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CHILDREN'S HEALTH AND COVID-19

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The cover photo represents a group of children wearing protective masks in the classroom. Masks are one of the most effective public health measures that we can use to protect ourselves and others from COVID-19. The image was taken from Adobe Stock #374754792.

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CHILDREN'S HEALTH AND COVID-19

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Summary of the National Advisory Committee on Immunization (NACI) Statement—Recommendations on Fractional Influenza Vaccine Dosing in the Event of a Shortage: Pandemic preparedness

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Abstract

Background: At the commencement of a pandemic, it is important to consider the impact of respiratory infections on the health system and the possibility of vaccine shortages due to increased demand. In the event of an influenza vaccine shortage, a strategy for administration of fractional influenza vaccine doses might be considered. This article reviews the available evidence for efficacy, effectiveness, immunogenicity and safety of fractional influenza vaccine dosing, and summarizes the National Advisory Committee on Immunization (NACI) recommendations on fractional dosing strategies by public health programs in Canada.

Methods: Two rapid literature reviews were undertaken to evaluate the efficacy, effectiveness, immunogenicity and safety of fractional influenza vaccine dosing via the intramuscular or intradermal route. The NACI evidence-based process was used to assess the quality of eligible studies, summarize and analyze the findings, and apply an ethics, equity, feasibility and acceptability lens to develop recommendations.

Results: There was limited evidence for the effectiveness of fractional influenza vaccine dosing. Fractional dosing studies were primarily conducted in healthy individuals, mainly young children and infants, with no underlying chronic conditions. There was fair evidence for immunogenicity and safety. Feasibility issues were identified with intradermal use in particular.

Conclusion: NACI recommended that, in the event of a significant population-level shortage of influenza vaccine, a full-dose influenza vaccine should continue to be used, and existing vaccine supply should be prioritized for those considered to be at high risk or capable of transmitting to those at high risk of influenza-related complications or hospitalizations. NACI recommended against the use of fractional doses of influenza vaccine in any population.

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Introduction

Influenza vaccination in Canada is provided annually through provincial and territorial seasonal influenza vaccine programs. Although provincial and territorial influenza vaccine programs vary across the country, all programs cover individuals who are at high risk of severe outcomes due to influenza and individuals that are capable of transmitting influenza to those at high risk

(e.g. household members, healthcare workers). Due to the rapid timelines required for vaccine production each year, any significant impact to the manufacturing process may cause delays in influenza vaccine delivery or decrease the overall number of doses produced, potentially resulting in vaccine shortages for a season. A significant and unexpected increase in demand for the influenza vaccine could also lead to insufficient supply, as the number of doses available is based on orders made primarily in the spring months in advance of the next influenza season. This could be particularly relevant at pandemic times, as it was for the 2020–2021 influenza season when increased demand for seasonal influenza vaccine was observed in the southern hemisphere as a result of the coronavirus disease 2019 (COVID-19) pandemic. A strategy for the administration of fractional influenza vaccine doses (i.e. less than a full-dose) might be considered in these situations, as the use of fractional doses would provide vaccine programs the ability to vaccinate a larger number of people with the amount of vaccine that is available when supply is limited. The objective of this advisory committee supplemental statement is to review the available evidence for efficacy, effectiveness, immunogenicity, and safety of fractional influenza vaccine dosing, and to provide guidance on potential fractional dosing strategies in the event of a significant influenza vaccine shortage in Canada.

In Canada, influenza vaccines are currently authorized for intramuscular (IM) administration only, apart from the live-attenuated influenza vaccine (LAIV), which is administered intranasally. Intradermal (ID) administration is not covered within influenza vaccine product monographs and would therefore be considered off-label. For the purposes of these recommendations, the National Advisory Committee on Immunization (NACI) considered two different fractional dosing strategies: 1) fractional IM administration of influenza vaccine; and 2) fractional ID administration of influenza vaccine.

Methods

To inform NACI's recommendations, two rapid literature reviews were undertaken by the Methods and Applications Group for Indirect Comparisons (MAGIC) through the Drug Safety and Effectiveness Network (DSEN) on the topic of fractional influenza vaccine dosing. The rapid review methods were specified *a priori* in a written protocol that included the research questions, search strategy, inclusion and exclusion criteria, and quality assessment. The NACI Influenza Working Group reviewed and approved the protocol. The search strategies were developed in consultation with an experienced librarian based on pre-defined population, intervention, control, outcomes, study design and timeframe, and the following research questions (1,2): What is the safety and effectiveness of using fractional dosing strategies to deliver IM seasonal influenza vaccines?; and What is the safety and effectiveness of using fractional dosing strategies to deliver seasonal influenza vaccine by ID administration?

The reviews were completed by MAGIC, with additional data extraction (notably immunogenicity outcomes as indirect evidence for effectiveness for IM administration of fractional doses) completed by the Public Health Agency of Canada (PHAC). For both reviews, EMBASE and MEDLINE electronic databases, Cochrane Library, Cochrane Central Register of Controlled Trials and international clinical trial registries were searched for IM vaccine publications in the last 20 years and ID vaccine publications in the last 10 years. Searches were restricted to articles published in English. Additionally, hand-searching of the reference lists of included articles and relevant systematic reviews was performed.

For the ID fractional dose review, the DSEN MAGIC team conducted all data extraction and performed a meta-analysis for effectiveness, immunogenicity, and safety outcomes. The risk of bias for the included ID studies was assessed using the Cochrane risk-of-bias tool for randomized trails.

For the IM fractional dose review, the DSEN MAGIC team extracted and narratively summarized the data for effectiveness and safety, and provided PHAC with a list of studies that assessed immunogenicity outcomes to be used as indirect evidence for effectiveness for IM administration of fractional doses. PHAC technical staff then extracted the immunogenicity data from these studies and summarized the evidence narratively. The level of evidence (i.e. study design and methodological quality of studies) included in the IM review were assessed independently by two reviewers with PHAC using the design-specific criteria outlined by Harris *et al.* (3).

A systematic assessment of ethics, equity, feasibility, and acceptability of influenza vaccine fractional dosing strategies was also conducted according to established NACI methods (4).

The body of evidence of benefits and harms was synthesized and analyzed according to NACI evidence-based process (5) to develop recommendations. Following thorough review of the evidence, NACI formulated, reviewed and approved recommendations. Full details and results are presented in the NACI *Recommendations on Fractional Influenza Vaccine Dosing* (6).

Results

Key characteristics of the studies included in the DSEN MAGIC team reviews and additional analyses by PHAC are summarized in **Table 1**.

Table 1: Characteristics of included studies providing evidence related to the comparative efficacy, effectiveness, and immunogenicity of fractional vs. full-dose influenza vaccine for intramuscular and intradermal administration

Author, year	Study design (vaccine)	Study population and setting	Outcomes
Intramuscular			
Antony *et al.*, 2020	Scoping review including RCTs, non-RCTs and observational studies Standard dose inactivated influenza vaccine	Individuals of all ages 10 RCTs presented data relevant for the systematic review (3 in adults and 9 in children)	Local, systemic and/or severe AEs
Robertson *et al.*, 2019	RCT 2016–2017 influenza season (7.5 mcg vs. 15 mcg dose of IIV4)	Healthy children 6–35 months of age • 7.5 mcg group (n=682) • 15 mcg group (n=682) US multi-centre study	Difference in seroconversion rate (15 mcg group–7.5 mcg group) post-vaccination GMT ratios (15 mcg group–7.5 mcg group) post-vaccination Local, systemic and/or severe AEs
Jain *et al.*, 2017	RCT 2014–2015 influenza season (7.5 mcg vs. 15 mcg dose of IIV4-Fluzone quadrivalent)	Healthy children 6–35 months of age • 7.5 mcg group (n=1,028) • 15 mcg group (n=1,013) Multi-centre study conducted in the US and Mexico	Seroprotection 28 days (or 56 days for unprimed individuals) post-vaccination Seroconversion 28 days (or 56 days for unprimed individuals) post-vaccination GMT rise 28 days (or 56 days for unprimed individuals) post-vaccination Local, systemic and/or severe AEs
Halasa *et al.*, 2015	RCT October 5, 2010 and March 2, 2012; the studies were conducted before the 2010–2011 and 2011–2012 influenza seasons (7.5 mcg vs. 15 mcg dose of IIV3-Fluzone)	Healthy children 6–35 months of age Primed individuals: 7.5 mcg group (n=9) and 15 mcg group (n=21) Naïve individuals: 7.5 mcg group (n=55) and 15 mcg group (n=119) US multi-centre study	Seroprotection 28 days (naïve individuals 28 days after 2nd dose of influenza vaccine) post-vaccination Seroconversion 28 days (naïve individuals 28 days after 2nd dose of influenza vaccine) post-vaccination Difference in GMT (15 mcg group–7.5 mcg group) 28 days after last vaccination Local, systemic and/or severe AEs
Pavia-Ruz *et al.*, 2013	RCT 2008–2009 influenza season (7.5 mcg vs. 15 mcg dose of IIV3-Fluarix or Fluzone)	Healthy children 6–35 months of age • Fluarix 7.5 mcg group (n=1,017) • Fluarix 15 mcg group (n=1,013) • Fluzone 7.5 mcg group (n=1,031) Multi-centre study conducted in the US, Hong Kong, Mexico, Thailand and Taiwan	Seroprotection 28 days (or 56 days for unprimed children) post-vaccination Seroconversion 28 days (or 56 days for unprimed children) post-vaccination GMT rise post-vaccination Local, systemic and/or severe AEs
Langley *et al.*, 2012	RCT 2008–2009 influenza season (7.5 mcg vs. 15 mcg dose of IIV3-Flulaval or Vaxigrip)	Healthy children 6–35 months of age • Flulaval 7.5 mcg group (n=164) • Flulaval 15 mcg group (n=167) • Vaxigrip 7.5 mcg group (n=43) Canadian multi-centre study	Seroprotection 28 days post-vaccination Seroconversion 28 days post-vaccination GMT ratios (Flulaval 15 mcg/Flulaval 7.5 mcg) 28 days post-vaccination (adjusted for prior influenza vaccination, baseline titer—pooled variance) Local, systemic and/or severe AEs
Della Cioppa *et al.*, 2011	RCT 2008–2009 influenza season (7.5 mcg vs. 15 mcg dose of IIV3 or IIV4)	Healthy children 6–35 months of age • IIV3 vaccine recipients: 7.5 mcg group (n=25), 15 mcg group (n=22) and IIV3-Vaxigrip 15 mcg group (n=26) • IIV4 vaccine recipients: 7.5 mcg group (n=25) and 15 mcg group (n=28) Multi-centre study conducted in Finland and Belgium Note: only a subset of study groups relevant for this review are presented in the systematic review	Seroprotection on day 50 Seroconversion on day 50 GMT rise on day 50 Local, systemic and/or severe AEs

