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EQUITY, DIVERSITY & INCLUSION IN PUBLIC HEALTH

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Vaccination of children in marginalized neighbourhoods: Equity and diversity challenges with COVID-19 vaccination campaigns

Cécile Rousseau[1]*, Caroline Quach[2], Ève Dubé[3], Anabelle Vanier-Clément[4], Tara Santavicca[4], Laurence Monnais-Rousselots[2]

Abstract

The coronavirus disease 2019 (COVID-19) pandemic has exacerbated social inequities along ethnic, racial and socio-economic lines, with significant harmful consequences for children. Building on the lessons learned from community-based initiatives, this commentary proposes a reflection around equity, diversity, and inclusion challenges embedded in child vaccination campaigns during an emergency context. We argue that building equitable and inclusive practices around marginalized communities' child vaccination is a multifaceted challenge. Beyond good intentions—wanting to protect children—the risks and benefits associated with highlighting diversity in each intervention need to be carefully considered, especially when it comes to a contested/polarizing procedure such as vaccination with a novel type of vaccine. Often, a one-size-fits-all approach negates and perpetuates structural inequities. In other cases, highlighting diversity and inequities may inadvertently increase stigma and discrimination, and further harm or infantilize targeted communities. By providing multiple perspectives, a transdisciplinary approach can support decision-making in a crisis context.

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Keywords: adolescent health/medicine, community health services, minority health, equity and inclusion

Introduction

The coronavirus disease 2019 (COVID-19) pandemic has exacerbated social inequities along ethnic, racial and socio-economic lines, with significant harmful consequences for children. In marginalized neighbourhoods, these structural and social inequities converge (1). Families' and children's environments have been shattered, while the priority was put on limiting viral transmission through vaccination and non-pharmacological interventions such as physical distancing and lockdown (2–6). In Montréal, Canada, children in lower-income households, racialized groups and in families born outside Canada were less likely to accept COVID-19 vaccination, and adolescents in the most deprived neighbourhoods were half as likely to get vaccinated for COVID-19 compared to their peers in the least deprived neighbourhoods (7).

In Montréal, a transdisciplinary program to mitigate pandemic-related inequities and associated social tensions, *Programme CoVivre - Institut universitaire SHERPA* (8–10), developed three initiatives to address challenges related to the mass vaccination campaign that started in December 2020: 1) the production of a guide to address ethno-racial differences in vaccine hesitancy; 2) the development of tools to decrease social tensions and bullying associated with the vaccination campaign for 12–17 years-old teenagers in schools and in multi-ethnic socio-economically deprived neighbourhoods; and 3) the development of tools to address parents' vaccine hesitancy regarding their 5–11-year-old's immunization. These initiatives aimed to transfer information and to buffer conflicts fuelled by the symbolic meaning associated with child vaccination in different faith and ethno-racial communities, but also in the majority in which diverse groups were opposed to vaccination.

All these interventions wove together different disciplinary expertise (paediatric, child mental health, anthropological and historical), to support the rapid production of tools in a crisis context. Building on the lessons learned from these initiatives, this paper aims to launch a reflection around equity, diversity, and inclusion challenges in a public health emergency context, to preserve, as much as possible, children's wellbeing. More specifically, we raise the following questions: To which extent

should vaccination-related programs directly address diversity? What are the possible benefits versus risks of stigmatization when highlighting minority communities' vulnerabilities to the pandemic direct and indirect impacts? Exposing the rationale underlying the chosen paths of action for these three initiatives, we argue that a transdisciplinary approach can play a key role to inform action when complex decisions are to be taken rapidly.

Addressing the cultural, social and historical dimensions of vaccine hesitancy

The development of a guide to address ethno-racial differences in vaccine hesitancy stemmed from the need to consider context and culture in improving confidence toward the vaccine (11,12). The objective was to raise practitioners' awareness about the impact of historical (e.g. abuse and medical experimentation on African American and Indigenous communities) and current collective experiences of oppression on the perception of institutional action, to improve cultural safety and establish a respectful dialogue about vaccination with communities.

This well-intentioned process rapidly uncovered problems associated with the oversimplification of very heterogeneous communities (such as Asian, Afro-Caribbean, Faith and First Nations communities), and the associated risks of stereotyping and stigmatizing them. The historical and social sciences perspectives in the team helped us to contextualize a large range of discourses and attitudes. In partnership with community stakeholders, these different perspectives informed our choices about the ways to represent diversity, while cautioning against a standardized use of the tools. The importance of gathering local data with which to develop tailored intervention was also highlighted.

Schools at the heart of the storm: Youth vaccination campaigns

In June 2021, at the launch of the 12–17 year-olds vaccination, the public divide between pro and anti-vaccines in Québec became heated, with threats, protests and aggression towards vaccination teams within schools. Schools' staff and parents were divided and bullying about vaccination decisions among peers became a worrisome issue. This fuelled fear in multi-ethnic neighbourhoods, jeopardizing the protective character of the schools as safe spaces of learning and inclusion, with youth refusing to attend schools while others would take a more provocative stance in response to the division of the adult community. To mitigate the impact of these tensions and re-establish a sense of community, the Programme CoVivre team began to develop tools for the school staff and for parents.

Although Montréal had an over-representation of minority and socio-economically deprived children among the non-vaccinated, we decided to develop tools which did not emphasize diversity, to rally the majority around the preservation of a protective school climate without stigmatizing the minorities. This decision was based on an appraisal of the social dynamics and included the input of a paediatric infectious disease specialist, to give more credibility to the proposed tools. In this case, the team felt that, given the adversarial tone of the public debate, emphasizing the vulnerability of migrants and ethno-racial communities in terms of vaccine hesitancy, could have increased their designation as scapegoats, because hesitant individuals were depicted as selfish or even criminal in the majority discourse. The tools were very well received and disseminated throughout the education and healthcare systems.

Supporting parental decision-making process about their children's vaccination

Building on the experience gained with the adolescent vaccination campaign, the team developed additional tools providing medical information, legitimizing vaccine hesitancy as a healthy process and supporting parental decision about the vaccination of their younger children (5–11 years old).

Given the paucity of data available at the time (13), the team relied on its medical experts to include up to date and nuanced information to support parents' informed consent. Rapidly, questions around the level of literacy and translations of the produced tools arose. An important dilemma was identified. On the one hand, the transmission of relatively complex information was seen as an exclusion process for parents with lower literacy level, even with a proper translation: on the other hand, oversimplifying the information, necessarily biased by our positive view of vaccination, could be paternalistic, depriving parents of a more comprehensive perspective. Unable to resolve this issue, we favoured a two-step process in which the full information pamphlets were translated and distributed, followed by a second version to be modified with community stakeholders and parents of different literacy levels, to allow communities and parents to determine what they considered essential information. The choice of the best channels to disseminate the information while maximizing trust and outreach was also discussed. Again, the team was conscious that with less time constraints, communities would have adapted the tools to their needs and concerns (14). Despite the urgency, the team's diversity enabled a reflection around the need to consider diversity and equity at each step of the process.

Conclusion

Building equitable and inclusive practices around marginalized communities' child vaccination is a multifaceted challenge (15). Beyond good intentions—everyone wants to protect children—there is a need to carefully consider the risks and benefits associated with highlighting diversity in each intervention, especially when it comes to a contested/polarizing procedure such as vaccination and novel vaccine. In some cases, as it has been strongly demonstrated during the current pandemic, a one-size-fits-all approach negates and perpetuates structural inequities. In other cases, highlighting diversity and inequities (even when real) may inadvertently increase stigma and discrimination, and further harm or infantilize targeted communities.

Our experience suggests that in this process, a transdisciplinary perspective may inform decision-making, during a pandemic and beyond. By providing different, sometimes opposing or complementary perspectives, this approach informs rapid action without replacing community consultation. It also supports the capacity to collectively endorse difficult choices in a context in which we always need to remember that our actions have multifaceted (and perhaps harmful) consequences.

Authors' statement

CR — Conceptualized, drafted the initial article, reviewed–revised the article
CQ — Completed, reviewed–revised the article, provided insights on specific discipline
ED — Completed, reviewed–revised the article, provided insights on specific discipline
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AV-C — Coordinator of the community interventions, reviewed the article, field insights
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All authors approved the final article as submitted and agree to be accountable for all aspects of the work.

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

Competing interests

None.

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Summary of an environmental scan of HIV and Hepatitis C programs, projects and initiatives in Saskatchewan

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Abstract

Background: In 2019, the human immunodeficiency virus (HIV) and hepatitis C (HCV) diagnosis rates in Saskatchewan (SK) were approximately twice the national rate. To address these high levels, Saskatchewan Stories, a community-based digital database, was developed to make information on Saskatchewan-based HIV and HCV programs, projects and initiatives (PPI) centrally and freely available. To begin populating this database, we conducted an environmental scan representing HIV and HCV PPI from January 1, 1980 to May 31, 2020.

Methods: MedLine, ERIC, ProQuest One Literature, Public Health Information database, SCOPUS and CINAHL were searched for both HIV and HCV articles. In addition, Bibliography of Native North Americans was searched for HIV and EMBSE (Ovid) and Indigenous studies portal (iPortal) were searched for HCV articles. Google Canada, Government of Saskatchewan, and Government of Canada websites were also searched.

Results: In total, 139 HIV-specific PPI and 29 HCV-specific PPI were found in the environmental scan (n=168). Among HIV PPI, 27% (n=38) were from academic literature while 73% (n=101) were from grey literature. Among HCV PPI, 41% (n=12) were from academic literature, while 59% (n=17) were from grey literature. HIV accounted for 83% of total PPI, compared to 17% for HCV.

Conclusion: This environmental scan is an important contribution to evidence-based practice and research in SK. It is particularly useful for organizations, researchers, policymakers and people living with HIV/HCV to develop new evidence-based PPI, to secure funding for PPI and to support individuals and communities in SK affected by HIV and HCV.

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Keywords: HIV, HCV, Saskatchewan, projects, programs, initiatives, Indigenous health, Indigenous culture

Introduction

Provincial rates of human immunodeficiency virus (HIV) and hepatitis C (HCV) in Saskatchewan (SK) are significantly higher than the national rate (1). Indeed, according to recent provincial reporting, the HIV diagnosis rate is over twice the national rate (16.4 per 100,000 compared to 6.9 per 100,000) (2), while the HCV diagnosis rate is nearly twice the national rate (52.5 per 100,000 compared to 30.4 per 100,000) (3). These two illnesses disproportionately affect Indigenous communities in SK; while Indigenous people represent about 16% of the SK population, they represent between 60% and 75% of new cases of both HIV and HCV in a given year (1–4).

Many community-based organizations (CBOs), non-profit organizations, volunteer groups, peer mentors and other supporters across SK provide services and support to both Indigenous and non-Indigenous clients and promote health and wellness through education and dissemination of information about sexually transmitted blood-borne infections (5–8). The Saskatchewan Stories (Sask Stories) project sought to create a digital database of programs, projects and initiatives (PPI) related to HIV and HCV that have taken place in SK from 1980 to 2020.

The Sask Stories database is a living platform for stakeholders, especially frontline service providers and CBOs to share evidence, resources and promising/wise practices. To assist with populating the database, we conducted an environmental scan of published (academic and grey literature) HIV and HCV PPI. While this article covers the results of the environmental scan, we are also currently gathering information from CBOs about PPI that have not been published online. These two processes are complementary and will paint a broad picture of the activities in SK that have aimed to address HIV and HCV over the last 40 years.

Methods

An environmental scan gathers information and identifies trends within a given field (e.g. HIV/HCV care and support), which could provide opportunities for developing a response plan to urgent health issues (9). Our environmental scan used a comprehensive search strategy following the methods used in Choo's conceptual framework for environmental scanning centered on information needs, information seeking and information use (10). The scan covered both academic and grey literature on HIV and HCV PPI from January 1, 1980, to May 31, 2020. The scan was conducted in the summer 2020.

To be included in this scan, studies, reports and/or web-based information had to meet the following inclusion criteria of terminology for PPI:

- Programs: services provided with a group to a distinct population
- Projects: activities undertaken by a group with a definitive start and end date
- Initiatives: actions to support programs and projects

Projects included the following inclusion criteria to help screen and select PPI for full review:

- Located fully or partially in SK
- About HIV and/or HCV
- Available in English
- Between January 1, 1980, and May 31, 2020, including any PPI that were ongoing

For literature to be included, it had to meet the following limits:

- Targeted toward people living with or at risk of HIV/HCV
- Full-text filter
- Boolean operators and search filters unique to each database

The dates of our study (1980–2020) provided opportunities to fill in gaps on HIV and HCV PPI published or reported during the AIDS epidemic (from the 1980s to early 1990s) and the academic and grey literature published in its wake.

Based on consultations with the Community Advisory Board (CAB) members for Sask Stories (including CBOs, clinicians, people with lived experience and Elders) and a health sciences librarian, a search strategy for collecting academic literature was developed. The same search strategy was applied for both HIV and HCV. The databases searched for published literature were MedLine, ERIC, ProQuest One Literature, Public Health Information database, SCOPUS and CINAHL. Bibliography of Native North Americans, EMBASE (Ovid) and Indigenous studies portal (iPortal) were searched for articles on HIV and HCV. Google Canada, the Government of Saskatchewan website and the Government of Canada website were also used to search for grey literature; only the first 10 pages of the Google search results were included for review, as the relevance to the topic searched dropped off significantly beyond the first 10 pages. Snowball sampling among the CAB members was used to identify additional organizations, community agencies and health services that supported people living with HIV and/or HCV.

This article is a summary of the resultant scan report and includes highlights of trends and varieties of the PPI. The full report, including methodology details (including search terms) and all extracted PPI data, data and annotated bibliography, can be found on the Sask Stories website.

Results

Academic and grey literature for HIV

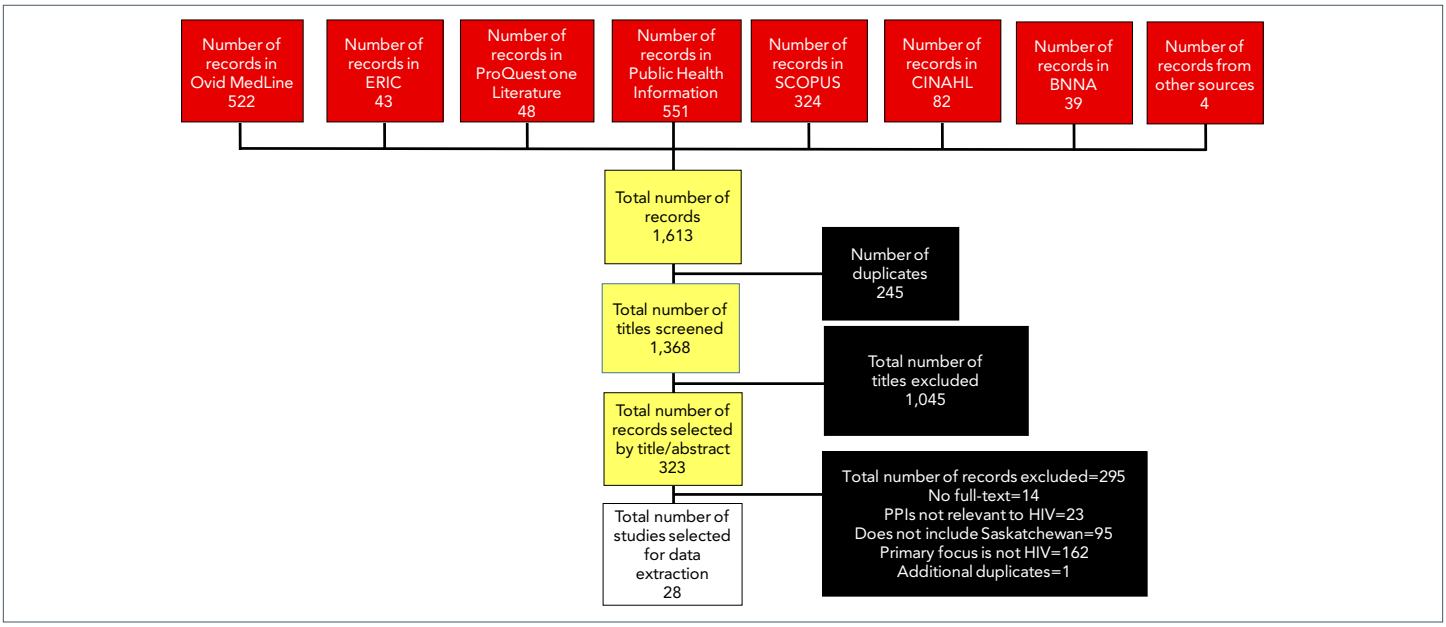
A total of 1,613 academic articles were retrieved, of which 245 were duplicate records. The abstracts of the remaining 1,368 articles were screened according to the inclusion criteria. A further 1,045 records were excluded based on title and abstract. A final 28 full-text articles were considered for review and data extraction (**Figure 1**). Among these 28 academic articles, a total of 38 PPI were identified, which included 23 projects, 9 programs and 6 initiatives. The reason for a higher number of PPI (n=38), compared to the number of academic articles (n=28) was that some articles referred to more than one PPI; for example, 17 PPI were stated as multiple combinations of a project, program and/or initiative within a single article (**Table 1**).

The grey literature search yielded 101 PPI. Among those, 18 were projects, 31 were programs and 51 were initiatives; however, one of these could not be classified as a program, project or initiative due to incomplete information (Table 1). Details on the scan results for HIV PPI can be found in the full report.

Academic and grey literature for HCV

The academic HCV literature search yielded an initial total of 1,061 articles; 326 were removed as duplicates and 406 were excluded as they did not meet the inclusion criteria. Finally, eight full-text articles were considered for data extraction (**Figure 2**). Twelve PPI were identified across eight academic articles, including two projects, seven programs and three initiatives specific to HCV in the context of SK (Table 1).

Figure 1: PRISMA chart of human immunodeficiency virus search



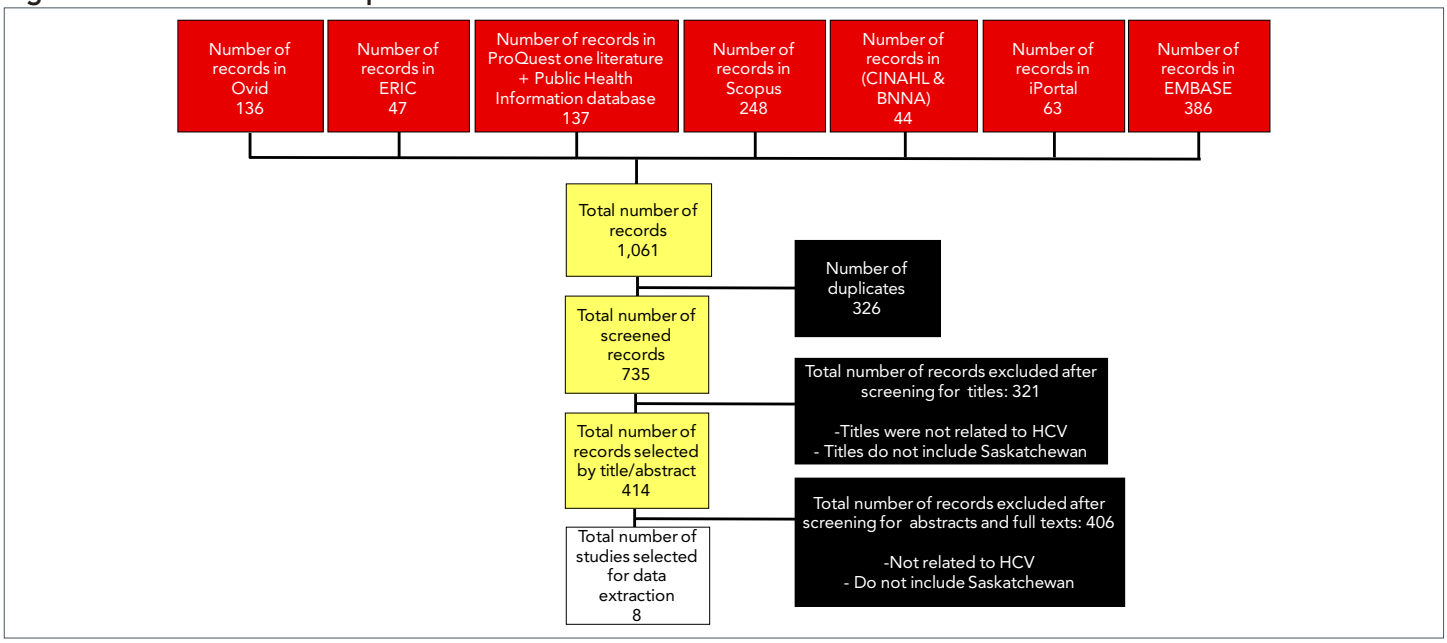
Abbreviations: BNNA, Bibliography of Native North Americans; HIV, human immunodeficiency virus; PRISMA, preferred reporting items for systematic reviews and meta-analysis

Table 1: Human immunodeficiency virus and hepatitis C search results for programs, projects and initiatives found within academic and grey literature[a]

PPI focus	Type of literature	Total	Projects	Programs	Initiatives	Not specified
HIV	Academic	38	23[b]	9[b]	6[b]	0
	Grey	101	18[b]	31	51	1
HCV	Academic	12	2	3	7[c]	0
	Grey	17	2[d]	6	9	0

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; PPI, programs, projects and initiatives
[a] Summary of final report
[b] Some programs, projects and initiatives included were identified as both a project, program and/or initiative
[c] Two sources have mentioned the same initiative for academic resources (HCV)
[d] Same project is mentioned in two different reports for grey literature (HCV)

Figure 2: PRISMA chart of hepatitis C virus search



Abbreviations: BNNA, Bibliography of Native North Americans; HCV, hepatitis C virus; PRISMA, preferred reporting items for systematic reviews and meta-analyses

Among the 17 grey literature sources, 2 projects, 6 programs and 9 initiatives for HCV were identified in the context of SK (Table 1). Among the PPI for projects, the same PPI was mentioned in two separate reports. Details on the scan results for HCV PPI can be found in the full report.

Combined HIV and HCV scan results for programs, projects and initiatives found within academic and grey literature

In total, 139 HIV-specific PPI and 29 HCV-specific PPI were identified (n=168). Of these PPI, 27% (n=38) and 41% (n=12) were found through academic literature, while 73% (n=101) and 59% (n=17) were from grey literature, for HIV and HCV, respectively. HIV accounted for 83% of total PPI, and HCV for 17% (**Table 2**). The academic articles have been summarized within an annotated bibliography in the final report.

Table 2: Combined scan results for programs, projects and initiatives found within academic and grey literature[a]

PPI focus	Total	Projects		Programs		Initiatives		Not specified	
		n	%	n	%	n	%	n	%
HIV (83% of total results)	139	41	29%	40	29%	57	41%	1	1%
HCV (17% of total results)	29	4	14%	13	45%	12	41%	0	0%

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus; PPI, programs, projects and initiatives
[a] Summary of final report

Discussion

To continue meeting the unique needs of people living with HIV and/or HCV, access to information about past and present PPI can guide organizations, individuals and communities to providing better access to care. This knowledge can be used to adapt or develop new PPI that are appropriate and context specific for SK's diverse communities. Access to this information allows stakeholders to identify promising and wise practices based on the evidence available to them. For instance, some PPI may be adaptable to the expressed needs of community, or to fit into an existing organizational structure. Adaptation is successful when proven interventions are incorporated into practice, or when appropriate models provide systematic guidance for PPI development (11). For SK's unique HIV epidemiologic profile, it is critical that relevant evidence supports culturally responsive and trauma-informed holistic PPI addressing HIV, HCV and health determinants. Although this is not a population-specific environmental scan, we acknowledge that the discourse of higher disease burden can further stigmatize Indigenous individuals and communities. One goal of our environmental scan is to honour the efforts of Indigenous and non-Indigenous communities and organizations that have led the design and implementation of various PPI in SK.

This environmental scan provides a compilation of published academic and grey literature about HIV and HCV-specific PPI in SK from 1980 to 2020. It represents the most comprehensive compilation of academic and grey literature specific to HIV and HCV in SK. Our results were not unexpected in the sense that, historically, there has been much more HIV-focused programming than HCV-focused programming in SK; however, we also know from our consultations with the Sask Stories CAB that there are several more HIV and HCV PPI, especially in rural, remote and Indigenous communities, than those that were found in our search. This can be explained by the fact that many of these PPI have not been published in either academic or grey literature and may not have an online or digital presence. Therefore, our next step is to identify PPI that have not been previously published on any platform. This will be accomplished with support from the CAB, the Indigenous Knowledge Facilitator and others who are currently leading this phase of consultations including conversations and updating information in the environmental scan that is incomplete or missing.

Conclusion

The information collected will be used to further develop the participatory database that serves as a central portal for SK's PPI. While a follow-up scan is needed to better reflect changes in PPI during the pandemic, we do not currently have the staff capacity to conduct an updated search (our funding ended in March 2022). This environmental scan is an important contribution to evidence-based practice and research in SK. It is particularly useful for organizations, researchers, policymakers and people living with HIV and/or HCV to develop new evidence-based PPI, to secure funding for PPI and to support individuals and communities in SK affected by HIV and HCV. Above all, it is a testament to the enormous labour and love of the people of SK working to address HIV and HCV.

Authors' statement

MG — Helped define search strategy, conducted environmental scan, drafted report
CM — Helped define search strategy, facilitated environmental scan, drafted report and manuscript
CH — Facilitated environmental scan, drafted report and manuscript
LC — Co-led project, helped define search strategy, reviewed manuscript
AK — Co-led project, helped define search strategy, reviewed manuscript

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

Competing interests
None.

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SURVEY REPORT

A cross-sectional investigation of HIV prevalence and risk factors among African, Caribbean and Black people in Ontario: The A/C Study

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Abstract

Background: The human immunodeficiency virus (HIV) epidemic has disproportionately affected African, Caribbean and Black (ACB) communities in Canada. We investigated the prevalence and factors associated with HIV infection among ACB people in Ontario.

Methods: A cross-sectional survey of first- and second-generation ACB people aged 15–64 years in Toronto and Ottawa (Ontario, Canada). We collected sociodemographic information, self-reported HIV status and offered dried blood spot (DBS) testing to determine the prevalence of HIV infection. Factors associated with HIV infection were investigated using regression models.

Results: A total of 1,380 people were interviewed and 834 (60.4%) tested for HIV. The HIV prevalence was 7.5% overall (95% confidence interval [CI] 7.1–8.0) and 6.6% (95% CI 6.1–7.1) in the adult population (15–49 years). Higher age (adjusted odds ratio [aOR] 2.8; 95% CI 2.77–2.82), birth outside of Canada (aOR 4.7; 95% CI 1.50–14.71), French language (aOR 9.83; 95% CI 5.19–18.61), unemployment (aOR 1.85; 95% CI 1.62–2.11), part-time employment (aOR 4.64; 95% CI 4.32–4.99), substance use during sex (aOR 1.66; 95% CI 1.47–1.88) and homosexual (aOR 19.68; 95% CI 7.64–50.71) and bisexual orientation (aOR 2.82; 95% CI 1.19–6.65) were associated with a positive HIV test. Those with a high school (aOR 0.01; 95% CI 0.01–0.02), college (aOR 0.00; 95% CI 0.00–0.01) or university education (aOR 0.00; 95% CI 0.00–0.01), more adequate housing (aOR 0.85; 95% CI 0.82–0.88), a higher social capital score (aOR 0.61; 95% CI 0.49–0.74) and a history of sexually transmitted infections (aOR 0.40; 95% CI 0.18–0.91) were less likely to have a positive HIV test.

Conclusion: Human immunodeficiency virus infection is linked to sociodemographic, socioeconomic, and behavioural factors among ACB people in Ontario.

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Keywords: HIV, high-risk populations, African Caribbean and Black, healthcare resource use, Canada

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Introduction

African, Caribbean and Black (ACB) people in Canada experience disproportionately high vulnerability to human immunodeficiency virus (HIV) due to intersecting social determinants that limit their ability to achieve optimal health outcomes (1). This is further aggravated by HIV-related stigma and discrimination towards communities affected by HIV (2,3). In Canada, ACB people constitute 2.5% of the population but 16% of people living with HIV (4). In the province of Ontario, ACB people constitute only 5% of the population but represent 25% of all new infections (4). Despite these figures, there is limited information on the HIV epidemic among ACB communities living in Canada, and there are currently no official estimates for HIV prevalence in ACB communities. Provincial surveillance data for HIV did not include ethnicity until recently (5,6), which may be a contributing factor. Despite being close to 40 years into the HIV epidemic, there are no racialized data on ACB people in Canada. As such, there is no agreed upon prevalence estimate for ACB people in Canada. Further, other systemic and structural factors may limit the capacity and resources to conduct research on ACB people, such as experiences of stigma and racial discrimination (2,3), alongside linguistic barriers (7) and migration-related issues (8).

Given that 52% of Canada's ACB population (over half a million people) live in Ontario (9), investigations to better understand their vulnerability to HIV infection are beneficial at the national level, including for Canada's planned response to reduce the burden and impact of sexually transmitted and blood-borne infections (10).

The purpose of this study (the A/C Study) is to inform policy and practice in Ontario, Canada regarding HIV care for ACB people by investigating the underlying factors that augment HIV risk and vulnerability of ACB people. In this paper, we report on the prevalence of HIV and factors associated with HIV infection.

Methods

We conducted a cross-sectional survey of ACB people in Toronto and Ottawa in Ontario, Canada from January to December 2019. The A/C Study was approved by the relevant Ethics Boards and the full protocol for the A/C Study is published elsewhere (11). Our study is reported according to the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) guidelines (12). Participants provided consent for the questionnaire, dried blood spot (DBS) and data linkage to administrative databases.

Eligibility

African, Caribbean and Black people were eligible to participate if they met the following criteria: were living in Toronto or Ottawa and their surrounding municipalities; were born in a Caribbean or Sub-Saharan African country or had a parent born in any of those countries; were 15 to 64 years old at the time of the survey; could communicate in English or French; and provided informed consent. The inclusion of youth as young as 15 years allowed us to capture their unique experiences and special safeguards were put in place, including counsellors and linkage to care (11).

Sampling

Our sample size estimation was informed by census and survey data on the distributions of ACB populations from the Caribbean and Africa in Toronto and Ottawa (13,14), a presumed 2% prevalence of HIV among first and second-generation ACB people and the Wilson confidence interval approach with continuity correction (15). This generated a sample size of 1,500, with 1,000 and 500 participants in Toronto and Ottawa, respectively.

Recruitment

Trained peer recruiters approached potentially eligible ACB people (social networks, events and venues populated by ACB people) to ask if they were interested in participating in the study.

Data collection

We obtained written informed consent for the interview and for collection of a DBS sample. Participants could consent for the interview alone or the interview and the DBS, but not the DBS alone.

The questionnaire was administered in French or English and included the following: socio-demographic information, sexual behaviour, substance use, blood donation, access to and use of health systems and services, and HIV testing, care and treatment. Further details on development and contents of the questionnaire can be found in the published protocol (11). A DBS sample was collected from all participants who consented to this part of the study; samples were tested by the Public Health Agency of Canada for antibodies against HIV. An honorarium of 40 CAD was offered to each participant. Participants were also offered a point-of-care HIV test.

