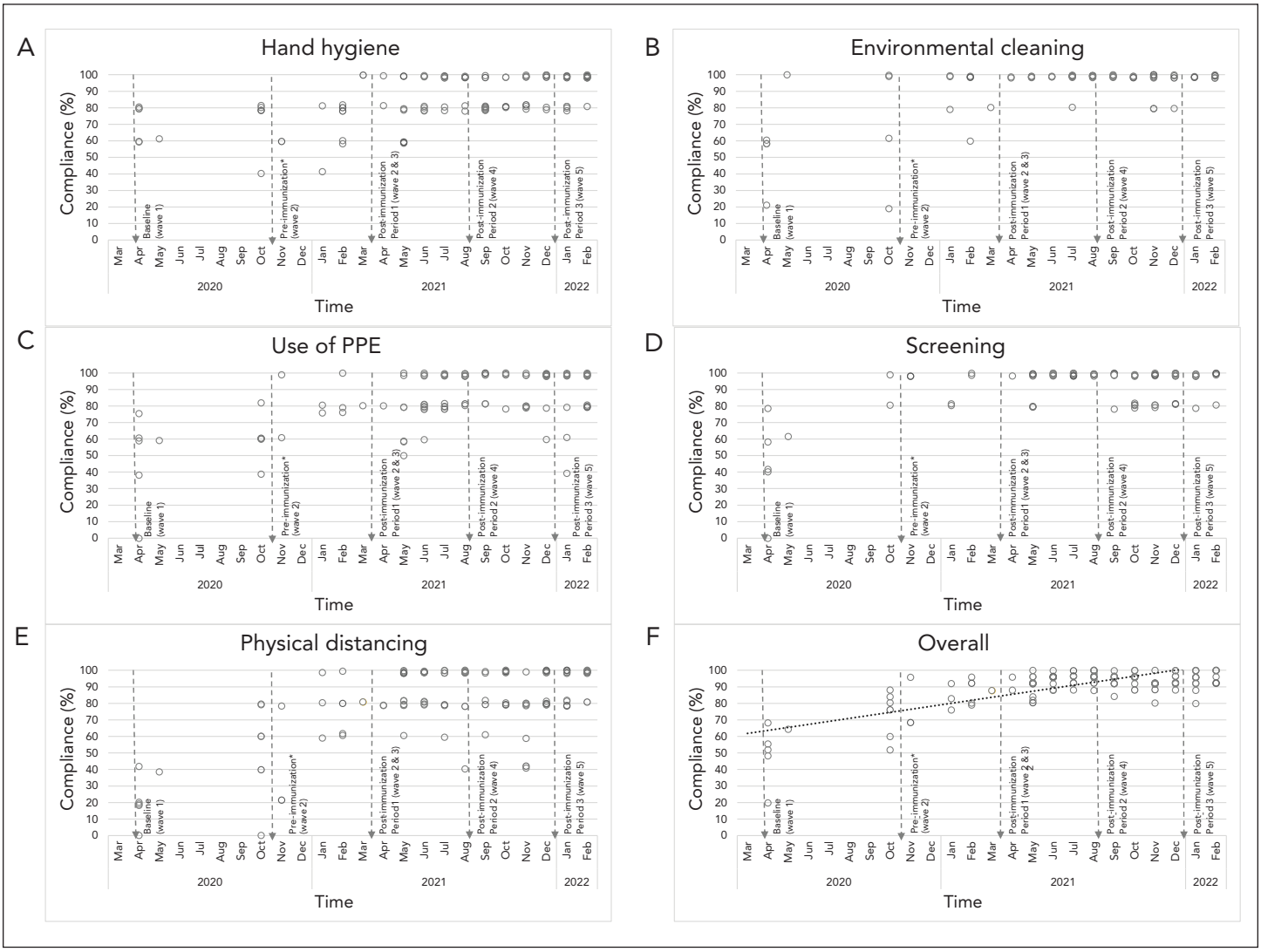
Table 3 summarizes the process measures of hub and spoke implementation. In total throughout the intervention, there were 4,051/4,142 emails sent/received by the hub, 631 on-site visits, 70 hub and spoke meetings, 9 town halls/webinar, 196 outbreak meetings, 49 vaccine support visits and 27 visits to support nasopharyngeal PCR testing. **Figure 1** depicts a scatter plot of adherence to IPAC practises over time where each point represents an on-site audit. Measurable improvements were observed across all areas, which were generally sustained (see trend line).

Table 3: Process measures in the 18 congregate care homes before and after implementation of "hub and spoke" program supporting response to the COVID-19 pandemic

Process measures	Baseline (Wave 1 pre-immunization, original virus)	Implementation period 1 pre-immunization (Wave 2, original virus)	Implementation period 2 post-immunization (Wave 2 and 3, Alpha variant)	Implementation period 3 post-immunization (Wave 4, Delta variant)	Implementation period 4 post-immunization (Wave 5, Omicron variant)
Total number of visits conducted by IPAC	N/A	98	193	209	131
Median weekly visits conducted by IPAC (IQR)	N/A	7 (3.8)	9 (4.0)	11 (2.5)	12 (2.0)
Total number of hub and spoke meetings	N/A	14	23	23	10
Median weekly hub and spoke meetings (IQR)	N/A	1 (0.0)	1 (0.0)	1 (0.5)	1 (0.5)
Total number of town halls/ webinars	N/A	6	1	2	0
Total number of outbreak meetings	N/A	50	58	16	72
Median weekly outbreak meetings (IQR)	N/A	4 (6.0)	4 (2.0)	1 (2.0)	6 (7.0)
Median weekly emails received from the homes (IQR)	N/A	27 (26.5)	66 (33.0)	26 (12.5)	154 (165.5)
Median weekly emails sent to the homes (IQR)	N/A	28 (21.5)	77 (37.0)	28 (9.5)	145 (99.0)
Total number of visits for vaccine support	N/A	N/A	24	15	10
Total number of visits for collecting PCR samples	N/A	16	8	0	3

Abbreviations: COVID-19, coronavirus disease 2019; IPAC, infection prevention and control; IQR, interquartile range; N/A, not applicable; PCR, polymerase chain reaction

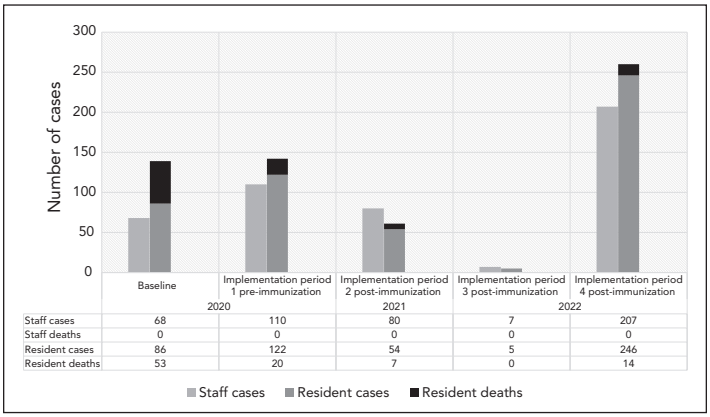
Figure 1: Scatter plots of the compliance with infection prevention and control practises of the 18 congregate care homes before and after implementation of "hub and spoke" program