Table 1: Characteristics of included studies providing evidence related to the comparative efficacy, effectiveness, and immunogenicity of fractional vs. full-dose influenza vaccine for intramuscular and intradermal administration (*continued*)

Author, year	Study design (vaccine)	Study population and setting	Outcomes
Intramuscular (*continued*)			
Skowronski *et al.*, 2011	RCT 2008–2009 influenza season (7.5 mcg vs. 15 mcg dose of IIV3-Vaxigrip)	Healthy children 6–23 months of age • 7.5 mcg group (n=124) • 15 mcg group (n=128) Canadian multi-centre study	Seroprotection 27–45 days after the 2nd dose Seroconversion 27–45 days after the 2nd dose GMT rise after the 2nd dose Local, systemic and/or severe AEs
Chi *et al.*, 2010	RCT 2007–2008 influenza season (9 mcg vs. 15 mcg dose of IIV3-Fluzone)	Adults 65 years of age and older without serious or unstable conditions • 9 mcg group (n=64) • 15 mcg group (n=65) US study	Seroprotection four weeks post-vaccination Local, systemic and/or severe AEs
Engler *et al.*, 2008	RCT 2004–2005 influenza season (7.5 mcg vs. 15 mcg dose of IIV3-Fluzone)	Healthy adults 18–64 years of age • 7.5 mcg group: 18–49 years old (n=284) and 50–64 years old (n=276) • 15 mcg group: 18–49 years old (n=274) and 50–64 years old (n=280) US multi-center study	RR of one or more medical visits for ILI involving the upper or lower respiratory tract Difference in seroconversion 21 days post-vaccination Difference in seroprotection 21 days post-vaccination Local, systemic and/or severe AEs
Belshe *et al.*, 2007	RCT 2006–2007 influenza season (3 mcg, 6 mcg, 9 mcg and 15 mcg doses of IIV3-Fluzone)	Healthy adults 18–49 years of age • 3 mcg group (n=29) • 6 mcg group (n=30) • 9 mcg group (n=32) • 15 mcg group (n=31) US single-site study	Seroconversion rate 28 days post-vaccination Seroprotection rate 28 days post-vaccination Local, systemic and/or severe AEs
Kramer *et al.*, 2006	RCT 2004–2005 influenza season (7.5 mcg vs. 15 mcg dose of IIV3-Fluzone)	Healthy adults healthcare workers 18 years of age and older • 7.5 mcg group (n=222) • 15 mcg group (n=222) US single-site study	RR of clinical diagnosis of influenza (ILI) for individuals vaccinated with a 7.5 mcg dose compared to 15 mcg vaccine dose Proportion of clinical diagnosis that was laboratory-confirmed influenza infection
Intradermal			
Egunsola *et al.*, 2020	Rapid review and meta-analysis including RCTs, non-RCTs and observational studies (ID administration of a 9 mcg vs. IM dose of 15 mcg of HA per influenza vaccine strain)	Individuals of all ages • 13,759 participants from RCTs • 164,021 participants from observational studies	RR of influenza infection and/or ILI from the ID administration of a 9 mcg of HA per strain dose of influenza vaccine compared to 15 mcg of HA per strain IM dose RR of seroconversion rate of ID compared to standard dose of IM administration RR of seroprotection rates for ID compared to standard dose of IM administration Risk of local AEs with ID compared to IM administration Risk of systemic AEs following vaccination with ID compared to IM vaccine

Abbreviations: AE, adverse event; GMT, geometric mean titre; HA, hemagglutinin; ID, intradermal; IIV3, trivalent inactivated influenza vaccine; IIV4, quadrivalent inactivated influenza vaccine; ILI, influenza-like-illness; IM, intramuscular; mcg, microgram; RCT, randomized controlled trial; RR, risk ratio; US, United States

Vaccine efficacy and effectiveness

Fractional intramuscular dosing (efficacy/effectiveness)

Two randomized clinical trials (RCTs) (7,8) were identified that assessed the efficacy of fractional IM administration of a 7.5 mcg of hemagglutin (HA) per strain dose versus a 15 mcg of HA per strain dose of the trivalent inactivated influenza vaccine (IIV3) against influenza-like-illness (ILI) during the 2004–2005 influenza season in the United States (US). Both studies were deemed to be good quality according to the criteria outlined by Harris *et al.* (3). The studies did not demonstrate a difference in efficacy between the full-dose (15 mcg) and the half-dose (7.5 mcg) of IIV3 against ILI.

Fractional intradermal dosing (efficacy/effectiveness)

Two studies (9,10) assessed the efficacy of fractional ID administration of influenza vaccine against laboratory-confirmed influenza infection or ILI in adults using IIV3. A meta-analysis of these two RCTs studies found no significant difference in the risk of influenza infection/ILI from the ID administration of a 9 mcg of HA per strain dose of influenza vaccine compared to 15 mcg of HA per strain IM dose (pooled risk ratio [RR]: 0.61, 95% CI, 0.19–1.91).

Immunogenicity

Overall, 10 RCTs and one meta-analysis of 16 RCTs reported immunogenicity outcomes for fractional doses of IM or ID influenza vaccine administration. The immunogenicity outcomes assessed by these studies included geometric mean-fold rise in hemagglutination inhibition (HI) titres (i.e. ratio of post to pre-vaccination geometric mean titre), seroprotection rate (i.e. proportion of participants with HI titres of at least 40 post-vaccination) and seroconversion rate (i.e. proportion of participants with at least a four-fold increase in HI titres post-vaccination, HI titre increase from less than 10 pre-vaccination to at least 40 post-vaccination, or both).

Fractional intramuscular dosing (immunogenicity)

Ten articles (8,11–19) were identified that assessed immunogenicity outcomes for fractional doses of influenza vaccines administered IM. All ten studies were RCTs deemed to be of good quality according to the Harris *et al.* criteria (3). Of these studies, two (8,11) were conducted in adults within the age range of 18 and 64 years and one (13) was conducted in adults of 65 years of age and older. The other seven studies (13–19) were all conducted in children within the age range of 6 to 35 months.

One study (8) in adults reported that the study groups that received a fractional dose of 7.5 mcg of HA per strain had statistically lower proportions of seroconversion and seroprotection post-vaccination than those who received the full-dose. Four studies (15–17,19) that statistically assessed the difference in immunogenicity between a full-dose and a half dose of influenza vaccine in children 6 to 35 months of age reported mixed results. Additional studies (one in adults and two in children) (13,17,19) that assessed varying fractional doses of influenza vaccine (3 mcg, 6 mcg, 7.5 mcg and 9 mcg of HA per strain) found that as the dose of influenza vaccine decreased, the immunogenic response also decreased. However, lower doses continued to meet criteria set for non-inferiority despite the reduced response compared to full-dose (according to current US Food and Drug Administration or previous European Medicines Agency criteria).

Fractional intradermal dosing (immunogenicity)

A meta-analysis (2) included 16 RCTs studies that assessed immunogenicity outcomes for fractional doses of influenza vaccine administered ID. The meta-analysis demonstrated no significant difference in the seroconversion rates for the study groups that had received fractionated doses (3 mcg, 6 mcg, 7.5 mcg or 9 mcg of HA per strain) by ID administration compared to 15 mcg of HA per strain dose given IM for all influenza strains. A meta-analysis was also performed for seroprotection rates compared to a full-dose of 15 mcg of HA strain per IM dose and found no significant difference for groups that received ID administration at doses of 3 mcg, 7.5 mcg or 9 mcg of HA per strain. Similarly, there was no significant difference in seroconversion or seroprotection rates between older adults that had received the fractional 9 mcg of HA per strain ID dose compared to those that received the full 15 mcg of HA per strain IM dose. However, seroprotection rates were significantly lower for those that had received a dose of 6 mcg of HA per strain for influenza A(H1N1) compared to a full IM dose.

Safety

Safety of the intramuscular route of administration

The rapid review identified seven studies (13–19) that assessed safety outcomes (local, systemic and severe (local, systemic and severe adverse events [AEs]) of fractional IM influenza vaccine in infants or toddlers in the range of 6 to 36 months of age. Three studies were identified in the rapid review that assessed safety of fractional IM influenza vaccination in adults: two of the studies (8,11) involved adults between the ages of 18–64 years (18–49 years and 18–65 years) and one study (12) included adults older than 65 years of age.

Safety of intradermal route of administration

Twenty-three studies (9,10,12,20–39) were identified that assessed the safety of ID administration of influenza vaccine and were able to be included in a meta-analysis performed by the DSEN MAGIC team. The studies identified included various fractional doses (3 mcg, 6 mcg, 9 mcg of HA per strain), as well as a full non-fractional dose (i.e. 15 mcg of HA per strain) of ID-administered influenza vaccine. Overall, there was fair evidence that fractional doses of influenza vaccine administered via the IM and ID routes do not result in a significant difference with regard to severe systemic AEs post-influenza vaccination. No significant increases in pain have been reported with ID influenza vaccine administration compared to IM administration; however, the risk of local AEs, such as ecchymosis, erythema, pruritus and swelling occurring post-vaccination at the injection site, is significantly higher with ID administration of influenza vaccine compared to IM administration.

Feasibility

Several feasibility issues were identified when considering fractional dosing of current influenza immunizations or administration of ID doses of influenza vaccines. Administering a fractional IM or ID dose would require administering a lower volume of vaccine to achieve the desired lower dose, which is only possible when influenza immunizations have been packaged as multi-dose vials and not as pre-filled syringes. The ID administration of vaccine requires a different gauge needle than IM administration, multi-dose vials (which are not always available midway in the season if supplies run low), and training and skill in ID administration that not all vaccinators will have. Significant training would also be required to ensure vaccinators are equipped in advance to provide ID influenza vaccinations and feel comfortable doing so. The number of vaccinators who are authorized and able to provide ID vaccination also vary by jurisdiction.