Statistical analysis

The primary outcome was the result of a DBS HIV test (positive/negative). Participant characteristics analyzed were age group, city, language in which the survey was completed, sex, gender identity, sexual orientation, place of birth, level of education, employment, ability to meet basic needs, housing situation, ever tested for sexually transmitted infections (STIs), self-reported HIV status and social capital index score (16). The social capital index score was estimated from levels of agreement or disagreement on individuals' perceptions about their neighbourhood (16).

We summarized continuous data with means and standard deviations, or medians (quartile 1; quartile 3). Categorical data was described using counts and percentages. We compared our sample to the 2016 Canadian Census profile (17), and weighted the data to match the age, sex, and city distribution of Black people in the Census. The prevalence of HIV was estimated as the proportion of people with a positive HIV test among those tested. We applied the coefficient of variation (CV)—as used by Statistics Canada—to determine which values were acceptable to report from small subgroups (18).

The factors associated with HIV infection were assessed using generalized linear models (GLM), adjusted for relevant covariates. Covariates were entered into separate models as blocks comprised of demographic (age [the six age groups were treated as ordinal], gender identity, level of education, place of birth, language, city), socioeconomic (employment status, ability to meet basic needs, housing situation, social capital index score) and sexual behaviour variables (age at first intercourse, substance use during sex, transactional sex, sexual orientation, ever had an STI test). We used robust standard errors to account for clustering within cities (Toronto and Ottawa). Only statistically significant covariates ($p<0.05$) were entered into the full model.

Model fit was assessed using the Akaike Information Criterion (AIC) by comparing full models to partial models (a lower AIC indicates a better fit). Multicollinearity was assessed using the variance inflation factor (VIF) with a VIF>25 suggestive of multicollinearity. The type 1 error rate was set at 5%. Adjusted odds ratios (aOR) and 95% confidence intervals (CIs) are reported. Data were analyzed using Stata version 16.0.

Results

Participant characteristics

We included a total of 1,380 people 15–64 years of age. More people were recruited from Toronto (n=854/61.9%), took the survey in English (n=1,276/92.5%) and were female (n=853/63.4%). Most participants reported ever being tested for STIs (n=762/63.8%) and HIV (n=950/74.6%), with most self-reporting their HIV status as negative (n=848/91.9%). Only 834 (60.4%) participants agreed to take the DBS. A full sociodemographic profile of the participants is shown in **Table 1**.

Table 1: Sociodemographic characteristics of participants by dry blood spot test result for human immunodeficiency virus (unweighted)

Variable	Positive test (n=67)		Negative test (n=767)		Not tested (n=546)		Total (n=1,380)	
	n	%	n	%	n	%	n	%
Age (years)[a]								
15–19	3	4.6	93	12.3	61	11.7	157	11.7
20–29	4	6.2	263	34.7	159	30.5	426	31.7
30–39	18	27.7	193	25.4	127	24.4	338	25.1
40–49	22	33.8	148	19.5	116	22.3	286	21.3
50–59	16	24.6	49	6.5	43	8.3	108	8.0
60–64	2	3.1	13	1.7	15	2.9	30	2.2
City								
Toronto	38	56.7	457	59.6	359	65.8	854	61.9
Ottawa	29	43.3	310	40.4	187	34.2	526	38.1
Language								
English	51	76.1	729	95.0	496	90.8	1,276	92.5
French	16	23.9	38	5.0	50	9.2	104	7.5
Sex[a]								
Male	26	40.6	279	36.9	186	35.5	491	36.5
Female	38	59.4	477	63.0	338	64.5	853	63.4
Intersex	0	0.0	1	0.1	0	0.0	1	0.1
Gender identity[a]								
Man	22	34.9	276	36.5	183	34.9	481	35.8
Woman	39	61.9	468	61.8	335	63.9	842	62.6
Trans persons	0	0.0	2	0.3	4	0.8	6	0.4
Non-binary persons	2	3.2	11	1.5	2	0.4	15	1.1

Table 1: Sociodemographic characteristics of participants by dry blood spot test result for human immunodeficiency virus (unweighted) (*continued*)

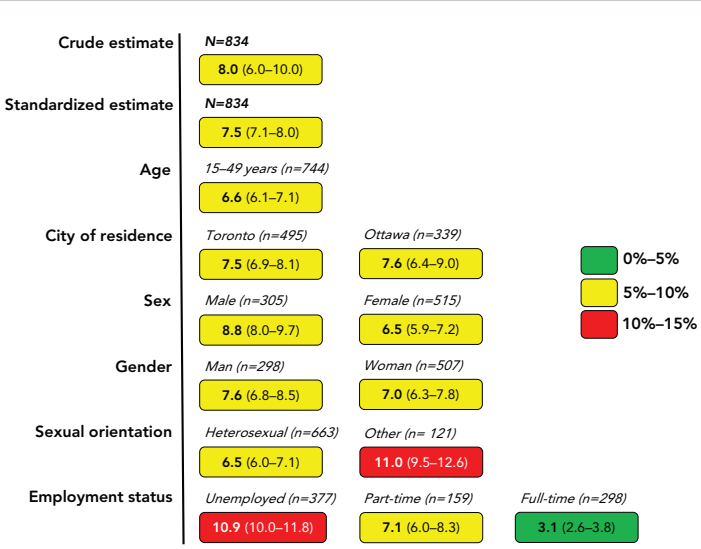
Variable	Positive test (n=67)		Negative test (n=767)		Not tested (n=546)		Total (n=1,380)	
	n	%	n	%	n	%	n	%
Sexual orientation								
Heterosexual	44	74.6	619	85.4	421	87.7	1,084	85.8
Homosexual	9	15.3	26	3.6	24	5.0	59	4.7
Bisexual	4	6.8	56	7.7	27	5.6	87	6.9
Other	2	3.4	24	3.3	8	1.7	34	2.7
Born in Canada[a]								
Yes	3	4.7	183	24.4	112	21.5	298	22.3
Education[a]								
University	4	6.6	10	1.3	16	3.1	30	2.3
College	15	24.6	174	23.1	120	23.3	309	23.3
High school	14	23.0	136	18.1	99	19.3	249	18.8
Less than high school	28	45.9	432	57.4	279	54.3	739	55.7
Employment								
Unemployed	46	68.7	331	43.2	264	48.4	641	46.4
Part-time	12	17.9	147	19.2	103	18.9	262	19.0
Full-time	9	13.4	289	37.7	179	32.8	477	34.6
Ability to meet basic needs[b]								
Not at all difficult	8	12.7	201	28.4	106	21.9	315	25.1
A little difficult	18	28.6	221	31.2	155	32.0	394	31.4
Fairly difficult	19	30.2	152	21.5	122	25.2	293	23.3
Very difficult	18	28.6	134	18.9	102	21.0	254	20.2
Housing situation[b]								
Not adequate	15	25.4	120	16.7	95	19.8	230	18.3
Barely adequate	8	13.6	85	11.8	63	13.1	156	12.4
Fairly adequate	21	35.6	276	38.4	196	40.7	493	39.2
Very adequate	15	25.4	238	33.1	127	26.4	380	30.2
Ever tested for STI[a]								
Yes	43	72.9	443	63.6	276	62.9	762	63.8
Self-reported HIV status[a]								
HIV+	47	82.5	4	0.8	24	7.0	75	8.1
HIV-	10	17.5	520	99.2	318	93.0	848	91.9

Abbreviations: HIV, human immunodeficiency virus; STI, sexually transmitted infections
[a] Missing fewer than 5%
[b] Missing 5%–10%

Prevalence of HIV infection

After weighting the sample according to age, sex and city of residence of the ACB people in Ontario, the prevalence was 7.5% (95% CI 7.1–8.0). The prevalence of HIV in the adult population (15–49 years) was 6.6% (95% CI 6.1–7.1). The prevalence in selected subgroups is shown in **Figure 1**.

Figure 1: Prevalence of human immunodeficiency virus in subgroups of African, Caribbean and Black people in Toronto and Ottawa, Ontario



Factors associated with HIV infection

In the demographic model, older people (aOR 1.86; 95% CI 1.58–2.18), people with non-binary gender identities (aOR 5.20; 95% CI 1.18–7.28; compared to men), people born outside of Canada (aOR 3.19; 95% CI 1.88–5.40) and people who completed the survey in French (aOR 8.11; 95% CI 2.34–28.14) were more likely to have a positive HIV test. Women (aOR 0.58; 95% CI 0.58–0.59) compared to men, and people with a high school education (aOR 0.15; 95% CI 0.05–0.46), college (aOR 0.08; 95% CI 0.07–0.08) or university (aOR 0.05; 95% CI 0.04–0.07) compared to people with less than high school education were less likely to have a positive test.

In the socioeconomic model, people who were unemployed (aOR 2.38; 95% CI 2.17–2.62) or only part-time employed (aOR 1.35; 95% CI 1.04–1.76) were more likely to have a positive HIV test. People with better housing situations (aOR 0.71; 95% CI 0.69–0.74) and with a higher social capital index score (aOR 0.55; 95% CI 0.51–0.60) were less likely to have a positive test.

In the behavioural model, people who identified as homosexual (aOR 8.63; 95% CI 5.86–12.72) and bisexual (aOR 2.45; 95% CI 1.25–4.8) were more likely to have a positive HIV test than those who identified as heterosexual. People with a higher age at first intercourse (aOR 0.91; 95% CI 0.88–0.95), people who reported substance use during sex (aOR 0.51; 95% CI 0.39–0.66), people who reported more sexual partners (aOR 0.78; 95% 0.74–0.82), and people who had ever had an STI test (aOR 0.51; 95% CI 0.27–0.94) were less likely to have a positive test.

In the full model (including demographic, socioeconomic and behavioural factors), older people (aOR 2.8; 95% CI 2.77–2.82), people born outside of Canada (aOR 4.7; 95% CI 1.5–14.71), people who completed the survey in French (aOR 9.83; 95% CI 5.19–18.61), people who were unemployed (aOR 1.85; 95% CI 1.62–2.11) or part-time employed (aOR 4.64; 95% CI 4.32–4.99), people who reported substance use during sex (aOR 1.66; 95% CI 1.47–1.88) and people who identified as homosexual (aOR 19.68; 95% CI 7.64–50.71) or bisexual (aOR 2.82; 95% CI 1.19–6.65) were more likely to have a positive HIV test. In contrast, people with a high school (aOR 0.01; 95% CI 0.01–0.02), college (aOR 0.00; 95% CI 0.00–0.01) or university education (aOR 0.00; 95% CI 0.00–0.01), compared to people with less than high school education, people who reported a more adequate housing situation (aOR 0.85; 95% CI 0.82–0.88), people with a higher social capital index score (aOR 0.61; 95% CI 0.49–0.74) and people who reported ever having an STI test (aOR 0.40; 95% CI 0.18–0.91) were less likely to have a positive test. The results of the models are shown in **Table 2**.

Discussion

In this study the overall adult prevalence of HIV infection was 6.6% (95% CI 6.1–7.1) and varied among subgroups; thus confirming the role of sociodemographic, socioeconomic and behavioural factors in HIV vulnerability. These findings were further highlighted in the multivariable analysis in which we identified age, education, place of birth, language, employment, housing, social capital, sexual orientation and STI testing behaviours to be associated with HIV infection.

This work highlights several key issues. First, 82.5% of people with a positive test self reported their positive HIV status; i.e., they were aware of their status. Awareness of HIV-positive status is the first of the UNAIDS 95-95-95 targets for 2030 (19), and this work confirms concerns that even if countries meet these targets on the national level, vulnerable sub populations may not. African, Caribbean and Black people in Ontario are 12.5% shy of the 2030 target. However, individuals may underreport their HIV-positive status for fear of stigma and discrimination, as shown in other studies (20).

In addition to factors that have been described in the literature, we found additional factors that may explain ACB people's vulnerability to HIV or the nefarious consequences of HIV infection. We found that people who reported a lower social capital were more likely to have HIV, suggesting that family and community supports can play a role in enhancing resilience

Table 2: Summary of generalized linear models for factors associated with a positive human immunodeficiency virus test

Partial models					Full model (n=348) AIC 4.105		
Block	Variable	aOR		*p*-value	aOR		*p*-value
		n	95% CI		n	95% CI	
Demographic (n=797) AIC 4.787	Age	1.86	1.58–2.18	<0.001	2.8	2.77–2.82	<0.001
	Gender identity						
	Man	1	1	N/A	1	1	N/A
	Woman	0.58	0.58–0.59	<0.001	1.16	0.83–1.62	0.393
	Other	5.20	1.18–7.28	<0.001	Omitted[a]		N/A
	Level of education						
	Less than high school	1	1	N/A	1	1	N/A
	High school	0.15	0.05–0.46	0.001	0.01	0.01–0.02	<0.001
	College	0.08	0.07–0.08	<0.001	0.00	0.00–0.01	<0.001
	University	0.05	0.04–0.07	<0.001	0.00	0.00–0.00	<0.001
	Place of birth						
	Canada	1	1	N/A	1	1	N/A
	Other	3.19	1.88–5.4	<0.001	4.7	1.5–14.71	0.008
	Language						
	English	1	1	N/A	1	1	N/A
	French	8.11	2.34–28.14	0.001	9.83	5.19–18.61	<0.001
	City						
	Toronto	1	1	N/A	Not included in model		
	Ottawa	0.79	0.62–1.01	0.064	Not included in model		
Economic (n=731) AIC 6.175	**Employment**						
	Unemployed	2.38	2.17–2.62	<0.001	1.85	1.62–2.11	<0.001
	Part-time	1.35	1.04–1.76	0.024	4.64	4.32–4.99	<0.001
	Full-time	1	1	N/A	1	1	N/A
	Ability to meet basic needs	0.89	0.73–1.08	0.223	Not included in model		
	Housing situation	0.71	0.69–0.74	<0.001	0.85	0.82–0.88	<0.001
	Social capital score	0.55	0.51–0.60	<0.001	0.61	0.49–0.74	<0.001
Behavioural (n=369) AIC 5.435	Age at first intercourse	0.91	0.88–0.95	<0.001	0.99	0.92–1.07	0.797
	Substance use during sex						
	No	1	1	N/A	1	1	N/A
	Yes	0.51	0.39–0.66	<0.001	1.66	1.47–1.88	<0.001
	Number of sexual partners	0.78	0.74–0.82	<0.001	0.80	0.69–0.93	0.004
	Transactional sex encounters	1.17	0.47–2.91	0.741	Not included in model		
	Sexual orientation						
	Heterosexual	1	1	N/A	1	1	N/A
	Homosexual	8.63	5.86–12.72	<0.001	19.68	7.64–50.71	<0.001
	Bisexual	2.45	1.25–4.8	0.009	2.82	1.19–6.65	0.018
	Other	1.02	0.03–32.11	0.992	6.92	0.53–89.73	0.139
	Ever had an STI test						
	No	1	1	N/A	1	1	N/A
	Yes	0.51	0.27–0.94	0.032	0.40	0.18–0.91	0.030

Abbreviations: AIC, Akaike information criterion; aOR, adjusted odds ratio; CI, confidence interval; N/A, not applicable; STI, sexually transmitted infections
[a] Omitted due to insufficient data

among ACB people. These mechanisms may work by buffering systemic disadvantages that predispose individuals to HIV (21), but also by promoting preventive behaviours.

African, Caribbean and Black people who were not born in Canada were more likely to have a positive HIV test. It is possible that those who were not born in Canada immigrated from countries with a high underlying prevalence of HIV. Also, we must consider that Black immigrants, irrespective of baseline risk, have other vulnerabilities related to income and employment that increase their risk of HIV, including culture shock, socioeconomic and racial disadvantage of immigrants (22).

People who completed the survey in French were also more likely to have a positive test. These individuals constitute an ethnic and linguistic minority in Ontario, and as a result may face additional socioeconomic barriers due to their language and migrant status. A scoping review on access to HIV care for Francophones in majority English-speaking provinces highlighted difficulties faced by healthcare professionals in providing care to French-speaking clients (7).

Increasing age was associated with a higher likelihood of a positive test. This finding is similar to national trends, which show an increasing prevalence in HIV from 15–19 years age group up to the 30–39 years age group, and then a steady decline (23). In our study, the 50–59 years age group had the highest HIV prevalence. It is possible that the older people have been living with HIV for longer, and have experienced other factors (e.g. advances in understanding about prevention and public health efforts in recent decades) that may increase longevity in people with HIV.

Previous STI testing was associated with lower HIV risk. We postulate that people who have a history of an STI test may have a better appreciation of their risk for STIs including HIV. Moreover, having an STI increases the risk of HIV infection (24); therefore, testing for and treating STIs would be expected to reduce HIV risk.

Overall, our findings corroborate previous research highlighting the need for information, testing and treatment services for ACB people (25), and a disconnect between perceived and actual risk for HIV infection (26). Even though we have discussed these factors separately, they do not exist in a vacuum and likely interact in complex ways to create vulnerability to HIV. While this study was conducted among ACB people, the findings may be true for other racialized or equity-seeking groups of people in Canada and serve to further our understanding of vulnerability to HIV.

Study limitations

This study is not without limitations. First, the planned sample size of 1,500 was not met; however, the sample size of 1,500 was based on an assumed prevalence of HIV of 2%. Given that the prevalence was higher, a smaller sample size would suffice. Second, this is a cross-sectional study, which precludes inferences about causality or the temporal nature of the associations reported here. Third, inaccuracies and non-response to certain questions were inevitable, leading to potential recall bias and social desirability bias. More so, despite weighting, the people who opted to take a DBS test may not be representative of the ACB population, and selection bias may be present. Fourth, the language in which participants chose to complete the questionnaire might not be a true reflection of their primary language of communication.

Study strengths

This study was led by ACB researchers, in line with the principles of autonomy and self-determination in community-led research, and ensured that those participants, recruiters and other community members were treated respectfully in a culturally appropriate manner. Our approach to knowledge translation prioritized the community and has been implemented so far through community presentations and a community report in French and English (27,28). This is the largest study of ACB people in Canada, with estimates of HIV prevalence by subgroups. Further details on the A/C Study can be accessed online.

Conclusion

African, Caribbean and Black people in Ontario are at a high risk of HIV infection and this risk is linked to sociodemographic, socioeconomic, and behavioural factors. Interventions to improve the social and economic wellbeing of ACB people by removing structural barriers to information, HIV testing, pre and post-exposure prophylaxis and other resources that curb transmission of HIV are needed. An ACB cohort study or linkage to administrative databases would be an ideal way to measure long-term trends in HIV risk, access to health services and health outcomes.

Authors' statement

LM — Writing–original draft
DOL — Writing–original draft; formal analysis; review and editing
LM — Design study; develop data collection instruments
WET — Design study; develop data collection instruments; review and editing
WH — Design study; develop data collection instruments; review and editing
LEN — Design study; develop data collection instruments; review and editing
JE — Design study; develop data collection instruments; review and editing
SB — Analysis review; review and editing

All authors reviewed and approved the final draft.

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

Competing interests

None.

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Effectiveness of non-pharmaceutical interventions to reduce SARS-CoV-2 transmission in Canada and their association with COVID-19 hospitalization rates

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Abstract

Background: Non-pharmaceutical interventions (NPIs) aim to reduce the incidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections mostly by limiting contacts between people where virus transmission can occur. However, NPIs limit social interactions and have negative impacts on economic, physical, mental and social well-being. It is, therefore, important to assess the impact of NPIs on reducing the number of coronavirus disease 2019 (COVID-19) cases and hospitalizations to justify their use.

Methods: Dynamic regression models accounting for autocorrelation in time series data were used with data from six Canadian provinces (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec) to assess 1) the effect of NPIs (measured using a stringency index) on SARS-CoV-2 transmission (measured by the effective reproduction number), and 2) the effect of the number of hospitalized COVID-19 patients on the stringency index.

Results: Increasing stringency index was associated with a statistically significant decrease in the transmission of SARS-CoV-2 in Alberta, Saskatchewan, Manitoba, Ontario and Québec. The effect of stringency on transmission was time-lagged in all of these provinces except for Ontario. In all provinces except for Saskatchewan, increasing hospitalization rates were associated with a statistically significant increase in the stringency index. The effect of hospitalization on stringency was time-lagged.

Conclusion: These results suggest that NPIs have been effective in Canadian provinces, and that their implementation has been, in part, a response to increasing hospitalization rates of COVID-19 patients.

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Introduction

Non-pharmaceutical interventions (NPIs) were implemented globally to reduce the transmission of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resulting levels of coronavirus disease 2019 (COVID-19) illnesses, hospitalizations and deaths. Non-pharmaceutical interventions were used before vaccines became widely available, and at the time of writing, continue to complement vaccination efforts. Non-pharmaceutical interventions include case detection and isolation, contact tracing and quarantine, travel restrictions, restrictive closures (gathering restrictions, nonessential business closures and school closures), curfews and personal measures including physical distancing and wearing masks. Non-pharmaceutical interventions act by reducing the rate of contacts among individuals (e.g. closure of nonessential businesses) and reducing the probability of transmission when contacts do occur (e.g. masking and physical distancing). Both contact rates and transmission probability are determinants of the effective reproductive number, R_t, (i.e. the average number of secondary cases generated by a typical infectious individual at time *t* in a population with atypical mixing resulting from some immunity and/or NPIs) (1). The very nature of NPIs, which aims at reducing social interactions, has been shown to negatively impact economies and the physical, mental and social well-being of the underlying population (2–4); therefore, assessment on the impact of NPIs to reduce the transmission of SARS-CoV-2 is important to justify and validate their implementation. A clearer understanding of the effectiveness of NPIs will also support future public health decisions regarding their use in response to potential successive waves of COVID-19 and potential future pandemics with similar modes of transmission.

Previous articles report evidence for and against the effectiveness of NPIs. Non-pharmaceutical interventions are associated with reducing confirmed case rates (5–7), and the strength of their effectiveness increases with earlier rather than later implementation (8). A recent review suggests that most studies report evidence for NPIs being effective (9). Evidence against the effectiveness of NPIs is largely centred on the types of NPIs measures and how they vary in their effectiveness (10–12). For example, restrictions to movement were not found to be associated with a reduction in the incidence (13). Also, lockdowns were not associated with a reduction in COVID-19 prevalence and mortality (14).

Even within Canada, there is varying evidence for the effectiveness of NPIs. Provinces and territories implemented NPIs differently through time in response to their COVID-19 situation. The predominant measures included school and workplace closures, public events cancellations, gathering restrictions, stay-at-home requirements, internal and interprovincial movement restrictions, testing policies and masking. Two recent articles assessing the effectiveness of NPIs used a standardized series of indicators and composite indices developed by the University of Oxford's Blavatnik School of Government to quantify provincial-level government NPIs over the duration of the COVID-19 pandemic (15). In one study, the stringency index was found to be associated with decreasing prevalence of COVID-19 over the first three waves in addition to the impact of vaccination but could not disentangle these effects (16). Another study focused largely on the pre-vaccination period of the pandemic and found that the effect of stringency to associate with a reduction in the daily case growth of COVID-19 was minimal to non-existent, over the first and second waves (17).

Here we aim to enhance understanding of the effectiveness—or not—of NPIs in Canada by assessing data from six provinces individually, given regional variations in the COVID-19 waves in Canada. We focused on the first and second waves of the pandemic. We accounted for possible confounding effects that might have arisen from the rollout of the first dose of vaccines and the first variant of concern during the latter months of the study period. We assessed associations with NPIs, as measured using a stringency index, from two perspectives. First, we expected 1) NPIs to reduce the frequency of infectious contacts, as measured by R_t, and 2) that the impact of NPIs should be time-lagged given the duration of the incubation period and surveillance activities (testing and reporting). Secondly, we assessed evidence that the strengthening of NPIs was in response to increasing hospitalization rates, with the intention of preventing healthcare systems from being overwhelmed. Hence, the objectives of this study were to measure the associations, at the provincial level, between 1) the stringency index of NPIs, stringency index (*sidx*), and transmission of SARS-CoV-2 (as measured by the effective reproduction number, R_t), and 2) the number of hospitalized COVID-19 patients and the intensity of the NPIs implemented, as measured by *sidx*.

Methods

Study design and population

This is an ecological study using the province as the unit of analysis. The study period was April 1, 2020, to March 31, 2021. This period excludes the first three months of 2020, before the World Health Organization declared global pandemic, when provincial health authorities were still establishing surveillance protocols. Furthermore, the study period includes the time period when NPIs were the main method of COVID-19 control—before vaccination may have had a significant impact on SARS-CoV-2 transmission in Canada (fewer than 2% of the population were fully vaccinated by March 31, 2021), though we do account for this effect as discussed below. The study period also contained the first two waves of the epidemic in Canada, and a significant part of the third wave. In this analysis, data from British Columbia (BC), Alberta (AB), Saskatchewan (SK), Manitoba (MB), Ontario (ON) and Québec (QC) were used because these provinces had the majority of cases (18).

Measurement and definition of SARS-CoV-2 transmission

Transmission of SARS-CoV-2 was estimated using the effective reproduction number R_t. The R_t is the average number of secondary infections generated by one case in a population in which some individuals are immune, and control measures may be in place (1). The lower bound of R_t is 0 with R_t<1 indicating decreasing transmission (i.e. the daily number of new cases is decreasing), R_t=1 indicating a stable rate of transmission (i.e. the infection is endemic), and R_t>1 indicating increasing transmission (i.e. the infection is spreading). The R_t was calculated from the number of new SARS-CoV-2 infections detected and reported by the provinces as temporally referenced by the date of reporting. The R library EpiEstim (version 2.2.3), with a 10-day sliding window on the reported infections, was used to estimate R_t (19). The serial interval was set at a mean of four days and a standard deviation of 4.75 days (20).

Measurement and definition of the stringency index

An adapted version of the methodology developed at the Blavatnik School of Government was used to generate a Canadian subnational dataset for NPIs implemented in response to COVID-19. Data were collected from publicly available sources, such as news articles and government press releases and briefings. These sources were identified and then coded using the indicators and codebook developed by Oxford Covid-19 Government Response Tracker, with an additional indicator being developed and coded to capture interprovincial travel restrictions: 0—No restrictions; 1—Recommend not to travel between provinces or territories; 2—Entrance into the province/territory from some provinces or territories is restricted (includes required quarantine period); 3—Entrance into the province/territory from all provinces or territories is restricted (includes required quarantine period). On a weekly basis, two team members independently coded the NPIs for each province and territory. The coded data from the two coders were then compared and any discrepancies were resolved by a third team member.

The Canadian subnational version of the Oxford's Stringency Index included the following modifications. First, indicators that did not vary in time or between provinces (i.e. international travel restrictions, federal public health information campaigns, public transport closures) were removed. Second, indicators that may influence infection transmission in Canada (interprovincial travel restrictions, testing policy, and masking policy) were added. The modified *sidx* was calculated using the same formula developed to calculate Oxford's Stringency Index but with a different set of indicators (**Table 1**).

Table 1: Comparison of modified stringency index and Oxford's stringency index

Indicator name	Oxford's stringency index	Modified stringency index
C1_School closing	Yes	Yes
C2_Workplace closing	Yes	Yes
C3_Cancel public events	Yes	Yes
C4_Restrictions on gatherings	Yes	Yes
C5_Close public transport	Yes	No
C6_Stay at home requirements	Yes	Yes
C7_Restrictions on internal movement	Yes	Yes
C8_International travel controls	Yes	No
H1_Public information campaigns	Yes	No
H2_Testing policy	No	Yes
H6_Facial coverings	No	Yes
X1: Interprovincial travel restriction	No	Yes

Note: Yes, included in the indicated stringency Index; No, not included in the indicated stringency index

Measurement and definition of the number of hospitalized COVID-19 patients

The number of hospitalized COVID-19 patients, *H*, was the daily number reported publicly by the provinces: Ontario, Alberta, Québec, British Columbia, Saskatchewan, and Manitoba.

Statistical model

A dynamic regression approach was used to measure the associations between *sidx* and R_t (i.e. study objective 1) and *sidx* and *H* (i.e. study objective 2). The outcomes, R_t or *sidx*, were modelled by non-stationary processes with time-dependent mean and variance and information from past observations. Given that classical regression analysis of non-stationary data can result in spurious model parameter estimates, this study used an autoregressive integrated moving average (ARIMA) modelling approach (21). More specifically, an extended version of the ARIMA model (ARIMAX) was used such that the outcome time series, y_t, was modelled as a function of *k* explanatory variables (x_{1t},…x_{kt}) by taking into account information from the past observation:

$$\nabla^d y_t = \nabla^d y_{t-1} * \theta_1 + \nabla^d y_{t-2} * \theta_2 + \ldots + \nabla^d y_{t-p} * \theta_p + \beta_1 * x_{1t} + \beta_2 * x_{2t} + \ldots + \beta_k * x_{kt} + \varepsilon_t + \alpha_1 * \varepsilon_{t-1} + \ldots + \alpha_q * \varepsilon_{t-q}$$

where the noise term ε_t is Gaussian with mean 0 and variance σ^2, and ∇^d is the differentiation operator and d is the degree of differencing. When d=1, the model is $\nabla^1 y_t = y_t - y_{t-1}$ and when d=2, $\nabla^2 y_t = \nabla^1(\nabla^1 y_t) = \nabla^1(y_t - y_{t-1}) = (y_t - y_{t-1}) - (y_{t-1} - y_{t-2}) = y_t - 2 * y_{t-1} + y_{t-2}$. Also, p is the number of the autoregressive (AR) terms of $\nabla^d y_t$ and q is the number of the moving average (MA) terms. Finally, $\theta_1, \theta_2, \ldots, \theta_p, \beta_1, \ldots \beta_{kt}, \alpha_1, \ldots, \alpha_q, \sigma$ are the model parameters. Overall, the model is denoted by ARIMAX (p, d, q), respectively. The ARIMAX models were built using the auto.arima function from the forecast package for R statistical software (22–24). This function finds the best fitting model while accounting

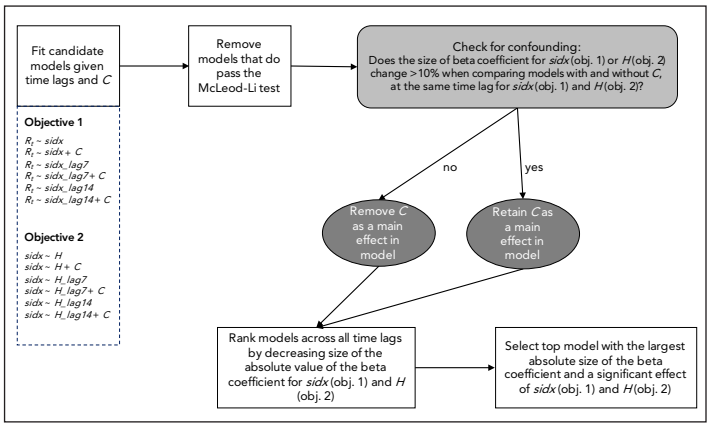
for autocorrelation using AR terms, differencing terms and MA terms. The auto.arima function selects a best fitting model among candidate models with differing in their number of AR and MA terms by minimising Akaike's information criterion for small sample sizes.