Abbreviation: PPE, personal protective equipment

The primary and secondary outcomes are described in **Table 4** and the results of logistic regression are shown in **Table 5**. **Figure 2** also depicts the total number of residents and staff cases as well as deaths during the study periods. The COVID-19-related mortality in residents decreased in implementation period 1 (OR=0.51, 95% CI, 0.30–0.88; p=0.01), which was sustained throughout the implementation periods. Resident case fatality decreased steadily from 38.1% at baseline to a nadir of 0%–5.1% (OR=0.08, 95% CI, 0.03–0.20, p<0.001). In the context of increased PCR testing (Table 4), resident case detection increased (OR=1.32, 95% CI, 1.02–1.71, p=0.03) during implementation period 1, then decreased post-immunization until the Omicron wave (period 4) when it peaked (OR=2.20, 95% CI, 1.75–2.77, p<0.001).

Figure 2: Number of COVID-19 resident and staff cases across 18 congregate care homes following implementation of "hub and spoke" program



	Baseline	Implementation period 1 pre-immunization	Implementation period 2 post-immunization	Implementation period 3 post-immunization	Implementation period 4 post-immunization
Staff cases	68	110	80	7	207
Staff deaths	0	0	0	0	0
Resident cases	86	122	54	5	246
Resident deaths	53	20	7	0	14

Abbreviation: COVID-19, coronavirus disease 2019

Table 4: Resident and staff outcomes in the 18 congregate care homes before and after implementation of '"hub and spoke" program supporting response to the COVID-19 pandemic

Outcome measures	Baseline (Wave 1 pre-immunization, original virus)	Implementation period 1 pre-immunization (Wave 2, original virus)	Implementation period 2 post-immunization (Wave 2 and 3, Alpha variant)	Implementation period 3 post-immunization (Wave 4, Delta variant)	Implementation period 4 post-immunization (Wave 5, Omicron variant)
Resident COVID-19-related mortality	2.3%	0.9%	0.3%	0.0%	0.6%
Resident case fatality rate	38.1%	14.1%	11.7%	0.0%	5.1%
Proportion of residents positive for SARS-CoV-2 by PCR[a]	6.0%	6.7%	2.9%	0.1%	11.4%
Percentage of staff positive for SARS-CoV-2 by PCR[a]	2.8%	4.9%	3.0%	0.0%	7.4%
Number of PCR tests for SARS-CoV-2 per 100 residents and staff—total (daily average)	314 (2.6)	5,214 (57.3)	4,048 (27.1)	390 (2.9)	1,875 (25.0)

Abbreviations: COVID-19, coronavirus disease 2019; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2
[a] Overall positivity-rate inclusive of community-acquired cases

Table 5: Logistic regression analysis, adjusting for correlation within homes, of outcome measures across 18 congregate care homes before and after implementation of "hub and spoke" program[a]

Outcome measure	OR	95% CI	*p*-value
COVID-19-related mortality			
Implementation period 1 pre-immunization (wave 2, original virus)	0.51	0.30–0.88	0.01
Implementation period 2 post-immunization (waves 2 and 3, Alpha variant)	0.18	0.08–0.40	<0.001
Implementation period 3 post-immunization (wave 4, Delta variant)	N/A	N/A	N/A
Implementation period 4 post-immunization (wave 5, Omicron variant)	0.23	0.12–0.43	<0.001
Case fatality rate			
Implementation period 1 pre-immunization (wave 2, original virus)	0.52	0.16–1.72	0.28
Implementation period 2 post-immunization (waves 2 and 3, Alpha variant)	0.30	0.08–1.12	0.07
Implementation period 3 post-immunization (wave 4, Delta variant)	N/A	N/A	N/A
Implementation period 4 post-immunization (wave 5, Omicron variant)	0.08	0.03–0.20	<0.001
Cases detected among residents			
Implementation period 1 pre-immunization (wave 2, original virus)	1.32	1.02–1.71	0.03
Implementation period 2 post-immunization (waves 2 and 3, Alpha variant)	0.53	0.39–0.73	<0.001
Implementation period 3 post-immunization (wave 4, Delta variant)	0.021	0.01–0.07	<0.001
Implementation period 4 post-immunization (wave 5, Omicron variant)	2.20	1.75–2.77	<0.001

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; N/A, non-applicable because no resident deaths during implementation period 3; OR, odds ratio
[a] Baseline (wave 1 pre-COVID-19 immunization, original virus) is the reference category

In secondary analysis, homes without pre-existing IPAC programs had higher baseline COVID-related mortality rate (OR=19.19, 95% CI, 4.66–79.02; $p<0.001$) and saw a larger overall decrease during implementation (3.76% to 0.37%–0.98%) as compared to homes with pre-existing IPAC programs (0.21% to 0.57%–0.90%) (Supplemental material, **Table S2**). In the sensitivity analysis, the reduction in COVID-related mortality among all CC homes remained significant following implementation of the intervention (Supplemental material, **Table S3**).

Discussion

In the present prospective study, the outcomes of residents across LTC, RH and other CC homes across northern Toronto improved steadily following wave one of the COVID-19 pandemic. Multiple factors likely contributed to better resident outcomes. Prior to COVID-19 vaccination being available in late 2020, these factors likely included earlier detection of cases through surveillance and testing, earlier initiation of supportive therapy, better coordination for those requiring transfer to hospital and increased human resources to support care needs. In addition, dexamethasone and tocilizumab utilization and changes in mechanical ventilation strategies for those transferred to hospital during the second wave onward were recognized interventions that led to improved outcomes of the most severe forms of COVID-19 (13–15). In the post-immunization period, resident outcomes improved further owing to high vaccine uptake including timely booster doses, along with the apparent association of the Omicron variant causing less severe disease, as well as broader access to therapeutics.

The implementation of the hub and spoke program helped to support many of these interventions, including adherence to IPAC practises, clinical management and vaccine delivery, and in doing so may have contributed to improved outcomes. Our program implementation was similar to others in both Canada and the United States that contributed to improved resident outcomes in LTC subsequent to the first wave of the COVID-19 pandemic (16–19). In Seattle, Washington, where the first reported LTC outbreak occurred in early 2020, a health system response was implemented that included improved communication around the status of LTC homes, early testing and isolation when COVID-19 cases were suspected in the home, and deployment of an on-site team in the case of a COVID-19 outbreak (19). One key difference with our hub and spoke model is that our team was on-site even in the absence of COVID-19 activity, working in partnership to strengthen IPAC in anticipation of future pandemic waves. We prospectively measured quantitative improvements in various IPAC practises over time.