The volume of vaccine to be administered is high even if using a fractional dose and would therefore require two ID injections if regular needles and syringes were used rather than just one. The majority of studies of administration of influenza vaccine by the ID route used micro-needle injectors for administration, which are not yet authorized or widely available in Canadian settings. Furthermore, the use of fractional doses is not covered within influenza vaccine product monographs and would therefore require a novel communication and consent plan for any off-label dosing if it were adopted. Finally, implementation of such an ID immunization program would require structured monitoring for any potential modification to a seasonal influenza vaccine program running low on vaccine and advanced planning would have to factor this in *a priori* as multi-dose vials are not always available midway in the season.

National Advisory Committee on Immunization recommendations for public health program decision-making

1. NACI recommends that, in the event of a significant population-level shortage of influenza vaccine, a full-dose influenza vaccine should continue to be used, and existing vaccine supply should be prioritized for those considered to be at high risk or capable of transmitting to those at high risk of influenza-related complications or hospitalizations. ***(Strong NACI Recommendation)***

- NACI concluded that there is fair evidence to recommend the use of a full-dose influenza vaccine (15 mcg or 60 mcg HA per strain, dependent on vaccine product) compared to a fractional dose for individuals at high risk or those capable of transmitting to those at high risk of influenza-related complications or hospitalizations. ***(Grade B Evidence)***

2. NACI recommends against the use of fractional doses of influenza vaccine in any population. ***(Discretionary NACI Recommendation)***

- NACI concluded that there is insufficient overall evidence at this time to recommend the use of fractional IM influenza vaccine doses. ***(Grade I Evidence)***
- NACI concluded that there is fair evidence that fractional ID influenza vaccine doses provide a sufficient immune response, but this route of administration is not feasible at this time. ***(Grade B Evidence)***

The detailed findings of the two rapid literature reviews, rationale and relevant considerations for these recommendations can be found in the NACI Statement, *Recommendations on Fractional Influenza Vaccine Dosing* (6).

Conclusion

In the event of a significant population-level shortage of the currently available influenza vaccine products, NACI recommends that full-dose influenza vaccine should continue to be used and existing vaccine supply should be prioritized for those considered to be at high risk or capable of transmitting to those at high risk of influenza-related complications or hospitalizations. NACI recommends against the use of fractional doses of influenza vaccines in any population.

Authors' statement

AS — Writing, original draft, review, editing
PDP — Writing, review, editing
KY — Review, editing
RH — Writing, review, editing

Competing interest

None.

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Summary of the National Advisory Committee on Immunization (NACI) Statement—Recommendation on Repeated Seasonal Influenza Vaccination

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Abstract

Background: Influenza vaccination is recommended annually; however, some studies have raised questions regarding whether repeated influenza vaccine administration may have unintended negative consequences for seasonal protection.

Methods: The National Advisory Committee on Immunization (NACI) Influenza Working Group undertook an overview of systematic reviews on the effects of repeated influenza vaccination on vaccine effectiveness, efficacy, and immunogenicity. A systematic assessment of programmatic factors was conducted according to established NACI methods. The NACI evidence-based process was used to critically appraise the available evidence and to review recommendations.

Results: The evidence base consisted of four eligible systematic reviews/meta-analyses. Repeated vaccination, including the current season, was consistently more effective than no vaccination in the current season. The evidence showed no significant difference or predictable trend in vaccine efficacy or effectiveness between vaccinations in two consecutive seasons compared to vaccination in the current season only.

Conclusion: Overall, NACI concluded that there is evidence to recommend annual influenza vaccination, irrespective of whether an individual received the seasonal influenza vaccine in previous seasons. It is neither currently feasible nor warranted to modify existing annual influenza vaccination programs to account for potential negative or positive interference. NACI continues to strongly recommend that seasonal influenza vaccine should be offered annually to everyone six months of age and older who does not have contraindications to the vaccine, irrespective of previous seasons' influenza vaccination status.

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Keywords: National Advisory Committee on Immunization, Canada, NACI, influenza, influenza vaccine, guidance, vaccine effectiveness, repeated vaccination

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Introduction

The influenza vaccine is a critical tool to protect against influenza-related disease and to reduce the influenza-associated burden on the Canadian healthcare system. Influenza vaccination is repeated annually due to waning immunity and the tendency of influenza viruses to mutate frequently, requiring changes in the vaccine formulation. To reduce the morbidity and mortality associated with influenza, National Advisory Committee on Immunization (NACI) recommends annual influenza vaccination for everyone six months of age and older who does not have contraindications to the vaccine (1).

A study published in the 1970s (2) raised questions about a potential negative impact of prior influenza vaccination on current season influenza vaccine effectiveness (VE) and conflicting results on whether repeated annual seasonal influenza vaccination could have unintended negative consequences for seasonal protection have also been reported (3–8). The degree to which repeated vaccination and other factors (e.g. vaccine strain match to circulating strains, initial exposure to influenza virus and egg-adaptive mutations) affect VE is still not fully understood and varies season to season. Furthermore, the complex interplay of factors affecting an individual's immune response to influenza vaccination makes it extremely difficult to make predictions far enough in advance of the next influenza season to help inform vaccine policy or administration practice changes.

NACI was asked to assess the effects of repeated influenza vaccination on VE, efficacy and immunogenicity with the purpose of evaluating the overall impact of this phenomenon and to provide an evidence base for population-level and individual-level vaccination decisions regarding annual influenza vaccination.

Methods

The NACI Influenza Working Group undertook an overview of existing systematic reviews according to a written protocol specified *a priori* that included review questions, search strategy, inclusion and exclusion criteria and quality assessment. The following research question and accompanying population, intervention, comparison(s) and outcome(s) (PICO) (**Table 1**) was developed to guide the evidence review: What are the effects of repeated seasonal influenza vaccination on VE, efficacy and immunogenicity?

Table 1: Population, intervention, comparator(s), outcome(s) criteria guiding NACI's evidence review

PICO	Criteria
Population	Adults and children
Intervention	Seasonal influenza vaccination in prior season(s) and current season
Comparison	Seasonal influenza vaccination in prior season(s) only OR in current season only OR unvaccinated in any season included in the study
Outcome	Vaccine efficacy or immunogenicity in the current season
Study design	Systematic review or meta-analysis

Abbreviation: NACI, National Advisory Committee on Immunization

To support this work, a systematic assessment of ethics, equity, feasibility, and acceptability of influenza vaccine guidance was also conducted according to established NACI methods (9). The NACI evidence-based process (10) was used to assess the available evidence and develop a new recommendation. Full details and results are presented in the NACI *Recommendation on Repeated Seasonal Influenza Vaccination* (11).

Results

The NACI's evidence base encompassed an overview of four systematic reviews (SRs)/meta-analyses (MAs) (12–15) on the effects of repeated influenza vaccination on vaccine efficacy or effectiveness, analyzing findings from a total of 24 unique primary studies. None of the SRs/MAs included primary studies that assessed immunogenicity. Based on the available evidence, NACI issued a new recommendation on repeated seasonal influenza vaccination.

Recommendation

NACI continues to recommend that seasonal influenza vaccine should be offered annually to everyone six months of age and older who does not have contraindications to the vaccine, irrespective of previous seasons' influenza vaccination status. (*Strong NACI Recommendation*)

- **NACI concludes that there is fair evidence to recommend annual influenza vaccination, irrespective of whether an individual received the seasonal influenza vaccine in previous seasons. (*Grade B Evidence*)**

Summary of evidence

- Repeated vaccination across seasons, including the current season, was consistently more effective than no vaccination in the current season.
- In general, the evidence shows no significant difference or predictable trend in vaccine efficacy or effectiveness between vaccinations in two consecutive seasons compared to vaccination in the current season only.
  - Of all the seasons investigated across many studies, only two influenza seasons indicated that VE of vaccination over consecutive seasons was statistically significantly lower than vaccination in the current season only. These notable seasons were influenza A(H3N2) in 2010–2011 (14) and influenza A(H3N2) in 2014–2015 (15). These findings were not statistically significant in all SRs/MAs that assessed VE in these two seasons; however, a trend towards lower VE for repeated vaccination was consistent for the 2014–2015 season across all studies (12,14).
- Evidence on the effects of repeated vaccination over three or more consecutive seasons was limited and is insufficient to draw firm conclusions at this time.

- Given the complex interplay between immune imprinting (such as previous exposures through vaccination and natural infection), circulating virus types and individual characteristics, it is not currently feasible nor warranted to modify existing annual influenza vaccination programs to account for potential negative or positive interference effects related to repeated influenza vaccination across seasons.

A complete review of evidence and full NACI recommendations are published in the new NACI *Recommendation on Repeated Seasonal Influenza Vaccination* (11). This guidance aligns with NACI's overarching recommendation for influenza vaccination and standard vaccine administration practices as detailed in the Canadian Immunization Guide and Annual NACI Statement on Seasonal Influenza Vaccine (1).

Conclusion

The body of evidence exploring whether repeated seasonal influenza vaccination can enhance or attenuate influenza vaccine immunogenicity and effectiveness continues to grow. Notably, a recent SR and MA commissioned by the World Health Organization (WHO) Strategic Advisory Group of Experts on Immunization (SAGE) Working Group on Influenza (16) examined the available evidence for the potential reduction in VE associated with repeated influenza vaccination. According to the WHO SAGE review, although vaccination in the previous year appears to attenuate VE, vaccination in two consecutive years affords better protection than not being vaccinated. Overall, the WHO SAGE review findings were in alignment with the conclusions of the recent NACI assessment: the effects of vaccination in the previous year were not consistent across seasons and further evaluation and investigation of whether VE is reduced by repeated vaccination would be needed prior to considering an alternative influenza vaccination regimen. New and emerging research priorities identified during NACI's recommendation development process, include the following:

- Effects of long-term repeated influenza vaccination on VE
- Effects of repeated influenza vaccination on VE stratified by age group and vaccine type
- Effects of repeated influenza vaccination on severe influenza-related outcomes, such as hospitalization and death
- Effects of repeated influenza vaccination that accounts for previous influenza exposure through vaccination and/or natural infection
- Immunological mechanisms underlying the effects of repeated influenza vaccination on VE

NACI will continue to monitor the evolving evidence and will update this guidance as needed.