Model building and selection

After time-lagging the explanatory data variables (i.e. *sidx* and *H*; see below), the data were averaged at seven-day non-overlapping periods. This reduces noise that can occur in health data for social factors (e.g. organization of surveillance and hospital) at the weekly level as observed in our data and does not inject more autocorrelation by using a moving average approach with overlapping periods (25). The statistical analysis was performed at the provincial level. The general formulation of candidate models for objective 1 was: $R_t \sim sidx$, and for objective 2 was: $sidx \sim H$. In both cases, the explanatory variable effects were also assessed with time lags at seven, and 14 days. Varying the length of the time lags enables a determination for how much time a change in *sidx* has a stronger impact on R_t (model for objective 1) or how much time a change in hospitalizations most influences the strength of NPI (model for objective 2). Varying the length of the time lags also allows accounting for likely differences among jurisdictions in the speed with which cases and hospitalizations are reported. Fitted models were disregarded if autoregressive conditional heteroscedasticity remained in the residuals, as tested using the McLeod-Li test, and allowing up to two violations for an assessment over five time-lag periods (26).

In our model building, we also consider the possibility of confounding effects of the more highly transmissible Alpha variant of concern (B.1.1.7), the winter months resulting in closer contacts as people spend more time indoors (27) as well as the introduction of vaccination which can all be associated with the exposures of interest (*sidx* or *H*) and the outcomes (R_t and *sidx*). Indeed, an increase in both R_t and *H* were observed during the end of our study period. Our study period was not long enough to disentangle the potential confounding effects which are not fully overlapping (i.e. vaccination from January to March 2021, and alpha increasing in dominance mostly in March 2021), and the study period only contains one winter from the end of December 2020 to March 2021. We therefore decide to use a period of time as a proxy combining all three effects and dichotomized time into a pre-vaccination/Alpha variant/winter (April–December 2020; coded as C=0) and the period when vaccination, the Alpha variant and winter were present (January–March 2021; coded as C=1). We tested for confounding by assessing if the change in the beta coefficient of *sidx* was greater than 10% between model formulations $R_t \sim sidx$ and $R_t \sim sidx + C$, for each time lag of *sidx*. If confounding existed, we retained the model with *C*, otherwise we retained the univariable model with *sidx*. We then ranked the retained models across the time lags, and no time lag, by the decreasing size of the beta coefficient for *sidx*, representing the variable effect size on the outcome variable. Final models were selected if the effect of *sidx* was significant at a *p*-value of 0.05 (**Figure 1**). For the second objective, we use the same approach given model formulations of $sidx \sim H$ and $sidx \sim H + C$. In the model results from both objectives, we report the Bayesian Information Criterion (BIC), which was calculated based on the maximum likelihood for each model, to enable comparisons among multiple models of the same province (28). Lower values of BIC indicate a more parsimonious model fit to the data. A difference in BIC (ΔBIC) of two or less indicates that the two models are equally effective in support of being the best model (29).

Figure 1: Summary of the model building and model selection approaches run separately for each province and objective



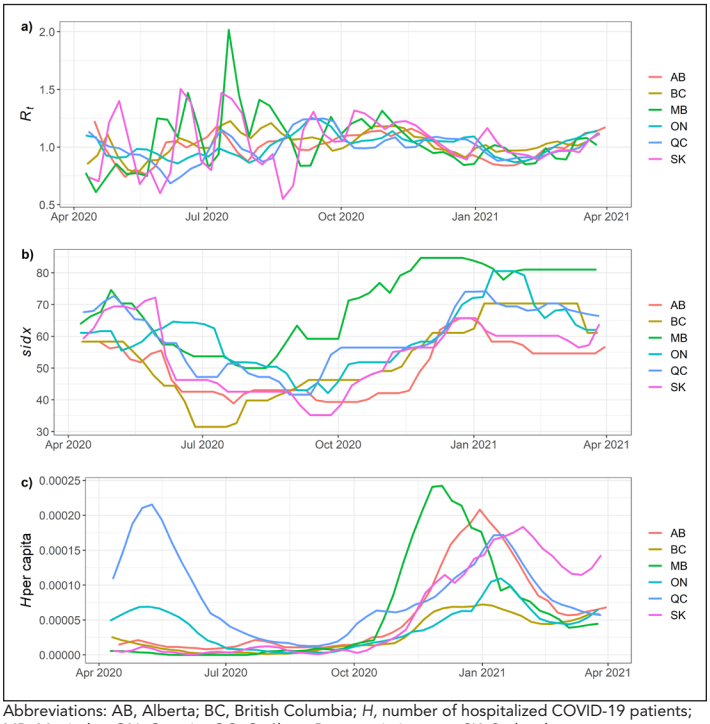
Abbreviations: *C*, period of time with combined effects of vaccination, Alpha variant and winter; *H*, number of hospitalized COVID-19 patients; lag7, time lags at seven days; lag14, time lags at 14 days; obj, objective; R_t, transmission rate; *sidx*, stringency index

Results

Temporal variation in R_t, *sidx*, and *H* were similar among the provinces during the study period (**Figure 2**). Visually, *sidx* and R_t were negatively associated (**Figure 3**), while *H* and *sidx* appeared positively associated (**Figure 4**). For objective 1, we found that *sidx* was significantly and negatively associated with R_t in all provinces except for BC. Alberta, SK, ON and QC had one final top selected model, while MB had three, with the top selected model having a lag of seven days for *sidx*. For the other provinces, the effects of *sidx* were lagged at 14 days for AB and QC, seven days for SK, but with no lag for ON (**Table 2**).

For objective 2, we found that *H* was significant and positively associated with *sidx* in all provinces except for SK. In BC, two models had effectively equal support for lagged effects of *H* at seven and 14 days, though the effect size of *H* was greater at 14 days. Alberta also had two models with equally effective support with *H* at 0 and seven days. The effect size was larger at seven days. For MB, there was only one model with a significant effect of *H*, which was lagged at seven days. Ontario and QC both had two models with significant effects of *H*. For ON, *H* was lagged at seven and 14 days, with the effect size being greater at 14 days. In QC, the effect size was greatest in the model with no time lag of *H*, as compared to a model a seven-day lag (**Table 3**).

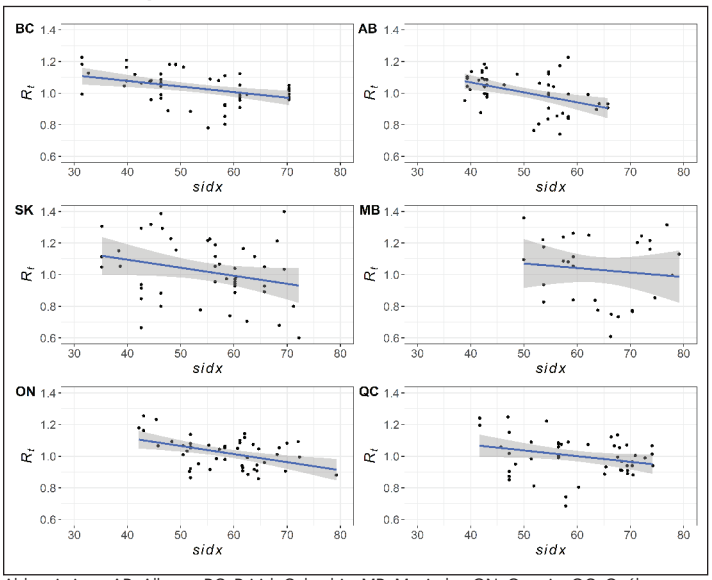
Figure 2: Study period time series at provincial level[a]



Abbreviations: AB, Alberta; BC, British Columbia; *H*, number of hospitalized COVID-19 patients; MB, Manitoba; ON, Ontario; QC, Québec; R_t, transmission rate; SK, Saskatchewan

[a] Study period time series at provincial level for a) transmission rate, R_t, b) stringency of NPIs, *sidx*, and c) number of hospitalized COVID-19 patients, *H*, per capita, for visual comparison. Data are averaged per week

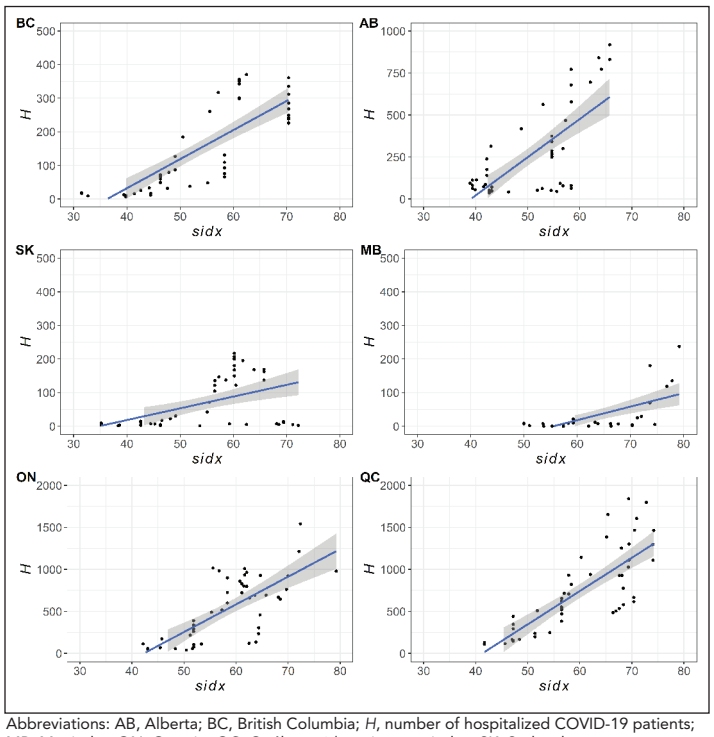
Figure 3: Scatter plot of stringency of non-pharmaceutical interventions against the transmission rate for six provinces in Canada[a]



Abbreviations: AB, Alberta; BC, British Columbia; MB, Manitoba; ON, Ontario; QC, Québec; R_t, transmission rate; *sidx*, stringency index; SK, Saskatchewan

[a] Data are averaged per week. A linear fitted line between *sidx* and R_t with standard errors are included to highlight the trend between the two variables

Figure 4: Scatter plot of stringency of non-pharmaceutical interventions against the number of hospitalized COVID-19 patients for six provinces in Canada[a]



Abbreviations: AB, Alberta; BC, British Columbia; *H*, number of hospitalized COVID-19 patients; MB, Manitoba; ON, Ontario; QC, Québec; *sidx*, stringency index; SK, Saskatchewan

[a] Data are averaged per week. A linear fitted line between *sidx* and *H* with standard errors are included to highlight the trend between the two variables

Our analysis suggests there was limited evidence for confounding effects of vaccination, the Alpha variant and winter, as modelled by *C*, on the outcome variables. For objective 1, there was only one model, as found for ON, with a significant effect *sidx* on R_t that also included a significant effect of *C*. All other models with significant effects of *sidx* did not retain *C* (Table 2). For objective 2, there were only two models, as found for AB and QC, that had a significant effect of *H* on *sidx* and retained the variable for *C* (Table 3). However, in both cases, the effect of *C* was not significant.

The full model results, with the AR and MA terms, are provided in the supplementary material for final models that contain a significant effect of *sidx* on R_t for objective 1, and of *H* on *sidx* for objective 2, at a *p*-value ≤0.05 (**Appendix**).

Table 2: Results from the final selected models at the provincial level for study objective 1[a,b]

Province	Model variables	BIC	M-Li	nV	*sidx*				*C*				nObs
					β	CI low	CI high	*p*-value	β	CI low	CI high	*p*-value	
BC	*sidx*_lag14	-116.8	0	5	-6.06E-03	-1.37E-02	1.54E-03	1.18E-01	N/A	N/A	N/A	N/A	50
	*sidx*_lag7	-115.6	1	2	-3.83E-03	-1.07E-02	3.02E-03	2.73E-01	N/A	N/A	N/A	N/A	50
	sidx	-115.2	1	1	-3.23E-03	-1.02E-02	3.70E-03	3.61E-01	N/A	N/A	N/A	N/A	50
AB	*sidx* + *C*	-114.9	1	2	-9.16E-04	-7.94E-03	6.11E-03	7.98E-01	-2.80E-02	-1.27E-01	7.08E-02	5.78E-01	51
	*sidx*_lag14	-125.2	1	0	-7.30E-03	-1.19E-02	-2.66E-03	2.04E-03	N/A	N/A	N/A	N/A	51
	*sidx*_lag7 + *C*	-115.1	1	0	2.70E-03	-6.74E-03	1.21E-02	5.75E-01	-4.04E-02	-1.42E-01	6.10E-02	4.34E-01	51
SK	*sidx*_lag14	-17.1	1	2	-2.78E-03	-1.06E-02	5.03E-03	4.85E-01	N/A	N/A	N/A	N/A	51
	sidx	-18.24	1	1	-4.98E-03	-1.25E-02	2.55E-03	1.95E-01	N/A	N/A	N/A	N/A	51
	*sidx*_lag7	-20.61	1	0	-7.83E-03	-1.55E-02	-1.80E-04	4.48E-02	N/A	N/A	N/A	N/A	51
MB	*sidx*_lag7	-8.776	1	0	-8.14E-03	-1.49E-02	-1.40E-03	1.80E-02	N/A	N/A	N/A	N/A	51
	sidx	-8.04	1	0	-7.62E-03	-1.44E-02	-8.74E-04	2.68E-02	N/A	N/A	N/A	N/A	51
	*sidx*_lag14	-7.489	1	0	-7.12E-03	-1.40E-02	-2.86E-04	4.11E-02	N/A	N/A	N/A	N/A	51
ON	*sidx* + *C*	-148.5	1	0	-4.30E-03	-8.51E-03	-8.79E-05	4.54E-02	-9.67E-02	-1.92E-01	-1.18E-03	4.72E-02	51
	*sidx*_lag7 + *C*	-149.6	1	0	-2.20E-03	-6.25E-03	1.84E-03	2.86E-01	-3.72E-02	-1.20E-01	4.53E-02	3.77E-01	51
	*sidx*_lag14 + *C*	-145.5	1	0	-1.01E-03	-5.32E-03	3.30E-03	6.46E-01	-4.83E-02	-1.33E-01	3.66E-02	2.65E-01	51
QC	*sidx*_lag14	-149.2	1	0	-7.66E-03	-1.30E-02	-2.29E-03	5.20E-03	N/A	N/A	N/A	N/A	51
	*sidx*_lag7 + *C*	-138.6	1	0	-2.42E-03	-8.34E-03	3.50E-03	4.22E-01	-1.63E-02	-8.34E-02	5.08E-02	6.33E-01	51
	sidx	-141.9	1	0	-2.15E-03	-7.75E-03	3.46E-03	4.53E-01	N/A	N/A	N/A	N/A	51

Abbreviations: AB, Alberta; β, beta coefficient; BC, British Columbia; BIC, Bayesian Information Criterion; *C*, period of time with combined effects of vaccination, Alpha variant and winter; CI, 95% confidence interval; lag7, time lags at seven days; lag14, time lags at 14 days; MB, Manitoba; M-Li, McLeod-Li test; N/A, not applicable; nObs, number of observations for model fitting; nV, number of violations in the McLeod-Li test; ON, Ontario; QC, Québec; R_t, transmission rate; *sidx*, stringency index; SK, Saskatchewan

[a] Results from the final selected models at the provincial level for study objective 1 of general model formulation: $R_t \sim sidx$ and assessing for confounding from vaccination, the Alpha variant and winter

[b] Models highlighted in grey were significant at *p*-value ≤0.05 and pass the McLeod-Li test with two or fewer violations. The models are ordered by the absolute value of the beta coefficient for *sidx*. Model estimates are shown for the beta coefficients, 95% confidence intervals and the *p*-value

Table 3: Results from the final selected models at the provincial level for study objective 2[a,b]

Province	Model variables	BIC	M-Li	nV	*H*				*C*				nObs
					β	CI low	CI high	*p*-value	β	CI low	CI high	*p*-value	
BC	*H*_lag14	260.3	1	0	6.44E-02	1.41E-02	1.15E-01	1.21E-02	N/A	N/A	N/A	N/A	51
	*H*_lag7	261.9	1	0	5.41E-02	1.87E-03	1.06E-01	4.23E-02	N/A	N/A	N/A	N/A	51
	H	265.2	1	0	2.34E-02	-2.73E-02	7.40E-02	3.66E-01	N/A	N/A	N/A	N/A	51
AB	*H*_lag7 + *C*	233.8	1	0	2.70E-02	1.50E-02	3.90E-02	1.02E-05	-4.48	-8.97	1.17E-02	5.06E-02	50
	H	231.1	1	0	2.60E-02	1.42E-02	3.78E-02	1.58E-05	N/A	N/A	N/A	N/A	50
	*H*_lag14	242.5	1	0	1.45E-02	1.26E-03	2.77E-02	3.18E-02	N/A	N/A	N/A	N/A	50
SK	*H*_lag7 + *C*	278.7	1	0	2.35E-02	-7.84E-02	1.25E-01	6.51E-01	2.12	-3.93	8.18	4.91E-01	50
	H + *C*	278.8	1	0	1.88E-02	-7.87E-02	1.16E-01	7.05E-01	2.68	-3.26	8.63	3.76E-01	50
	*H*_lag14 + *C*	278.9	1	0	1.63E-03	-1.01E-01	1.04E-01	9.75E-01	2.47E	-3.49	8.43	4.16E-01	50
MB	*H*_lag7	233.4	1	0	2.88E-02	2.70E-04	5.73E-02	4.79E-02	N/A	N/A	N/A	N/A	51
	*H*_lag14	236.1	1	0	1.49E-02	-1.45E-02	4.42E-02	3.20E-01	N/A	N/A	N/A	N/A	51
	H + *C*	254	1	0	7.63E-03	-2.26E-02	3.79E-02	6.21E-01	-2.04	-5.96	1.88	3.08E-01	51
ON	*H*_lag14	266	1	0	1.55E-02	7.74E-03	2.32E-02	8.77E-05	N/A	N/A	N/A	N/A	51
	*H*_lag7	269.1	1	0	1.40E-02	5.78E-03	2.23E-02	8.52E-04	N/A	N/A	N/A	N/A	51
	H	273.8	1	0	1.02E-02	-4.22E-04	2.08E-02	5.98E-02	N/A	N/A	N/A	N/A	51
QC	*H* + *C*	243.5	1	0	8.36E-03	1.29E-03	1.54E-02	2.05E-02	-2.48	-5.29	3.36E-01	8.44E-02	51
	*H*_lag7	229.9	1	0	6.90E-03	4.02E-04	1.34E-02	3.74E-02	N/A	N/A	N/A	N/A	51
	*H*_lag14 + *C*	247.5	1	0	3.13E-03	-3.51E-03	9.77E-03	3.55E-01	-2.34	-4.84	1.68E-01	6.75E-02	51

Abbreviations: AB, Alberta; β, beta coefficient of the variable; BC, British Columbia; BIC, Bayesian Information Criterion; *C*, period of time with combined effects of vaccination, Alpha variant and winter; CI, 95% confidence interval; *H*, number of hospitalized COVID-19 patients; lag7, time lags at seven days; lag14, time lags at 14 days; MB, Manitoba; M-Li, McLeod-Li test; N/A, not applicable; nObs, number of observations for model fitting; nV, number of violations in the McLeod-Li test; ON, Ontario; QC, Québec; *sidx*, stringency index; SK, Saskatchewan

[a] Results from the final selected models at the provincial level for study objective 2 of general model formulation: *sidx* ~ *H* and assessing for confounding from vaccination, the Alpha variant and winter

[b] Models highlighted in grey were significant at *p*-value ≤0.05 and pass the McLeod-Li test with two or fewer violations (nV). The models are ordered by the absolute value of the beta coefficient for the number of hospitalized COVID-19 patients. Also shown are the 95% confidence intervals for beta

Discussion

This study used a dynamic regression approach to assess the impact of NPIs as measured by the Canadian subnational stringency index, *sidx*, to reduce the transmission of SARS-CoV-2 as measured by R_t and explore the potential for the number of hospitalized COVID-19 patients, *H*, to drive the level of *sidx*. Our results provide empirical evidence for the associations that *sidx* has with R_t and *H* at the provincial level in Canada. There already exists empirical evidence for the effect of NPIs to reduce the burden of COVID-19 in other countries (5–7,9), but at the time of writing, this effect was less understood in Canada, with studies reporting varying to non-effects of NPIs (16,17,30,31).

Stratifying the analysis by province facilitated the interpretation of the effects of *sidx* and *H* given interprovincial differences in testing activities and mitigation strategies. At the provincial level, statistical results suggest that for most provinces, increasing *sidx* had a significant and time-lagged effect to decrease R_t. Though the effect of *sidx* was negative, it was not significantly associated with R_t for BC (where *sidx* and R_t showed a broadly negative relationship for all provinces [Figure 3]). For the second objective, increasing *H* was significantly associated with increasing *sidx*, with a time-lagged effect, in all provinces except for SK. For SK, the effect of *H* on *sidx* was positive, but not significant (where *sidx* and *H* showed a broadly positive association for all provinces [Figure 4]). For both objectives, there were interprovincial inconsistencies in the length of the lagged effects of *sidx* (objective 1) and *H* (objective 2). It is possible that the inconsistencies relate to provincial differences in reporting and compliance to NPIs. The proportion of cases reported can vary within and among provinces (32). This may be caused by 1) differences in testing criteria and rates and 2) underreporting due to socio-demographic factors that influence both willingness to be tested and access to provincial testing centres (33,34). Testing criteria changed over time and differed among the provinces. Proportionally few asymptomatic people were likely to be tested, except in healthcare, long-term care and at certain times when resources enabled a wider population testing criteria through contact tracing (32). Reporting inconsistencies would decrease the accuracy of R_t to represent the true level of transmission and thus reduce the ability to detect an association between *sidx* and R_t. The absence of a detectable effect of *H* on *sidx* for SK may relate to interprovincial variation in the epidemics, in that, the actual numbers of cases were mostly lower in SK, for the study period, compared to the other, larger provinces.

Interpretation of time-lagged effects of *sidx* on R_t also requires consideration of the calculation of R_t, which used the date of case reporting. The combined incubation period of infection (35), time from symptom onset to obtaining a positive polymerase chain reaction result, and then time lag from case detection to reporting of the case has been internally estimated by the Public Health Agency of Canada at up to 14 days. This means that the R_t used in this study is a delayed measure of the transmission rate for a particular day. Therefore, the time-lagged effects of *sidx* on R_t found in this study, at seven to 14 days, may in fact be identifying more rapid effects of public health measures on transmission.

Modelling studies suggest that early implementation of restrictive NPIs is optimal to maximize their effect and minimize their duration (36). However, the time-lagged effect of *H* on *sidx* suggests that the provinces implemented and strengthened NPIs in response to a growing number of hospitalized COVID-19 patients rather than preventively.

Modelling studies initially suggested that restrictive closures would not be needed to control the COVID-19 epidemic in Canada with case detection and isolation and contact tracing and quarantine (test-and-trace), combined with physical distancing measures (37–39). Clearly, repeated resurgence of the epidemic, combined with the findings here suggest that test-and-trace capacity has not been sufficient and restrictive closures (which comprise most of the components of the *sidx*) have had to be implemented to control the epidemic.

We did not find strong evidence for confounding. This may be in part due to our proxy variable combining effects that were expected to differ in the direction of their association, such that, vaccination should reduce R_t, while the alpha variant and more time spent indoors during the winter should associate with an increase in R_t. The analysis occurred using data prior to significant vaccination of the Canadian population so it is likely that the elucidated relationships provide evidence of genuine associations between cases, hospitalizations and NPIs.

Study strengths and limitations

The strength of our study largely centres on our statistical approach and model structure. A similar study assessing for the impact of NPIs using stringency as a composite measure on the daily growth rate of cases did not identify a significant association over a similar study period from February 2020 to February 2021 (17). We argue that our model structure is better suited to model non-stationary time-dependent data by accounting for complex temporal dynamics of the time series using the MA and AR terms (40). Vickers *et al*. (17) used a random effect that can only account for the autocorrelation within defined time periods. By using autoregressive functions, we were able to account for any serial dependence in the data throughout the study time period. The McLeod-Li test validated the effectiveness of the model structure (26). Furthermore, through this model structure, we could use fixed effects to assess for time-lagged effects of *sidx*, unlike the approach by Vickers *et al*. (17). Finally, this is the first study that explicitly tests for the effect that *H* may have on the implementation of *sidx* in strength and timing.

An important limitation in our study is that the stringency indices, as developed by the Blavatnik School of Government, and as adapted for this study, do not account for public compliance (15), upon which the success of NPIs to reduce the burden

of COVID-19 depends. Interprovincial differences in the level of public compliance to NPIs were present during the study period. Analysis of survey data during the time period of this study indicates that compliance to NPIs tends to be lower in AB and SK, and higher in ON and QC (41,42). Furthermore, the level of public compliance is influenced by the ability of governments to clearly communicate the importance of having NPIs, the timeliness of implementation, clarity and consistency of enforcement, and public understanding and attitudes towards NPIs (43–46). In Canada, public healthcare is the mandate of the provincial governments, and sociodemographics varies among the provinces, therefore accounting for reporting differences and compliance at the provincial level should strengthen the associations of *sidx* with R_t, and *sidx* with *H*.

Another limitation arises from *sidx* being a composite index derived from multiple NPIs without weighting the strength of their contribution to limit infectious contacts. Analysis of Canadian data provides evidence that the effectiveness of NPIs depends on the type of measure (30,31). A greater understanding of the NPI measures at the individual level would benefit future policy development and implementation for using any one measure against COVID-19 or other respiratory illnesses with similar or great public health impacts.

Conclusion

Results from this study provide evidence that NPIs, as measured by a composite stringency index, are associated with reducing cases in Canada; while the strength of the stringency of NPIs was driven, in part, by the number of hospitalized COVID-19 patients. The timing of NPIs, as measured by lagging *sidx* at 0, 7 and 14 days, to reduce SARS-CoV-2 transmission, as measured by the effective reproduction number, was not consistent across the studied provinces. This may be caused by interprovincial differences in reporting of COVID-19 and the level of population compliance to NPIs. Future work should focus on these factors, particularly the effect of NPIs to reduce SARS-CoV-2 transmission as modified by measures of compliance and assessing for varying effects of individual NPIs.

Authors' statement

EER — Conceived the study, analyzed the data, interpreted the results, drafted and edited the manuscript, critical review of the manuscript
BPA — Conceived the study, developed the stringency index adapted for a Canadian context, interpreted the results, drafted and edited the manuscript
HC — Interpreted the results, drafted and edited the manuscript, critical review of the manuscript
CAC — Developed the stringency index adapted for a Canadian context, interpreted the results, drafted and edited the manuscript
DC — Conceived the study, calculated the measure of the transmission rate of SARS-CoV-2, analyzed the data, interpreted the results, drafted and edited the manuscript
SM — Provided statistical advice, interpreted the results, drafted and edited the manuscript, critical review of the manuscript
BD — Conceived the study, developed the stringency index adapted for a Canadian context, interpreted the results, drafted and edited the manuscript
BRN — Provided statistical advice, interpreted the results, drafted and edited the manuscript
NHO — Conceived the study, interpreted the results, drafted and edited the manuscript, critical review of the manuscript

All authors approved the final version of the manuscript.

Competing interests

None.

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Appendix

This document provides the full model parameter estimates for the top ranked models, per province and objective, for models containing a significant effect of sidx (objective 1) or H (objective 2).

Table A1: Model formulation and ARIMAX (p, d, q) for provinces

Province	Model formulation	ARIMAX (p, d, q)[a]	Parameter	Beta coefficient		*p*-value
				n	95% CI	
British Columbia	*sidx* ~ *H*_lag14	ARIMAX (2, 0, 0)	ar1	1.22	0.969 to 1.48	4.86e-21
			ar2	-0.352	-0.647 to -0.057	1.93e-02
			intercept	44.6	35.3 to 53.9	7.71e-21
			*H*_lag14	0.0644	0.0141 to 0.115	1.21e-02
Alberta	R_t ~ *sidx*_lag14	ARIMAX (2, 0, 0)	ar1	1.19	0.917 to 1.45	5.06e-18
			ar2	-0.567	-0.841 to -0.294	4.79e-05
			intercept	1.38	1.15 to 1.61	6.19e-31
			*sidx*_lag14	-0.0073	-0.0119 to -0.00266	2.04e-03
	sidx ~ *H*_lag7 + *C*	ARIMAX (0, 1, 0)	*H*_lag7	0.027	0.015 to 0.039	1.02e-05
			C	-4.48	-8.97 to 0.0117	5.06e-02
Saskatchewan	R_t ~ *sidx*_lag7	ARIMAX (0, 0, 1)	ma1	0.76	0.55 to 0.97	1.32e-12
			intercept	1.46	1.04 to 1.88	1.00e-11
			*sidx*_lag7	-0.00783	-0.0155 to -0.00018	4.48e-02
Manitoba	R_t ~ *sidx*_lag7	ARIMAX (0, 0, 1)	ma1	0.584	0.361 to 0.806	2.65e-07
			intercept	1.61	1.14 to 2.08	2.71e-11
			*sidx*_lag7	-0.00814	-0.0149 to -0.0014	1.80e-02
	sidx ~ *H*_lag7	ARIMAX (0, 1, 1)	ma1	0.456	0.181 to 0.731	0.00115
			*H*_lag7	0.0288	0.00027 to 0.0573	0.04790
Ontario	R_t ~ *sidx* + *C*	ARIMAX (0, 1, 0)	*sidx*	-0.0043	-0.00851 to -8.79e-05	0.0454
			C	-0.0967	-0.192 to -0.00118	0.0472
	sidx ~ *H*_lag14	ARIMAX (1, 0, 1)	ar1	0.698	0.413 to 0.982	1.59e-06
			ma1	0.487	0.156 to 0.818	3.96e-03
			intercept	51.4	45.7 to 57.1	1.05e-70
			*H*_lag14	0.0155	0.00774 to 0.0232	8.77e-05
Québec	R_t ~ *sidx*_lag14	ARIMAX (1, 0, 1)	ar1	0.744	0.527 to 0.962	2.02e-11
			ma1	0.775	0.566 to 0.984	3.88e-13
			intercept	1.48	1.14 to 1.83	2.11e-17
			*sidx*_lag14	-0.00766	-0.013 to -0.00229	5.20e-03
	sidx ~ *H* + *C*	ARIMAX (1, 0, 1)	ar1	0.899	0.778 to 1.02	6.17e-48
			ma1	0.75	0.48 to 1.02	5.15e-08
			intercept	56.6	46.4 to 66.8	1.52e-27
			H	0.00836	0.00129 to 0.0154	2.05e-02
			C	-2.48	-5.29 to 0.336	8.44e-02

Abbreviations: ar, autoregressive term; ARIMAX, autoregressive integrated moving average extended; *C*, period of time with combined effects of vaccination, Alpha variant and winter; CI, 95% confidence interval; lag7, time lags at seven days; lag14, time lags at 14 days; MA, moving average; R_t, transmission rate; *sidx*, stringency index
[a] ARIMAX (p,d,q) denotes the number of autoregressive terms, p, degree of differencing, d, and number of moving average terms, q

Modelling COVID-19 transmission using IDSIM, an epidemiological-modelling desktop app with multi-level immunization capabilities

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has placed unprecedented demands on local public health units in Ontario, Canada, one of which was the need for in-house epidemiological modelling capabilities. The objective of this study is to develop a native Windows desktop app for epidemiological modelling, to be used by public health unit epidemiologists to predict COVID-19 transmission in Durham Region.