A number of important insights arose during implementation of this model of care. First, the weekly meetings and on-site visits created a strong partnership that resulted in improved coordination at multiple levels. For example, surveillance and testing were facilitated resulting in improved turnaround times from specimen collection to result reporting. These newly detected cases were managed in real-time and residents with acute illness were identified based on early warning signs, and in many instances, we were able to facilitate transfers to the hospital directly to an inpatient unit while bypassing the emergency department. Second, the use of virtual platforms allowed teams from multiple institutions to meet seamlessly across different physical locations and to provide consultative services to residents and families in their home. At the same time, we found that virtual care was not a substitute to going on-site to assess IPAC practises and residents in-person on a regular basis. One of our program successes was the on-site presence that is crucial to supporting implementation within the workflow of the home. Third, the adoption of this model resulted in better coordination of resources compared to each CC home navigating the COVID-19 pandemic on its own. For example, the improved visibility around the IPAC status of each home in north Toronto allowed for both hospital and other community care agency resources to be deployed to homes in response to their needs, which prevented critical shortages in human resources and supplies that were seen during the first wave of the COVID-19 pandemic (4,7).

Limitations

Our study has several important limitations. First, it is an observational study describing program implementation and the resident outcomes may be influenced by other confounding factors including the changing context of the pandemic outlined in Table 1. However, many of these protective measures were facilitated through the hub and spoke model. In addition, similar improvements were not observed in the homes with pre-existing IPAC programs, suggesting that the IPAC capacity-building contributed to the improved outcomes among homes that lacked formal IPAC programs at the start of the pandemic. Second, we cannot fully exclude the role of survivor bias leading to improved outcomes in these homes following wave one of the pandemic; however, a sensitivity analysis, which at least partially adjusted for this, still found a significant improvement in resident outcomes following implementation of the intervention. Finally, this evaluation focused only on one hub and spoke intervention implemented in Ontario, Canada, and implementation may have varied elsewhere. Nevertheless, our evaluation provides lessons learned regarding successful implementation of this model.

Conclusion

The outcomes of older adults residing in CC homes steadily improved throughout the first two years of the COVID-19 pandemic. While this finding is multifactorial, integration with the local hospital partner supported key interventions known to protect residents. Further longitudinal support in IPAC is needed beyond the COVID-19 pandemic to improve the safety of CC environments in Canada.

Authors' statement

CKC and MM contributed equally to the article and are considered co-lead authors.

All authors had access to the data and contributed to the preparation of this manuscript.

Competing interests

JAL has received payment for expert testimony requested by hospitals of the Ontario Hospital Association, Seneca College, and Ministry of the Attorney General of Ontario. No other competing interests declared.

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Supplemental material

These documents can be accessed on the Supplemental material file.

Table S1: Infection prevention and control audit tool for congregate care homes
Table S2: Resident COVID-19-related mortality in congregate care homes with or without pre-existing infection prevention and control program before the pandemic
Table S3: Sensitivity analysis comparing baseline versus implementation period 1 with COVID-19 recovered residents excluded

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Treatment of severe human mpox virus infection with tecovirimat: A case series

Koray K Demir[1], Michaël Desjardins[1,2,3], Claude Fortin[1,2], Simon Grandjean-Lapierre[1,2,3], Arpita Chakravarti[1,2], François Coutlée[1,2,3], Gerasimos Zaharatos[4], Jean Morin[5], Cécile Tremblay[1,2,3]*, Jean Longtin[6]

Abstract

Background: Tecovirimat (TCV, TPOXX®) is an orthopox-specific antiviral drug indicated for the treatment of smallpox. There is also a mechanistic basis for its use in mpox infection. However, its approval was based on animal studies, and its efficacy and side-effect profile in human patients with disease is unknown.

Methods: During the 2022 international mpox epidemic, clinicians in Canada were permitted by Health Canada to access TCV for severe cases of mpox disease. We describe the use of TCV in nine adults with severe mpox virus infection in Montréal, Canada.

Results: Five patients were treated for severe and potentially life-threatening head and neck symptoms, while four were treated for genitourinary or anorectal disease. Two-thirds of patients were also treated for suspected bacterial superinfection. All patients recovered (median time to resolution of severe symptoms: nine days) without relapse or hospital readmission. No patients reported adverse events attributable to TCV and no patients stopped their treatment early.

Conclusion: Our experience suggests that TCV is well tolerated and may accelerate recovery in severe cases. These preliminary, observational data may also be explained by concomitant treatment for superinfection and are limited by the absence of a control group. Controlled, clinical trials should be conducted to clarify the attributable benefit of TCV in severe mpox infection.

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Affiliations

[1] Division of Infectious Diseases, Department of Medicine, Centre Hospitalier de l'Université de Montréal, Montréal, QC

[2] Department of Microbiology, Immunology and Infectious Diseases, Université de Montréal, Montréal, QC

[3] Hospital Research Centre, Centre Hospitalier de l'Université de Montréal, Montréal, QC

[4] Division of Infectious Diseases, Department of Medicine, Jewish General Hospital, Montréal, QC

[5] Pharmacy Department, Centre Hospitalier de l'Université de Montréal, Montréal, QC

[6] Division of Infectious Diseases, Department of Medicine, CHU de Québec, Québec City, QC

***Correspondence:**
cecile.tremblay@umontreal.ca

Introduction

The mpox virus is an orthopoxvirus that causes human mpox infection, a disease classically characterized by systemic symptoms associated with a disseminated vesiculo-pustular rash. Though most cases are self-limited, severe illness and death can occur in a subset of the population, depending on the viral clade and patient-specific risk factors (1). Fortunately, the case fatality rate in the ongoing 2022 international outbreak has been below 1%, though severe symptoms requiring emergency consultation and hospitalization have been frequently reported (2). Patients do not typically receive specific antiviral therapy, as effective treatments for mpox have not generally been widely available.

Tecovirimat (TCV, TPOXX®, formerly ST-246) is a first in class antiviral drug that was designed for the treatment of variola virus, which causes smallpox in humans. Its molecular target, the p37 protein, is a highly conserved molecule among orthopoxviruses which is responsible for transit of virions outside the cell and is indispensable for virulence (3). Because variola virus is no longer in circulation, clinical efficacy was extrapolated from animal studies in which subjects were inoculated with other orthopoxviruses, including lethal doses of mpox in non-human primates. In these experiments, survival was 95% among non-human primates infected with mpox that received TCV, as compared to 5% in non-human primates that received

placebo, with benefits also seen in number of lesions and viral load (4). A subsequent clinical trial in healthy human volunteers confirmed that a treatment course of 14 days was generally well tolerated, with only 1% of patients discontinuing treatment due to adverse events associated with TCV (4). Based on these data, the United States Food and Drug Administration approved TCV under its Animal Rule in 2018 (5).

To our knowledge, TCV had only been used in disparate, exceptional circumstances for the off-label treatment and prophylaxis of different orthopoxviruses (6–10). Its use in multiple patients with severe manifestations of disease has not been reported. We describe the outcomes of nine patients with severe mpox infection who received TCV as part of their treatment.