Authors' statement

AS — Writing, original draft, review, editing
KY — Review, editing
JP — Writing, review, editing

The National Advisory Committee on Immunization (NACI) *Recommendation on Repeated Seasonal Influenza Vaccination* was prepared by: K Young, MK Doll, J Przepiorkowski, L Zhao, R Harrison, I Gemmill, J Papenburg, and A Sinilaite, on behalf of NACI Influenza Working Group, and was approved by NACI.

Competing interests

None.

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Resource use and disease severity of children hospitalized for COVID-19 versus multisystem inflammatory syndrome in children (MIS-C) in Canada

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Abstract

Background: Direct comparisons of paediatric hospitalizations for acute coronavirus disease 2019 (COVID-19) and multisystem inflammatory syndrome in children (MIS-C) can inform health system planning. We describe the absolute and relative hospital burden of acute paediatric COVID-19 and MIS-C in Canada.

Methods: This national prospective study was conducted via the Canadian Paediatric Surveillance Program from March 2020–May 2021. Children younger than 18 years old and hospitalized for acute COVID-19 or MIS-C were included in the analysis. Outcomes included supplemental oxygen (low-flow oxygen or high-flow nasal cannula), ventilation (non-invasive or conventional mechanical), vasopressors, paediatric intensive care unit (PICU) admission, or death. Adjusted risk differences (aRD) and 95% confidence intervals (CI) were calculated to identify factors associated with each diagnosis.

Results: Overall, we identified 330 children hospitalized for acute COVID-19 (including five deaths) and 208 hospitalized for MIS-C (including zero deaths); PICU admission was required for 49.5% of MIS-C hospitalizations versus 18.2% of acute COVID-19 hospitalizations (aRD 20.3; 95% CI, 9.9–30.8). Resource use differed by age, with children younger than one year hospitalized more often for acute COVID-19 (aRD 43.4% versus MIS-C; 95% CI, 37.7–49.1) and more children 5–11 years hospitalized for MIS-C (aRD 38.9% vs. acute COVID-19; 95% CI, 31.0–46.9).

Conclusion: While there were more hospitalizations and deaths from acute paediatric COVID-19, MIS-C cases were more severe, requiring more intensive care and vasopressor support. Our findings suggest that both acute COVID-19 and MIS-C should be considered when assessing the overall burden of severe acute respiratory syndrome coronavirus 2 in hospitalized children.

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Keywords: COVID-19, intensive care, multisystem inflammatory syndrome in children, MIS-C, paediatrics, hospitalizations, resource use, surveillance, SARS-CoV-2

Introduction

Along with hospitalization for acute coronavirus disease 2019 (COVID-19), multisystem inflammatory syndrome in children (MIS-C) has emerged as a serious yet infrequent complication of paediatric severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Though MIS-C was first described in the United Kingdom in April 2020, to date, few studies have directly compared characteristics and outcomes associated with these two diagnoses (1–4). Case series describing MIS-C indicate higher proportions of severe disease relative to acute COVID-19, despite much lower incidence of MIS-C in the community, estimated at 316 cases per million SARS-CoV-2 infections among those younger than 21 years of age (5–7). Differences in the associated use of hospital resources (e.g. ventilation or hemodynamic support requiring intensive care) between these two disease entities are not well known and may have implications for future paediatric pandemic planning. We aimed to describe the absolute and relative hospital burden of acute paediatric COVID-19 infection and MIS-C during the first fifteen months of the pandemic in Canada, prior to the emergence of the Omicron variant and the approval of SARS-CoV-2 vaccines for use in children.

Methods

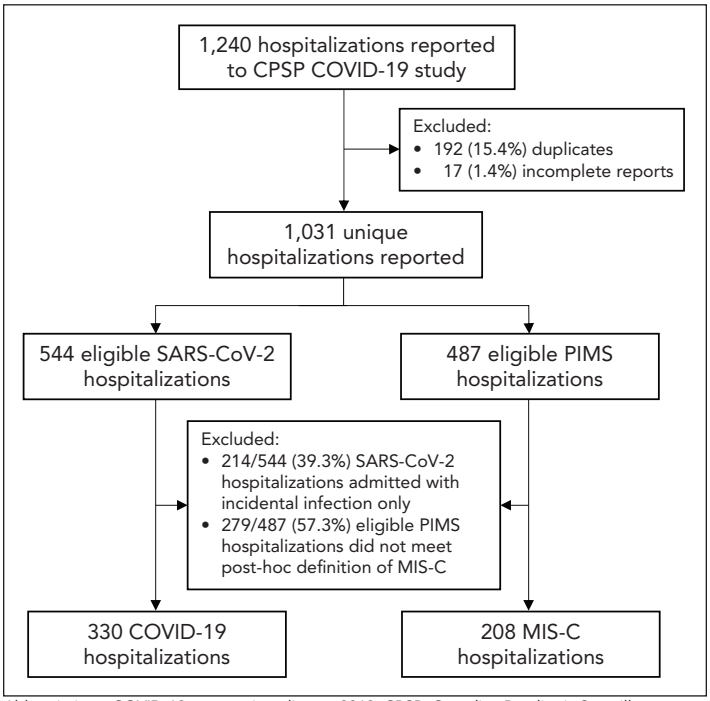
We conducted a national prospective study via the Canadian Paediatric Surveillance Program (CPSP) from March 2020–May 2021, during which time ancestral SARS-CoV-2 lineages and later the Alpha (B.1.1.7) variant of concern were dominant. The CPSP is a public health surveillance network that includes more than 2,800 paediatricians and paediatric subspecialists across Canada, who were surveyed weekly and asked to voluntarily report any incident cases to this study. In addition to the survey report, study co-investigators from 13 university health centres across Canada actively reported all cases from their institutions. Cases of children younger than 18 years of age and hospitalized with acute SARS-CoV-2 infection or paediatric inflammatory multisystem syndrome (PIMS) were eligible to be reported. While cases were reported based on a surveillance definition of PIMS, we applied a post-hoc case definition of MIS-C according to the World Health Organization (8). By definition, all patients with MIS-C had a documented linkage to SARS-CoV-2 (i.e. positive polymerase chain reaction, rapid antigen or serology test, or a close contact with microbiologically confirmed SARS-CoV-2). For all SARS-CoV-2 hospitalizations, the reporting physician indicated whether the hospitalization was due to acute COVID-19 or if incidental infection was identified upon routine screening; this was confirmed by dual case adjudication by the study team to ensure consistency. We therefore compared two mutually exclusive groups for this analysis: children hospitalized for acute COVID-19 versus children hospitalized for MIS-C. Further details regarding the study design are described elsewhere, and surveillance definitions are available (9–11).

Baseline characteristics and severity outcomes were ascertained for both case definitions using a standardized case report form. Severity outcomes included requirements for supplemental oxygen (either low-flow oxygen or high-flow nasal cannula), ventilation (either non-invasive, conventional mechanical or high-frequency oscillatory ventilation), vasopressors, paediatric intensive care unit (PICU) admissions or death. Characteristics were summarized using medians, interquartile ranges (IQR), frequencies and percentages. Frequencies between one and four were reported as "fewer than five" while some larger frequencies were presented as ranges to prevent back calculation, in accordance with CPSP privacy policy. Adjusted risk differences (aRD) were calculated to identify factors associated with each diagnosis, adjusting for age, sex, presence of one or more comorbid conditions, and the timing of hospitalization (classified in five three-month periods from March 2020–May 2021). Differences in continuous variables (i.e. age and PICU length of stay) were assessed using Wilcoxon rank-sum tests. The temporal lag (in weeks) between all Canadian SARS-CoV-2 case counts (ascertained from the Public Health Agency of Canada) (12) and hospitalizations reported to CPSP were assessed using Spearman's rank correlation coefficient. The p-values <0.05 were considered statistically significant. Analyses were conducted in Stata v17.0 (13).

Results

Overall, 330 children hospitalized for acute COVID-19 and 208 hospitalized for MIS-C were reported during the surveillance period (**Figure 1**, **Table 1**). The median age among acute COVID-19 patients (1.9 years; IQR 0.1–13.3) was significantly younger than those with MIS-C (8.1 years; IQR 4.2–11.6; $p<0.001$). More children younger than one year of age were hospitalized for acute COVID-19 than with MIS-C (aRD 43.4%; 95% CI, 37.7–49.1), while more children aged 5–11 years were hospitalized for MIS-C than acute COVID-19 (aRD 38.9%; 95% CI, 31.0–46.9). Chronic comorbid conditions were more common amongst acute COVID-19 patients (43.0% vs. 15.9% with MIS-C; aRD 38.0%; 95% CI, 31.0–45.1).

Figure 1: Flowchart of hospitalizations reported to the Canadian Paediatric Surveillance Program COVID-19 study

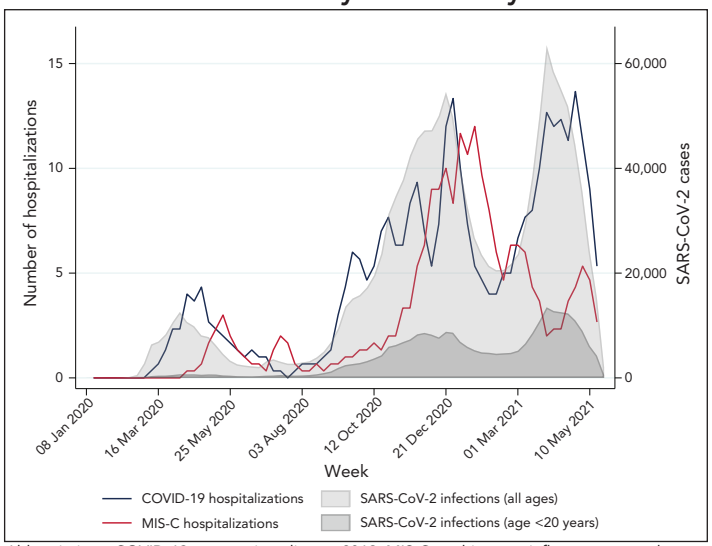


Abbreviations: COVID-19, coronavirus disease 2019; CPSP, Canadian Paediatric Surveillance Program; MIS-C, multisystem inflammatory syndrome in children; PIMS, paediatric inflammatory multisystem syndrome; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

The PICU admission was required for 49.5% of MIS-C hospitalizations versus 18.2% of acute COVID-19 hospitalizations (aRD 20.3; 95% CI 9.9–30.8), though the proportion of children younger than five years of age admitted to PICU was similar (19.7% vs. 15.4%; **Table 2**). The median length of PICU stay was one day greater for acute COVID-19 (four days; IQR 2–7) than MIS-C (three days; IQR 2–4; $p=0.04$). Vasopressor use was more common for MIS-C than acute COVID-19 at all ages (35.6% vs. 2.4%; aRD 23.1%; 95% CI, 15.8–30.4). The proportion of all patients requiring supplemental oxygen and mechanical ventilation were similar (24.6% and 10.9% for acute COVID-19 vs. 30.3% and 9.6% for MIS-C, respectively). Five deaths due to acute COVID-19 were reported versus zero due to MIS-C.