Methods: The developed app is an implementation of a multi-stratified compartmental epidemiological model that can accommodate multiple virus variants and levels of vaccination, as well as public health measures such as physical distancing, contact tracing followed by quarantine and testing followed by isolation. It was used to investigate the effects of different factors on COVID-19 transmission, including vaccination coverage, vaccine effectiveness, waning of vaccine-induced immunity and the advent of the Omicron variant. The simulation start date was November 22, 2021.

Results: For the Delta variant, at least 90% of the population would need to be vaccinated to achieve herd immunity. A Delta-variant-only epidemiological curve would be flattened from the start in the absence of immunity waning and within six months in the presence of immunity waning. The percentage of infections caused by the Omicron variant was forecast to increase from 1% to 97% in the first month of the simulation. Total Omicron infections were forecasted to be reduced, respectively, by 26% or 41% if 3,000 or 5,000 booster doses were administered per day.

Conclusion: For the Delta variant, both natural and vaccination-induced immunity are necessary to achieve herd immunity, and waning of vaccine-induced immunity lengthens the time necessary to reach herd immunity. In the absence of additional public health measures, a wave driven by the Omicron variant was predicted to pose significant public health challenges with infections predicted to peak in 2–3 months from the start of the simulation, depending on the rate of administration of booster doses.

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Keywords: COVID-19, compartmental epidemiological model, IDSIM app, vaccination levels, immunity waning, variants

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Introduction

On March 11, 2020, the World Health Organization declared the coronavirus disease 2019 (COVID-19) epidemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a pandemic. Like other affected countries, Canada and its provinces instituted emergency public health measures to control virus transmission, in the form of masking mandates, detection, isolation and quarantine, international travel restrictions, work from home, school and business closures and even stay-at-home orders (1). Some of these measures came at great economic cost and having an inordinately large number of infections was unacceptable due to the strain they would have placed on medical services. Therefore, it became very important to model the pandemic and to use model predictions to assess demands on the health system and to guide policy decisions around public health measures.

At the federal level, the Public Health Agency of Canada created a Canadian COVID-19 modelling network made up of federal, provincial, territorial and university-based modellers and epidemiologists (2). Modelling results were used to inform policies, guide public health action and communicate with the public.

In the Province of Ontario, the COVID-19 Modelling Consensus Table was created in March 2020 to bring together multiple groups of experts, health system leaders and senior decision makers and to generate consensus estimates based on multiple modelling results and expert opinions. Such estimates were used to inform policy decisions on public health measures, to communicate with the public, and to evaluate health system status and demands (3).

To model COVID transmission under different scenarios, a vast number of models were being developed in Canada and around the world using an array of software packages. For example, modelling efforts at the Public Health Agency of Canada resulted in the development of both compartmental (4) and agent-based models (5). The former was implemented using the Analytica software package, while the latter was implemented using the AnyLogic software package. Another compartmental model was developed by Tuite *et al.* (6) with the specific aim of modelling COVID transmission in Ontario. In Europe, a team centred at the University of Cambridge developed another compartmental model (7) and implemented it using a pre-packaged initial-value ordinary-differential solver developed in the Python programming language. Virtually all available models were focused on evaluating non-pharmaceutical interventions (e.g. testing and tracing, physical distancing). They did not have the ability to simulate the effect of vaccines, especially those administered in multiple doses, or the waning of vaccine-induced protection. Available models were also not convenient for individual public health units (PHUs) because they required familiarity with specific software packages used to implement them. In practice, this meant that a multidisciplinary team consisting of both epidemiologists and computational scientists was needed to correctly and efficiently use the models and corresponding software packages.

In the summer of 2020, as the province of Ontario was recovering from the first wave of COVID-19 infections, it became clear that a second wave was developing. Local PHUs were called upon to make forecasts about the future evolution of cases, estimate demands on hospitals and recommend public health interventions at a time when modelling resources, both computational and human, were scarce. Modelling results prepared at the national or provincial level by sizeable teams of epidemiologists and mathematicians were only partially applicable to local situations.

The Regional Municipality of Durham, which comprises areas to the east of Toronto and has a population of approximately 750,000, was facing challenges common to all Ontario PHUs. To alleviate the shortage of modelling resources, Durham Region Health Department established a collaboration with Ontario Tech University to develop in-house COVID-19 epidemiological modelling capabilities. The immediate objective was to create a model and software package in the form of a Windows desktop app to be used by staff epidemiologists for making forecasts and informing policy decisions without the need for high-performance computing systems or extensive training.

For simplicity and practicality, a dynamic compartmental (deterministic) model developed by the Public Health Agency of Canada (4) was initially adopted. This initial model consisted of seven compartments (susceptible, exposed, exposed quarantined, infectious, infectious isolated, hospitalized, and removed), and allowed for only one ancestral strain. It was implemented as a Modern Fortran (Fortran with object-oriented programming features) code with an Excel/Visual-Basic user interface. As variants emerged and vaccines became available, additional capabilities were added to the model and the implementation was switched to a native MS-Windows desktop app with a Modern Fortran computational backend. The app was named IDSIM (Infectious-Disease SIMulator). This work presents the (November 2021) IDSIM model and illustrates some of its capabilities by performing four simulations of COVID-19 transmission under different conditions.

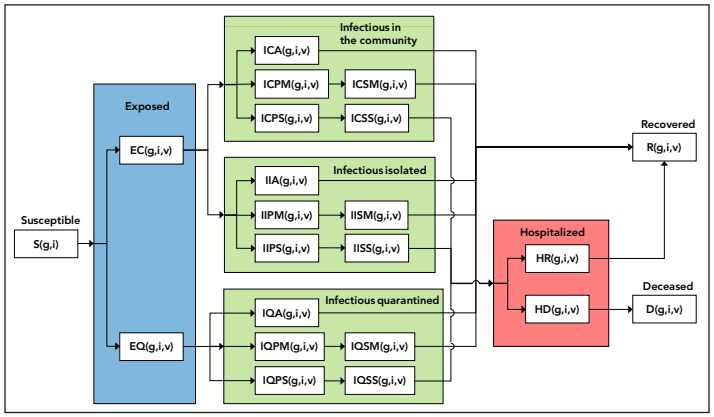
Epidemiological model

The epidemiological model is a multi-stratified compartmental model that can accommodate multiple virus variants and levels of vaccination, as well as public health measures such as physical distancing, contact tracing followed by quarantine and testing followed by isolation.

Compartments and flowchart

The diagram of the epidemiological model is shown in **Figure 1**.

Figure 1: Compartmental model diagram



Abbreviations: EC, exposed in the community (not quarantined); EQ, exposed quarantined; D, deceased; HR, hospitalized recovering; HD, hospitalized dying; ICA, infectious, in the community, asymptomatic; ICPM, infectious, in the community, pre-symptomatic, will progress to mild symptoms; ICPS, infectious, in the community, pre-symptomatic, will progress to severe symptoms; ICSM, infectious, in the community, symptomatic, mild symptoms; ICSS, infectious, in the community, symptomatic, severe symptoms; IIA, infectious isolated asymptomatic; IIPM, infectious isolated pre-symptomatic, will progress to mild symptoms; IIPS, infectious isolated pre-symptomatic, will progress to severe symptoms; IISM, infectious isolated symptomatic mild; IISS, infectious isolated symptomatic severe; IQA, infectious quarantined asymptomatic; IQPM, infectious quarantined pre-symptomatic, will progress to mild symptoms; IQPS, infectious quarantined pre-symptomatic, will progress to severe symptoms; IQSM, infectious quarantined symptomatic mild; IQSS, infectious quarantined symptomatic severe; R, recovered; S, susceptible

The population in each compartment is categorized by combined stratum (subscript g), immunization status (subscript i) and variant (subscript v). The differential equations governing transition from one compartment to another are presented in the **Appendix**.

Variants

The variant subscript v, applies to all compartments other than the one comprised of susceptible individuals.

Combined strata

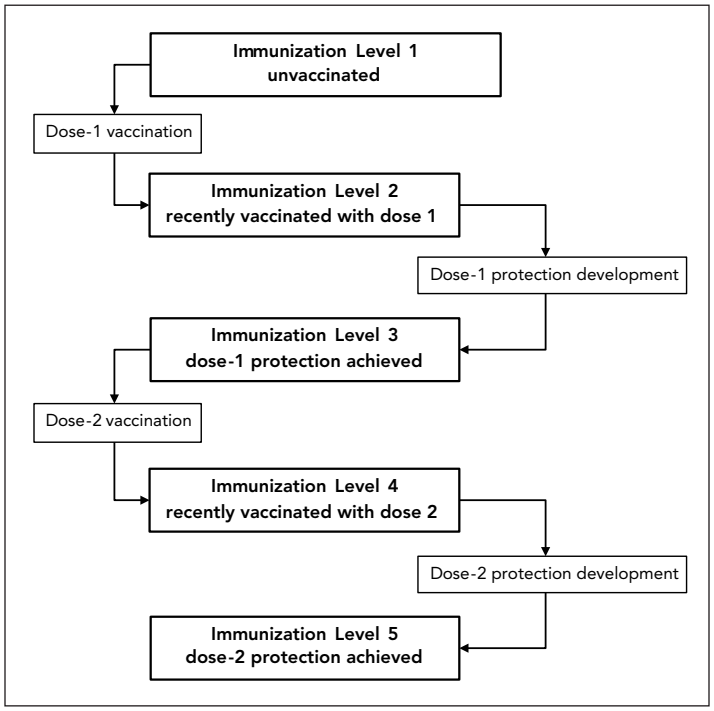
Each combined stratum is a combination of strata corresponding to multiple stratifications. For example, if a particular population were stratified by age into two strata, those under 50 years and those 50 years and older, and by gender into two strata, female and male, then subscript g would take values between 1 and 4, corresponding to the four combined strata: females under 50 years, females 50 years and older, males under 50 years, and males 50 years and older.

Immunization status

The immunization status can have as many levels as necessary, identified by subscript i. For example, subscript i could take values between 1 and 5, with the following meanings: 1) not vaccinated; 2) first dose administered, first dose protection not yet achieved; 3) first dose protection achieved; 4) second dose administered, second dose protection not yet achieved and 5) second dose protection achieved.

Persons advance from one immunization level to the next either through vaccination or the passing of time. Using the example above, individuals would move from level 1 to level 2 and from level 3 to level 4 through vaccination (defined by the number of people being vaccinated daily), and from level 2 to level 3 and from level 4 to level 5 by the simple passing of time (defined by the average time necessary to achieve protection after vaccination). This is illustrated in **Figure 2**.

Figure 2: Example of immunization levels



Transmission model

Persons become exposed through contact with one or multiple infectious individuals. The exposure rate is characterized by the number of contacts per individual per day and by the probability of transmission with contact. The former is characterized by an average number of daily contacts for the population. The latter is characterized by an average number for the population which is then modulated by variant-dependent and vaccination-level-dependent factors.

Stratification parameters

Each stratification can have a different number of strata. Each stratum is defined by the following parameters:

- Fraction of population belonging to the stratum
- Susceptibility modulator (a factor that multiplies the probability of transmission with contact for susceptible individuals belonging to the stratum)
- Severity modulator (a factor that multiplies the fraction of symptomatic individuals in the stratum that go on to develop severe symptoms). For example, in the 80 years and older age group, a value greater than one would be appropriate to represent the higher probability of severe outcomes for that age group

Variant parameters

Each variant, including the ancestral strain, is defined by the following parameters:

- Latency time (since exposure)
- Incubation time (since exposure)
- Time to hospitalization for severe cases (since exposure)
- Time to recovery for non-severe cases (since exposure)
- Time to recovery after hospitalization (for severe cases that recover)
- Time to death after hospitalization (for severe cases that do not recover)
- Probability of transmission with contact
- Fraction of infectious individuals that are symptomatic
- Fraction of infectious symptomatic individuals that have severe symptoms
- Fraction of hospitalized individuals that recover

Immunization-level parameters

Each immunization level is defined by the following parameters:

- Transmissibility factor (a factor, usually less than or equal to one, that multiplies the probability of transmission with contact for infectious individuals with a specific vaccination level)
    - For infectious individuals who are unvaccinated or recently vaccinated (before developing protection), this factor would be one. For individuals who are both vaccinated and infectious and who have already developed some protection, the factor would normally be less than one to represent the fact that those individuals are less contagious
- Susceptibility factor (a factor, usually less than or equal to one, that multiplies the probability of transmission with contact for susceptible individuals with a specific vaccination level)
    - For susceptible individuals who are unvaccinated or recently vaccinated (before developing protection), this factor would be one. For susceptible individuals who have already developed some protection, the factor would normally be less than one to represent the fact that those individuals are less likely to become infected. This factor is essentially equal to one minus the vaccine efficacy
- Severity factor (a factor, usually less than or equal to one, that multiplies the fraction of symptomatic individuals with severe symptoms)
    - For infectious symptomatic individuals who are unvaccinated or recently vaccinated (before developing protection), this factor would be one. For infectious symptomatic individuals who have already developed some protection, the factor would normally be less than one, to represent the fact that those individuals are less likely to develop severe symptoms
- Rate at which individuals move from one immunization level to the next, expressed as either of the following:
    - Persons vaccinated per unit time (day)
    - Average time (days) before protection level changes following vaccination

Parameters for public health measures

Public health measures are characterized by the following parameters:

- Fraction of exposed individuals that are successfully quarantined
- Fraction of infectious individuals that are tested and successfully isolated
- Coefficient for additional unspecified public health measures. This general factor, usually less than or equal to 1, appears in the force of infection to account for measures such as mask wearing or physical distancing. It can also be manually adjusted to fit model predictions to actual recorded data

Modelling of decrease in vaccine protection over time and of third dose

The multi-level immunization status can be used to model the decrease in vaccine protection and subsequent need for a third doses once the protection has decreased to a certain level. An example is to use eight immunization levels as follows:

- Not vaccinated
- First dose administered, protection after first dose not yet achieved
- First dose administered, protection after first dose achieved
- Second dose administered, protection after second dose not yet achieved
- Second dose administered, protection after second dose achieved
- Second dose protection decreased
- Third dose administered, protection after third dose not yet achieved

- Third dose administered, protection after third dose achieved

Progression from level 5 to level 6 happens through the passage of time (e.g. three months for a 20% decrease in vaccine protection). Progression from level 6 to level 7 happens through administration of the third vaccine dose. Progression from level 7 to level 8 happens through the passage of time (e.g. two weeks for increased protection to develop).

Model assumptions

In its current form, the model makes several assumptions:

- Recovery from one variant offers full and permanent immunity against all variants
- Breakdown by strata in a particular stratification is independent of the other stratifications. As with the previous stratification example, if 50% of the population were female and 50% of the population were male, that is assumed to be true both for persons under 50 years and for persons 50 years and older. Similarly, if 60% of the population is under 50 years and 40% is 50 years and older, then that is assumed to be true for both male and female populations
- All severe cases are hospitalized
- The number of contacts per day per person is the same for all combined strata and independent of the vaccination level of an individual. Quarantined, isolated and hospitalized individuals are assumed to have no contacts

Simulation starting and end points

Initial conditions at "Day 0" can be specified in detail, including the population of each compartment by stratum, vaccination status and variant. This allows simulations to start from realistic data acquired in the field rather than from generic assumptions of one infectious individual. The end point of a simulation can be saved and used as the starting point of a new simulation, thus allowing the indefinite extension of the simulation time interval.

Time-dependent epidemiological parameters

Time-dependent parameters can be simulated by assuming them to be constant over finite time intervals, with step changes from one interval to the next. For example, the simulation of an entire year can be performed in 30-day intervals, with parameters updated at the start of each simulation interval.

COVID-19 transmission simulations

Four simulations were performed to investigate the effect of specific factors on COVID-19 transmission in Durham Region:

- Simulation 1: Effect of different vaccination coverage values with vaccination being the only public health measure, assuming no waning of vaccine-induced immunity over time
- Simulation 2: Effect of different vaccine effectiveness values with specified public health measures in place, assuming no waning of vaccine-induced immunity over time
- Simulation 3: Effect of waning vaccine-induced immunity after three months, assuming specified public health measures
- Simulation 4: Effect of the advent the Omicron variant, and impact of COVID-19 booster vaccines on transmission and severity of Delta and Omicron variants assuming specified health measures and waning of vaccine-induced immunity over time

Pfizer-BioNTech (Comirnaty, BNT162b2) and Moderna (Spikevax, mRNA-1273) were the two main types of COVID-19 vaccines offered in Durham Region. Vaccine effectiveness against COVID-19 infection dropped between three and six months. It was assumed that individuals in Durham Region received their second dose, on average, four months prior to the simulation start date.

Stratification by age group was not used. This simplification was adopted because reliable age-dependent data such as transmissibility, severity and vaccine efficacy were not available. While age-dependent contact matrices for a period pre-dating COVID-19 were available (8) they were not used, because such matrices would have had an effect on the overall simulation results only if transmissibility and vaccine efficacy were also broken down by age groups.

General simulation parameters are shown in **Table 1** and were based on information available in November 2021. The best estimates for some of the parameters in Table 1 (e.g. latency period, incubation period, duration of hospital stay, vaccine effectiveness, severity) have since changed. Parameters specific to individual simulations are shown in **Table 2**. For all simulations, Day 0 was November 22, 2021.

Results and discussion

The first simulation was performed to quantify the impact of different vaccination proportions on COVID-19 transmission assuming vaccination was the only public health control measure and no additional vaccinations during the simulation period.

Table 1: General simulation parameters

Parameter	Value	Source
Number of strata	1	User specified
Number of infectious individuals on Day 0	200 active cases reported on Day 0. For each reported case, there are three undetected cases in the community, for a total of 800 infectious individuals	PHU data, (9)
Number of contacts per day	10	(10,11)
Latency period	3 days for Delta 1 day for Omicron	(12–14)
Incubation time	5 days for Delta 3 days for Omicron	(12–15)
Time to hospitalization (from exposure)	10 days for Delta and Omicron	PHU data
Time to recovery for non-severe (from exposure)	14 days for Delta and Omicron	PHU data
Time to recovery after hospitalization	14 days for Delta 10 days for Omicron	PHU data, (14)
Time to death after hospitalization	15 days for Delta and Omicron	PHU data
Probability of transmission with contact	0.058 for Delta (estimated based on R_0, infectious period and contact rate) 0.232 for Omicron	(16,17)
Fraction symptomatic (of infectious)	0.85 for Delta & Omicron	PHU data
Fraction severe (of symptomatic)	0.03 for Delta 0.012 for Omicron	PHU data, (18)
Fraction recovered after hospitalization	0.6 for Delta 0.8 for Omicron	PHU data, (19)
Transmissibility factor for unvaccinated	1 for Delta and Omicron	(20)
Susceptibility factor for unvaccinated	1 for Delta and Omicron	(20)
Severity factor for unvaccinated	1 for Delta and Omicron	(19)
Transmissibility factor after 1 dose	0.8 for Delta and Omicron	(20)
Susceptibility factor after 1 dose	0.7 for Delta and Omicron	(20,21)
Severity factor after 1 dose	0.3 for Delta and Omicron	(19)
Transmissibility factor after 2 doses	0.5 for Delta 0.6 for Omicron	(20)
Susceptibility factor after 2 doses	0.2 for Delta 0.6 for Omicron	(20,22,23)
Severity factor after 2 doses	0.2 for Delta 0.3 for Omicron	(13,24)
Transmissibility factor after 3 doses	0.5 for Delta 0.5 for Omicron	(20)
Susceptibility factor after 3 doses	0.1 for Delta 0.3 for Omicron	(22)
Severity factor after 3 doses	0.06 for Delta 0.1 for Omicron	(13,24)
Fraction of population with 1 dose on Day 0	0.01–0.03	PHU data
Fraction of population with 2 doses on Day 0	0.72–0.74	User specified
Fraction of population with 3 doses on Day 0	0	User specified
Number of exposed individuals on Day 0	218	PHU data
Infectious period	11 days for Delta 13 days for Omicron	Calculated based on recovery period
Population	738,000	Census data
Number of recovered persons on Day 0	110,700	PHU data
Number of deceased persons on Day 0	389	PHU data

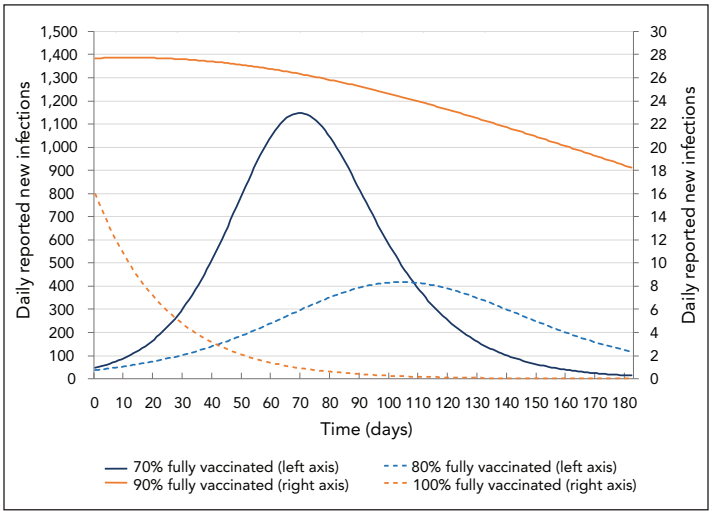
Abbreviation: PHU, public health unit

Table 2: Specific simulation parameters

Parameter	Simulation 1: Different vaccination coverage values	Simulation 2: Different vaccine effectiveness values	Simulation 3: Cases with and without waning immunity	Simulation 4: Evolution of Delta and Omicron variants and effect of booster doses
Distribution of variants on Day 0	100% Delta			99% Delta and 1% Omicron
Vaccination levels	Unvaccinated Two doses	Unvaccinated Dose 1 Dose 2	Unvaccinated Dose 1 Dose 2 Reduced immunity	Unvaccinated Dose 1 Dose 2 (reduced immunity) Dose 3
Vaccination coverage	Compare transmission under different vaccination proportions: 70%, 80%, 90% and 100%	Start with a vaccination coverage of 2% for Dose 1, 72% for Dose 2 400 Dose 1 administrated per day 300 Dose 2 administrated per day		Start with a vaccination coverage of 1% for Dose 1, 74% for Dose 2 and 0% for Dose 3 500 Dose 1 administrated per day 200 Dose 2 administrated per day 3,000 or 5,000 Dose 3 administered per day
Public health measures	Public health measure coefficient is 1, no isolation and no quarantine	Public health measure coefficient is 0.8 (fitted to match the estimated value of $R_t \approx 1$ for Durham Region on Day 0) All the cases reported are isolated and 5% of exposed are quarantined		
Vaccine effectiveness	Vaccine effectiveness is 80% Vaccine reduces transmission by 50% after Dose 2 and reduces severity by 85%	Compare the following: Effectiveness rate of 33% for Dose 1 and 80% for Dose 2 Effectiveness rate of 56% for Dose 1 and 87% for Dose 2	Effectiveness at two weeks: 33% for Dose 1; 80% for Dose 2 Transmissibility at two weeks: 83% for Dose 1; 50% for Dose 2	Omicron variant is four times as transmissible as the Delta variant
Waning immunity after vaccination	None	None	Vaccine effectiveness 12 weeks Dose 2: 45% Transmissibility 12 weeks after Dose 2: 76%	Reduced protection for individuals who had only two doses of vaccine

Figure 3 shows simulation results for daily reported new infections for different vaccination proportions. Results predicted that the number of daily reported COVID-19 cases would significantly decrease with increased vaccination proportions; however, even with an 80% vaccination coverage, there would still be a very high number of daily reported cases. At least 90% of the total population would need to be vaccinated to control an epidemic consisting of the Delta variant. In reality, it would have been hard to reach such high vaccination coverage, particularly when younger age groups were ineligible for vaccination. The results suggest that even small increases in vaccination coverage can significantly reduce COVID-19 transmission but that other control measures would also be needed. Public health control measures other than vaccination can include case detection, contact tracing and quarantine, physical distancing, limiting social gatherings, mask use, self-monitoring and other "lockdown" measures.

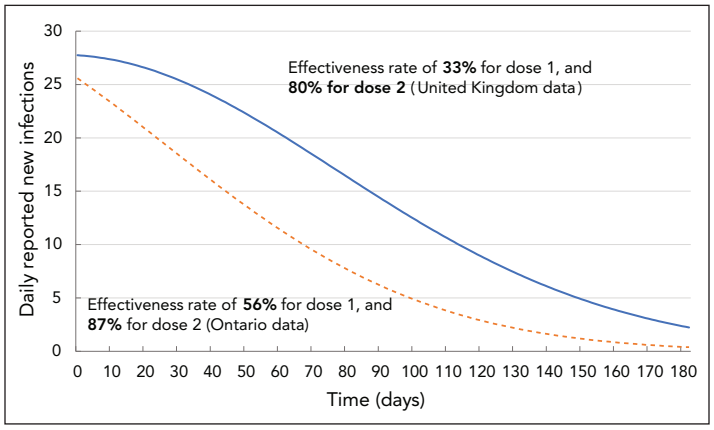
Figure 3: Impact of different vaccination coverage values on COVID-19 transmission



Note: Left vertical axis is used for the plots corresponding to 70% and 80% vaccine coverage and right vertical axis is used for the plots corresponding to 90% and 100% vaccine coverage

The second simulation evaluated the impact of two different vaccine effectiveness values on COVID-19 transmission under the specific public health control measures in effect in Durham Region in November 2021, as shown in Table 2. The two sets of values for vaccine effectiveness were drawn from United Kingdom (UK) (20) and an Ontario (21) study. The Ontario study found a higher vaccine effectiveness than the UK study. Under the control measures in effect in November 2021, the effective reproduction number, R_t, estimated based on daily case data, was approximately 1.0. To account for all public health measures not explicitly modelled (e.g. masking, physical distancing) the public health measure coefficient was manually fitted, so on Day 0, the predicted R_t matched the estimated $R_t \approx 1$ in Durham Region for the month of November 2021. The starting population vaccination fraction was 2% for dose-1 and 72% for dose-2. Each day, 400 people were assumed to be vaccinated with the first dose and 300 people vaccinated with the second dose. This corresponded to 92% of the total population having completed two doses by the end of the 180-day simulation period. Simulation results for the two sets of vaccine effectiveness data are shown in **Figure 4**.

Figure 4: Impact of different vaccine effectiveness values on COVID-19 transmission

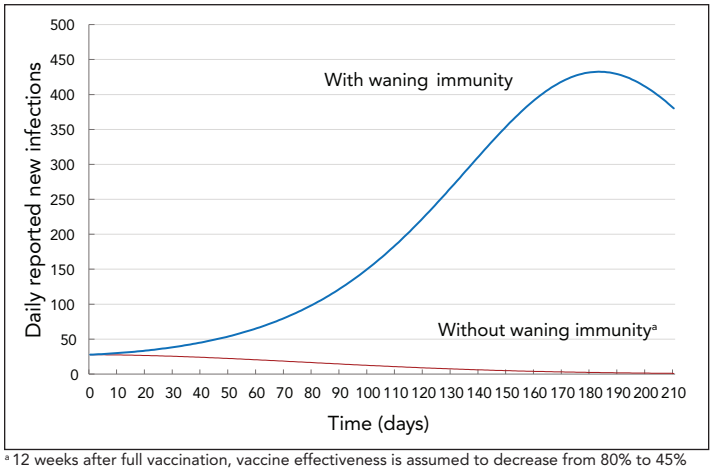


With then-current (November 2021) vaccination and other public health control measures, it was projected that the daily new infections (assuming only Delta variant) would decrease over time. However, at day 90, the projection based on the UK vaccine-effectiveness data showed twice the number of daily reported infections than the projection based on the Ontario vaccine-effectiveness data.

In addition to comparing the effectiveness of different control measures, the modelling application can also be used to understand the impact of waning vaccine-induced immunity on COVID-19 transmission.

The third simulation was performed to estimate the impact of decreasing vaccine effectiveness over time. It compared the case of no immunity waning to the case of immunity waning after three months. To account for all public health measures not explicitly modelled, the public health measure coefficient was manually fitted so, on Day 0, the predicted R_t matched the estimated $R_t \approx 1$ in Durham Region for the month of November 2021. Results are shown in **Figure 5**.

Figure 5: Impact of waning vaccine-induced immunity on COVID-19 transmission



[a] 12 weeks after full vaccination, vaccine effectiveness is assumed to decrease from 80% to 45% and the reduction of transmissibility in vaccinated people is assumed to drop from 50% to 24%

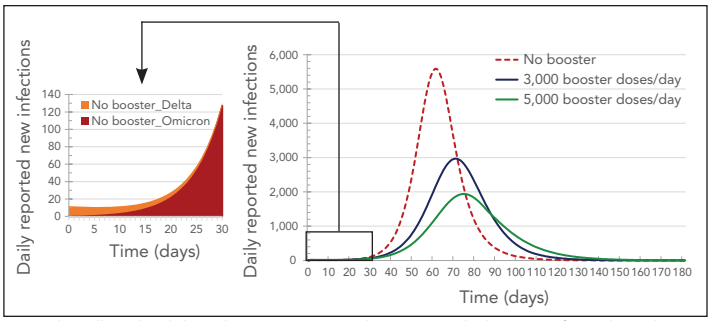
Under the then-current (November 2021) vaccination program and other public health measures, assuming no waning of immunity after vaccination, the epidemiological curve was projected to be flattened from the beginning and daily reported new infections to be decreasing. The waning of immunity reduces the likelihood of being protected from COVID-19 infection (vaccination effectiveness) and increases the likelihood of fully-vaccinated people transmitting the disease. Assuming waning immunity, the number of daily reported new infections was forecast to be higher and the epidemiological curve to flatten six months into the simulation period.

The modelling application can also simulate disease transmission with multiple variants. The fourth simulation investigated the advent of the Omicron variant in addition to the Delta variant, as well as the effectiveness of a third dose (booster) of messenger ribonucleic acid (mRNA) vaccine in preventing COVID-19 infection, hospitalization and death. The Omicron variant was assumed to be four times as transmissible as the Delta variant (21). On Day 0 of the simulation, 99% of the existing infections were assumed to be due to the Delta variant and 1% to the Omicron variant. To account for all public health measures not explicitly modelled, the public health measure coefficient was manually fitted so, on Day 0, the predicted R_t matched the estimated $R_t \approx 1$ in Durham Region for the month of November 2021. The COVID-19 infections, hospitalizations and deaths were compared for three scenarios: 1) no third (booster) dose of mRNA vaccine; 2) 3,000 booster doses administrated per day; and 3) 5,000 booster doses administrated per day. The booster-dose coverage was assumed to start at 0% on Day 0 of the simulation and booster doses were assumed to be administered until booster coverage reached 93% of the eligible population (18 years of age or older). It would have taken

180 days to reach 93% booster coverage with 3,000 booster doses being administered per day and 110 days to reach that coverage level with 5,000 booster doses being administered per day.