Methods

In May 2022, multiple outbreaks of mpox virus infection were reported among gay and bisexual men in Europe and North America. Since then, over 60,000 cases have been declared in 104 countries (11). In Canada, Montréal was quickly recognized as the national epicentre of the 2022 mpox epidemic, with nearly all Canadian cases being concentrated in the city's downtown area.

In response to the growing number of cases in Montréal, a multifaceted public health campaign was launched, including variola immunization for people at high risk of infection and community awareness efforts in 2SLGBTQI+ venues. In addition, the federal government authorized the use of TCV for certain cases under a special access program, requiring centralized approval from a coordinating infectious diseases physician and pharmacist. Since mpox is a generally self-limited illness, TCV was restricted to patients who were deemed to have severe symptoms, or in other exceptional circumstances, at the judgment of the treating infectious diseases specialist.

To be eligible to receive TCV, patients were first required to have polymerase chain reaction-confirmed orthopoxvirus infection in at least one clinical specimen. Testing was performed at the provincial public health laboratory (*Laboratoire de santé publique du Québec*, Montréal, Québec) using primers and probes specific for human orthopoxviruses, which in the current epidemiologic setting were considered diagnostic of mpox infection. Confirmatory testing with an mpox-specific polymerase chain reaction assay was performed subsequently at the National Microbiology Laboratory, in Winnipeg, Manitoba.

Two Letters of Authorization were issued by Health Canada pursuant to C.08.010 of the Food and Drug Regulations Special Access Programme, authorizing the use of TCV for emergency treatment of patients. Informed consent was obtained from eligible individuals to ensure they were well informed of the possible risks and benefits of the drug and its development status and that a report on the outcome and results would be provided to Health Canada. The Council for International Organizations of Medical Sciences form was used to report any serious and/or unexpected adverse drug reactions.

Eligible and consenting patients received TCV free of charge at a dose of 600 mg by mouth, twice daily for 14 days as part of their clinical care. All patients were followed until the end of therapy to determine their clinical evolution.

Results

Between May 12 and June 14, 2022, mpox infection was confirmed in 135 individuals in the Province of Québec, Canada. Nine patients (7%) presented with severe symptoms of mpox infection and received TCV. All patients were adult men (mean age: 40 years) who acquired their infection after sexual contact with other men. Five patients (55%) were people living with human immunodeficiency virus (HIV) and on antiretroviral therapy at the time of infection, with undetectable HIV viral loads and a median CD4 cell count of 513 cells/uL. One patient had a CD4 cell count of 100 cells/uL. No patient had received smallpox immunization prior to their infection, though one patient had received the non-replicating, third generation smallpox vaccine (Imvanune®) the day he presented to care with active lesions.

Patients received TCV a median of nine days after onset of symptoms. Five patients were considered to have severe head and neck symptoms (including dysphagia and dysphonia) including one patient who presented with trismus and one with a peritonsillar abscess. Four patients were treated for highly symptomatic genital and/or anorectal lesions. Six patients were concomitantly treated for bacterial superinfection, of whom two had positive throat cultures for *Streptococcus pyogenes*. Three patients were hospitalized during their care. None required admission to the intensive care unit or surgical intervention during their stay. The full characteristics of patients are shown below in **Table 1**.

At the time of writing, all patients experienced resolution of the symptoms that justified TCV use (median length of use prior to recovery: nine days). No patients were re-hospitalized for clinical deterioration and no patients died. No patients described adverse drug reactions attributable to TCV and no patients stopped the medication early.

Table 1: Clinical characteristics of the patients at baseline

Characteristic	Patients (n=9)	%
Mean age, years (range)	40	29–63
Sex (n, %)		
Male	9	100%
Female	0	0%
Epidemiological risk factors and comorbidities (n, %)		
Male sexual partners	9	100%
Prior smallpox immunization	0	0%
Median duration of symptoms before treatment, days (range)	9	5–22
Hospitalized	3	33%
Suspected or proven bacterial superinfection[a]	6	66%
Human immunodeficiency virus	5	55%
Median CD4 count of patients living with human immunodeficiency virus (cells/uL)	513	N/A
Median viral load	Undetectable	Undetectable
Symptoms (n, %)		
Head and neck	5	55%
Neurological	2	22%
Genitourinary and anorectal	5	55%
Fever	5	55%
Lymphadenopathy	9	100%
Myalgias	3	33%

Abbreviation: N/A, not applicable
[a] Culture proven *Streptococcus pyogenes* infection, including one peritonsillar abscess

Discussion

This is the first Canadian case series of TCV use during a mpox outbreak for severely symptomatic cases. All patients experienced rapid clinical improvement. The medication was well tolerated, without any patient-reported adverse events. These findings are globally consistent with trial data that show improved clinical outcomes in non-human primates and a favourable adverse event profile. Our data also align with a large American case series of patients who received TCV and were at risk of severe disease (12). In the American experience, only a small proportion of patients reported minor adverse events and 90% of patients were cured at the time of the post-treatment follow-up.

A unique feature of our study is that all patients in our cohort presented with severe manifestations of disease, including concern of possible impending respiratory compromise. This is a historically rare manifestation of mpox infection, which was not reported among adults in a previous North American outbreak caused by contact with prairie dogs (13). It is possibly more common in this current outbreak as a function of direct viral inoculation in oropharyngeal mucosa during suspected person-to-person sexual transmission and severe manifestations have more recently been described (2). While previous uses of TCV did not specifically address this patient population, we were reassured to note that all patients progressed favourably despite their initial severe manifestations.

In addition, over half of patients in our cohort had suspected or culture-proven bacterial superinfection of their viral lesions. Though superinfection has been reported in previous mpox outbreaks, it is not common (1). However, because of some patients abnormally severe presentations and clinical concern for possible bacterial infection, several in our cohort were also treated with antibiotics. This is similar to another cohort in the United Kingdom (14) and could have contributed to the globally favourable outcomes seen in our group. In both cases of culture-positive bacterial infection, *Streptococcus pyogenes* was isolated in throat cultures; therefore, one could surmise that oropharyngeal mpox lesions might have served as a portal of entry.

None of the patients in this study had been vaccinated for smallpox prior to the onset of their symptoms—either in the setting of the current outbreak or in their youth. Data from cohorts in historically endemic countries suggests that patients with prior variola virus immunization have less severe disease (15). The impact of antivirals in these cases has not yet been studied and thus remains uncertain.

Limitations

The limitations of this study include its observational nature, the small number of cases and our inability to follow their evolution with a prospective assessment of blood, urine and upper respiratory tract viral loads. We are unable to draw firm conclusions from this cohort in the absence of a control group, and our results are primarily hypothesis-generating.

Conclusion

Overall, our experience suggests that TCV appears to be a safe adjunct to supportive care in the treatment of mpox infection and may accelerate recovery in severe cases. Because mpox is generally a self-limited condition and because of the presence of other variables, such as treated bacterial superinfection, the magnitude of TCV's clinical impact in this setting remains uncertain. Controlled, clinical trials should be conducted to clarify the attributable benefit of tecovirimat in severe mpox infection.