Acute paediatric COVID-19 hospitalization trends lagged behind all Canadian SARS-CoV-2 infection waves by one week (Spearman's $\rho=0.89$), versus a lag of six weeks for MIS-C hospitalizations (Spearman's $\rho=0.82$; **Figure 2**).

Figure 2: Time series of acute COVID-19 hospitalizations[a], multisystem inflammatory syndrome in children hospitalizations[a] and SARS-CoV-2 infection[b] across Canada from January 2020 to May 2021[c]



Abbreviations: COVID-19, coronavirus disease 2019; MIS-C, multisystem inflammatory syndrome in children; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2
[a] Younger than 18 years
[b] All ages or younger than 20 years
[c] Data for COVID-19 and MIS-C hospitalizations represent the three-week moving average of cases included in this study. SARS-CoV-2 infections were ascertained from the Public Health Agency of Canada, available at https://health-infobase.canada.ca/covid-19/epidemiological-summary-covid-19-cases.html, and reflect the date of illness onset

Discussion

Understanding the severity and associated in-hospital resource use required to manage acute paediatric COVID-19 and MIS-C is necessary to anticipate acute health system needs, and to make informed decisions regarding preventative measures including SARS-CoV-2 vaccination. Based on national surveillance data from March 2020 to May 2021, acute COVID-19 was found to have resulted in more paediatric hospitalizations and deaths and longer PICU stays, while MIS-C resulted in more PICU admissions and more frequent need for hemodynamic support. In this study, half of hospitalized MIS-C patients required intensive care, consistent with prior studies from the United Kingdom (44%) and the United States (64%) during the first year of the pandemic (14,15). While PICU admissions among MIS-C patients were often initiated due to shock, these patients were likely stabilized rapidly with immune modulation and vasopressor support. This may explain the shorter PICU stays relative to patients with acute COVID-19, who typically require PICU admission due to

Table 1: Characteristics of children hospitalized for acute COVID-19 and multisystem inflammatory syndrome in children

Characteristic	Diagnosis		aRD[a], %	95% CI	*p*-value
	COVID-19	MIS-C			
Total hospitalizations, N[b]	330	208	-	-	-
Age (years), median (IQR)[c]	1.9 (0.1–13.3)	8.1 (4.2–11.6)	-	-	<0.001
Age (years), n (%)					
Younger than 1	140 (42.4)	9 (4.3)	43.4	37.7–49.1	<0.001
1–4	68 (20.6)	52 (25.0)	−2.9	−10.4–4.6	0.45
5–11	30 (9.1)	98 (47.1)	−38.9	−46.9–−31.0	<0.001
12–17	92 (27.9)	49 (23.6)	−1.6	−9.6–6.4	0.69
Sex, n (%)					
Female	145 (43.9)	76 (36.5)	6.2	−4.9–17.3	0.27
Male	185 (56.1)	132 (63.5)	−6.2	−17.3–4.9	0.27
Comorbid conditions, n (%)[d]					
None/unknown	188 (57.0)	175 (84.1)	−38.0	−45.1–−31.0	<0.001
1 or more	142 (43.0)	33 (15.9)	38.0	31.0–45.1	<0.001
Population group, n (%)					
White	75 (22.7)	63 (30.3)	−12.4	−22.8–−2.0	0.02
South Asian	40 (12.1)	25 (12.0)	1.4	−6.0–8.7	0.71
Arab/West Asian	39 (11.8)	16 (7.7)	4.4	−2.3–11.1	0.20
Black	39 (11.8)	29 (13.9)	−2.2	−9.5–5.1	0.56
Indigenous	28 (8.5)	9 (4.3)	4.8	−0.6–10.3	0.08
East/Southeast Asian	18 (5.5)	12 (5.8)	3.0	−2.2–8.1	0.26
Latin American	5 (1.5)	18 (8.7)	−7.5	−13.3–−1.7	0.01
Unknown	92 (27.9)	49 (23.6)	-	-	-

Abbreviations: aRD, adjusted risk difference; CI, confidence interval; COVID-19, coronavirus disease 2019; IQR, interquartile range; MIS-C, multisystem inflammatory syndrome in children; -, not applicable

[a] All comparisons adjusted for age category, sex, comorbid conditions, and timing of hospitalization. Positive risk differences indicate a characteristic was more common for acute COVID-19 while negative risk differences indicate a characteristic was more common for MIS-C

[b] Overall, 544 hospitalized children with severe acute respiratory syndrome coronavirus 2 infection were reported to the Canadian Paediatric Surveillance Program, among whom 330 children were admitted due to acute COVID-19; 493 hospitalized children were reported with suspected paediatric inflammatory multisystem syndrome, among whom 208 children met the World Health Organization definition of MIS-C

[c] Continuous age was missing for four patients with acute COVID-19, though categorical age could still be determined

[d] Comorbidities were reported as any of the following conditions: congenital heart disease, diabetes, gastrointestinal/liver disease, genetic/metabolic conditions, hematologic disorders, immunodeficiencies, malignancies, neurologic or neurodevelopmental conditions, obesity, pulmonary disease (i.e. asthma or other chronic lung disease), renal disease, rheumatologic/autoimmune disorders, tracheostomy, transplants or other conditions

Table 2: Outcomes of acute COVID-19 and multisystem inflammatory syndrome in children hospitalizations, overall and by age category

Outcome[a]	Diagnosis		aRD[b], %	95% CI	*p*-value
	COVID-19	MIS-C			
All hospitalizations					
Supplemental oxygen	81/330 (24.6)	63/208 (30.3)	−5.6	−15.2–3.9	0.25
Ventilation	36/330 (10.9)	20/208 (9.6)	1.7	−4.9–8.2	0.62
Vasopressors	8/330 (2.4)	74/208 (35.6)	−23.1	−30.4–−15.8	<0.001
PICU admission	60/330 (18.2)	103/208 (49.5)	−20.3	−30.8–−9.9	<0.001
PICU length of stay (days)	4 (2–7 days)	3 (2–4 days)	-	-	0.04
ECMO	0/330 (0.0)	0/208 (0.0)	-	-	-
Death	5/330 (1.5)	0/208 (0.0)	-	-	-
Age younger than 5 years					
Supplemental oxygen	36/208 (17.3)	10/61 (16.4)	−0.1	−13.0–12.6	0.98
Ventilation	18–21/208 (8.7–10.1)[c]	Fewer than 5/61 (fewer than 8.2)	12.8	7.0–18.5	<0.001
Vasopressors	5–7/208 (2.4–3.4)[c]	8/61 (13.1)	−4.7	−12.1–2.6	0.21
PICU admission	32/208 (15.4)	12/61 (19.7)	2.5	−8.8–13.8	0.66
PICU length of stay (days)	4 (2–6 days)	3 (1–3 days)	-	-	0.02
Age 5–11 years					
Supplemental oxygen	8/30 (26.7)	37/98 (37.8)	−12.9	−35.0–9.3	0.25
Ventilation	Fewer than 5/30 (fewer than 16.7)	7–10/98 (7.1–10.2)[c]	−9.8	−18.5–−1.1	0.03
Vasopressors	0/30 (0.0)	42/98 (42.9)	-	-	-
PICU admission	7/30 (23.3)	61/98 (62.2)	−34.5	−57.7–−11.3	0.004
PICU length of stay (days)	2 (1–9 days)	3 (2–4 days)	-	-	0.68
Age 12–17 years					
Supplemental oxygen	37/92 (40.2)	16/49 (32.7)	−9.2	−27.2–8.9	0.32
Ventilation	11–14/92 (12.0–15.2)[c]	6–9/49 (12.2–18.4)[c]	−6.9	−25.1–11.3	0.46
Vasopressors	Fewer than 5/92 (fewer than 5.4)	24/49 (49.0)	−43.5	−63.3–−23.8	<0.001
PICU admission	21/92 (22.8)	30/49 (61.2)	−38.1	−57.2–−19.0	<0.001
PICU length of stay (days)	6 (3–8 days)	4 (2–5 days)	-	-	0.11

Abbreviations: aRD, adjusted risk difference; CI, confidence interval; COVID-19, coronavirus disease 2019; ECMO, extracorporeal membrane oxygenation; MIS-C, multisystem inflammatory syndrome in children; PICU, paediatric intensive care unit; -, not applicable

[a] Descriptive statistics are presented as frequency and proportions, or medians and interquartile ranges

[b] All comparisons adjusted for sex, comorbid conditions, and timing of hospitalization. Comparisons for all hospitalizations also adjust for age category. Positive risk differences indicate an outcome was more common for acute COVID-19 while negative risk differences indicate an outcome was more common for MIS-C

[c] Frequencies and percentages are reported using ranges to prevent back calculation of frequencies fewer than five

respiratory distress and/or exacerbation of chronic comorbid conditions (e.g. neurologic or respiratory disease). The higher vasopressor and intensive care requirements for MIS-C, with similar rates of respiratory support requirements, are consistent with multiple United States studies (2,16). A small number of acute COVID-19-related deaths were reported versus no MIS-C-related deaths, in part due to complications from chronic comorbid conditions among children with severe COVID-19 (17).