Figure 6 shows the forecast impact of the Omicron variant and the third dose of vaccine on disease transmission. The number of new Omicron-variant infections was projected to surpass the number of new Delta-variant infections after just two weeks from Day 0, in the middle of December 2021. Within a month, Omicron was projected to become the dominant variant and account for the majority (97%) of infections. Similar results were found by the Ontario COVID-19 Science Advisory Table (25).

Figure 6: Impact of booster doses on COVID-19 transmission with two variants



Note: The callout details how the Omicron variant becomes vastly dominant after only 30 days in the no-booster scenario

Simulation results suggested that booster doses would have a dramatic impact on COVID-19-related infections, hospitalizations (including inpatients and intensive care units) and deaths (Figure 6, **Figure 7** and **Figure 8**). It was forecast that over a quarter of infections (26%) would be prevented if 3,000 booster doses were administered each day in Durham Region, and 41% of infections would be prevented if 5,000 booster doses were administered each day. Administering 5,000 booster doses each day was forecast to also prevent more than half of the hospitalizations and almost half of the deaths (**Table 3**, **Table 4** and Figure 8).

Figure 7: Impact of booster doses on severity of COVID-19 infections with two variants

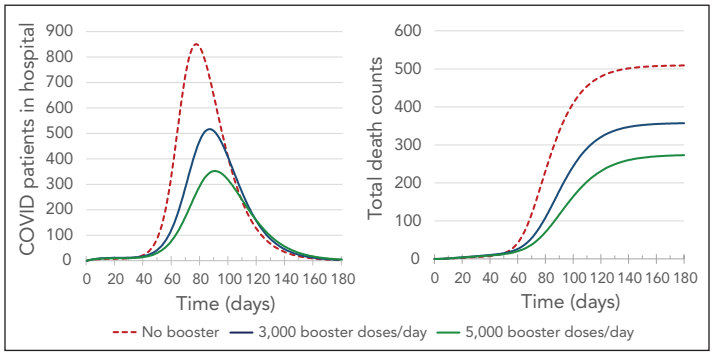


Figure 8: COVID-19 infections, hospitalizations and deaths by vaccine status with 5,000 booster doses administered per day

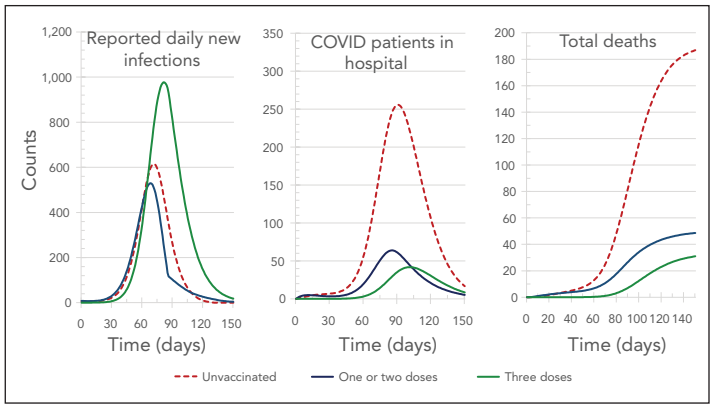


Figure 8 shows the forecast number of daily reported new infections, patients in hospital on a given day, and total deaths by vaccination status for the 5,000 booster-dose per day scenario. Although vaccinated people were predicted to account for almost three quarters of the COVID-19 infections by day 180, they were predicted to account for only 30% of severe cases (measured by hospitalizations and deaths).

Table 3: Counts of infections, hospitalizations and deaths over the simulation period (180 days) and percentage decrease compared to the "no-booster" scenario

Group	Total infections	% decrease in total infections	Highest hospitalizations on a single day	% decrease in hospitalization peak	Total hospitalizations	% decrease in total hospitalizations	Total deaths	% decrease in total deaths
No booster	558,841	-	851	-	2,558	-	509	-
3,000 booster doses/day	411,500	26%	517	39%	1,766	31%	357	30%
5,000 booster doses/day	328,533	41%	352	59%	1,354	47%	273	46%

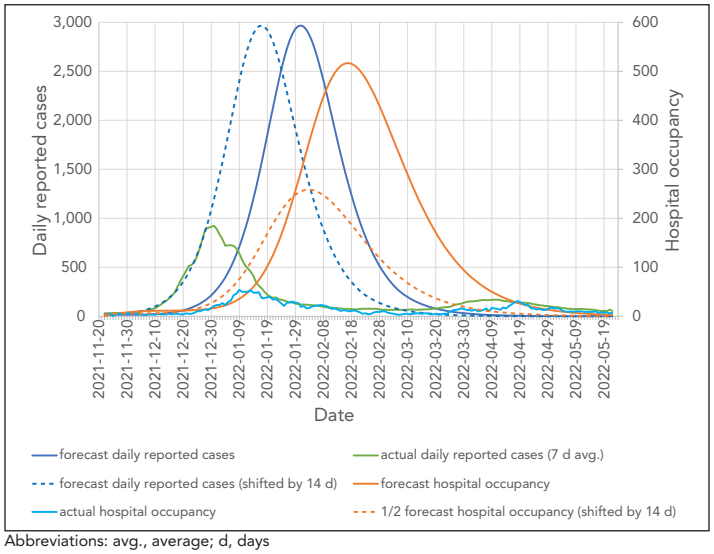
Abbreviation: -, not applicable

Table 4: Counts and proportion of infections, hospitalizations and deaths over the simulation period (180 days) by vaccination status assuming 5,000 booster doses administered per day

Indicator	Counts				Proportions		
	Unvaccinated	1 or 2 doses	3 doses	Total	Unvaccinated	1 or 2 doses	3 doses
Total infections	90,288	74,919	163,327	328,533	27%	23%	50%
Hospitalization peak	256	64	42	362	71%	18%	12%
Total hospitalizations	946	241	167	1354	70%	18%	12%
Total deaths	190	50	33	273	70%	18%	12%

It is informative to compare actual data with the simulation results that are closest to the scenario that developed in real life, namely the fourth simulation—assuming 3,000 booster doses administered per day. Actual hospital occupancy data were not directly available and were estimated based on daily admissions data from the PHU assuming an average hospital stay for the Omicron-dominated wave of five days. The average hospital stay was estimated based on the age-specific average hospital length of stay for an Omicron-dominated wave (26) and the age distribution of hospital admissions for the Durham-Region PHU. The comparison is shown in **Figure 9** for daily reported cases and hospital occupancy. A detailed analysis of what simulation-parameter values would lead to the best agreement between forecast and actual numbers would involve rigorous model calibration using least square minimization analysis, which was not part of the work reported here, so only a rough analysis is provided with the caveat to treat this simple analysis with caution. Figure 9 shows that the actual daily reported cases begin to increase substantially approximately two weeks earlier than predicted by the simulation. We hypothesize that this is because on Day 0 of the simulation, the Omicron wave was already more advanced than assumed. In other words, the 1% Omicron prevalence assumed in the simulation was likely a more accurate description of the situation on November 8, 2021, rather than on November 22, 2021. For hospital occupancy, it would first appear that the forecast and actual numbers increase at the same time; however, that is an artifact of assuming an average hospital stay of 10 days, whereas the actual hospital stay for the Omicron-driven wave was approximately five days. This means that hospital occupancy was overestimated by a factor of approximately two. To estimate agreement if the starting point of the simulation was moved back to November 8, 2021, and if the hospital stay was assumed to be five days instead of 10, one can look at the dashed lines in Figure 9, which show the forecast number of reported cases and half the forecast hospital occupancy with both curves shifted back in time by 14 days. The agreement between the forecast and the actual reported daily infections is now quite good for the first ~50 days of the simulation (up to near the end of December). After December 28, 2021, the forecast and actual curve begin to diverge markedly, with the actual number of reported new infections decreasing abruptly while the forecast number continues to increase. This could be attributed to a combination of factors such as change in public behaviour (presumably as a consequence of public messaging, since public health measures had not been changed at that point) and a change in testing and reporting rules for new infections on December 31, 2021 (27). Forecast hospital occupancy also looks close to the actual one for the first two months of the simulation once the time shift and length of hospital stay are accounted for. The forecast hospital-occupancy curve leads the actual hospital occupancy curve by approximately two days, which may be explained by an underestimation of the time between symptom onset and hospitalization for hospitalized Omicron cases.

Figure 9: Comparison of simulated results with actual data



Abbreviations: avg., average; d, days

Limitations

Limitations of the current model include the assumption of full and permanent immunity after infection and the assumption that infection with one variant will offer immunity against all other variants.

Conclusion

A new, easy-to-use epidemiological-modelling desktop app was developed based on a multi-compartment deterministic epidemiological model. The app can be downloaded from the IDSIM website. The app can model different levels of vaccine-

induced immunity, as well as the developing and waning of immunity with time after vaccination. The functionality of the app was demonstrated by using it to simulate the effects of specific factors on COVID-19 transmission. Simulation results yielded several conclusions:

- For the Delta variant, herd immunity is not achievable through vaccination only. To maintain a reproduction number below one, public health measures need to be in place until natural immunity achieved through infection with the virus, along with immunity through vaccination, brings the overall immunity to the level necessary for herd immunity. Herd immunity is even harder to achieve with the more transmissible Omicron variant.
- Waning vaccine-induced immunity prolongs the time public health measures need to stay in place and the time necessary to approach herd immunity through additional infections.
- The Omicron variant quickly outcompeted the Delta variant. Results suggested this to happen within two weeks of the simulation start and the number of daily new cases was projected to start decreasing after two to three months, depending on the rate of administration of booster doses.
- Booster doses have an important contribution to mitigating the effects of waning immunity and immune evasion by reducing COVID-19 infections, hospitalizations and deaths.
- The IDSIM app can assist PHUs by providing control over what simulations they require depending upon the local situation and ever-changing face of COVID-19, including new variants and sub-variants, changing vaccine eligibility, coverage and effectiveness and shifting public health measures. The tool provides PHU-specific results that can be used to enhance other local, provincial, national and international information. In Durham Region, weekly projections were produced for Health Department leadership and shared with the local hospital network to help prepare for possible surges in cases and hospitalizations.

The model is currently being extended to include options to model reinfection with either the same or a different variant, as well as stratum-specific number of contacts per day. The inclusion of these new features will allow more realistic simulations, including the study of annual, possibly seasonal, epidemics under endemic conditions.

While COVID-19 provided the impetus for this work, the developed model and desktop app are flexible enough to be applicable to other communicable diseases being monitored by PHUs. Thus, it is expected that IDSIM will be a welcome addition to the tools in current use by epidemiologists in PHUs.

Authors' statement

The following are each author's contributions to the reported work.
EN — Conceptualization, methodology, software, writing–original draft, writing–review and editing, supervision, project administration, funding acquisition
MP — Conceptualization, methodology, writing–review and editing, supervision
FX — Conceptualization, methodology, formal analysis, investigation, data curation, writing–original draft, writing–review and editing, visualization
PS — Conceptualization, methodology, software, writing–review and editing, visualization
AP — Conceptualization, methodology, data curation, writing–review and editing
The content and view expressed in this article are those of the authors and do not necessarily reflect those of the Government of Canada.

Competing interests

None.

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Appendix: Model equations

A.1 Notations

The equations in this appendix use the following notations.

General parameters, quantities and identifiers

N_s Number of stratifications

k Stratification index $(k = 1,2...N_s)$

n_k Number of strata in stratification k

s_k stratum index for stratification k $(s_k = 1,2...n_k)$

g Combined-stratum index $(g = \{s_1, s_2 ... s_{N_s}\})$

n_s Total number of combined strata $(n_s = \prod_{k=1}^{N_s} n_k)$

C Compartment identifier. The compartment identifiers are described in section 2.1 of the main paper. For example, $C=EQ$ denotes the "Exposed Quarantined" compartment.

$N^C_{g,i,\mathrm{v}}(t)$ Number of individuals in compartment C belonging to combined stratum g, with immunization level i, affected by variant v, at time t. For example, $N^{EQ}_{g,i,\mathrm{v}}(t)$ denotes the number of exposed quarantined individuals.

N Total population

χ Probability of transmission with contact (with an infectious individual)

Φ Contact rate (number of contacts [with other individuals] a [susceptible] individual has per unit time [day])

Stratification parameters

α^{sus}_{k,s_k} Susceptibility modulator for stratum s_k of stratification k

α^{sus}_g Susceptibility modulator for combined stratum g

$$(\alpha^{sus}_g = \prod_{k=1}^{N_s} \alpha^{sus}_{k,s_k})$$

α^{sev}_{k,s_k} Severity modulator for stratum s_k of stratification k

α^{sev}_g Severity modulator for combined stratum g

$$(\alpha^{sev}_g = \prod_{k=1}^{N_s} \alpha^{sev}_{k,s_k})$$

Variant parameters

T^{lat}_{v} Latency time (since exposure) for variant v

T^{inc}_{v} Incubation time (since exposure) for variant v

T^{hos}_{v} Time to hospitalization for severe cases (since exposure) for variant v

T^{rec-ns}_{v} Time to recovery for non-severe cases (since exposure) for variant v

$T^{hos-rec}_{\mathrm{v}}$ Time to recovery after hospitalization (for severe cases that recover)

$T^{hos-dec}_{\mathrm{v}}$ Time to death after hospitalization (for severe cases that do not recover)

χ_{v} Probability of transmission with contact

$\gamma^{sym}_{\mathrm{v}}$ Fraction of infectious individuals that are symptomatic

$\gamma^{sev}_{\mathrm{v}}$ Fraction of infectious symptomatic individuals that have severe symptoms

$\gamma^{hos-rec}_{\mathrm{v}}$ Fraction of hospitalized individuals that recover

Immunization parameters

$\theta^{tra}_{i,\mathrm{v}}$ Transmissibility factor for variant v and immunization level i

$\theta^{sus}_{i,\mathrm{v}}$ Susceptibility factor for variant v and immunization level i

$\theta^{sev}_{i,\mathrm{v}}$ Severity factor for variant v and immunization level i

R^{vac}_i Persons with immunity level i vaccinated per unit time (day)

T^{vac}_i Time (days) spent in immunity level i before advancing to immunity level $i+1$

Note: For immunization levels, i, for which progression to level $i+1$ happens through vaccination, $R^{vac}_i \neq 0$ and $\frac{1}{T^{vac}_i} = 0$

For immunization levels, i, for which progression to level $i+1$ happens through the simple passage of time (such as in the case of developing protection after vaccination or in the case of

$R_i^{vac} = 0$ and $\frac{1}{T_i^{vac}} \neq 0$ protection waning),

In short, either R_i^{vac} or T_i^{vac} but not both, apply to any immunity level *i*, and $\frac{R_i^{vac}}{T_i^{vac}} = 0$ as .

Parameters for public health me ures

γ^q Fraction of exposed individuals that are successfully quarantined

γ^{ti} Fraction of infectious individuals that are tested and successfully isolated

σ^{phm} Coefficient for additional, unspecified, public health measures

A.2 Force of infection

The force (risk) of infection is a susceptible individual's probability of exposure per unit time. The force of infection is denoted by $\lambda_{g,i,v}(t)$ and has the following expression:

$$\lambda_{g,i,v}(t) = \sigma^{phm}\alpha_g^{sus}\theta_{i,v}^{sus}\sum_{i'}\theta_{i',v}^{tra}\chi_v\Phi\frac{1}{N-\sum_{g'',i'',v''}N_{g'',i'',v''}^{D}(t)}\sum_{g'}\sum_{C\in\text{infectious in the community}}N_{g',i',v}^{C}(t) \quad \#1$$

#1

For a small number of deaths, $\sum_{g',i'',v'} N_{g',i'',v'}^{D}(t) \quad N$,

the force of infection can be approximated by:

$$\lambda_{g,i,v}(t) \quad \sigma^{phm}\alpha_g^{sus}\theta_{i,v}^{sus}\sum_{i'}\theta_{i',v}^{tra}\chi_v\Phi\frac{1}{N}\sum_{g'}\sum_{C\in\text{infectious in the commuity}}N_{g',i',v}^{C}(t) \quad \#2$$

A.3 Vaccination

Only individuals who are susceptible or otherwise in the community (neither isolated nor quarantined) and not symptomatic are vaccinated under normal circumstances. Consequently, the number of "vaccinable" persons with immunization level *i*, at any given time is:

$$N_i^{vac}(t) = \sum_g N_{g,i}^{S}(t) + \sum_g\sum_v N_{g,i,v}^{EC}(t) + \sum_g\sum_v N_{g,i,v}^{ICA}(t) + \sum_g\sum_v N_{g,i,v}^{ICPM}(t) + \sum_g\sum_v N_{g,i,v}^{ICPS}(t) \quad \#3$$

If exposed and infectious individuals are much fewer than the susceptible ones, it can be assumed that only susceptible individuals are being vaccinated and then the number of vaccinable individuals can be approximated as:

$$N_i^{vac}(t) \quad \sum_g N_{g,i}^{S}(t) \quad \#4$$

This work assumes that only susceptible individuals are being vaccinated.

With the above notations, the balance equations for each compartment are written as below.

A.4 Balance equations

$$\frac{d}{dt}N_{g,i}^{S}(t) = -\left(\sum_v \lambda_{g,i,v}(t)\right)\times N_{g,i}^{S}(t) + R_{i-1}^{vac}\frac{N_{g,i-1}^{S}(t)}{N_{i-1}^{vac}(t)} + \frac{1}{T_{i-1}^{vac}}N_{g,i-1}^{S}(t) - R_i^{vac}\frac{N_{g,i}^{S}(t)}{N_i^{vac}(t)} - \frac{1}{T_i^{vac}}N_{g,i}^{S}(t) \quad \#5$$

The fourth and fifth terms on the right represent the rate at which persons with current immunization level *i* move to immunization level *i+1*. As explained in the note for the immunization parameters, only one of the two terms is nonzero. Similarly, terms two and three on the right represent the rate at which persons with current immunization level *i-1* move to immunization level *i*, and only one of them is nonzero.

$$\frac{d}{dt}N_{g,i,v}^{EC}(t) = \left(1-\gamma^q\right)\lambda_{g,i,v}(t)\times N_{g,i,v}^{S}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{EC}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{EC}(t) \quad \#6$$

$$\frac{d}{dt}N_{g,i,v}^{EQ}(t) = \gamma^q\lambda_{g,i,v}(t)\times N_{g,i,v}^{S}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{EQ}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{EQ}(t) \quad \#7$$

$$\frac{d}{dt}N_{g,i,v}^{ICA}(t) = \left(1-\gamma_v^{sym}\right)\left(1-\gamma^{ti}\right)\frac{1}{T_v^{lat}}\times N_{g,i,v}^{EC}(t) - \frac{1}{T_v^{rec-ns}-T_v^{lat}}\times N_{g,i,v}^{ICA}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{ICA}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{ICA}(t) \quad \#8$$

$$\frac{d}{dt}N_{g,i,v}^{ICPM}(t) = \left(1-\alpha_g^{sev}\gamma_v^{sev}\right)\gamma_v^{sym}\left(1-\gamma^{ti}\right)\frac{1}{T_v^{lat}}\times N_{g,i,v}^{EC}(t) - \frac{1}{T_v^{inc}-T_v^{lat}}\times N_{g,i,v}^{ICPM}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{ICPM}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{ICPM}(t) \quad \#9$$

$$\frac{d}{dt}N_{g,i,v}^{ICPS}(t) = \alpha_g^{sev}\gamma_v^{sev}\gamma_v^{sym}\left(1-\gamma^{ti}\right)\frac{1}{T_v^{lat}}\times N_{g,i,v}^{EC}(t) - \frac{1}{T_v^{inc}-T_v^{lat}}\times N_{g,i,v}^{ICPS}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{ICPS}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{ICPS}(t) \quad \#10$$

$$\frac{d}{dt}N_{g,i,v}^{IIA}(t) = \left(1-\gamma_v^{sym}\right)\gamma^{ti}\frac{1}{T_v^{lat}}\times N_{g,i,v}^{EC}(t) - \frac{1}{T_v^{rec-ns}-T_v^{lat}}\times N_{g,i,v}^{IIA}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{IIA}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{IIA}(t) \quad \#11$$

$$\frac{d}{dt}N_{g,i,v}^{IIPM}(t) = \left(1-\alpha_g^{sev}\gamma_v^{sev}\right)\gamma_v^{sym}\gamma^{ti}\frac{1}{T_v^{lat}}\times N_{g,i,v}^{EC}(t) - \frac{1}{T_v^{inc}-T_v^{lat}}\times N_{g,i,v}^{IIPM}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{IIPM}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{IIPM}(t) \quad \#12$$

$$\frac{d}{dt}N_{g,i,v}^{IIPS}(t) = \alpha_g^{sev}\gamma_v^{sev}\gamma_v^{sym}\gamma^{ti}\frac{1}{T_v^{lat}}\times N_{g,i,v}^{EC}(t) - \frac{1}{T_v^{inc}-T_v^{lat}}\times N_{g,i,v}^{IIPS}(t) + \frac{1}{T_{i-1}^{vac}}N_{g,i-1,v}^{IIPs}(t) - \frac{1}{T_i^{vac}}N_{g,i,v}^{IIPS}(t) \quad \#13$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IQA}(t)=\left(1-\gamma_{\mathrm{v}}^{sym}\right)\frac{1}{T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{EQ}(t)-\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IQA}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{IQA}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{IQA}(t) \quad \#14$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IQPM}(t)=\left(1-\alpha_{g}^{sev}\gamma_{\mathrm{v}}^{sev}\right)\gamma_{\mathrm{v}}^{sym}\frac{1}{T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{EQ}(t)-\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IQPM}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{IQPM}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{IQPM}(t) \quad \#15$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IQPS}(t)=\alpha_{g}^{sev}\gamma_{\mathrm{v}}^{sev}\gamma_{\mathrm{v}}^{sym}\frac{1}{T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{EQ}(t)-\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IQPS}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1}^{IQPS}(t)-\frac{1}{T_{i}^{vac}}N_{g,i}^{IQPS}(t) \quad \#16$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{ICSM}(t)=\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{ICPM}(t)-\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{ICSM}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{ICSM}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{ICSM}(t) \quad \#17$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{ICSS}(t)=\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{ICPS}(t)-\frac{1}{T_{\mathrm{v}}^{hos}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{ICSS}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{ICSS}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{ICSS}(t) \quad \#18$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IISM}(t)=\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IIPM}(t)-\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{IISM}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{IISM}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{IISM}(t) \quad \#19$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IISS}(t)=\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IIPS}(t)-\frac{1}{T_{\mathrm{v}}^{hos}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{IISS}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{IISS}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{IISS}(t) \quad \#20$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IQSM}(t)=\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IQPM}(t)-\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{IQSM}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{IQSM}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{IQSM}(t) \quad \#21$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{IQSS}(t)=\frac{1}{T_{\mathrm{v}}^{inc}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IQPS}(t)-\frac{1}{T_{\mathrm{v}}^{hos}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{IQSS}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{IQSS}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{IQSS}(t) \quad \#22$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{HR}(t)=\gamma_{\mathrm{v}}^{hos-rec}\times\frac{1}{T_{\mathrm{v}}^{hos}-T_{\mathrm{v}}^{inc}}\times\left[N_{g,i,\mathrm{v}}^{ICSS}(t)+N_{g,i,\mathrm{v}}^{IISS}(t)+N_{g,i,\mathrm{v}}^{IQSS}(t)\right]-\frac{1}{T_{\mathrm{v}}^{hos-rec}}\times N_{g,i,\mathrm{v}}^{HR}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{HR}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{HR}(t) \quad \#23$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{HD}(t)=\left(1-\gamma_{\mathrm{v}}^{hos-rec}\right)\times\frac{1}{T_{\mathrm{v}}^{hos}-T_{\mathrm{v}}^{inc}}\times\left[N_{g,i,\mathrm{v}}^{ICSS}(t)+N_{g,i,\mathrm{v}}^{IISS}(t)+N_{g,i,\mathrm{v}}^{IQSS}(t)\right]-\frac{1}{T_{\mathrm{v}}^{hos-dec}}\times N_{g,i,\mathrm{v}}^{HD}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{HD}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{HD}(t) \quad \#24$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{R}(t)=\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{ICA}(t)+\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{ICSM}(t)+\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IIA}(t)+\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{IISM}(t)+\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{lat}}\times N_{g,i,\mathrm{v}}^{IQA}(t)+\frac{1}{T_{\mathrm{v}}^{rec-ns}-T_{\mathrm{v}}^{inc}}\times N_{g,i,\mathrm{v}}^{IQSM}(t)+\frac{1}{T_{\mathrm{v}}^{hos-rec}}\times N_{g,i,\mathrm{v}}^{HR}(t)+\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{R}(t)-\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{R}(t) \quad \#25$$

$$\frac{d}{dt}N_{g,i,\mathrm{v}}^{D}(t)=\frac{1}{T_{\mathrm{v}}^{hos-dec}}\times N_{g,i,\mathrm{v}}^{HD}(t) \quad \#26$$

In balance equations #6 to #25, corresponding to any compartment *C* other than *S*, the two terms on the right-hand side of type $\frac{1}{T_{i-1}^{vac}}N_{g,i-1,\mathrm{v}}^{C}(t)$ and $\frac{1}{T_{i}^{vac}}N_{g,i,\mathrm{v}}^{C}(t)$ represent, respectively, the rate at which persons with current immunization level *i-1* move to immunization level *i* and the rate at which persons with current immunization level *i* move to immunization level *i+1*, through the passage of time. Depending on the desired type of simulation, one or both terms can be zero (See also previous note for the immunization parameters).

Demographic patterns of exposure and transmission for a rural Canadian community outbreak of COVID-19, 2020

Kaitlin Patterson[1]*, Mathieu Chalifoux[2], Rita Gad[2], Shannon Leblanc[2], Paige Paulsen[2], Louise Boudreau[3], Theresa Mazerolle[4], Mariane Pâquet[2]

Abstract

Background: A coronavirus disease 2019 (COVID-19) community outbreak was declared October 5–December 3, 2020, in the Restigouche region of New Brunswick, Canada. This article describes the epidemiological characteristics of the outbreak and assesses factors associated with its transmission in rural communities, informing public health measures and programming.

Methods: A provincial line list was developed from case and contact interviews. Descriptive epidemiological methods were used to characterize the outbreak. Incidence rates among contacts, and by gender for the regional population were estimated.

Results: There were 83 laboratory-confirmed cases of COVID-19 identified during the observation period. The case ages ranged from 10–89 years of age (median age group was 40–59 years of age) and 51.2% of the cases were male. Symptom onset dates ranged from September 27–October 27, 2020, with 83% of cases being symptomatic. A cluster of early cases at a social event led to multiple workplace outbreaks, though the majority of cases were linked to household transmission. Complex and overlapping social networks resulted in multiple exposure events and that obscured transmission pathways. The incidence rate among men was higher than women, men were significantly more likely to have transmission exposure at their workplace than women, and men were the most common index cases within a household. No transmission in school settings among children was documented despite multiple exposures.

Conclusion: This investigation highlighted the gendered nature and complexity of a COVID-19 outbreak in a rural Canadian community. Targeted action at workplaces and strategic messaging towards men are likely required to increase awareness and adherence to public health measures to reduce transmission in these settings.

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Keywords: COVID-19, Canada, outbreak, emerging infectious diseases, household transmission, workplace transmission, gender, rural communities

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Introduction

The Restigouche region is located in north-central part of New Brunswick and has a population of 30,955 residents over a land mass of 8,580 km^2 (1). With a population density of 3.6 people per km^2, and no urban centres with a population over 30,000 people, Restigouche is considered to be a rural region (1). Between January 1 and October 4, 2020, the Restigouche region reported only 98 cases and relatively low community transmission rates of coronavirus disease 2019 (COVID-19). Here we describe a community outbreak within the Restigouche region where multiple chains of transmission resulted in 83 cases of COVID-19 identified between October 5 and November 4, 2020. The outbreak was declared on October 9, 2020, following the identification of an initial cluster of seven cases following a social gathering.

There is a paucity of reporting on rural COVID-19 outbreaks with complex overlapping social networks in the published literature. Because many rural and remote areas have limited capacity to manage and treat COVID-19, essential services may be rapidly paralyzed as individuals are implicated in outbreaks as either cases or contacts. Therefore, evidence is needed to inform targeted public health measures and programming for outbreak prevention and management in these rural communities. The objectives of this outbreak analysis are to describe the outbreak, to assess factors that led to spread and transmission and to inform recommendations for public health measures and programming in rural communities.

Methods

Public health nurses from both of New Brunswick's health networks (*Réseau de santé Vitalité* and Horizon Health Network) led data collection through case investigations and contact tracing interviews. The New Brunswick Department of Health also requested the assistance of the Canadian Field Epidemiology Program to provide epidemiological support to the investigation team, and the investigation was completed collaboratively between these agencies.

Sources of data included detailed case and contact interviews, a provincial case and contact line, and documentation of public health measures implemented during the outbreak (e.g. web pages, press releases, internal government documents).

Outbreak cases were defined as those with a laboratory-confirmed case using polymerase chain reaction (PCR) tests with nucleic acid detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), were a resident and/or visitor to the Restigouche region, whose episode date occurred from September 27, 2020, to November 5, 2020 (inclusive), and their source of acquisition was not travel-associated. Each case was assigned an episode date for analysis using either the date of symptom onset, or for asymptomatic cases the date of their positive laboratory specimen collection. The outbreak was declared over on December 3, 2020 (28 days or two COVID-19 incubation periods) from the last confirmed case on November 4, 2020 (2).

Investigation methods included descriptive epidemiology (e.g. frequency tables, epidemiological curves) using the available data collection tools, and additional case interviews to inform the extent of the outbreak and development of the social network diagrams. To examine potential transmission settings, we defined cluster events/locations where three or more cases were epidemiologically linked.

When multiple exposure settings were identified, a setting of most likely transmission was assigned for each case (family/household, social interaction and/or workplace), from likeliest to least likely. To ascertain most likely exposure settings, we examined the infectious period of cases present at each setting based on symptom onset date (if symptomatic) or specimen collection date (if asymptomatic) and risk of exposure. Cases who were secondary cases within their household (as defined by symptom onset date or testing date) were categorized as household exposure.

All cases were interviewed to identify how the case may have been exposed (backwards contact tracing) and any contacts the case may have exposed (forward contact tracing). At the outset of the outbreak, there were no public health recommendations for people in the community to wear a mask and no vaccine was available. Individuals that had close contact (i.e. less than two meters away for 15 or more minutes) with cases during their infectious period were classified as contacts, as per recommendations outlined by the Canadian government at the time of this outbreak. We calculated the secondary attack rate among contacts by dividing the number of known contacts that subsequently became cases by the total number of identified contacts.

We calculated the regional incidence rates overall and by age and gender. Gender, as part of the case investigation form, was defined as the socially constructed roles, behaviours, expressions and identities of girls, women, boys, men and gender diverse people (options for this variable were male, female, another gender or unknown). For the overall incidence rate, we divided the total number of laboratory-confirmed cases by the number of Restigouche residents according to the 2016 census (1). Then we divided the number of laboratory-confirmed cases by age/gender by their respective resident populations according to the census.