Authors' statement

KKD — Original draft, collection of data, review draft manuscript
MD — Conceptualization, methodology, supervision of the project, collection of data, review draft manuscript
JL — Conceptualization, methodology, supervision of the project, collection of data, review draft manuscript

CT — Conceptualization, methodology, supervision of the project, collection of data, review draft 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

CT is the Pfizer/Université de Montréal Chair on HIV Translational Research.

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Summary of the NACI Statement on Public Health Level Recommendations on the Use of Pneumococcal Vaccines in Adults, Including the Use of 15-valent and 20-valent Conjugate Vaccines

Aleksandra Wierzbowski[1], Robert Pless[1], Kyla J Hildebrand[2] on behalf of the National Advisory Committee on Immunization (NACI)*

Abstract

Background: Age and certain medical/social conditions are risk factors for invasive pneumococcal disease (IPD). For prevention of IPD, the National Advisory Committee on Immunization (NACI) has recommended the 23-valent polysaccharide pneumococcal vaccine, PNEU-P-23, for adults 65 years of age and older and adults over 18 years of age living with certain underlying conditions. NACI has also recommended 13-valent conjugate pneumococcal vaccine, PNEU-C-13, for adults; however, in publicly funded programs, this recommendation is limited to individuals with risk factors for IPD. Two new conjugate vaccines, PNEU-C-15 and PNEU-C-20, have been authorized by Health Canada for prevention of IPD in adults. This article summarizes NACI public health recommendations for pneumococcal vaccines in adults given these new conjugate vaccines that provide additional serotype coverage over PNEU-C-13.

Methods: Key studies evaluating the immunogenicity and safety of PNEU-C-15 and PNEU-C-20 were reviewed. The Grading of Recommendations, Assessment, Development and Evaluations framework methodology was used to assess the certainty of evidence.

Results: The PNEU-C-15 and PNEU-C-20 vaccines showed comparable immune responses, and safety profiles for all mild, moderate, and severe adverse events, to the currently used vaccines. No data were available on the efficacy or effectiveness of PNEU-C-15 or PNEU-C-20. Economic evidence and feasibility assessments supported the use of the PNEU-C-20 vaccine.

Conclusion: NACI recommends PNEU-C-20 for adults 65 years of age and older, 50–64 years of age and living with factors placing them at higher risk of pneumococcal disease, and 18–49 years of age with immunocompromising conditions, with PNEU-C-15+PNEU-P-23 an alternative.

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Keywords: pneumococcal infection, invasive pneumococcal disease, vaccines/conjugate, pneumococcal vaccines, immunization schedule, public health recommendations, economic analysis

Affiliations

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

[2] NACI Pneumococcal Working Group Chair, Department of Pediatrics, Faculty of Medicine, University of British Columbia, Vancouver, BC

***Correspondence:**

naci-ccni@phac-aspc.gc.ca

Introduction

Pneumococcal disease (PD) includes both invasive pneumococcal diseases (IPD), such as meningitis, bacteremia, bacteremic pneumonia and empyema, and non-invasive pneumococcal disease, such as community-acquired pneumonia, sinusitis, and acute otitis media. The burden of disease is predominately attributable to a small number of the more than 100 identified

serotypes of a *Streptococcus pneumoniae* bacteria. Invasive pneumococcal disease is most common in the very young, the elderly and individuals living with medical conditions and/or other risk factors that place them at higher risk of IPD.

The incidence of IPD in adults in Canada increased from 2001 to 2004, followed by relatively stable incidence in the subsequent 15 years. It was highest in adults 65 years of age and older, with incidence proportional to age starting at 50 years of age, and higher in Northern Canada compared to the rest of the country. Furthermore, the proportion of IPD caused by vaccine targeted serotypes have remained relatively stable since 2016 (1,2). Current National Advisory Committee on Immunization (NACI) recommendations for the prevention of IPD in adults include two vaccines: a 23-valent polysaccharide pneumococcal vaccine, PNEU-P-23 (Pneumovax®); and a 13-valent conjugate pneumococcal vaccine, PNEU-C-13 (Prevnar 13®). The PNEU-P-23 vaccine is recommended for routine immunization against IPD for all adults 65 years of age and older and adults 18–64 years of age with underlying medical conditions or social factors that put them at higher risk of IPD. The PNEU-C-13 vaccine, in series with PNEU-P-23, is recommended for adults 18 years of age and older and living with immunocompromising conditions resulting in high risk of IPD. A complete list of conditions that increase the risk of IPD along with dose and schedule of recommended vaccinations is available in the Pneumococcal Vaccine Chapter of the *Canadian Immunization Guide* (3).

Two new conjugate pneumococcal vaccines for adults, PNEU-C-15 (Vaxneuvance™) and PNEU-C-20 (Prevnar 20®) were authorized by Health Canada on November 16, 2021, and May 9, 2022, respectively. The PNEU-C-15 vaccine was first authorized for adults 18 years of age and older with an indication for prevention of IPD caused by 15 serotypes of *S. pneumoniae* (PNEU-C-13 plus serotypes 22F and 33F) (4). The PNEU-C-20 vaccine is authorized for adults 18 years of age and older with an indication for prevention of pneumonia and IPD caused by 20 serotypes of *S. pneumoniae* (PNEU-C-13 plus serotypes 8, 10A, 11A, 12F, 15B, 22F and 33F) (5). Complete details can be found in the NACI statement, *Public health level recommendations on the use of pneumococcal vaccines in adults, including the use of 15-valent and 20-valent conjugate vaccines*. PNEU-C-15 (Vaxneuvance™) has also recently been authorized for use in infants, children and adolescents from six weeks through 17 years of age and is under review by NACI for use in paediatric programs.

The objective of this article is to summarize the NACI recommendations (6) on the use of PNEU-C-15 and PNEU-C-20 vaccines in adults.

Methods

The NACI reviewed evidence pertaining to the burden of IPD in the adult population, along with the safety, immunogenicity, efficacy, and effectiveness of the vaccines, along with an economic analysis and application of the Ethics, Equity, Feasibility and Acceptability (known as EEFA) framework. Clinical trials were assessed via a targeted review, and a health economic model was created by the Public Health Agency of Canada (PHAC) to assess cost-effectiveness in the Canadian population and was used in a multi-model comparison in combination with other cost effectiveness models. The knowledge synthesis was performed by the NACI Secretariat and reviewed by the Pneumococcal Working Group. The Grading of Recommendations, Assessment, Development and Evaluations framework methodology was used to assess certainty of the evidence and arrive at recommendations. For complete details of the methods refer to the NACI statement (6).

Results

The burden of IPD in the adult population since the introduction of paediatric pneumococcal vaccination programs in 2002 has been relatively stable; however, despite being strongly recommended for vaccination, the oldest adults (65 years of age and older) continue to have consistently higher incidence rates than younger cohorts with the exception of infants and children under five years of age.