Despite comparable absolute rates of overall in-hospital resource use, there were important age differences in disease severity and the ensuing strategies used to support these patients. Infants (i.e. younger than one year old) rarely required hospitalization for MIS-C, presenting with lower rates of shock, coagulopathy and myocarditis relative to older children (11,18). Conversely, infants were the most commonly hospitalized age group for acute COVID-19, in part due to the routine practice of admitting febrile

infants for investigations and empiric treatment (19). Meanwhile, the requirement for hemodynamic support among children five years of age and older with MIS-C (43–49%) likely led to the high proportion of PICU admission among this age group relative to acute COVID-19, in keeping with other published literature (3).

While our study period ended prior to dominance of the Delta and Omicron lineages, these and future SARS-CoV-2 lineages may affect the relative in-hospital burden of acute COVID-19 infection and MIS-C. Studies from Denmark and Israel have found the incidence of MIS-C during Omicron waves fell to one tenth that of prior waves, after accounting for vaccination status (20,21). Declines in the proportion of MIS-C patients admitted to PICU have also been observed (e.g. 61% during pre-Delta waves to 52% during the Delta wave in the United States (22); 49% during Delta waves to 21% during Omicron waves in Israel (21)), though this may also reflect increased physician knowledge of MIS-C and refinement of supportive and treatment strategies. Uptake of paediatric and adolescent SARS-CoV-2 vaccines may also alter the relative in-hospital burden of disease, having shown effectiveness against both severe COVID-19 and MIS-C (23,24).

Limitations

There are several limitations to this study. First, the voluntary nature of CPSP reporting means that not all paediatric hospitalizations in Canada were identified. The number of hospitalizations reported in this study may therefore differ from provincial reports, which use administrative data. Moreover, the limited availability of molecular and serologic testing during the early pandemic likely resulted in some cases failing to meet the case definition of MIS-C. Data were also collected prior to emergence of the Delta and Omicron variants, and before implementation of paediatric and adolescent SARS-CoV-2 vaccine programs. The PICU admission criteria may have differed by age, centre and diagnosis. Nevertheless, this study provided a unique opportunity to compare children hospitalized for acute COVID-19 infection and MIS-C using data ascertained with the same surveillance methods, timeframe and patient population, with physician case review to ensure all reported cases met the case definitions.

Conclusion

Our findings suggest that both acute COVID-19 and MIS-C need to be considered when assessing the overall burden of SARS-CoV-2 in hospitalized children, and have implications for future pandemic planning with respect to hospital resource use. Given the high proportion of children requiring PICU support for MIS-C, in tandem with the limited number of specialized hospital beds, it is clear these resources need to be anticipated for future pandemic waves. Moreover, given the low overall rates of vaccination among children younger than 12 years of age (25), awareness of disease severity from both acute COVID-19 and MIS-C may inform parents and policymakers in their decision-making regarding paediatric vaccines.

Authors' statement

DSF — Conceptualization, methodology, validation, formal analysis, investigation, data curation, writing (original draft)
CMH — Conceptualization, methodology, validation, investigation, writing (review & editing), supervision, funding acquisition
OD — Investigation, writing (review & editing)
TET — Investigation, writing (review & editing)
MPM — Investigation, writing (review & editing)
RAB — Investigation, writing (review & editing)
MK — Validation, investigation, data curation, writing (review & editing)
MLT — Methodology, validation, investigation, data curation, writing (review & editing), project administration
KB — Investigation, writing (review & editing)
GBB — Investigation, writing (review & editing)
CB — Investigation, writing (review & editing)
TLB — Investigation, writing (review & editing)
SMB — Investigation, writing (review & editing)
KC — Investigation, writing (review & editing)
CC — Investigation, writing (review & editing)
ND — Investigation, writing (review & editing)
EJD — Investigation, writing (review & editing)
JEE — Investigation, writing (review & editing)
CF — Investigation, writing (review & editing)
AF — Investigation, writing (review & editing)
SF — Investigation, writing (review & editing)
RG — Investigation, writing (review & editing)
KTK — Investigation, writing (review & editing)
BL — Investigation, writing (review & editing)
RML — Investigation, writing (review & editing)
BWM — Investigation, writing (review & editing)
JO — Investigation, writing (review & editing)
JP — Investigation, writing (review & editing)
CMP — Investigation, writing (review & editing)
VEP — Investigation, writing (review & editing)
JPPG — Investigation, writing (review & editing)
RP — Investigation, writing (review & editing)
MS — Investigation, writing (review & editing)
MIS — Investigation, writing (review & editing)
RP — Investigation, writing (review & editing)
KAT — Investigation, writing (review & editing)
IVT — Investigation, writing (review & editing)
EH — Conceptualization, investigation, writing (review & editing), supervision
RS — Conceptualization, investigation, writing (review & editing), supervision
RSMY — Conceptualization, investigation, writing (review & editing), supervision
FK — Conceptualization, methodology, investigation, writing (review & editing), supervision
SKM — Conceptualization, methodology, investigation, writing (review & editing), supervision
CPSP COVID-19 Study Team — Investigation, writing (review & editing)
F Kakkar and S Morris were co-senior authors.

Competing interests

CMH is the Director of Children's Mental Health of Ontario, and the Director of Medical Affairs for the Canadian Paediatric Society and Canadian Paediatric Surveillance Program. MPM has received consulting fees from Sobin and Abbvie and payment for expert testimony from the Canadian Medical Protective Association. RAB has received honoraria and participated in advisory boards with SOBI, Roche, Amgen, and AbbVie. KB served as Past President of the Community Paediatrics Section of the Canadian Paediatric Society and has received royalties from Brush Education. TLB is an employee of the Public Health Agency of Canada (PHAC). KC is Chair of the Acute Care Committee of the Canadian Paediatric Society and is past-president of the Emergency Medicine Section of the Canadian Paediatric Society. EJD is Chair of the Scientific Research Committee and a director of Epilepsy Canada. She is also a member of Partners Against Mortality in Epilepsy and the advisory boards of Cardiol, Pendopharm and Stoke Therapeutics. CF is Chair of the Scientific Steering Committee for the Canadian Paediatric Surveillance Program, former Chair of the Specialty Committee in Paediatrics of the Royal College of Physicians and Surgeons of Canada, former president of the Canadian Paediatric Society, and member of the Executive as Secretary of the Canadian Critical Care Society. She has received reimbursement for travel expenses from Canadian Paediatric Society and the Royal College of Physicians and Surgeons of Canada. She has also received an honorarium for a presentation at a continuing education conference from the Université de Sherbrooke. SF is the President of the Association of Medical Microbiology and Infectious Disease Canada and has received consulting fees from Toronto Metropolitan University. RML has received honoraria for serving as a consultant to Sobi, Novartis, Sanofi, and Eli Lilly, as chair for data monitoring committees for Eli Lilly and Novartis, and from the Canadian Rheumatology Association. JP has received consultant fees from AbbVie, honoraria from AbbVie, AstraZeneca and Seegene, and he received respiratory virus testing materials from Seegene for his institution. He has participated in *ad hoc* advisory board meetings for AbbVie and Merck and is a voting member of the National Advisory Committee on Immunization. RP is a consultant for Verity Pharmaceuticals. MS is supported via salary awards from the BC Children's Hospital Foundation and the Michael Smith Foundation for Health Research and has been an investigator on projects funded by GlaxoSmithKline, Merck, Moderna, Pfizer, Sanofi-Pasteur, Seqirus, Symvivo and VBI Vaccines. All funds have been paid to his institute, and he has not received any personal payments. MIS is an employee of the Public Health Agency of Canada. EH has participated in advisory board meetings of CSL-Behring and Takeda, data safety monitoring boards of Rocket Pharmaceutical and Jasper Therapeutics, and has patent applications with Immugenia and Immune Biosolutions. RS has received honoraria and served on an advisory board and as a consultant with Novartis, honoraria from Canadian Rheumatology Association, is a board member for Rheumatology for All, and her institution receives funding from Bristol Myers Squibb for a patient registry for which she is Principal Investigator. RSMY has received grant funding from CFI, CIHR, Genome Canada, PHAC and the COVID-19 Immunity Task Force, and The Arthritis Society; is a member of the Science and Industry Advisory Committee at Genome Canada and Medical Advisory Board at Kawasaki Disease Canada; and a member of a data safety monitoring board for a study on IL-1 inhibitors for Kawasaki Disease. FK has received honoraria for presentations given to the Association des Pédiatres du Québec and receives CMV testing kits from Altona Diagnostics. SKM has received honoraria for lectures from GlaxoSmithKline, was a member of ad hoc advisory boards for Pfizer Canada and Sanofi Pasteur, and is an investigator on an investigator led grant from Pfizer. DSF, OD, TET, MK, and MLT have no conflicts of interest to report.

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EPIDEMIOLOGICAL STUDY

Description of COVID-19 outbreaks in childcare facilities in Alberta, March 2020 to December 31, 2021

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Abstract

Background: Children attending childcare are vulnerable to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, and mitigation measures such as masking, distancing, enhanced hygiene are not feasible for this population. Describing outbreak growth during the coronavirus disease 2019 (COVID-19) pandemic in childcare centres may provide insight into how to best mitigate the risks of COVID-19 and other infectious diseases in these settings. This article describes the childcare outbreaks and associated cases in Alberta at different time periods throughout the pandemic.

Methods: Our observational analysis used data on outbreaks and associated cases tracked through the Alberta Health Services Communicable Disease Outbreak Management database. We included all COVID-19 outbreaks opened in childcare facilities (March 2020 to December 31, 2021). We compared the characteristics of outbreaks and cases during each wave of the pandemic.

Results: There were a total of 841 childcare outbreaks, including 4,613 cases (70.2% in children and 29.8% adults). Many characteristics of outbreaks and cases varied across pandemic waves, including attack rates (12.1%–28.7% in adults and 5.8%–16.3% in children), percent of cases in children (56.4%–77.3%), and percent of outbreaks with a child index case (34.0%–70.1%). The overall average cases/outbreak was 5.5 (range: 1–68), and case examples of large outbreaks showed that delaying testing and attending daycare while symptomatic seemed to drive higher transmission.

Conclusion: Waves had different outbreak and case characteristics, for both adults and children. Transmission may happen more readily among adults and among children than between those two groups. Measures shown to be effective to reduce transmission in other settings can be implemented here, such as vaccination, strictly enforcing the exclusion of those symptomatic, and facilitating rapid testing.