Cross tabulations (chi-squared or Fisher's exact for categorical or binary variables) and t-tests (for continuous variables) were used

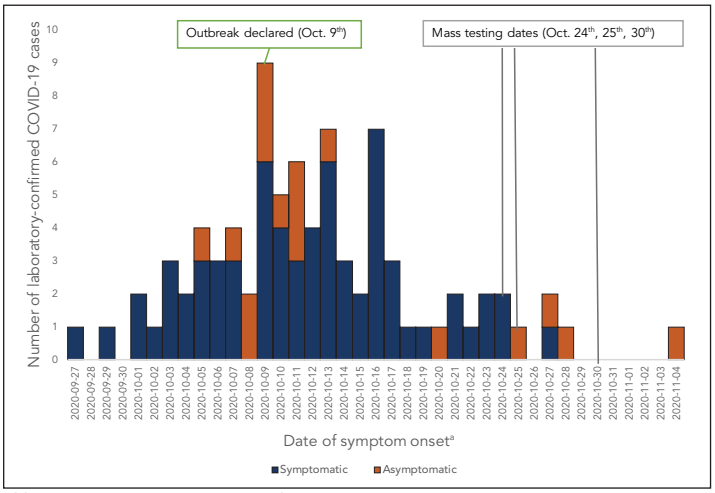
to examine differences in severity outcomes, number of contacts, exposures and testing delays by age and gender. Descriptive statistics were conducted using STATA, the charts were produced using excel and the social network diagram was produced in R.

Results

Case and testing demographics

A total of 83 laboratory-confirmed cases were associated with the community outbreak in Restigouche region between September 27, 2020, and November 5, 2020 (**Figure 1**) and 5,312 tests were conducted. None of the cases was genetically sequenced. Additionally, during the outbreak, three mass testing days were offered for asymptomatic individuals in Restigouche region (1,985 tests were conducted October 24, 25 and 30 during this mass testing). Slightly more females (58%) were tested than males (42%), and the majority (65%) of the tests were conducted among 40–79 year-olds.

Figure 1: Number of confirmed outbreak cases of COVID-19 in Restigouche region, New Brunswick by date of symptom onset[a] (n=83), between September 27 and November 5, 2020



Abbreviation: COVID-19, coronavirus disease 2019
[a] For asymptomatic cases the date of specimen collection was used

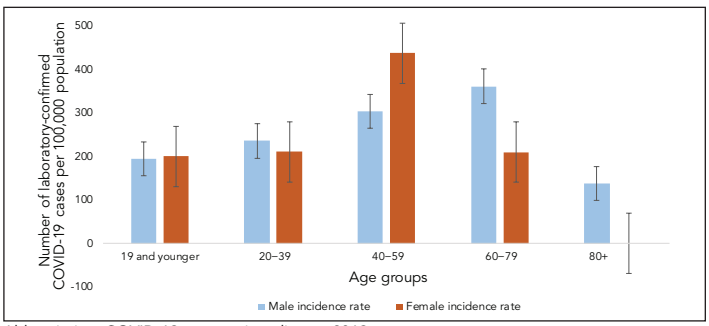
The overall test positivity rate was 1.70% (2.76% excluding the mass testing) during the outbreak period. Among the laboratory confirmed cases, the highest proportion of cases was among 40–49 year-olds (38%), and 52% of cases were male (**Table 1**). Overall, males had a higher incidence rate than females (**Figure 2**). None of the cases reported identifying as "another gender" or "unknown".

Table 1: Descriptive data on confirmed COVID-19 cases in Restigouche region, New Brunswick between September 27 and November 5, 2020

Characteristics	Number of confirmed cases	
	n	%
Age (years)	**83**	**100**
19 and younger	10	12.1
20–39	13	15.7
40–59	32	38.6
60–79	27	32.5
80 and older	1	1.2
Gender		
Male	43	51.8
Female	40	48.2
Symptoms at time of interview		
Asymptomatic	14	16.9
Symptomatic	69	83.1
Severity[a]		
Hospitalizations	5	6.0
Intensive care unit admissions	3	3.6
Mechanical ventilation	2	2.4
Deceased	2	2.4
Testing delay among symptomatic cases		
Range in time to testing after symptom onset (days)	0–12	N/A
Mean time to testing after symptom onset (days)	2.78	N/A
Median time to testing after symptom onset (days)	3	N/A
Contacts[b]		
Range in number of contacts	0–34	N/A
Mean number of contacts	6.43	N/A
Median number of contacts	4.5	N/A

Abbreviations: COVID-19, coronavirus disease 2019; N/A, not applicable
[a] Severity categories are not mutually exclusive. A total of five cases were hospitalized, among those five, three were admitted to the intensive care unit, among those three, two required mechanical ventilation and both of those cases died
[b] These numbers exclude cases 19 years of age and under due to the large influence of the number of school contacts

Figure 2: Incidence rate of COVID-19 confirmed cases by age and gender in the Restigouche region, New Brunswick identified between September 27 and November 5, 2020



Abbreviation: COVID-19, coronavirus disease 2019

An initial cluster of seven cases was identified following a social gathering; no masking or physical distancing was reported among individuals attending the event. Symptom onset date and contact tracing were used to identify the probable source case (earliest symptom onset date with laboratory-confirmed COVID-19). None of the early cases had any travel exposure history or contact with known cases outside of the community. Because Restigouche region is on the border of New Brunswick and Québec, and as the Québec regions (Gaspésie–Îles-de-la-Madeleine and Bas Saint Laurent) bordering New Brunswick were experiencing community transmission and several outbreaks in the weeks leading up to this outbreak (3), the most likely introduction was as a result of interprovincial travel. As part of the "Atlantic Bubble", New Brunswick borders were controlled for interprovincial travel outside the Atlantic Provinces (4); however, residents on both sides of the Québec/New Brunswick border were exempt from travel restrictions if they were travelling for essential reasons (e.g. work, school and emergency services) (5). There was a series of indoor and outdoor events/gatherings held in the weeks prior to the identification of the outbreak that were mentioned during case investigations that did not fall within standard exposure periods (e.g. more than 14 days prior to episode onset). However, these events had both Québec and New Brunswick residents in attendance and may mean that some early cases were undetected.

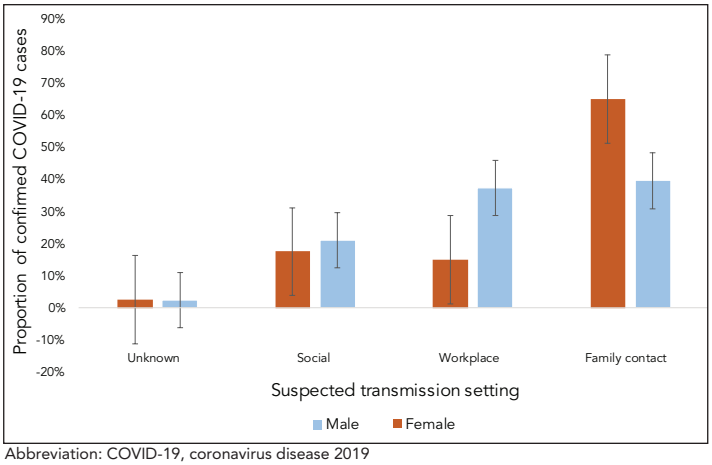
The mean number of contacts per case was 6.43, with a total of 470 contacts of adult cases identified. Both men and women had similar mean numbers of reported contacts (6.25 and 6.61, respectively), but the median number of contacts for men was higher (6 versus 4). Of these contacts, 39 subsequently tested positive, resulting in a secondary attack rate of approximately 8.2% among identified case contacts. The remaining cases were not identified through contact tracing prior to testing positive for COVID-19. Forty-two were linked to cases through backwards contact tracing.

Among laboratory confirmed cases, men aged 20–39 years sought testing significantly longer after symptom onset (3.57 days after symptom onset) than women (1.2 days after symptom onset) ($p>0.05$). Additionally, cases aged 60 years or older (4.64 days after symptom onset) sought testing significantly ($p>0.01$) longer after symptom onset than cases younger than 60 years of age (2.63 days after symptom onset). Men and women had similar proportions of asymptomatic cases at time of testing, hospitalizations, admissions to intensive care units, mechanical ventilations, and deaths.

Among cases younger than 19 years of age, 210 contacts were identified and isolated (mean number of contacts per case was 23.33, significantly higher than cases older than 19 years of age). There were no secondary cases identified and no transmission observed in schools, school buses or child/youth-related activities. All adolescent cases were linked to household contacts (none were the primary case of the household) and resulted in no secondary transmission to non-household contacts, despite exposing contacts during their infectious periods.

Among all cases, there were significant differences in exposure by gender (**Figure 3**). Women were most likely to be exposed by family and/or household members (67% vs. 40% $p>0.05$) whereas men were more likely to be exposed at their workplace or through social interactions (60% vs 37% $p>0.05$).

Figure 3: Transmission settings for COVID-19 outbreak in Restigouche region, New Brunswick by gender, identified between September 27 and November 5, 2020

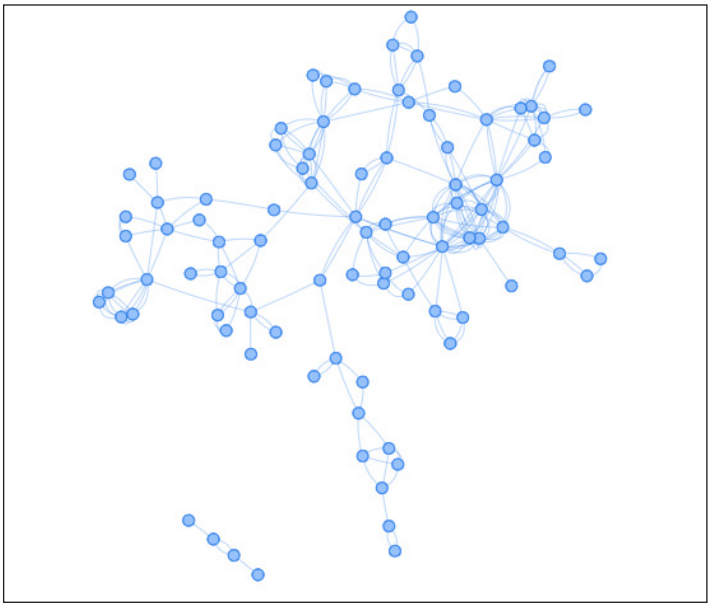


Abbreviation: COVID-19, coronavirus disease 2019

Clusters

Through case interviews, contact tracing and analysis of the local line list, we were able to link all cases to two main transmission chains (**Figure 4**). Additionally, we identified a total of seven clusters of three or more confirmed cases associated with settings, events or locations where transmission may have occurred. A social event likely preceded the majority of transmission chains identified during the community outbreak.

Figure 4: Network analysis of Restigouche region, New Brunswick COVID-19 cases between September 27 and November 5, 2020[a,b]



Abbreviation: COVID-19, coronavirus disease 2019
[a] Each node represents a case
[b] Due to privacy considerations, the sequence of cases and clusters are not identified in this figure

We also identified clusters among social outings with overnight stays and at several workplaces. Finally, we identified one family cluster we were unable to connect with other chains of transmission (Figure 4).

Discussion

Introduction of COVID-19 into Restigouche region most likely occurred through travel for essential reasons across the New Brunswick-Québec borders, given the strict provincial border quarantine measures and absence of evidence of ongoing community transmission prior to the outbreak. The leading hypotheses are linked to a series of indoor and outdoor events/gatherings held in the weeks prior to the identification of the outbreak. These events had both Québec and New Brunswick residents in attendance. Interprovincial spread of COVID-19 cases due to land travel has been difficult to track throughout Canada, as each case is reported to the public health unit of their residence. Alternatively, it is possible COVID-19 was circulating undetected within the community from another source of introduction, and it was only identified upon reaching a critical threshold, resulting in rapid spread (6). However, undetected widespread community transmission in this case is unlikely, given the relatively short duration and small number of cases linked to this outbreak.

Globally, men have a higher proportion of COVID-19 case counts than women, and experience more severe illness and higher mortality (7). In this outbreak, we also found that the incidence rate among men was significantly higher than among women and that men were more likely to be the index case in workplaces and households, despite fewer men getting tested. Research of other health outcomes has found that male gender expectations within communities and work environments can drive various high-risk behaviours (e.g. poor health seeking behaviours and drinking and driving) (8). Emerging evidence on COVID-19 has found that women are more likely than men to follow government recommendations, take health precautions (e.g. mask-wearing, physical distancing, handwashing and staying at home) and encourage others to take health precautions (9,10). Decreasing adherence to public health measures for COVID-19, such as staying at home, physical distancing and reducing contacts, has been observed over time regardless of gender (11). We also observed that older adults had longer delays in testing and had more contacts than younger adults. Often, older adults delayed seeking care because they underestimated the seriousness of their condition and attributed severity of symptoms as inevitable due to their age (12). Alternatively, older adults may have delayed seeking care because they had issues accessing transportation or don't know where to seek help (12).

Perception of risk of COVID-19 exposure may be underestimated in areas with low community transmission and case numbers. Several case contacts identified through backwards contact tracing were not initially reported as contacts as they did not meet the "two metres/15-minute interaction" criteria to be classified as a contact during the outbreak time period. This lack of reporting may have been as a result of a reluctance to disclose those interactions, or because individuals underestimated the time or overestimated the distance of their interactions (13). Another possibility is that transmission occurred despite those adhering to the two metres/15-minute interaction rule; however, most cases in this outbreak were linked to close contact with a known case. In backward contact tracing studies, an over dispersion effect has been observed, where the likelihood of transmission varies by case, and that certain events and individuals lead to a large number of secondary cases (14). It is possible that not all exposures to cases and/or events were captured.

Complex social networks that led to multiple exposures and transmissions throughout the region were identified. Other rural outbreaks of COVID-19 have been similarly characterized, and alternative approaches have been used to classify exposures and households where these networks occur (15). Modelling has demonstrated that full lockdowns for 14 days in these tightly connected communities can reduce significantly both the extent of the outbreak and the length, potentially reducing cases by 95% (16).

No transmission in schools or between children was detected in this outbreak, despite children being in contact during their infectious period. At the time of the outbreak, children were required to wear masks, all extracurricular activities were cancelled and most schools were using classroom cohorts to mitigate potential spread. Two hundred and ten individuals were required to isolate for 14 days after their last identified exposure in school settings; no cases were subsequently identified among these contacts. This finding is similar to evidence from the global literature that secondary cases in school environments between children are rare for COVID-19, especially when public health measures, such as masking, are being followed (17,18).

Recommendations/implications for public health

Public health moved quickly to contain the outbreak presented here using enhanced non-pharmaceutical public health measures (including mandatory masking in public placement, workplace assessments, gathering limits) and the closure of nonessential services. As the Canadian population is increasingly vaccinated, and public health measures are reduced, it is likely that under-vaccinated populations and areas may experience increased numbers of cases and outbreaks. Early evidence is emerging that in rural areas, COVID-19 vaccine hesitancy is higher and vaccine coverage is lower than in urban areas (19).

In preparing for future outbreaks and emergence of cases the following should be considered, particularly if more transmissible variants are introduced:

- Public health education about the efficacy of public health measures (e.g. mask wearing and physical distancing) has been effective in increasing voluntary compliance with jurisdictional rules and recommendations (6); however, targeted messaging by gender and age is likely required to increase adherence to public health measures specifically among older men (7). In particular, the identification of trusted messengers (e.g. group leaders, peers, friends, family) has been effective in advocating for public health measures, including vaccination, in targeted groups and rural and remote communities (20).
- Less stringent approaches to managing contacts related to school exposures may be warranted; however, risk will be dependent on community rates of transmission, the nature of the exposure, age demographic of students, rates of vaccination and the variant in circulation.
- Communication of risks related to travel and exposure to individuals who have travelled may be necessary in low-prevalence areas, where risks may be perceived as non-existent.
- If staffing and resources permit, utilizing both forward and backward contact tracing is preferable, using backward contact tracing has resulted in identifying 2–3 times more cases (21). In rural and/or remote regions often with little to no incidence of COVID-19, identifying the source(s) of infection is critical for controlling spread and prevention strategies in the future (22).
- The number of significant interactions not recognized as such was large in this rural setting. Investigations in these settings may benefit from a broader set of criteria for identifying contacts, including lower thresholds for defining exposure interactions (23). Individuals may perceive a fifteen-minute interaction as less time (e.g. "I only stopped in to say hi") (24). Improving the clarity of public health measures and addressing changes to the measures are critical for acceptance and adherence (25). While these changes may not be feasible for public health follow-up due to limited resources, this clarification will support individual's ability to assess risk and make decisions in the context of outbreaks and more transmissible variants.

Limitations

Several limitations warrant discussion. First, because 30% of cases presented as asymptomatic certain dynamics of transmission may have been misclassified. In these cases, we used a combination of exposure information and specimen collection date to assess plausibility. Second, we relied on self-reported exposure information, and we only implemented backward contact tracing in the middle of the outbreak. This may have resulted in missed exposures and or transmission events. Third, we did not have any genomic data to identify whether the outbreak was linked to one or more introductions. At the time of this outbreak investigation, whole genome sequencing was not available in New Brunswick. All whole genome sequencing was conducted through the National Microbiology Laboratory in Winnipeg, Manitoba and because 95% of the cases were linked epidemiologically, sequencing the outbreak cases was not a high priority.

Conclusion

This investigation highlighted the gendered nature and complexity of a COVID-19 outbreak in a rural Canadian community. Targeted action at workplaces and strategic messaging towards men are likely required to increase awareness and adherence to public health measures to reduce transmission in these settings.

Authors' statement

KAP — Conceptualized, obtained datasets, methodology, analyzed and interpreted data, drafted and revised the manuscript
MC — Conceptualized, obtained datasets, methodology, interpreted data, revised the manuscript
RRG — Conceptualized, obtained datasets, interpreted data, revised the manuscript
SL — Conceptualized, obtained datasets, interpreted data, revised the manuscript
PP — Analyzed and interpreted data, and revised the manuscript
LB — Conceptualized, collected data, obtained datasets, interpreted data, revised the manuscript
TM — Conceptualized, collected data, obtained datasets, interpreted data, revised the manuscript
MP — Conceptualized, obtained datasets, methodology, interpreted data, revised the manuscript

Competing interests

None.

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National Influenza Annual Report, Canada, 2021–2022: A brief, late influenza epidemic

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Abstract

Canadian seasonal influenza circulation had been suppressed since the beginning of the coronavirus disease 2019 (COVID-19) pandemic. This suppression was reported globally and generated concern that the return of community influenza circulation could be intense and that co-circulation of influenza and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was possible and potentially severe. Community circulation of influenza returned to Canada during the 2021–2022 influenza season. The influenza epidemic began in week 16 (mid-April 2022) and lasted only nine weeks. This epidemic was driven by influenza A(H3N2) and was exceptionally late in the season, low in intensity and short in length. Community co-circulation of influenza and SARS-CoV-2 was observed in Canada for the first time during the 2021–2022 seasonal influenza epidemic. The unusual characteristics of the 2021–2022 influenza epidemic suggest that a breadth of factors moderate transmission dynamics of the two viruses. Concerns of an intense seasonal influenza epidemic did not come to fruition during the 2021–2022 season; therefore, high influenza susceptibility remains, as does predisposition to larger influenza epidemics. Ongoing circulation of SARS-CoV-2 creates uncertainty about dynamics of future influenza epidemics, but influenza vaccination remains a key public health intervention available to protect Canadians. Public health authorities need to remain vigilant, maintain surveillance and continue to plan for both heightened seasonal influenza circulation and for the potential for endemic co-circulation of influenza and SARS-CoV-2.

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

Introduction

In March 2020, widespread non-pharmaceutical interventions (NPIs) such as masking, border and travel measures and physical distancing were implemented in Canada and globally to curtail the spread of coronavirus disease 2019 (COVID-19). Since their implementation, typical seasonal influenza activity has been suppressed globally, and Canadian influenza activity remained at interseasonal levels through the entire 2020–2021 influenza season (1–7).

Suppression of influenza circulation raised concern that a resurgence of influenza would be observed with relaxation of NPIs (8). Natural infection or annual vaccination is required to gain immunity to seasonal influenza strains. Waning immunity, antigenic drift and a larger cohort of young children without exposure to natural infection may have increased the population susceptible to seasonal influenza. This increased susceptibility creates a population-level predisposition to high-intensity seasonal influenza epidemics (9).

Of additional concern, influenza resurgence could coincide with continued waves of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Co-circulation of these high burden viruses would pose a threat to public health and place pressure on health systems. Public health surveillance is essential to plan for and mitigate this threat.

Seasonal influenza activity re-emerged in Canada during the 2021–2022 influenza season. This surveillance report summarizes the 2021–2022 Canadian influenza season through analysis of FluWatch core indicators.

Methods

Design

FluWatch is a long-standing national surveillance system that monitors the spread of influenza and influenza-like illness (ILI) in Canada. FluWatch is a composite surveillance system consisting of virological surveillance, influenza and ILI activity level surveillance, syndromic surveillance, outbreak surveillance, severe outcome surveillance and vaccine monitoring. Annually, influenza surveillance is conducted across Canada from epidemiological week 35 to week 34 of the following year. For the 2021–2022 Canadian influenza season, this surveillance period began on August 28, 2021, and ended on August 27, 2022.

Indicator definitions and data sources

FluWatch indicator definitions and data sources are summarized in **Table 1**, as is a single external SARS-CoV-2 indicator and data source that was included in analyses.

Table 1: FluWatch components, indicators, and data sources used to describe the 2021–2022 Canadian influenza season

Component	Indicator	Operational definition	Description of data source
FluWatch			
Virological	Weekly percentage of RT-PCR influenza tests positive.	Numerator: weekly number of influenza detections. Denominator: total weekly number of influenza tests reported.	Respiratory Virus Detections Surveillance System: Laboratory test counts are reported by public health laboratories from all P/Ts, and five hospital laboratories/networks. Primary surveillance target populations are acute respiratory infection cases at emergency departments, hospitalized severe acute respiratory virus infection cases, and influenza outbreak cases. Outpatient ILI cases may be targeted, but testing is typically limited to higher-risk individuals and algorithms vary by P/T. Case-level data is available for a subset of detections.
	Counts of influenza detections by age group, type, and/or subtype.	N/A	
Influenza/ILI activity levels	Weekly influenza/ILI activity level, based on activity within each influenza surveillance region over the preceding week.	Four levels of activity used for weekly classification: No activity: no laboratory-confirmed influenza detections during reporting week. Sporadic: sporadic ILI cases and influenza detections, but no outbreaks. Localized: increased ILI cases, influenza detections, and outbreaks occurring in less than 50% of the surveillance region. Widespread: increased ILI cases, influenza detections, and outbreaks occurring in 50% or more of the surveillance region.	Epidemiologists from all P/Ts report weekly influenza/ILI activity level for influenza surveillance regions.
Syndromic	Weekly percentage of patients seen by primary healthcare providers with ILI.	ILI: acute onset of respiratory illness with fever and cough and one or more of sore throat, arthralgia, myalgia or prostration. Numerator: weekly number of patients seen with ILI. Denominator: total weekly number of patients seen.	Sentinel Primary Care Provider ILI: Primary healthcare providers across Canada report on patients presenting with ILI.
	Weekly percentage of FluWatchers participants reporting ILI.	ILI: acute cough and fever. Numerator: weekly number of participants reporting ILI. Denominator: total weekly participants reporting.	FluWatchers: Volunteer participants across Canada report episodes of cough and fever experienced in the preceding week via an online questionnaire.
Outbreaks	Number of weekly laboratory-confirmed influenza outbreaks by setting.	Outbreak: two or more cases of ILI reported in the setting during a seven-day period with at least one case laboratory-confirmed as influenza.	Epidemiologists from all P/Ts report weekly. All P/Ts report outbreaks in hospitals and long-term care facilities. Some report in additional settings such as remote/isolated communities, schools/daycare, and "other" settings (includes locations such as retirement homes, assisted living, shelters and correctional facilities).

Table 1: FluWatch components, indicators, and data sources used to describe the 2021–2022 Canadian influenza season (*continued*)

Component	Indicator	Operational definition	Description of data source
FluWatch (*continued*)			
Severe outcomes	Weekly/cumulative influenza-associated hospitalization rates per 100,000 population.	Hospitalization rate: Numerator: number of influenza-associated hospitalizations. Denominator: combined population of reporting P/Ts.	Provincial/Territorial Severe Outcome Surveillance: Nine P/T Ministries of Health (AB, MB, SK, NS, NB, NL, PE, YT and NT) report laboratory-confirmed influenza-associated hospitalizations, ICU admissions and deaths.
	Counts of weekly influenza-associated hospitalizations, ICU admissions and deaths.	N/A	
	Counts of weekly influenza-associated hospitalizations, ICU admissions, and deaths among paediatric population by age group, type and/or subtype.	N/A	IMPACT: Sentinel network that reports paediatric laboratory-confirmed influenza-associated hospitalizations (16 years and younger). Detailed case-level data is reported by the network's 12 paediatric hospitals across eight P/Ts (BC, AB, SK, MB, ON, QC, NS and NL).
	Counts of weekly influenza-associated hospitalizations, ICU admissions and deaths among adult population by age group, type and/or subtype.	N/A	CIRN–SOS: Sentinel hospital network that reports adult laboratory-confirmed influenza-associated hospitalizations (16 years and older). Detailed case-level data is reported by the network's nine hospitals across four P/Ts (AB, ON, QC and NS).
Viral characterization	Counts and proportions of influenza isolates antigenically similar to the vaccine strains.	N/A	National Microbiology Laboratory: P/T public health laboratories forward a subset of influenza isolates to the National Microbiology Laboratory from cases detected throughout the season. Specimens undergo genetic characterization, antigenic characterization, and/or antiviral susceptibility testing. Genetic characterization is established by sequencing the HA gene of the influenza viruses to compare their genetic properties. Antigenic characterization is established by HA inhibition assay. Drug susceptibility is determined by chemiluminescence assay.
	Counts and proportions of influenza isolates susceptible to antivirals.	N/A	
Vaccine monitoring	Percentage of Canadian adults who received the seasonal influenza vaccine during the current influenza season.	N/A	Public Health Agency of Canada's Seasonal Influenza Immunization Coverage Survey: Annual telephone survey conducted in January and February to assess seasonal influenza vaccine coverage among adults aged 18 years and older.
	Effectiveness of seasonal influenza vaccination against laboratory-confirmed influenza-associated medically attended illness and hospitalization.	VE estimates are estimated by test negative design and calculated as: $VE = 100\% \times \left(1 - \frac{O_{pos}}{O_{neg}}\right)$ where O_{pos} is the odds of vaccination among those testing positive for influenza and O_{neg} is the odds of vaccination among those testing negative.	SPSN and CIRN-SOS: These networks calculate and report vaccine effectiveness against laboratory-confirmed influenza-associated medically attended illness and hospitalization, respectively.
External			
SARS-CoV-2 virological	Seven-day moving average percentage of SARS-CoV-2 tests positive.	Numerator: number of SARS-CoV-2 detections over the previous seven days. Denominator: total SARS-CoV-2 tests over the previous seven days.	Publicly available data from the Public Health Agency of Canada (10). SARS-CoV-2 case and testing data published by provincial and territorial partners are collated and published.

Abbreviations: AB, Alberta; BC, British Columbia; CIRN-SOS, Canadian Immunization Research Network Severe Outcome Surveillance; HA, hemagglutinin; ILI, influenza-like illness; IMPACT, Canadian Immunization Monitoring Program ACTive; ICU, intensive care unit; MB, Manitoba; N/A, not applicable; NB, New Brunswick; NL, Newfoundland and Labrador; NT, Northwest Territories; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; P/T, provinces and territories; QC, Québec; RT-PCR, reverse transcription polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SK, Saskatchewan; SPSN, Canadian Sentinel Practitioner Surveillance Network; VE, vaccine effectiveness; YT, Yukon

Statistical analysis

Data cleaning, manipulation, and analysis of counts, rates and proportions were all performed in SAS v9.4. Visualizations of analyses were prepared in Microsoft Excel. Comparisons to pre-pandemic indicator data were presented where possible. Seasons used for comparison varied by data source, depending on stability, data quality and data comparability over time (**Table 2**).

Results

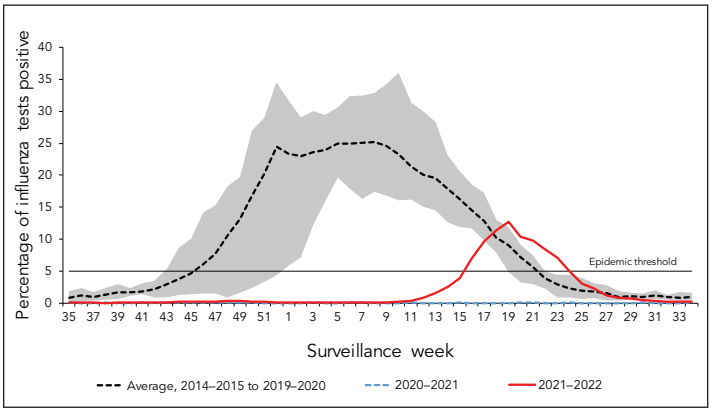
Virological

Early in the season, an increase in sporadic detections was recorded from week 48 to 51 (late-November to late-December 2021; 231 detections) but remained well below the seasonal epidemic threshold (5% or more tests positive and 15 or more detections). Detections then decreased, with fewer than 10 weekly detections reported from week 3 to 8 (late-January to late-February 2022). In week 16, influenza activity surpassed the epidemic threshold, and a national influenza epidemic was declared in Canada for the first time in two years.

The 2021–2022 seasonal influenza epidemic began exceptionally late in the season and lasted nine weeks, from week 16 to 25 (late-April to mid-June 2022; **Figure 1**). Nationally, in pre-pandemic seasons, epidemics have typically begun around week 47 (mid to late-November) and lasted 27 weeks on average.

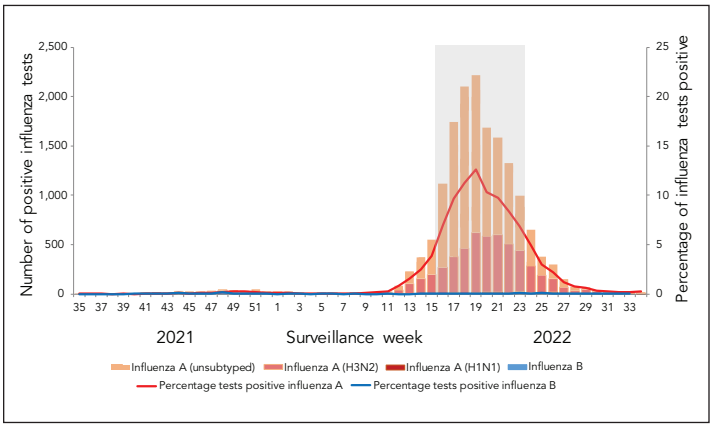
During the 2021–2022 influenza season, a total of 16,126 laboratory-confirmed influenza detections were reported out of 751,900 total laboratory tests (**Table 3**). Considerable geographic variation was observed, as the majority of detections were recorded in Québec (47%), Alberta (17%) and British Columbia (10%). Nearly all of the detections were influenza A (99%) and the influenza A(H3N2) subtype predominated, accounting for 98% of the 5,240 subtyped influenza A specimens (**Figure 2**).