There are currently no efficacy or effectiveness data available for PNEU-C-15 or PNEU-C-20 for any adult indication. Authorization was based on an assessment of the immune responses using opsonophagocytic activity assays of both vaccines compared to currently recommended vaccines.

For PNEU-C-15, in immunocompetent pneumococcal vaccine-naïve adults 65 years of age and older and for shared serotypes, PNEU-C-15 demonstrated overall similar immune responses, including for serotype 3, compared to PNEU-C-13, although seroresponses varied (7–11). Studies comparing PNEU-C-15 to PNEU-P-23 showed similar results, although seroresponse was higher with serotype 3 with PNEU-C-15 (7).

For PNEU-C-20, non-inferiority criteria were met in vaccine-naïve populations over 60 years of age; however, there was an observed lower proportion of seroresponders compared to PNEU-C-13 for shared serotypes (12,13).

Persistence of immune responses over a 12-month period for both PNEU-C-15 and PNEU-C-20 were comparable to PNEU-C-13.

Data on local and systemic adverse events (AE), both solicited and unsolicited, were collected in similar fashion for both vaccines, with shorter follow-up periods for solicited events after each dose and follow-up for up to six months for serious adverse events (SAE).

There was little to no difference reported in clinical trials between PNEU-C-15 and PNEU-P-23 or PNEU-C-13 for all mild/moderate and severe systemic AEs occurring within 14 days of vaccination as well as reported SAEs up to six months after vaccination in all evaluated populations, including in adults 65 years of age and older with an immunocompromising condition (7–11). There was also little to no difference in AEs for PNEU-C-15 administered concomitantly with quadrivalent influenza vaccine in vaccine-naïve adults (11).

There was little to no difference between PNEU-C-20 and PNEU-C-13 in all mild/moderate and severe systemic AEs up to seven days post vaccination and SAEs up to one month post vaccination for vaccine-naïve adults aged 60 years or older (12,13). For adults 65 years of age and older who have previously been vaccinated with PNEU-P-23 (one to five years prior), SAE up to six months and systemic AEs seven days after vaccination were similar between PNEU-C-20 and PNEU-C-13 (14).

A systematic review of economic analyses conducted in the United States found that PNEU-C-20 use in older adults was generally associated with increased quality-adjusted life years, with lower incremental cost-effectiveness ratios when the vaccine was used in those 65 years of age and older compared to programs in those 50 years of age and older. Incremental cost-effectiveness ratio estimates for PNEU-C-15 use in series with PNEU-P-23 at those six years of age showed variability across studies (16).

A cost-utility model developed by PHAC was used to evaluate the cost-effectiveness of different age-based recommendations. The analysis indicated that PNEU-C-20 used alone is likely a cost-effective strategy for those 65 years of age and older. Compared to PNEU-C-20, PNEU-C-15 is unlikely to be a cost-effective option. Results of the multi-model comparison were consistent with the PHAC economic evaluation.

The PNEU-C-20 vaccine covers more than 90% of serotypes included in PNEU-P-23 and could be offered in immunization programs as a single dose. A single dose vaccine schedule minimizes complexity and cost in a vaccine program and can facilitate vaccination of populations that are otherwise difficult to reach to complete a series requiring multiple doses. To optimize the protection of PNEU-C-15, PNEU-P-23 would also need to be offered in a multi-product, two-dose series.

Recommendations

Following the review of available evidence, NACI made the following recommendations for public health level decision-making. A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present. A discretionary recommendation may be considered for some populations/individuals in some circumstances. Alternative approaches may be reasonable.

The full statement contains a more detailed explanation of the recommendations and a management options table (6). This information should be reviewed in order to inform decision-making; in particular for individuals who have not been included in their respective provincial or territorial publicly funded program. In considering NACI recommendations for publicly funded immunization programs and for the purposes of publicly funded program implementation, provinces and territories may take into account other local operational factors.

For adults not previously vaccinated with a pneumococcal vaccine, or adults whose vaccination status is unknown

1. **The NACI recommends that the pneumococcal conjugate vaccine PNEU-C-20 should be offered to pneumococcal vaccine naïve adults or adults whose vaccination status is unknown and who are ≥65 years of age and, or 50–64 years of age living with risk factors placing them at higher risk of pneumococcal disease, or who are 18–49 years of age living with immunocompromising conditions. *(Strong NACI recommendation)***
   Individuals at increasing age and/or with certain underlying medical conditions (both non-immunocompromising and immunocompromising) and other factors, including community-level risk, are at higher risk of IPD. Adults 65 years of age and older have the highest incidence rate of IPD compared to other adult age groups, and the current uptake of pneumococcal vaccines in this age group is well below national goals. Age-based recommendations may need to be modified for communities with younger age distributions, such as First Nations, Métis, or Inuit communities, where autonomous decisions should be made by Indigenous Peoples with the support of healthcare and public health partners in accordance with the *United Nations Declaration on the Rights of Indigenous Peoples.*

2. **The NACI recommends that PNEU-C-15 followed by PNEU-P-23 may be offered as an alternative to PNEU-C-20 to pneumococcal vaccine naïve adults or adults whose vaccination status is unknown and who are ≥65 years of age, 50–64 years of age living with risk factors placing them at higher risk of pneumococcal disease, or who are 18–64 years of age living with immunocompromising conditions. *(Discretionary NACI recommendation)***

Although PNEU-C-15 is not expected to yield the same population-level epidemiological benefits as PNEU-C-20 and requires a second dose with PNEU-P-23, it is anticipated that it will improve disease outcomes compared to offering PNEU-P-23 alone. As to timing of the doses, an interval of one year is recommended for adults 65 years of age and older and adults 50–64 years of age who are living with risk factors for pneumococcal disease. An interval of eight weeks is recommended for adults who are 18–64 years of age and living with immunocompromising conditions to allow for quicker completion of the series, however a longer interval may result in less blunting of immune responses and could be considered if risk of pneumococcal infection is low.

For adults previously vaccinated with a pneumococcal vaccine

3. **The NACI recommends that the pneumococcal conjugate vaccine PNEU-C-20, should be offered to adults ≥65 years of age who have been previously immunized with PNEU-P-23 alone, or PNEU-C-13 and PNEU-P-23 in series, if it has been at least 5 years from the last dose of a previous pneumococcal vaccine (PNEU-P-23 or PNEU-C-13). *(Strong NACI recommendation)***
   If PNEU-C-20 is not available there may be a benefit to offering PNEU-C-15 to adults 65 years of age and older who have received PNEU-P-23 alone. There is limited benefit to giving PNEU-C-15 to individuals who received PNEU-C-13 as it will only offer protection against two additional serotypes. In addition, for those adults 65 years of age and older who are also at the highest risk of IPD, an additional dose of PNEU-P-23 may be offered one year following PNEU-C-15 (or PNEU-C-13 had they received it prior to availability of PNEU-C-15).