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Keywords: COVID-19, childcare, outbreaks, Alberta, surveillance

Introduction

The Province of Alberta experienced five transmission waves of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, the causative agent of coronavirus disease 2019 (COVID-19), between March 2020 and March 2022. Early in the pandemic, children were reported to be less susceptible than adults to both infection and to severe outcomes such as hospitalization (1,2), with a high percentage having asymptomatic infection (3). Since then, much work has gone into understanding the infection in children (4–8), with studies noting that children are indeed at risk of infection, severe illness and long-term consequences (9), and are able to transmit the infection to others. Several studies have examined transmission

and outbreaks in the childcare setting (10–16), some noting low transmission (10,12,17,18) or a higher attack rate or proportion of cases in adults (13,14). However, most of these studies examined transmission during the earlier phases of the pandemic in 2020 before more transmissible variants of concern (VOC) were circulating, and none compared outbreak characteristics in the same jurisdiction across different time points during the pandemic.

Setting

The Province of Alberta has a population of 4.48 million (19). Statistics Canada estimated that 41% of Albertan children under the age of six years were enrolled in childcare between November 2020 and January 2021, and 54% between 2019 and 2020 (20). Childcare includes daycares, home-based care ("day homes"), preschools and out-of-school care. In these settings, children are in close contact with caregivers and other children in distinct cohort groups that typically have limited contact with other cohorts in the facility. Additionally, when public health restrictions do not otherwise limit cohort size, it is typical for facilities to group children and caregivers from multiple cohorts together, especially at drop-off and pick-up times, increasing the total number of individuals that interact. The staff-to-child ratios in childcare facilities range from 1:3 for infants, to 1:15 for children six years and older (21). Day homes are smaller groups and are limited to six children (not including the day home provider's children), with not more than three children under three years of age (21).

Children attending childcare are vulnerable to acquiring SARS-CoV-2, largely because public health measures such as masking and distancing are not feasible for this group. Within this setting, the children eat meals in close proximity to multiple people every day and have poor hygienic practices (22). Additionally, for most of our analysis period, only a small proportion of their close contacts in the daycare setting was vaccine-eligible and young children continue to have low vaccination coverage. Even though all children six months and older have been eligible since August 2022, as of December 19, 2022, only 38.9% of children 5–11 years and 3.5% of children 6 months–4 years had two doses of a COVID-19 vaccine (23) and, due to current approvals for strain-specific boosters, it is likely children will continue to lag behind adults for some time.

From the beginning of the SARS-CoV-2 pandemic until December 31, 2021, childcare settings and those who attended them were often prioritized for public health measures, including increased tracking of outbreaks and contact tracing and availability of vaccines and polymerase chain reaction (PCR) testing. We detail these measures, along with others relevant to households, and the timelines they were implemented in the **Appendix**. These details may provide important context to understand the outbreaks, such as who was eligible for PCR testing at any given time. Documenting policy changes will assist future outbreak epidemiologists in understanding why we found the transmission patterns we did.

Objective

Outbreaks of infectious illnesses in childcare facilities are not solely a phenomenon of the SARS-CoV-2 virus, as outbreaks of gastrointestinal and influenza-like illnesses have also been detected in these settings (22). The COVID-19 pandemic and the near-universal contact tracing brought about by the emergency provide interesting insights into the contextual factors that can exacerbate or mitigate the spread of infectious disease in childcare settings. Our objective is to provide aggregate surveillance data on outbreaks in childcare in Alberta in each pandemic wave through a descriptive statistical analysis of outbreaks and linked cases, and detailed case examples. Our summary description of all COVID-19 outbreaks tracked throughout the pandemic in Alberta is useful to public health practitioners interested in understanding the characteristics of such outbreaks in these settings and fills a gap in the literature on childcare outbreaks that will enable academic researchers to design more targeted analyses.

Methods

Our surveillance period begins with the first identified case of COVID-19 linked to a childcare facility in Alberta in May 2020 and ends with the end of childcare outbreak tracking on December 31, 2021. During this time period, Alberta experienced five transmission waves, which we differentiated based on the dominant variants and the active case counts.

Databases

We collected data on cases linked to outbreaks in childcare facilities using Alberta Health's COVID-19 dataset that integrates data elements from several systems to provide a comprehensive COVID-19 cases and outbreak dataset. The Provincial Surveillance information system is a laboratory surveillance system that receives results for all notifiable diseases from laboratory surveillance conducted by Alberta Precision Labs (24,25). The communicable disease reporting system and the Communicable Disease Outbreak Management system contain information on COVID-19 cases and the data integration and measurement reporting system contains up-to-date information on people admitted and discharged from hospitals in Alberta (including for cases of multisystem inflammatory syndrome in children [MIS-C]). Reporting requirements changed throughout the pandemic and a detailed description of these requirements can be found in the Appendix. Vaccination data for cases was accessed from the Immunization and Adverse Reaction to Immunization database.

Defining case and outbreak characteristics

We included only laboratory-confirmed COVID-19 cases. Throughout the pandemic, all cases were tested voluntarily,

although the eligibility for PCR testing changed over time (see **Supplemental material**). The definition of an outbreak in a childcare setting also changed over time (see Supplemental material). All childcare outbreaks were handled by specialized outbreak contact tracing teams who worked with facility managers to identify cases, risks and plan mitigation strategies. Cases that attended a facility being tracked as an outbreak were linked via an outbreak investigation number. Throughout the pandemic, when an outbreak was identified in the childcare setting, exposed persons at the facility were notified, either required or recommended to quarantine, and encouraged to get PCR testing.

We identified probable outbreak index cases by their symptom onset date (SOD); cases with the same onset date were both counted as probable index cases (as such, there are more index cases than outbreaks). If a facility had two children with the same SOD it was categorized as "child index" and if it had two adults with the same SOD it was categorized as "adult index". There were 39 outbreaks where both an adult and child had the same SOD, and these have been excluded when comparing outbreaks by index case age group. We defined each case's infectious period as 48 hours prior to symptom onset, or 48 hours prior to a positive test result if the case was asymptomatic at the time of testing (26).

We report vaccination status of cases 12 years of age and older, as vaccines for children five years of age and older were not available until November 24, 2021. We considered a vaccine dose as valid if it was received 14 days or more before the SOD. We used vaccination data and the SOD to determine if the case was vaccinated at the time of their SOD, and we also reported if they were vaccinated by March 2022.

When reporting on severe outcomes, we included individuals who had a positive COVID-19 test at the time of hospitalization and children who were hospitalized at a later point for MIS-C. The MIS-C cases were reported by clinicians to the communicable disease team who provided weekly reports to public health surveillance partners.

Outbreaks were included in waves based on the date the outbreak was opened, and cases were included in waves based on the date the case was reported. Due to low numbers of cases linked to childcare outbreaks in wave 1, we combined waves 1 and 2 in our reporting.

Statistics and descriptive analyses

We summarized the characteristics of cases linked to childcare outbreaks that were open over the course of the pandemic from March 2020 to December 31, 2021. We used R to analyze the data and conduct descriptive analysis, as well as Excel and Stata to conduct descriptive analysis and add summary variables. Contact tracers recorded information on the total populations of children and adults at risk in a facility, and attack rates were calculated as the number of lab-confirmed cases of COVID-19 out of the at-risk population. However, not all outbreaks that had the attack rate calculations performed by the investigators were precise, as there were 4/808 outbreaks (0.5%) reported as greater than 100%. These are likely errors. We did not identify a standard policy for how population at risk was defined.

Outbreak case examples

We selected two outbreaks from each time period to examine outbreaks in these settings in more detail: from each time, we selected one of the largest outbreaks and one outbreak that had "average" characteristics (based on the number of cases, attack rate, duration and having an index case carrying the most common variant identified in that wave).

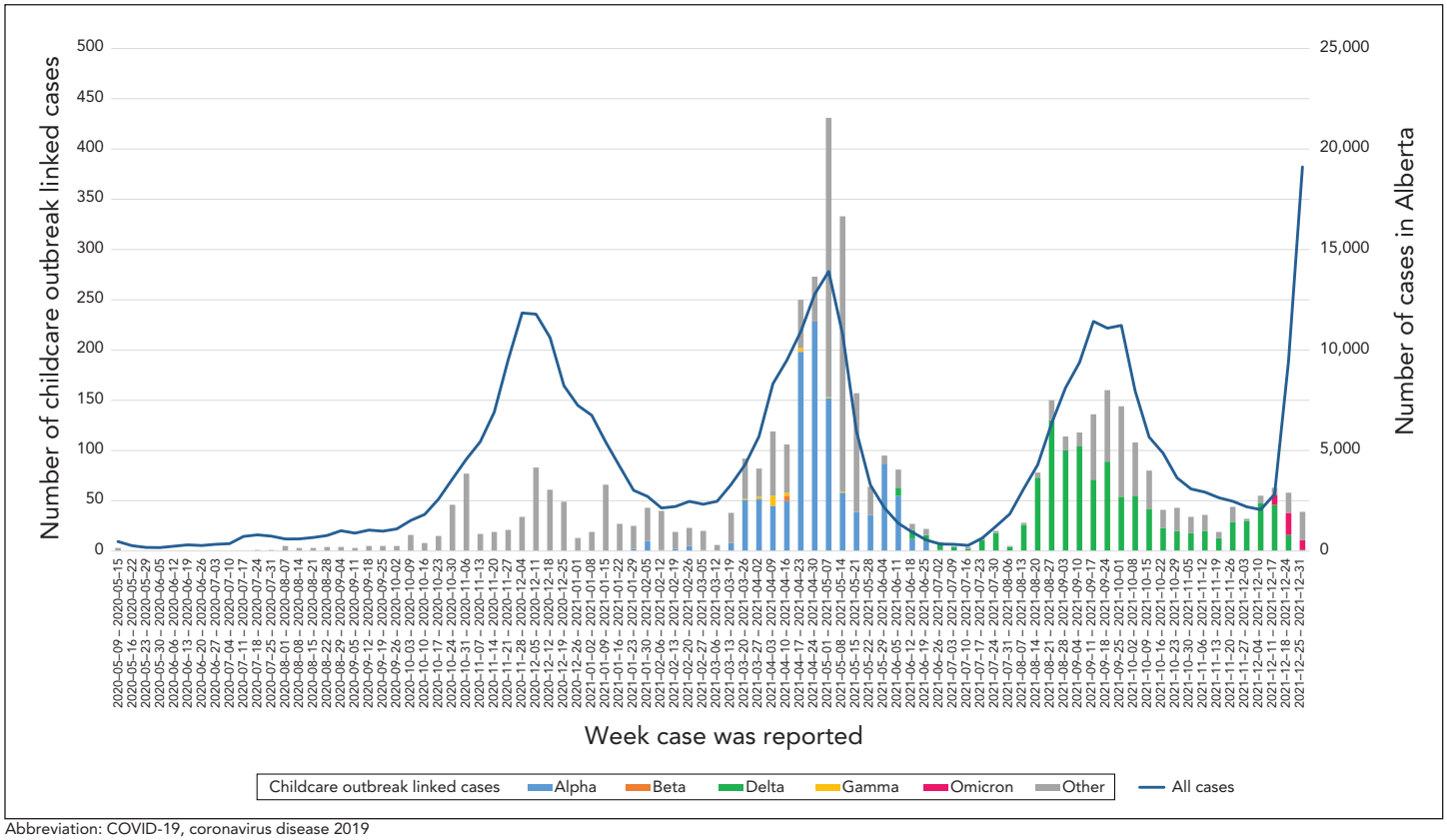
After extracting the cases linked to each of our identified outbreak, we manually searched the Communicable Disease Outbreak Management system for cases in the same household as each outbreak case. Household contacts were not included in attack rate calculations; they were included to demonstrate the context in which they arose and to describe the impact they had in the community. We used individual contact tracing notes and outbreak reports to describe the example outbreaks, although we obscured details to protect privacy. These data sources are often inconsistent and not all details about outbreak characteristics and dynamics are available for every case or outbreak. For example, few reports mention the proportion of staff in the facility who were vaccinated, and information about secondary transmission to cases not at the facility was inconsistently available throughout the pandemic.