Figure 1: Percentage of influenza tests positive in Canada by surveillance week[a,b]



[a] Comparison of 2021–2022 influenza season to previous seasons, 2014–2015 to 2019–2020 and 2020–2021
[b] The shaded area represents the maximum and minimum percentage of tests positive reported by week from 2014–2015 to 2019–2020. The epidemic threshold is 5% tests positive for influenza. When it is exceeded, and a minimum of 15 weekly influenza detections is reported, a seasonal influenza epidemic is declared

Figure 2: Number of positive influenza tests and percentage of tests positive in Canada, by type, subtype and surveillance week for the 2021–2022 influenza season[a]



[a] The shaded area indicates weeks where the positivity rate was at least 5% and a minimum of 15 positive tests were observed, representing the 2021–2022 seasonal influenza epidemic

Table 2: Summary of pre-pandemic data availability of FluWatch components for historical comparisons by influenza season

Influenza season	FluWatch component					
	Virological	Sentinel primary care provider ILI	FluWatchers	Outbreaks	P/T-SOS[a]	IMPACT
2014–2015	Yes	Yes	No	No	No	Yes
2015–2016	Yes	Yes	No	No	No	Yes
2016–2017	Yes	Yes	Yes	No	Yes	Yes
2017–2018	Yes	Yes	Yes	No	Yes	Yes
2018–2019	Yes	Yes	Yes	Yes	Yes	Yes
2019–2020[b]	Yes	Yes	Yes	Yes	Yes	Yes

Abbreviations: ILI, influenza-like illness; IMPACT, Canadian Immunization Monitoring Program ACTive; P/T-SOS, Province/Territory Severe Outcomes Surveillance
[a] Only cumulative end-of-season data is available prior to the 2019–2020 season
[b] In weekly comparisons to the 2019–2020 season, data from week 11 onwards is excluded due to the COVID-19 pandemic

Table 3: Number of laboratory tests, detections, and percentage positivity by province/territory for the 2021–2022 Canadian influenza season

Province/territory	Influenza tests	Influenza detections			Peak weekly influenza percent positivity		Cumulative influenza percent positivity	
		All influenza	Influenza A	Influenza B	%	95% CI[a]	%	95% CI[a]
Newfoundland and Labrador	15,930	327	327	0	7.9	6.0–9.8	2.1	1.8–2.3
Prince Edward Island	2,807	65	65	0	25.5	13.1–38.0	2.3	1.8–2.9
Nova Scotia	27,351	431	422	9	8.3	6.1–10.4	1.6	1.4–1.7
New Brunswick	21,601	495	495	0	25.9	21.6–30.3	2.3	2.1–2.5
Québec	131,566	7,634	7,524	110	26.6	25.3–27.9	5.8	5.7–5.9
Ontario	105,633	904	897	7	6.4	5.4–7.5	0.9	0.8–0.9
Manitoba	60,920	577	577	0	9.4	7.4–11.3	0.9	0.9–1.0
Saskatchewan	32,914	781	781	0	13.5	10.8–16.2	2.4	2.2–2.5
Alberta	102,875	2,716	2,713	3	11.9	10.6–13.1	2.6	2.5–2.7
British Columbia	225,352	1,558	1,462	96	3.9	3.2–4.5	0.7	0.7–0.7
Yukon Territory	5,511	21	14	7	33.3	0.0–71.1	0.4	0.2–0.5
Northwest Territories	2,263	207	207	0	31.5	23.4–39.6	9.1	8.0–10.3
Nunavut	17,177	410	410	0	53.8	44.8–62.9	2.4	2.2–2.6
Canada	751,900	16,126	15,894	232	12.6	12.1–13.1	2.1	2.1–2.2

Abbreviation: CI, confidence interval
[a] Binomial proportion Wald confidence interval

This influenza season was of low intensity, with weekly activity peaking in week 19 (mid-May 2022) at 12.6% tests positive, far below pre-pandemic seasonal peaks that averaged 31.5%. While influenza testing practices have changed during the COVID-19 pandemic, reflected by the total influenza test volume (n=751,900 vs an average of n=317,963 pre-pandemic), the elevated test volume does not account for the observed low peak epidemic percent positivity. Despite elevated testing, only 2,223 influenza detections were reported during the week 19 peak, much lower than the pre-pandemic average peak weekly detections (n=4,303). The 16,126 total detections were also quite low compared to the average 48,478 detections during pre-pandemic seasons.

Detailed information on age and influenza type/subtype was received for 14,159 laboratory-confirmed influenza detections of which 49% (n=7,169) were among individuals aged 0–19 years. Nearly half of influenza A(H3N2) detections (46%) were among individuals aged 0–19 years, an unusually young case distribution for an A(H3N2) dominant epidemic. In pre-pandemic seasons, an average of 17% of influenza A(H3N2) detections were among this age group (**Table 4**).

Table 4: Number and percentage of seasonal influenza A(H3N2) detections in Canada by age group[a]

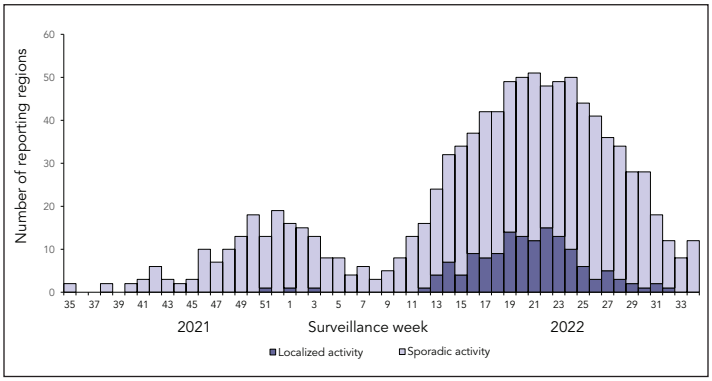
Age group (years)	Influenza season													
	2014–2015		2015–2016		2016–2017		2017–2018		2018–2019		2019–2020		2021–2022	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
0–4	811	7%	77	8%	839	7%	682	7%	275	5%	218	10%	573	19%
5–19	959	8%	104	10%	1,081	10%	709	7%	506	10%	267	12%	798	27%
20–44	1,686	14%	168	17%	1,816	16%	1,387	14%	660	13%	352	16%	805	27%
45–64	1,678	13%	212	21%	1,986	18%	1,597	16%	722	14%	323	15%	292	10%
65 and older	7,325	59%	457	45%	5,487	49%	5,882	57%	2,950	58%	991	46%	511	17%
Total	12,459	N/A	1,018	N/A	11,209	N/A	10,257	N/A	5,113	N/A	2,151	N/A	2,979	N/A

Abbreviation: N/A, not applicable
[a] Comparison of 2021–2022 influenza season to previous seasons, 2014–2015 to 2019–2020

Influenza/influenza-like illness activity levels

From week 40 (early-October) onwards, sporadic influenza activity was reported by at least one region in Canada in each week of the 2021–2022 influenza season. Nationally, the number of surveillance regions reporting sporadic or localized influenza activity reached a small peak in week 52 (late-December) and a larger peak in week 21 (late-May; **Figure 3**). Activity remained within peak levels from early-May to late-June. The first small peak mostly consisted of sporadic activity, whereas localized activity was more frequently reported during the second larger peak and was reported in multiple regions across Canada. Reported levels never exceeded localized activity.

Figure 3: Number of influenza surveillance regions reporting sporadic or localized activity by week in Canada, 2021–2022 influenza season

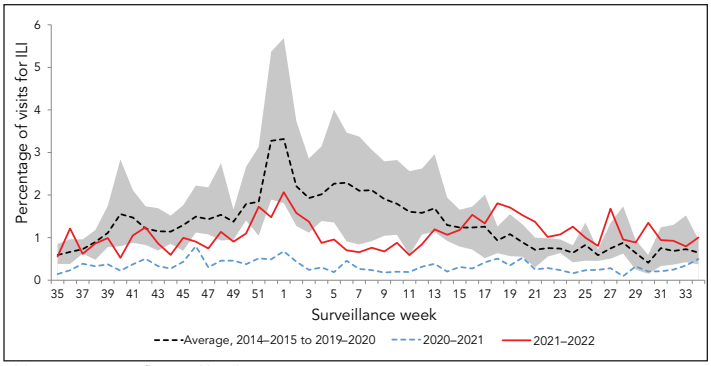


Syndromic—Sentinel primary healthcare provider influenza-like illness surveillance

During the 2021–2022 season, a weekly average of only 50 sentinel primary care providers reported to the ILI surveillance program with a weekly average of 3,769 total patients seen; both metrics were lower than historical levels. On average, in pre-pandemic seasons, 134 sentinel providers reported to the surveillance program and 7,688 total patients were seen each week.

The weekly percentage of visits to primary care providers due to ILI ranged from 0.5% to 2.1% (**Figure 4**). There was no single defined peak in ILI visits observed this season, while in pre-pandemic seasons a peak was typically observed in late-December/early-January, with an average of 3.4% visits due to ILI at this time of season. From the start of the season to mid-April (week 35 to 15), weekly percentage of visits due to ILI were almost exclusively below historical averages. From week 16 onwards (mid-April), the weekly percentage of visits due to ILI was above historical averages following an increase in weekly ILI visits at a time of typical decrease. This late increase in ILI coincided with the late seasonal influenza epidemic.

Figure 4: Percentage of visits for ILI reported by sentinel primary care providers in Canada by surveillance week[a,b]



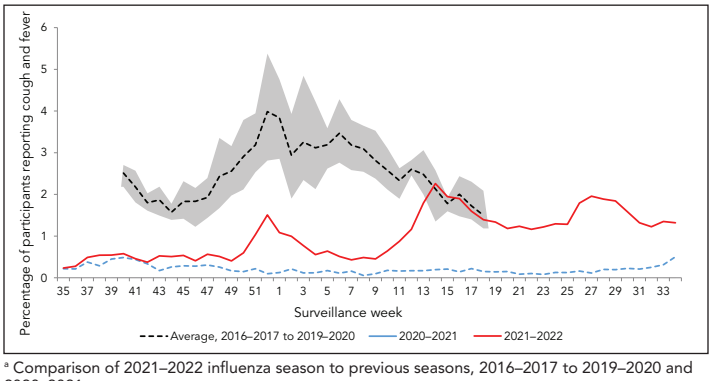
Abbreviation: ILI, influenza-like illness
[a] Comparison of 2021–2022 influenza season to previous seasons, 2014–2015 to 2019–2020 and 2020–2021
[b] The shaded area represents the maximum and minimum percentage of visits for ILI reported by week from 2014–2015 to 2019–2020

Syndromic—FluWatchers

During the 2021–2022 season, an average of 12,045 FluWatchers participants reported each week. Overall, a total of 18,124 participants reported at least once this season, completing a total of 619,322 questionnaires.

The percentage of FluWatchers reporting ILI remained very low for the majority of the 2021–2022 season (**Figure 5**). From the beginning of the season to early-April (week 39 to 13), this percentage remained far below pre-pandemic levels. Despite this, a peak was observed in week 52 (early-January) at 1.5%. Five weeks later, a subsequent higher peak occurred in week 14 (early-April) at 2.3%, reaching expected levels for the first time of the season. A final peak in FluWatcher-reported ILI was observed in week 27 (early-July) at 2.0%.

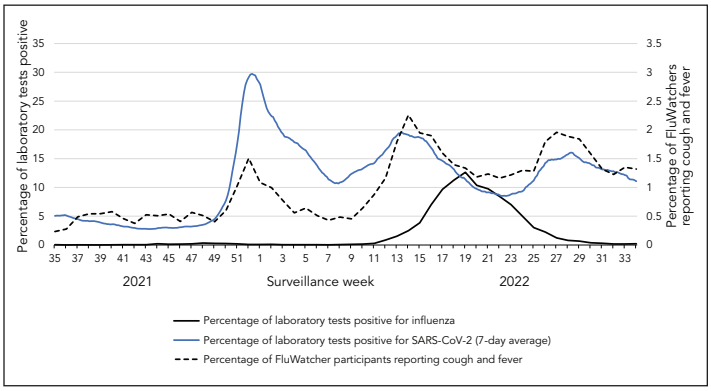
Figure 5: Percentage of FluWatcher participants reporting cough and fever in Canada by surveillance week[a,b]



[a] Comparison of 2021–2022 influenza season to previous seasons, 2016–2017 to 2019–2020 and 2020–2021
[b] The shaded area represents the maximum and minimum percentage of percentage of participants reporting cough and fever by week, from 2016–2017 to 2019–2020

The percentage of FluWatchers reporting ILI aligned well with the percentage of SARS-CoV-2 laboratory tests that were positive in Canada (**Figure 6**). The first peak in FluWatchers ILI (week 52; 1.5%) occurred concurrently with SARS-CoV-2 activity reaching its maximum peak during the surveillance period. The highest peak in FluWatchers ILI (week 14; 2.3%) occurred during a smaller SARS-CoV-2 activity peak, and as influenza activity was approaching its highest peak of the season. During the third peak in FluWatchers ILI (week 27; 2.0%), ILI increased with SARS-CoV-2 activity while influenza positivity decreased.

Figure 6: Percentage of influenza and SARS-CoV-2 laboratory tests positive and percentage of FluWatchers reporting cough and fever in Canada by surveillance week, 2021–2022 influenza season



Abbreviation: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

Outbreaks

During the 2021–2022 season, 91 laboratory-confirmed influenza outbreaks were reported. The majority of laboratory-confirmed outbreaks (88%) were reported from week 11 to 24 (mid-March to mid-June), with the highest number of outbreaks in any given week (n=9) reported in week 16. Of reported laboratory-confirmed outbreaks, 49% were in long-term care facilities (n=45) and 38% were in facilities categorized as "other" (e.g. retirement homes, correctional facilities). All but one laboratory-confirmed outbreak were due to influenza A, and 96% (n=44) of outbreaks with subtype information were due to influenza A(H3N2).

This season, there were fewer laboratory-confirmed influenza outbreaks reported and a lower proportion of outbreaks occurred in long-term care facilities compared to recent pre-pandemic seasons. In the 2018–2019 and 2019–2020 seasons respectively, there were 978 and 1,038 total laboratory-confirmed outbreaks reported with 64% and 62% of outbreaks occurring in long-term care facilities.

Severe outcomes—Provincial/Territorial Severe Outcome Surveillance

During the 2021–2022 influenza season, 776 influenza-associated hospitalizations were reported by participating provinces and territories. Nearly all hospitalizations were associated with influenza A (99.6%), and among hospitalizations with subtype information, 99.5% (n=407) were associated with influenza A(H3N2).

The annual seasonal hospitalization incidence was nine hospitalizations per 100,000 population, much lower than rates recorded in pre-pandemic seasons where on average 42 hospitalizations per 100,000 population were recorded (**Table 5**). Similar to previous seasons, the annual seasonal hospitalization rates were highest among adults aged 65 years and older (21 per 100,000) and children aged 0–4 years (19 per 100,000). However, in past seasons of predominant influenza A(H3N2) circulation, hospitalization rates have been much higher among adults aged 65 years and older, relative to younger age groups (Table 5).

Table 5: Estimated annual seasonal incidence of influenza hospitalizations (per 100,000 population) in Canada by age group[a]

Age group (years)	Influenza season (predominant influenza of season)				
	2016–2017 (H3N2)	2017–2018 (H3N2 & B)	2018–2019 (H1N1)	2019–2020 (H1N1 & B)	2021–2022 (H3N2)
0–4	46	70	98	77	19
5–19	9	17	21	16	7
20–44	5	12	15	14	5
45–64	15	41	40	23	6
65 and older	128	280	127	76	21
Overall	30	64	45	30	9

[a] Comparison of 2021–2022 season to previous seasons, 2016–2017 to 2019–2020

The majority of this season's influenza-associated hospitalizations (94%) occurred from week 14 to 26, corresponding to the brief influenza epidemic experienced this season. While brevity contributes to this season's lower annual hospitalization incidence, weekly incidence peaked at 1.2 hospitalizations per 100,000; lower than the 2019–2020 season, which peaked at 2.9 hospitalizations per 100,000 and featured 13 consecutive weeks with a hospitalization rate greater than 1.2 per 100,000.

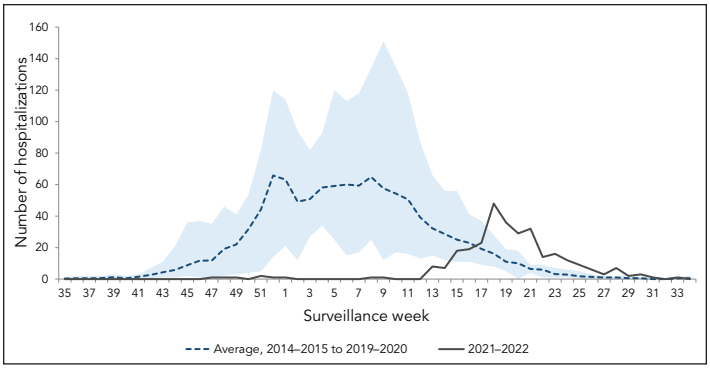
A total of 69 intensive care unit (ICU) admissions and 22 deaths were reported this season by participating provinces and territories. Of hospitalized cases, 9% were admitted to ICU; which is comparable to pre-pandemic seasons (average 11%; range 4%–17%). The ICU admissions were most common among adults 65 years of age and older (30%) and 45–64 years of age (26%). Deaths were most common among adults 65 years of age and older (59%).

Severe outcomes—Canadian Immunization Monitoring Program ACTive

The Canadian Immunization Monitoring Program ACTive (IMPACT) network preliminarily reported 303 influenza-associated paediatric hospitalizations during the 2021–2022 influenza season—far fewer than reported in pre-pandemic seasons. From 2014–2015 to 2019–2020, an average of 1,057 paediatric hospitalizations were reported, with 593 hospitalizations during the 2016–2017 season being the lowest reported in a single season.

Weekly preliminary paediatric hospitalizations remained below expected pre-pandemic levels for most of the 2021–2022 season

Figure 7: Preliminary number of influenza-associated paediatric hospitalizations reported by IMPACT, by week of admission[a,b]



Abbreviation: IMPACT, Canadian Immunization Monitoring Program ACTive
[a] Comparison of 2021–2022 influenza season to previous seasons, 2014–2015 to 2019–2020
[b] The shaded area represents the maximum and minimum hospitalizations reported by week of admission, from 2014–2015 to 2019–2020

but increased late in the season peaking in week 18 (early-May; n=48; **Figure 7**). This peak was of low intensity and late compared to prior seasons; on average, pre-pandemic paediatric hospitalizations peaked at 93 weekly hospitalizations, and peak weekly hospitalizations occurred no later than week 9.

Almost all hospitalizations were associated with influenza A (99%), and among the 96 hospitalizations with subtype information, 98% were associated with influenza A(H3N2). Age distribution of paediatric hospitalizations was similar to pre-pandemic seasons, with hospitalized cases most commonly reported in patients younger than two years of age (32%).

There were 30 ICU admissions and fewer than five deaths reported this season. Of hospitalized cases, 10% were admitted to ICU; lower than pre-pandemic seasons (average 18%). The highest proportion of ICU admissions was reported among patients 10–16 years (30%) and 2–4 years of age (23%).

Severe outcomes—Canadian Immunization Research Network Severe Outcome Surveillance

A total of 30 influenza-associated hospitalizations were reported through the Canadian Immunization Research Network Severe Outcome Surveillance (CIRN-SOS) during the 2021–2022 influenza season. There were too few hospitalizations to analyze temporality or severity trends.

Viral characterization

From September 1, 2021 to August 27, 2022, the National Microbiology Laboratory (NML) characterized 277 influenza viruses, far fewer than during a typical influenza surveillance season (1,171 to 3,857 viruses from 2014–2015 to 2019–2020). All 277 influenza viruses were influenza A (266 A(H3N2), 11 A(H1N1)).

Of the 266 influenza A(H3N2) viruses genetically characterized, sequence analysis of the hemagglutinin gene indicated that 100% of these viruses belonged to genetic clade 3C.2a1b.2a.2.

A total of 277 influenza viruses were antigenically characterized (n=266 influenza A(H3N2) and 11 influenza A(H1N1)). Among these viruses, 19% of A(H3N2) viruses (n=51) were antigenically similar to the egg-propagated A(H3N2) reference virus used in the production of the 2021–2022 Northern Hemisphere influenza vaccine, while 91% of A(H1N1) viruses (n=10) were similar to the cell-propagated A(H1N1) reference virus.

Two-hundred and fifty-nine influenza viruses (246 A(H3N2) and 11 A(H1N1)) were tested for antiviral resistance, with 100% of viruses sensitive to each oseltamivir and zanamavir.

Vaccine monitoring—Vaccine coverage

Vaccine coverage for the 2021–2022 influenza season was similar to the previous season. Thirty percent of adults 18–64 years of age received their influenza vaccine. Vaccine coverage was higher among seniors aged 65 years and older (71%) and adults aged 18–64 years with chronic medical conditions (38%). Overall vaccine coverage was higher amongst females compared to males.

Vaccine monitoring—Vaccine effectiveness

Using a test-negative design, the Canadian Sentinel Practitioner Surveillance Network (SPSN) reports adjusted vaccine effectiveness (VE) of 36% (95% confidence interval (CI): −38–71) against medically-attended illness due to late-season influenza A(H3N2) clade 3C.2a1b.2a.2 viruses (11). This estimate is adjusted for age group, province, comorbidity and calendar month, and is based on 327 specimens collected from week 10 to 26 (early-March to early-July 2022).

Given the low-intensity community circulation of influenza this season, estimates of seasonal influenza vaccine effectiveness in

preventing hospitalization for laboratory-confirmed influenza are not available for the 2021–2022 season.

Discussion

The 2021–2022 Canadian influenza season saw the return of community influenza circulation. A national seasonal influenza epidemic was declared for the first time since the 2019–2020 season. Starting in mid-April and lasting only nine weeks, the 2021–2022 Canadian influenza season was later and shorter than usual and dominated by influenza A(H3N2).

The COVID-19 pandemic and response disrupted seasonal transmission patterns of influenza and other respiratory viruses. The NPIs put in place to address the COVID-19 pandemic, such as masking, border and travel measures and physical distancing, contributed to these disruptions. Associations between NPIs and decreased transmission of influenza and SARS-CoV-2 have been demonstrated (12–16). The aforementioned factors, as well as other factors such as antagonistic viral interference, which has been observed between influenza and other seasonal respiratory viruses (17,18), may have contributed to the early-season suppression of influenza. The breadth of these factors continues to create uncertainty about the dynamics of influenza and SARS-CoV-2 co-circulation.

Seasonal influenza activity increased late in the season to reach the epidemic threshold at a time that corresponded to elevated SARS-CoV-2 transmission, demonstrating that community-level co-circulation of these viruses is possible. When influenza activity reached 5% of tests positive in Canada, the SARS-CoV-2 7-day average of test positivity was 17.6% and never dropped below 8.5% during the influenza epidemic (Figure 6). However, the 2021–2022 Canadian seasonal influenza epidemic peaked when SARS-CoV-2 percentage positivity was decreasing. Globally, peaks in influenza percentage positivity have thus far occurred at times when SARS-CoV-2 percentage positivity is relatively low or declining; a trend observed at some World Health Organization regional levels as well (19). Factors that modulate transmission of both viruses, such as viral interference, NPIs, vaccination, social mixing patterns and climatic conditions, require further study in combination to explain these trends.

There was evidence of influenza and SARS-CoV-2 co-circulation activity in ILI reports from FluWatchers. Reported ILI activity broadly aligned with SARS-CoV-2 laboratory activity, but the magnitude of the two indicators did not align precisely. Fluwatchers ILI activity increased but remained below expected levels during the most intense SARS-CoV-2 activity peak. The highest peak in FluWatchers ILI activity was later reported during a period of influenza and SARS-CoV-2 co-circulation. These findings highlight potential usefulness of FluWatchers for signal detection, but also highlight the lack of specificity of the case definition.

In Canada, the seasonal epidemic was driven by the spread of influenza A(H3N2). Influenza A(H3N2) case distribution tends to skew towards older adults, but this was not observed during the 2021–2022 season. The proportion of A(H3N2) infections detected among children and teenagers was nearly three times higher than typical, and hospitalization rates were similar among children aged 0–4 years and adults aged 65 years and older—atypical for a season dominated by A(H3N2). This unusual age distribution has a complex set of possible explanations, including more restrictive NPIs among vulnerable older adults differentially impacting influenza transmission in this group. Immunologic factors including increased susceptibility among the large cohort of young children unexposed to influenza infection may also play a role.

There was no evidence of increased severity of influenza cases among FluWatch indicators. The proportion of hospitalized cases admitted to ICU was either within or below expected levels. While a scarcity of documented cases has limited assessment, there was some early evidence of synergistic effects on severity of cases co-infected with influenza and SARS-CoV-2 (20–23). FluWatch surveillance indicators are not well equipped to assess these effects.

Increased population-level influenza susceptibility was a concern coming into the 2021–2022 season. Several modelling studies demonstrated that pandemic-related conditions could cause greater seasonal influenza epidemic intensity, but that the complexity of transmission dynamics cause uncertainty in both the magnitude and timing (8,24,25). The 2021–2022 influenza epidemic highlighted this uncertainty, being late and low intensity. Influenza susceptibility remains higher than typical pre-pandemic years, and predisposition to larger influenza epidemics also remains (9); however, the likelihood of an intense influenza season is influenced by the ongoing COVID-19 pandemic and response, and population susceptibility to influenza cannot be considered in isolation.

With influenza susceptibility remaining high, the importance of seasonal influenza vaccination to reduce susceptibility is highlighted. The SPSN reported 36% VE against illness due to the influenza A(H3N2) clade 3C.2a1b.2a.2 viruses that predominated this season (95% CI: −38–71). These viruses are considered antigenically-distinct from the 2021–2022 vaccine strain instead belonging to clade 3C.2a1b.2a.1, but the estimate is very similar to VE estimates against influenza A(H3N2) recently reported from the United States (35%; 95% CI: 19–47) for the period spanning October 2021 to April 2022 (26) and from Europe (35%; 95% CI: 6–54) spanning October 2021 to March 2022 (27). Findings from SPSN, as well as strain characterization results from NML, reinforce the World Health Organization's decision to switch to a more representative clade 3C.2a1b.2a.2 strain for the northern hemisphere 2022–2023 A(H3N2) vaccine component (28).

Conclusion

The 2021–2022 Canadian influenza season was highlighted by the return of epidemic-level influenza activity. The 2021–2022 influenza epidemic was late, low-intensity and brief, and was influenced by the ongoing COVID-19 pandemic. Over the past two years, relatively few Canadians have been infected with influenza, rendering the population more susceptible to the seasonal influenza strains that are likely to circulate in the upcoming years. Ongoing circulation of SARS-CoV-2 creates great uncertainty regarding when an intense influenza epidemic may reoccur in Canada. Public health authorities need to remain vigilant and continue to plan for seasonal influenza circulation and to maintain laboratory diagnostics and surveillance capacity to help prevent the spread and impact of influenza. Influenza vaccination remains a key public health intervention available to protect Canadians.

Authors' statement

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

Competing interests

None.

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Surveillance of laboratory exposures to human pathogens and toxins, Canada, 2021

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Abstract

Background: The Laboratory Incident Notification Canada surveillance system monitors laboratory incidents that are mandated to be reported under the *Human Pathogens and Toxins Act* and the *Human Pathogens and Toxins Regulations*. This article describes laboratory exposure incidents that occurred in Canada in 2021 and individuals affected in these incidents.

Methods: We extracted all laboratory incidents occurring in licensed Canadian laboratories in 2021 from the Laboratory Incident Notification Canada system and analyzed them using the software R. We calculated the rate of exposure incidents and performed descriptive statistics by sector, root cause, activity, occurrence type and type of pathogen/toxin. Analysis of the education level, route of exposure, sector, role and laboratory experience of the affected persons was also conducted. We conducted seasonality analysis to compare the median monthly occurrence of exposure incidents between 2016 and 2020 to monthly incidents in 2021.

Results: Forty-three exposure incidents involving 72 individuals were reported to Laboratory Incident Notification Canada in 2021. There were two confirmed laboratory-acquired infections and one suspected infection. The annual incident exposure rate was 4.2 incidents per 100 active licenses. Most exposure incidents involved non-Security Sensitive Biological Agents (n=38; 86.4%) and human risk group 2 (RG2) pathogens (n=27; 61.4%), with bacteria (n=20; 45.5%) and viruses (n=16; 36.4%) as the most implicated agent types. Microbiology was the most common activity associated with these incidents (n=18; 41.9%) and most incidents were reported by the academic sector (n=20; 46.5%). Sharps-related (n=12; 22.2%) incidents were the most common, while human interaction (e.g. workload constraints/pressures/demands, human error) (n=29, 28.2%) was the most common root cause. Most affected individuals were exposed through inhalation (n=38; 52.8%) and worked as technicians or technologists (n=51; 70.8%). Seasonality analyses revealed that the number of exposure incidents reported in 2021 were highest in September and May.

Conclusion: The rate of laboratory incidents was slightly lower in 2021 than in 2020. The most common occurrence type was sharps-related while issues with human interaction was the most cited root cause.

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

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Introduction

Working with human pathogens and toxins (HPTs) in laboratory settings poses a risk of exposure for personnel. The risk of laboratory-acquired infections (LAIs) has driven the development of biosafety oversight measures around the world, such as regulated laboratory safety practices and mandatory reporting of exposures in various settings. In the United States, Belgium and the United Kingdom, LAIs are monitored by a number of different agencies and systems with various levels of regulatory authority (1–3). In comparison, Canada has a mandated comprehensive exposure reporting system at the federal level, established to collect all laboratory incidents related to HPTs.

The Public Health Agency of Canada's (PHAC) Centre for Biosecurity administers and enforces the *Human Pathogens and Toxins Act* (HPTA) and the *Human Pathogen and Toxins Regulations* (HPTR), which were enacted to promote safety and security of the public against the risks of working with HPTs in hospital, academic, public and private laboratories. The HPTA came into effect in 2015, fulfilling its directions through the HPTR. The HPTA classifies HPTs into risk groups (RG) based on their potential to cause harm to the health of both an individual and the community (4). The RG1 pathogens are those that are not capable of or are unlikely to cause disease in humans and are associated with low risk to both individuals and the community. The RG2 pathogens can cause serious disease in an individual but is unlikely to do so, and the risk of community spread is low. The RG3-classified pathogens are likely to cause serious disease in an infected individual, but the risk of spread to the public is low. The RG4 category is reserved for HPTs that are likely to cause harmful and serious disease in an individual and are of concern for spread to others in the community. A subset of HPTs has been determined to pose increased biosecurity risk due to their potential in being used as a biological weapon, and are classified as Security Sensitive Biological Agents (SSBAs). Under the HPTA, all Canadian laboratory facilities are required to obtain a license if conducting any controlled activities with RG2, RG3, or RG4 HPTs (5).

The HPTA outlines actions to be undertaken by laboratories, such as the mandatory timely reporting of incidents involving RG2 pathogens or above in the following instances (6): exposures and suspected or confirmed laboratory-acquired infections/intoxication; inadvertent possession, production and/or release of an HPT; missing, lost, or stolen biological agent, including SSBAs not received within 24 hours of expected arrival; and changes affecting biocontainment, including changes to the physical structure of the facility, to any equipment or to the standard operating procedures.