4. **The NACI recommends that the pneumococcal conjugate vaccine PNEU-C-20 may be offered to adults 65 years of age and older who have been previously immunized with PNEU-C-13 alone, if it has been 1 year from the last dose of PNEU-C-13. *(Discretionary NACI recommendation)***
   Offering PNEU-C 20 is intended to expand serotype coverage offered by PNEU-C-13. A shorter interval of eight weeks may be considered to align with operational considerations for immunization clinics and/or programs. The additional benefit of offering PNEU-C-15 is limited; however, PNEU-C-15 in series with PNEUP-23 or PNEU-P-23 alone can be considered if PNEU-C-20 is unavailable or inaccessible.

For hematopoietic stem cell transplant (HSCT) recipients

5. **NACI recommends pneumococcal conjugate vaccine PNEU-C-20 should be offered to adults 18 years old or older who received a hematopoietic stem cell transplant (HSCT) after consultation with transplant specialist. A primary series of 3 doses of PNEU-C-20 starting 3–9 months after transplant should be administered at least 4 weeks apart, followed by a booster dose of PNEU-C-20 12–18 months post-transplant (6–12 months after the last dose of PNEU-C-20). *(Strong NACI recommendation)***
   The recommended timing of PNEU-C-20 for hematopoietic stem cell transplant recipients should be determined in consultation with the recipient's transplant specialist. The PNEU-C-15 vaccine may be considered if PNEU-C-20 is unavailable or inaccessible, to ensure the needed protection.

Conclusion

Prior to the authorization by Health Canada of PNEU-C-15 and PNEU-C-20 for adults, NACI's recommendation for adults 65 years of age and older was for the use of PNEU-P-23, with PNEU-C-13 only recommended for individuals at highest risk of IPD, such as those with immunocompromising conditions. Conjugate vaccines induce immunological memory and provide longer duration of protection in part due to the ability for boosting by involving T lymphocytes in a way that polysaccharide vaccines cannot. For this reason, conjugate vaccines may provide more durable protection and may result in fewer cases of pneumococcal disease. The new vaccines offer an opportunity to protect adults and further reduce the burden of disease; therefore, NACI is recommending their use more widely in the publicly funded immunization programs.

Both PNEU-C-20 and PNEU-C-15 have shown robust immune responses in adults previously vaccinated with pneumococcal vaccines and have demonstrated a comparable safety profile to PNEU-C-13 in all adult population studied. However, PNEU-C-20 is anticipated to yield greater population-level epidemiological benefits over the use of PNEU-C-15.

It should be further noted that, at this time, no PNEU-C-20 studies in immunocompromised adults have been conducted but PNEU-C-20 is expected to be similarly efficacious as PNEU-C-13 against disease attributable to the 13 matched serotypes, including in hematopoietic stem cell transplant recipients.

NACI only supports the continued use of PNEU-C-13 and PNEU-P-23 in adults when PNEU-C-15 and/or PNEU-C-20 are unavailable or inaccessible.

At this time, there are no public health level recommendations on the use of PNEU-C-15 or PNEU-C-20 for adults 18–49 years of age with non-immunocompromising risk factors that place them at high risk of IPD, as additional analyses on the cost-effectiveness of conjugate PNEU-C-15 and PNEU-C-20 in this population are needed. The PNEU-C-15 or PNEU-C-20 vaccines may be considered at clinical discretion for these individuals. While PNEU-P-23 and PNEU-C-13 continue to be available and jurisdictions continue providing these vaccines for this group, previous NACI recommendations remain for this group.

Authors' statement

AW — Writing, original draft, review, editing
RP — Writing, review, editing
KH — Review, editing

Competing interests

None.

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NACI Pneumococcal Working Group Members: KJ Hildebrand (Chair), J Bettinger, N Brousseau, P De Wals, D Fisman, J Kellner, A McGeer, J Papenburg, S Rechner, and G Tyrell.

Ex-officio representatives: G Coleman (Biologic and Radiopharmaceutical Drugs Directorate [BRDD] Health Canada [HC]), M Kobayashi (Centers for Disease Control and Prevention [CDC] United States), AY Li (Vaccine Preventable Diseases Surveillance [VPDS] Public Health Agency of Canada [PHAC]), I Martin (National Microbiology Lab [NML] PHAC), G Metz (Vaccine Safety [VS] PHAC), and A Monohan (First Nations and Inuit Health Branch [FNIHB], Indigenous Services Canada [ISC]).

PHAC Participants: A Wierzbowski, R Pless, N Islam, AY Li, I Martin, A Stevens, C Tremblay, A Tuite, and K Young.

NACI Members: S Deeks (Chair), R Harrison (Vice-Chair), M Andrew, J Bettinger, N Brousseau, H Decaluwe, P De Wals, E Dubé, V Dubey, KJ Hildebrand, K Klein, J Papenburg, A Pham-Huy, B Sander, S Smith, and S Wilson.

Liaison representatives: L Bill/M Nowgesic (Canadian Indigenous Nurses Association), LM Bucci (Canadian Public Health Association), E Castillo (Society of Obstetricians and Gynaecologists of Canada), J Comeau (Association of Medical Microbiology and Infectious Disease Canada), J Macneil (Centers for Disease Control and Prevention, United States), L Dupuis (Canadian Nurses Association), D Fell (Canadian Association for Immunization Research and Evaluation), S Funnell (Indigenous Physicians Association of Canada), J Hu (College of Family Physicians of Canada), M Lavoie (Council of Chief Medical Officers of Health), D Moore (Canadian Paediatric Society), M Naus (Canadian Immunization Committee), and A Ung (Canadian Pharmacists Association).

Ex-officio representatives: V Beswick-Escanlar (National Defence and the Canadian Armed Forces), E Henry (Centre for Immunization and Respiratory Infectious Diseases [CIRID], PHAC), M Lacroix (Public Health Ethics Consultative Group, PHAC), C Lourenco (Biologic and Radiopharmaceutical Drugs Directorate, Health Canada), D MacDonald (COVID-19 Epidemiology and Surveillance, PHAC), S Ogunnaike-Cooke (CIRID, PHAC), K Robinson (Marketed Health Products Directorate, HC), M Routledge (National Microbiology Laboratory, PHAC), and T Wong (First Nations and Inuit Health Branch, Indigenous Services Canada).

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Update on mpox (monkeypox) in Canada, February 2023

Source: Public Health Agency of Canada. Emerging Science Group: Living evidence profile on the 2022 monkeypox outbreak, Highlights up to December 15, 2022. Full report available from: ocsoevidence-bcscdonneesprobantes@phac-aspc.gc.ca

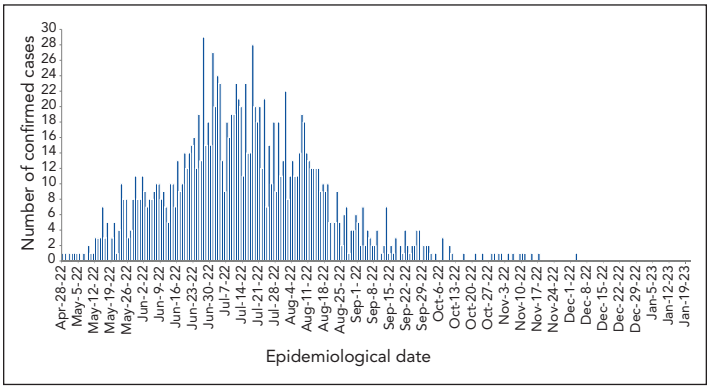
Introduction

In May 2022, cases of monkeypox—recently renamed mpox by the World Health Organization (WHO)—started to appear in non-endemic countries. As of January 2023, cases have now been reported in over 100 countries (1). In July 2022, the WHO declared the mpox outbreak a Public Health Emergency of International Concern. This update describes the clinical features of the 2022 mpox outbreak, and provides an overview of the outbreak in Canada, the national public health response, and the implications for emerging pathogen outbreak preparedness in the future.

Current situation in Canada

Cases of mpox have been reported by nine provinces and the Yukon, but were largely centred in Ontario, Québec and British Columbia. The epidemic in Canada peaked in late June/early July when 25–30 new cases were being reported per day. Since the peak, the number of cases has declined rapidly, with only occasional cases reported since mid-November (**Figure 1**). As of January 20, 2023, Canada reported a cumulative total of 1,460 cases, with 44 reported hospitalizations and no deaths (2).

Figure 1: Epidemic curve of mpox epidemic in Canada as of January 20, 2022



Notes: Epidemiological date represents the earliest of symptom onset, lab report, or public health report date. Figure 1 represents the epidemic curve of confirmed mpox cases in Canada between April 28, 2022 and January 20, 2023 (n=1,396). The number of confirmed cases differs from the total number of publicly reported cases in Canada (n=1,460) as it excludes cases for which no case report form was received by the Public Health Agency of Canada (PHAC) from provincial or territorial partners. As of January 20, 2023, no new cases have been reported to PHAC since December 14th, 2022 (last case reported with an epidemiological date of December 3rd, 2022) (2)

Epidemiologic and clinical features of 2022 mpox outbreak

The outbreak began in May 2022, and some 680 studies had been published by mid-December 2022. Based on the global scientific literature, the median incubation period spans 7–9.6 days from exposure until the appearance of first symptoms, with a range of 2–21 days. This current estimate is similar to historical data for this disease.

Data obtained globally, including from a study in Montréal, Québec, show the mpox outbreak largely affected the gay, bisexual and men who have sex with men (gbMSM) community, and transmission was predominantly associated with intimate sexual contact (3). Other exposures not associated with intimate contact occurred among household members who had close (non-sexual) contact. Sporadic cases of mpox among healthcare workers were reported, but only a small number of cases, all outside Canada, were associated with workplace exposure. Fomite transmission was rare, based on a small number of transmission events in healthcare workers, and contaminated piercing and tattoo establishments, despite the fact the mpox virus can survive on hard surfaces for days.

The clinical presentation of cases in the 2022 outbreak had notable new characteristics when compared with historical descriptions. Most cases had at least one skin lesion and, in about half of the cases, lesions appeared before other symptoms—including fever, headache and malaise. Often the first lesion appeared at the place of inoculation and then spread to other areas of the body; for many cases, the first lesion was in the mouth or anogenital region. Mpox lesions can be hard to differentiate from lesions of other sexually transmissible infections, such as chancre or syphilis. Furthermore, some cases presented with few or no lesions, had lesions that did not spread or had asynchronous lesions (appearing at different stages of development). Proctitis and pharyngitis were common and were sometimes accompanied by significant pain. Some cases required health care, largely for pain control or treatment of secondary infections. Symptoms usually lasted 2–4 weeks. Vision impairment due to ocular mpox is rare but has been reported. Other complications, such as myocarditis or encephalitis, have also been described.

There are eight recent studies reporting on the clinical use and safety of tecovirimat (TPOXX) or cidofovir for treatment of mpox, but there is limited evidence on treatment effectiveness. Emerging data on the Bavarian Nordic vaccine, Imvamune®, has shown variable effectiveness across studies. The early COSMOS study, with data up to October 31, 2022, found vaccine efficacy was 37% after one dose and 69% after two doses, with no difference by sex, immune status or type of injection (4). However, a more recent publication estimated 86% effectiveness from a single subcutaneous dose (5)

Canada's response

Health is a shared responsibility in Canada; so the mpox outbreak required a federal/provincial/territorial (FPT) public health response plan to contain it (6). The objectives of this plan were to reduce the impact of mpox, stop the chains of transmission, minimize the risk that mpox becomes established in Canada, and ensure the clinical and public health response were based on the best available evidence.

Canada's National Microbiology Laboratory was the first to provide diagnostic testing for mpox and worked closely with provincial and territorial (PT) public health laboratories to increase their testing capacity. Information on testing procedures was developed and distributed locally. The Public Health Agency of Canada (PHAC) established a national surveillance system, in collaboration with FPT partners. The PT health authorities compiled and forwarded de-identified data to PHAC, which collated the data to produce national statistics, and shared regular reports with the WHO.

Federal/provincial/territorial collaboration led to clinical and public health guidance documents that were distributed nationally, such as the case and contact management guidance (7) and guidance on reducing the risk of spread in community settings (8). PHAC and PTs facilitated the deployment of nearly 100K doses of Imvamune vaccine across the country, and implemented vaccine safety surveillance through systems already in place. The National Advisory Committee on Immunization issued vaccine guidelines for at-risk populations (9). PHAC's Chief Public Health Officer and Chief Science Officer established an expert panel to engage researchers and clinical experts from across Canada to share knowledge and shape the national public health response. PHAC participated in the World Health Organization Research and Development Blueprint meetings held to discuss mpox science and research gaps, and how best to assess vaccine effectiveness. These science leadership activities helped to inform domestic science and research priorities, which in turn were leveraged for funding of international mpox research by the Canadian Institutes of Health Research and the International Development Research Centre.

Federal/provincial/territorial collaboration also included partnerships with community organizations, particularly those serving the gbMSM population and focusing on sexual health. This led to raised awareness about the mpox outbreak at PRIDE events, including information on ways to limit its spread, including vaccination. Surveys of high-risk populations during the outbreak indicated that, 40%–69% of people reduced their number of sexual partners to reduce their risk of mpox infection and transmission.

Conclusion

Work continues across Canada and abroad to increase our understanding of the virus and our ability to prevent, detect and treat new cases. The response to mpox occurred while the Canadian health system and public health authorities were dealing with the continuing COVID-19 pandemic, resurgent respiratory infections, and the need to ensure domestic preparedness due to the Sudan virus outbreak in Uganda. Addressing these epidemics illustrates the urgent and ongoing need for Canada's clinical and public health systems further develop and sustain their capacity to detect and manage multiple national infectious disease emergencies simultaneously.

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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

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