In December 2015, the Laboratory Incident Notification Canada (LINC) Surveillance System was launched to implement and oversee requirements of reporting incidents involving RG2 HPTs and above, as outlined in the HPTR. The LINC receives reports from all licensed laboratories in Canada describing exposure and non-exposure laboratory incidents that involve HPTs. A total of 279 exposure incidents were reported between 2016 and 2020, involving a total of 596 individuals in private, public, hospital and academic laboratories (7–11). In light of the ongoing coronavirus disease 2019 (COVID-19) pandemic, there has been a heightened awareness and public interest in biosafety and biosecurity.

The objective of this annual report is to describe the distribution of laboratory incidents reported to LINC in 2021 and the associated factors, including activity, sector, agent, occurrence type, root causes and the number and characteristics of people exposed.

Methods

Data sources

Since the launch of the LINC surveillance system, regulated parties are required to submit their notification reports for laboratory exposure incidents, including suspected or confirmed LAIs, via the PHAC's Biosecurity Portal. Forms are standardized to capture select information for exposure incidents. Data are captured via the Microsoft Customer Relationship Management system and reviewed for accuracy and completeness by LINC team members. Data from exposure incidents that occurred between January 1, 2021, and December 31, 2021, including incidents reported in this period without a specified incident date, were used in this analysis. If more than one follow-up report was submitted, data from the most recent report were used. Extracted data were cleaned by investigating any outliers, correcting for spelling errors, and removing duplicate entries. Reporting is voluntary when the agent or incident is not under the purview of the HPTA. This includes incidents involving agents in their natural environment or classified as RG1. These reports are sometimes submitted to LINC at the discretion of the reporter, and are often incomplete as a follow-up is not required. Consequently, these reports are excluded from the analysis (ruled out).

Within the scope of the HPTA/HPTR, an exposure incident is defined as a laboratory incident that could have resulted in intoxication/infection or did result in a suspected or confirmed LAI (4,6). A non-exposure incident refers to any of the following: 1) the inadvertent possession, production or release of a pathogen or toxin; 2) a missing, lost or stolen pathogen or toxin; or 3) an SSBA not being received within 24 hours of expected arrival.

Analysis

We extracted LINC surveillance data to Microsoft Excel on February 28, 2022, and performed descriptive statistics in R 4.0.2. Cross validation of all findings were performed in SAS EG 7.1. Exposure incidents, including suspected and

confirmed LAIs, were classified as either confirmed or ruled out incidents after the investigation was detailed in follow-up reports. The affected persons were ruled out if the event itself was ruled out, or if the person was otherwise determined not to be exposed. Annual numbers of exposure incidents between 2016 and 2020 were updated using the most recent data to account for changes in status of historic reports as LINC continuously receives new data; therefore, it should be noted that some discrepancies may exist between the values for this and past years' annual reports.

Among confirmed exposure incidents, we analyzed the number of incidents at the level of the report and the affected individual, of which there may be more than one per report. For each incident report, we examined the distribution of the sector, main activity, root cause(s) of the incident, occurrence type, and implicated pathogen/toxin involved, along with reporting delays. For each affected person, we examined the distribution of the highest level of education, years of laboratory experience, route of exposure, sector and regular role. In light of the ongoing COVID-19 pandemic, investigations specific to severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) were highlighted in the analysis.

We compared the number of exposure incidents over time from 2016 to 2021, and calculated the exposure incident rate per 100 active licenses, which has been described in detail in previous reports (8,9). Finally, we performed an analysis of seasonality trends to compare the monthly occurrence of exposure incidents from between 2016 and 2021. The monthly exposure incidents for the five-year period were calculated by obtaining the median number of exposures for each month. The median was chosen over the mean as it provides a better measure of central tendency of exposure incidents by dampening noise from outlier data.

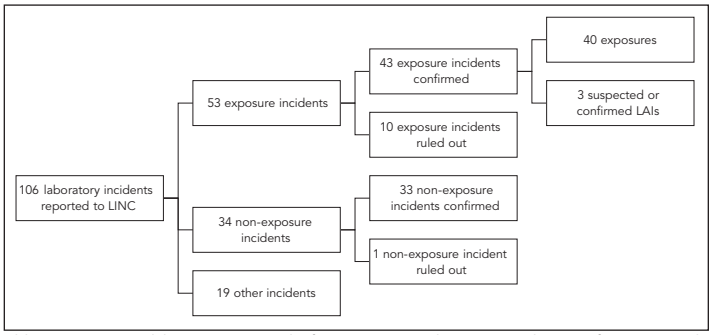
Results

Between January 1 and December 31, 2021, LINC received 106 reports on laboratory incidents: 53 exposure reports; 34 non-exposure reports; and 19 other reports involving changes affecting biocontainment (**Figure 1**). Among the exposure incidents, two resulted in confirmed LAIs, one involved a suspected LAI and ten were ruled out (Figure 1). One non-exposure report was ruled out. Initially, a total of 83 people were reportedly exposed in these laboratory incidents, but upon further investigation, 11 people were ruled out.

In 2021, there were 1,027 active licenses in Canada permitting the use of HPTs; therefore, the exposure incident rate was 4.2 incidents per 100 active licenses in 2021 (**Figure 2**).

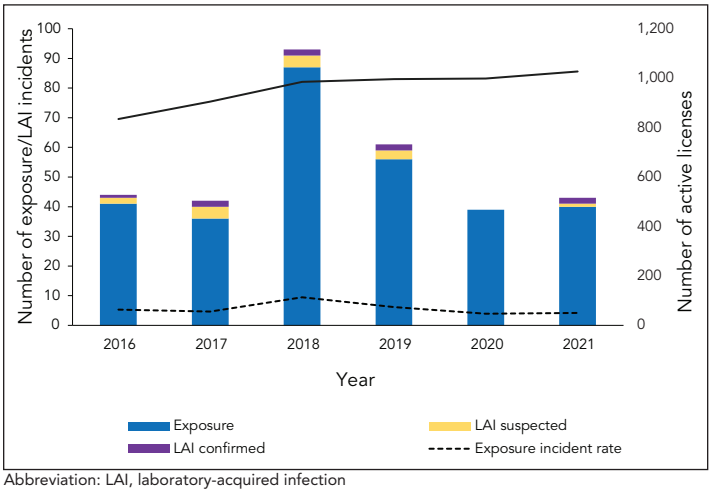
Between 2016 and 2020, the median number of exposure incidents per month varied with the lowest being 2.5 incidents per month in June and August, and the highest being

Figure 1: Types of incidents reported to Laboratory Incident Notification Canada and exposure incidents included in analysis, Canada, 2021



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

Figure 2: Confirmed exposure incidents, suspected and confirmed laboratory-acquired infections and exposure incident rate, Canada, 2016–2021



Abbreviation: LAI, laboratory-acquired infection

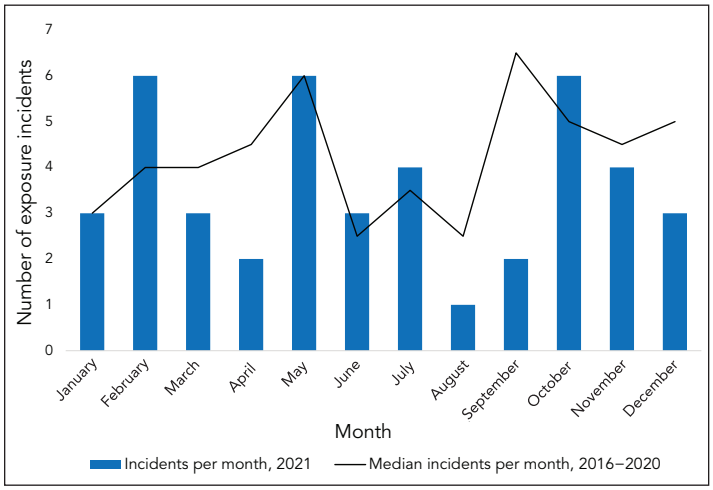
6.5 incidents per month in September (**Figure 3**). In comparison, the number of exposure incidents in 2021 also varied with the lowest in August (one incident per month) and the highest in February, May and October (six incidents per month).

Exposure incidents by main activity and sector

Among the exposure incidents reported, microbiology was the most common activity being performed during the incident (n=18; 41.9%), followed by *in vivo* animal research (n=12; 27.9%). Less frequently reported activities included animal care, cell culture, autopsy/necropsy, molecular investigation, microscopy or other (n=13; 30.2%). Definitions of the main activities are included in **Appendix Table A1**.

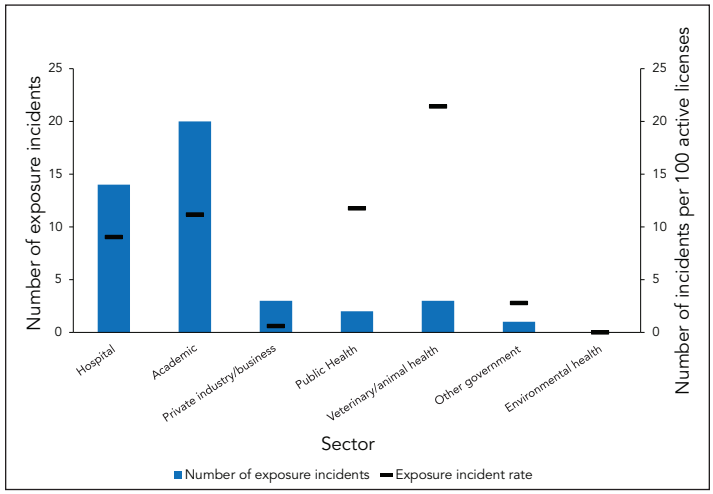
Most exposure incidents occurred in the academic sector (n=20; 11.2 per 100 active licenses), followed by the hospital sector (n=14; 9.0 per 100) (**Figure 4**). The veterinary/animal health sector had the highest rate of exposure incidents per 100 active licenses (21.4 per 100), followed closely by the public health sector (11.8 per 100). The environmental health sector had no reported incidents in 2021.

Figure 3: Seasonality analysis using median confirmed exposure incidents[a] per month, Canada, 2016–2021



[a] Exposure incidents include those that involved a suspected or confirmed laboratory-acquired infection

Figure 4: Confirmed exposure incidents and active licenses by sector reported to Laboratory Incident Notification Canada, Canada, 2021



Implicated human pathogens and toxins

A total of 44 pathogens and toxins were implicated in the 43 exposure incidents; one incident implicated two pathogens. Of the 44 pathogens and toxins, most exposure incidents involved non-SSBA (n=38; 86.4%) and human RG2 pathogens (n=27; 61.4%) (**Table 1**). Bacteria (n=20; 45.5%) and viruses (n=16; 36.4%) were the most implicated agent types, while no submitted reports involved parasites. The most common RG2 agents involved in exposure incidents were *Neisseria meningitides* and *Streptococcus agalactiae* (n=3; 6.8% each). The most common RG3 agent was SARS-CoV-2 (n=6; 13.6%). *Vaccinia virus* was the agent involved in the suspected LAI and *Salmonella enterica* and *Staphylococcus aureus* were involved in the two confirmed LAIs.

Table 1: Human pathogens or toxins involved in reported exposure incidents by risk group level and security sensitive status, Canada, 2021 (N=44)

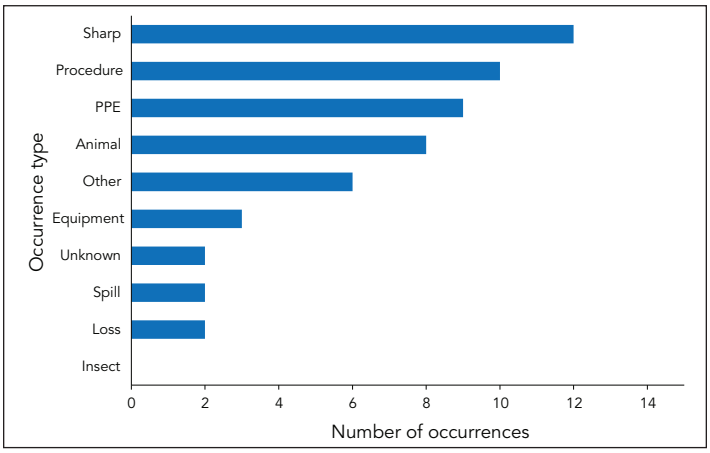
Biological agent type by risk group	Non-SSBA		SSBA		Unknown		Total	
	n	%	n	%	n	%	n	%
RG2	**27**	**61**	**0**	**0**	**0**	**0**	**27**	**61**
Bacteria	15	34	0	0	0	0	15	34
Fungus	0	0	0	0	0	0	0	0
Parasite	0	0	0	0	0	0	0	0
Prion	2	5	0	0	0	0	2	5
Toxin	1	2	0	0	0	0	1	2
Virus	9	20	0	0	0	0	9	20
Unknown	0	0	0	0	0	0	0	0
RG3	**11**	**25**	**5**	**11**	**0**	**0**	**16**	**36**
Bacteria	1	2	3	7	0	0	4	9
Fungus	2	5	2	5	0	0	4	9
Parasite	0	0	0	0	0	0	0	0
Prion	1	2	0	0	0	0	1	2
Toxin	0	0	0	0	0	0	0	0
Virus	7	16	0	0	0	0	7	16
Unknown	0	0	0	0	0	0	0	0
Bacteria[a]	**0**	**0**	**0**	**0**	**1**	**2**	**1**	**2**
Total	**38**	**86**	**5**	**11**	**1**	**2**	**44**	**100**

Abbreviations: RG2, risk group 2; RG3, risk group 3; SSBA, security sensitive biological agents
[a] This agent was identified as *Brucella* spp., but was not given a risk group as no species was identified

Occurrence types

Figure 5 presents the 54 types of occurrences reported in the 43 exposure incident reports. Sharps-related incidents were the most common (n=12; 27.9% of reports), followed by procedure-related incidents (n=10; 23.3% of reports) and personal protective equipment (PPE)-related incidents (n=9; 20.9% of reports). Definitions of occurrence types are provided in **Table A2**.

Figure 5: Reported occurrence types involved in reported exposure incidents, Canada, 2021 (N=54)



Abbreviation: PPE, personal protective equipment

Root causes and areas for laboratory safety improvement

In total, 103 root causes were identified in the 43 exposure reports through investigation of their follow-up reports (**Table 2**), giving an average of 2.4 root causes per report. The most cited root causes included issues with human interaction (n=29, 67.4%) and standard operating procedures (n=20, 46.5%), followed by issues with equipment (n=16, 37.2%) and training (n=14, 32.6%).

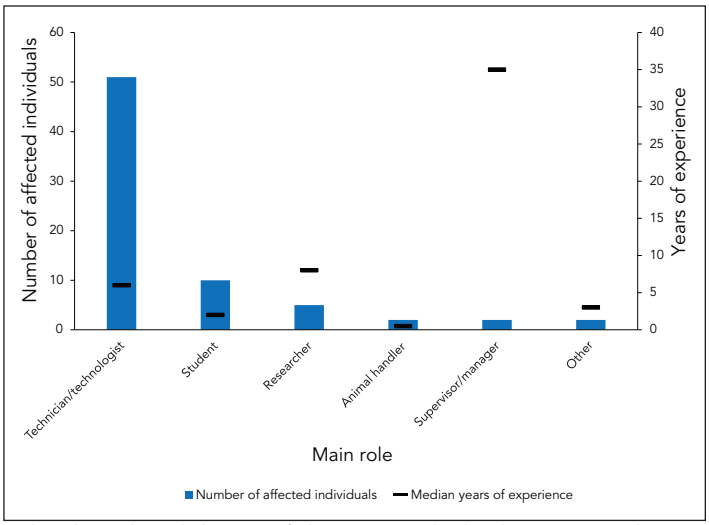
Exposed individuals

In total, 72 individuals were exposed through the 43 confirmed exposure incidents reported to LINC. Most exposed individuals had a technical/trades diploma (n=47; 65.3%) or Bachelor's degree (n=10; 13.9%). Other highest reported education levels included Master's degree (n=4; 5.6%) and MD/PhD (n=3; 4.2%).

Among exposed individuals, most worked as a technician or technologist (n=51; 70.8%), student (n=10; 13.9%) or researcher (n=5, 6.9%). Other roles reported included supervisor/manager (n=2; 2.8%) and animal handler (n=2; 2.8%). The median number of years of experience was six years among technicians/technologists and two years among students (**Figure 6**).

Among the 72 exposed individuals, most were exposed to HPTs through inhalation (n=38; 52.8%) or through needle/sharps (n=12; 16.7%) (data not shown). Other reported routes of exposure included absorption through contact with mucous membranes or skin, and injection/inoculation.

Figure 6: Individuals affected in exposure incidents reported by number of years of laboratory experience and main role[a], Canada, 2021 (N=72)



[a] Other roles are those which reporters feel are not captured in the other categories, such as clinical veterinarians

Time between the incident and the reporting date

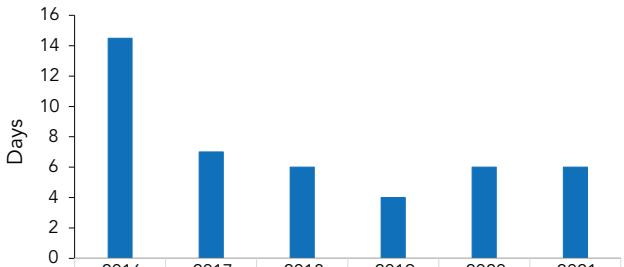
In 2021, 58.1% (n=25) of all exposure reports (n=43) were submitted to LINC within one week of the incident. The median number of days from incident occurrence to LINC reporting was six days in 2021, the same as in 2020 (**Figure 7**).

Table 2: Root causes reported in follow-up reports of exposure incidents, Canada, 2021 (N=103)

Root cause	Examples of areas of concern	Citations	
		n	%[a]
Human interaction	A violation (cutting a corner, not following correct procedure, deviating from standard operating procedure)	29	67.4%
	An error (a mistake, lapse of concentration, or slip of any kind)		
Standard operating procedure	Documents were followed as written but not correct for activity/task	20	46.5%
	Procedures that should have been in place were not in place		
	Documents were not followed correctly		
Equipment	Equipment quality control needed improvement	16	37.2%
	Equipment failed		
	Equipment was not appropriate for purpose		
Training	Training not in place but should have been in place	14	32.6%
	Training not appropriate for task/activity		
	Staff were not qualified or proficient in performing task		
Communication	Communication did not occur but should have	10	23.3%
	Communication was unclear, ambiguous, etc.		
Management and oversight	Supervision needed improvement	10	23.3%
	Lack of auditing of standards, policies and procedures		
	Risk assessment needed improvement		
Other	Not applicable	4	9.3%

[a] Denominator for percentage calculations is the total number of reports (n=43). The percentages add to more than 100% because each report may have multiple root causes. The percentages here represent the proportion of reports that indicate the given root cause, for example, 67.4% of reports selected human interaction as one of their root causes

Figure 7: Time between the date of the incident and the date report was submitted to Laboratory Incident Notification Canada, Canada, 2016–2021



	2016	2017	2018	2019	2020	2021
25th percentile	3.75	3	2	2	2	2
Median	14.5	7	6	4	6	6
75th percentile	42.75	18.5	20.5	9	15	13

Median time between incident date and reporting date

Discussion

The LINC received 43 mandatory incident exposure reports in 2021, of which two resulted in a confirmed LAI and one led to a suspected LAI; a slight increase from 2020. As with previous years' reports, exposures occurred primarily while performing microbiological and *in vivo* animal research and mostly across hospital and academic sectors (7–11). Most incidents involved non-SSBAs and RG2 organisms, with bacteria and viruses being the most implicated agent type. Exposures mainly occurred as a result of breaches in operating procedures, sharps-related events, and failure of or inadequate PPE.

SARS-CoV-2 exposures

The year 2021 is the first full year of data for exposure incidents that occurred during the COVID-19 pandemic. The SARS-CoV-2 was the most commonly implicated agent across all pathogen groups, which may be explained, in part, by the heightened laboratory activities focused on COVID-19 treatment, vaccination and understanding of SARS-CoV-2 pathogenicity. It should be noted that as per the HPTA, reported exposure incidents involving SARS-CoV-2 did not include exposure incidents occurring during diagnostic activities.

Comparison of 2021 data with pre-pandemic levels shows some reduction in the number of laboratory exposure incidents and LAIs, suggesting that reduced laboratory personnel and laboratory work due to lockdowns and workplace closures, increased use of PPEs and renewed focus on biosafety may have had an impact on the occurrence of laboratory incidents. Data from exposure incidents once laboratory activities have fully resumed will be key in identifying further trends in laboratory incident occurrences.

Seasonal variation in exposure incidents

An analysis of the median exposure incidents per month from 2016 to 2020 demonstrates marked seasonal variation, with the highest number of incidents occurring in September and May, and the lowest number in January, June and August (Figure 3). We posit that these dips in exposure incident activity may be explained by lower staff levels during summer holidays, followed by an increase in September with lab members returning to the office as well as students returning to academic labs. Similarly, the peak in May might be representative of an influx of new lab members during the summer hiring period, as well as students taking on summer work terms.

Trends in the occurrence of exposure incidents observed in 2021 were similar to the median number of incidents per month between 2016 and 2020, with exception to September 2021. Only two incidents were reported in September, as compared to an expected 6.5 incidents. Investigation into the roles of the individuals involved, their years of experience, and the licence sector provided no further information on why fewer incidents were reported in September 2021. A lack of student presence on campuses as well as reduced staffing capacities in labs as a result of the COVID-19 pandemic may have impacted these numbers.

Human interaction as a root cause of incidents

Human interaction was cited as a root cause of exposure incidents in nearly 70% of reports, representing a 20% increase as compared to 2019. These incidents are frequently cited with other root causes, such that human interaction may equally impact other areas of concern such as training, equipment, standard operating procedures and communication. Consequently, human interaction represents an important area for improvement in laboratory biosafety. Indeed, a 2017 biosafety risk assessment of laboratory accidents in the United States identified human error as the key driver of laboratory biosafety accidents, but there are limited data quantifying the extent to which human interaction plays a role in laboratory biosafety (12). Additional details on root causes from exposure reports submitted to PHAC may provide an opportunity to further explore these trends and bridge this knowledge gap.

Strengths and limitations

The main strength of this study is the collection of laboratory incident data through a standardized and mandatory reporting system across Canada. Public Health Agency of Canada's Biosecurity Portal provides an accessible and easy-to-use method for reporting key information regarding laboratory exposure incidents. Consequently, this allows for near real-time assessment of biosafety risks and trends in HPT exposures. Efficient communication with other members of the Centre of Biosecurity, such as the inspections team, allows for rapid identification of trends in reporting and the potential for risk mitigation of incidents at licensed facilities.

As with previous years, under-reporting of laboratory exposure incidents remains a possible limitation for this analysis, and the magnitude is currently unknown. To mitigate these issues, the Centre for Biosecurity offers alternate methods of incident declaration, including fax, email and telephone calls, hosts training sessions and sends out quarterly newsletters to

regulated parties alerting them of changes to the Canadian Biosafety Standards and their duty to report laboratory exposure incidents, in an effort to improve reporting compliance. In addition, inspectors check for and encourage reporting of incidents when inspecting regulated laboratories.

It is also important to note that the dearth of available information regarding laboratory incidents in other jurisdictions makes it particularly difficult to compare reporting trends observed outside of Canada. Laboratory incidents are frequently reported as case studies in other countries, so there is a lack of centrally located or easily accessible data on this subject. Canada is a unique example of a country with a centrally developed and standardised system to consistently collect information on laboratory incidents.

Finally, the LINC system does not currently support the collection of the total number of personnel or distribution of roles within laboratories. The number of active licenses is used as a proxy for workforce size, which limits the opportunity to provide more comprehensive analyses of exposure incidence rates. As such, caution should be used when interpreting this data at the laboratory level.

Conclusion

The rate of laboratory exposure incidents in 2021 was similar to that reported in 2020. Disruptions to laboratory work in light of the ongoing COVID-19 pandemic may have contributed to lower rates of laboratory exposure incidents as compared to previous years. Despite this, analysis of reports from regulated parties has shown sustained trends in the characteristics of laboratory exposure incidents in Canada, including occurrence type, root causes and sectors involved, which may help to further inform guidelines to improve biosafety and biosecurity in Canada.

Authors' statement

ERT and MEJ contributed equally to this article.

Competing interests

None.

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Appendix

Table A1: Definitions of main activity

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

Table A2: Definitions of occurrence type

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

Abbreviation: PPE, personal protective equipment

Circular logic and flawed modelling compromises non-pharmaceutical intervention article's conclusions

Jennifer Grant[1]*, Martha Fulford[1], Richard Schabas[1]

Abstract

Assessing the value of non-pharmaceutical interventions (NPIs) in response to coronavirus disease 2019 is a critical exercise to ensure optimal response to future pandemics. To be credible, evaluations should be impartial and rely on robust data and methodologies. Unfortunately, the assessment by Ogden *et al*. fails on all these accounts and instead further confounds the issue by reliance on models with incorrect underlying assumptions, circular reasoning and inappropriate assignment of causality. Ironically, instead of supporting the argument for NPIs, the authors detract from their argument by making unconvincing points supported by poor analysis.

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Introduction

Canada's early response to coronavirus disease 2019 (COVID-19) was largely based on non-pharmaceutical interventions (NPIs)—school and business closures, stay at home orders, curfews, travel restrictions, mandatory public masking and quarantine—that were initially based on little or no evidence (1,2). These measures were not part of existing pandemic plans and, furthermore, they ignored the overarching principles of pandemic planning to "minimize serious illness and overall deaths" and "minimize societal disruption" (3). Subsequent publications evaluating NPIs have been observational and ecological with almost no high-quality science. Those randomized, cluster randomized trials and robust case-control studies that have been done show weak effects of most NPIs (4–6) while robust and growing literature demonstrate the counter-balancing adverse effects of NPIs (7–9). It is vitally important that we try to assess the effectiveness and the costs of each of these interventions dispassionately, based on real-world data. Unfortunately, the article "Counterfactuals of effects of vaccination and public health measures on COVID-19 cases in Canada: What could have happened?" by Ogden *et al.* (10) is superficial, deeply flawed and provides a disservice to the evaluation of these important issues.

1. Confusing case fatality rate with infection fatality rate and reported cases with total infections

The first paragraph claims that the infection fatality rate (IFR) early in the pandemic was 1%. An IFR of 1% is a massive overestimate—infection fatality rates were around 0.2% (11–13) prior to vaccination, and the less virulent Omicron variant has an estimated IFR of 0.006% (14). Instead, the number being quoted is closer to the case fatality rate. The error results from reporting 3.3 million cases (8% of the population), when in fact, this number is likely closer to 25 million (60% of the population) (15,16). This means that the authors were either unaware of the distinction between case and infection rates or were intentionally reporting them incorrectly. Either option is concerning and should have been corrected prior to publication.

2. Uncritical reliance on flawed and discredited mathematical models

In this article, Ogden *et al.* use a model (17) that presumes efficacy of NPIs to prove that NPIs have efficacy. This circular reasoning alone should have disqualified this article at the stage of peer review. If that were not enough, the authors project "almost a million deaths" in Canada, based on their model. Not

only would this be a rate fourteen times higher than that actually experienced in Sweden (18), it would also have required an IFR of at least 3%—at least an order of magnitude higher than evidence-based estimates pre-vaccine (13).

3. Attributing causality to temporal correlation where it fits its narrative but ignoring temporal correlations that do not

A brief look at the main graphic of the article (Figure 1) shows arrows that deviate from the vertical, with explanatory arrows off-set horizontally with little explanation as to why the specific distance or angle was chosen. There are also places where, despite no obvious change in stringency, case counts go up or down or there is no obvious temporal correlation between the measure and the change in cases. These are not scientifically valid data without strong numeric evaluation and justification.

4. Failure to consider other explanations

Population mortality rates in British Columbia were 2.5 times lower than Québec and lower than most other parts of the country, yet British Columbia had a lower stringency than most provinces (19); keeping schools open from June 2020 onwards. In fact, mortality data do not generally follow stringency indexes (6) and likely have complex explanations such as age structure (5), obesity rate (20), population density (21) and economic disparity (22).

5. Choosing inappropriate comparators

The authors choose to present specific countries—two isolated islands (New Zealand and Australia) and a country without functional land borders (South Korea)—whose outcomes were favourable early in the pandemic. However, substantial cultural, genetic, geographic and social differences may also explain lower impact early in the pandemic. The authors also conveniently forget that these countries have subsequently had massive outbreaks during the Omicron era. In fact, the heavy impact of the Omicron wave on Pacific Rim countries suggests that factors other than social choices played a role.

6. No consideration of the short and long-term costs of the interventions

Even if deemed effective in preventing disease, an honest evaluation of the impact of NPIs must also consider their costs. The British Columbia Centre for Disease Control has tracked some of these harms, which include extreme social isolation of seniors, worsening both their mental and physical health (23). For example, there was an increase in falls, which are linked with increased mortality (24). Another example is the marked increase in substance abuse in younger individuals such that overdoses were a much larger cause of death in this group than COVID-19 (25). This is also seen in the StatsCan mortality report (26), which documented an increase in non-COVID-19 deaths in Canadians under the age of 45 years. We are only beginning to understand the impact of the delay in cancer diagnoses and its effect on mortality (27).

7. Failure to disclose important conflicts of interest

The authors of this article disclose no competing interests; however, two authors are senior scientists at the Public Health Agency of Canada (one is the Chief Public Health Officer for Canada) and four are directly employed by the federal government. As key leaders responsible for decision making, they can hardly be viewed as not having competing interests in the favourable evaluation of pandemic management.

Conclusion

Canada and the world need rigorous analysis of the effectiveness and the costs of the NPI's used to try to control COVID-19 case-counts. This analysis must be disinterested and based on comprehensive data sets. Unfortunately, this article's failure to use real-world data, apply scientific rigour and dispassionately consider alternate hypotheses marks it as unscientific. The *Canada Communicable Disease Report* should not have accepted or published this study because of its lack of scientific merit and its obvious conflict of interest.

Authors' statement

All authors contributed equally.

Competing interests

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Response from the Editor-in-Chief

In this "Letter to the Editor", Grant *et al*. have purported a "Failure to disclose important conflict of interest" in that the authors of this paper disclose no competing interests when such interests appear to be present.

As part of the editorial process, each author and co-author must submit the International Committee of Medical Journals Editors (ICMJE) Form for Disclosure of Potential Conflicts of Interest. If an author fails to comply with this rule, their name is removed from the author list and put in the "Acknowledgement" section at the end of the article. For this article, all seven authors provided their declaration and none of them had any relevant financial activities outside the submitted work, any patents, whether planned, pending or issued, that were broadly relevant to the work, and no other relationships, conditions, circumstances that present a potential conflict of interest beside being employees at the Public Health Agency of Canada.

As for Grant *et al*.'s comment "The *Canada Communicable Disease Report* should not have accepted or published this study because of its lack of scientific merit and its obvious conflict of interest", the journal ensures scientific rigour through a double-blind review process and, specifically for this article, two reviewers from separate academic institutions provided their comments. Neither reviewer recommended that this study not be published.

CCDR

CANADA COMMUNICABLE DISEASE REPORT

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