Each outbreak is reported using the earliest symptom onset as "Day 1", and each additional case is added based on when their symptoms started. Contact tracing in daycare settings ended early in wave 5 and we were not able to select a large and small outbreak for that wave; instead, we selected two outbreaks with confirmed Omicron cases.

Results

The first childcare-associated case of COVID-19 in Alberta was identified in May 2020. Between then and December 31, 2021, there were 841 individual cases of COVID-19 at a childcare facility that met the definition of an outbreak and were tracked, with 4,613 associated cases. Of the 841 outbreaks, 63% (n=531) included at least one VOC case confirmed through screening or genotyping. The earliest outbreak due to a VOC SARS-CoV-2 variant was identified in January 2021 and was an Alpha variant (**Figure 1**). **Table 1** summarizes the characteristics of the outbreaks and **Table 2** details the average attack rate in each wave, for children and adults separately. Wave 3 stands out as having the highest number of outbreaks, the highest average cases/outbreak, the longest average duration and the highest average attack rates in both children and adults.

Figure 1: Epidemic curve of childcare associated COVID-19 cases compared to all cases in Alberta from May 2020 to December 2021[a]



Abbreviation: COVID-19, coronavirus disease 2019
[a] Cases are dated based on when the lab-confirmed case was reported to Alberta Health

Table 1: Characteristics of childcare facility outbreaks opened during each wave of the COVID-19 pandemic, based on the date that the outbreak was opened

Characteristic	All	95% CI	Waves 1 & 2 May 10, 2020–Feb 25, 2021		Wave 3 Feb 26, 2021–Jul 1, 2021		Wave 4 Jul 2, 2021–Dec 15, 2021		Wave 5 Dec 16, 2022–Dec 31, 2022	
			n	95% CI	n	95% CI	n	95% CI	n	95% CI
Total outbreaks	841	N/A	144	N/A	336	N/A	331	N/A	30	N/A
Most common variant identified through genotyping	23.9% Alpha	22.7–25.1	95.0% Not genotyped	93.2–96.4	49.0% Alpha	46.9–51.1	67.3% Delta	64.9–69.7	33.8% Omicron	25.8–42.7
Average number of cases/outbreak	5.5	5.1–5.9	5.2	4.4–6.1	6.6	5.8–7.4	4.6	4.2–5.1	3.8	2.8–4.8
Percent of outbreaks with two or fewer cases	30.2	27.1–33.4	31.9	24.4–40.2	24.1	19.6–29.1	35.0	29.9–40.5	36.7	19.9–56.1
Outbreak average duration (days)[a]	9.7	9.0–10.4	9.1	7.2–11.1	10.3	9.2–11.5	9.4	8.4–10.4	9.0	5.7–12.3
Percent of outbreaks with a probable child index	55.1	51.6–58.5	34.0	26.3–42.4	48.5	43.1–54.0	70.1	64.8–75.0	63.3	43.9–80.1
Average percent of child cases	68.6	66.7–70.6	56.4	51.5–61.4	65.4	62.6–68.2	77.3	74.3–80.3	68.1	54.7–81.5
Average percent of child cases when probable index is an adult, N=339	46.8	44.1–49.6	43.2	37.8–48.6	49.7	45.9–53.4	47.4	41.1–53.6	31.7	12.1–51.4
Average percent of child cases when probable index is a child, N=463	85.4	83.7–87.1	80.8	73.8–87.9	80.4	77.4–83.4	89.6	87.5–91.7	89.1	80.5–97.7
Percent of index cases tested within one day of symptom onset, N=968	40.0	36.9–43.1	51.4	43.7–59.1	40.6	35.7–45.6	34.6	29.8–39.7	30.8	15.9–52.4

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; N/A, not applicable
[a] Calculated as the number of days between symptom onset of first case and last case

Table 2: Attack rates in children and adults stratified by the age category of the index case

Characteristic	All	95% CI	Waves 1 & 2 May 10, 2020–Feb 25, 2021		Wave 3 Feb 26, 2021–Jul 1, 2021		Wave 4 Jul 2, 2021–Dec 15, 2021		Wave 5 Dec 16, 2022–Dec 31, 2022	
			n	95% CI	n	95% CI	n	95% CI	n	95% CI
Average % attack[a]	13.4	12.2–14.6	12.6	10.2–14.9	18.2	15.8–20.6	9.6	8.3–10.9	7.5	4.9–10.1
Average % attack in only children	11.8	10.6–13.0	8.9	7.1–10.7	16.3	14.0–18.7	9.1	7.7–10.6	5.8	3.4–8.2
Average % attack in only children when probable index is an adult, N=314	10.4	8.8–12.0	8.5	6.1–10.8	13.3	10.3–16.3	7.9	5.6–10.3	4.9	-0.1–9.9
Average % attack in only children when probable index is a child, N=457	12.3	10.7–13.9	9.7	6.6–12.9	18.3	14.6–21.9	9.2	7.5–10.9	6.3	3.5–9.1
Average % attack in only adults	21.4	19.3–23.6	28.5	21.4–35.5	28.7	25.0–32.4	12.1	9.9–14.3	14.3	6.9–21.6
Average % attack in only adults when probable index is an adult, N=314	32.6	28.9–36.4	37.3	26.7–47.9	35.0	30.5–39.5	25.2	19.1–31.3	25.7	11.5–39.9
Average % attack in only adults when probable index is a child, N=457	12.8	10.4–15.2	13.2	6.6–19.7	22.6	16.8–28.4	6.4	4.7–8.0	7.6	0.0–15.2

Abbreviation: CI, confidence interval
[a] 33 outbreaks did not have information on the total population at risk, so attack rates could not be calculated

Table 3 summarizes the characteristics of cases associated with the outbreaks and Figure 1 is an epidemiologic curve of all childcare outbreak linked cases compared to the province-wide cases. Overall, cases in the childcare setting peaked along with cases in the community. Wave 4 had the highest proportion of cases being children. There were no deaths in our population, 0.4% of adults were admitted to the intensive care unit and 2.2% of adults and 0.3% of children were admitted to hospital. As there were so few cases of MIS-C, we did not report these separately from other types of childhood hospitalization.

Table 3: Characteristics of cases linked to any childcare facility outbreak during each wave of the COVID-19 pandemic, based on the date the case was reported[a]

Characteristic of cases	All	95% CI	Waves 1 & 2 May 10, 2020–Feb 25, 2021		Wave 3 Feb 26, 2021–Jul 1, 2021		Wave 4 Jul 2, 2021–Dec 15, 2021		Wave 5 Dec 16, 2022–Dec 31, 2022	
			n	95% CI	n	95% CI	n	95% CI	n	95% CI
All (N)	4,613	N/A	758	N/A	2,207	N/A	1,518	N/A	130	N/A
Age (%)										
Younger than 1 year	0.3	0.2–0.5	-	N/A	-	N/A	0.2	0.0–0.6	0	N/A
1–2 years	18.5	17.4–19.7	17.2	14.5–20.0	21.9	20.2–23.7	15.0	13.2–16.8	10.8	6.0–17.4
3–4 years	27.8	26.5–29.1	24.9	21.9–28.2	26.4	24.5–28.3	31.7	29.4–34.1	22.3	15.5–30.4
5–9 years	21.0	19.9–22.3	13.6	11.2–16.2	17.4	15.8–19.0	29.1	26.8–31.5	32.3	24.4–41.1
10–19 years	2.6	2.1–3.1	3.6	2.4–5.1	1.7	1.2–2.3	3.4	2.6–4.5	-	N/A
20–29 years	7.6	6.8–8.4	10.3	8.2–12.7	7.7	6.7–8.9	5.8	4.7–7.1	10.0	5.4–16.5
30–39 years	8.6	7.8–9.4	12.4	10.1–15.0	8.6	7.5–9.9	6.6	5.4–8.0	8.5	4.3–14.6
40–49 years	8.3	7.6–9.2	12.3	10.0–14.8	9.4	8.2–10.7	4.7	3.7–5.9	9.2	4.9–15.6
50–59 years	4.3	3.7–4.9	4.2	2.9–5.9	5.3	4.4–6.4	2.8	2.0–3.7	4.6	1.7–9.8
60 years and older	1.0	0.7–1.4	1.5	0.7–2.6	1.1	0.7–1.6	0.7	0.3–1.3	-	N/A
Child (younger than 18 years)	69.1	67.7–70.4	57.4	53.8–60.9	67.1	65.1–69.0	78.1	75.9–80.1	66.9	58.1–74.9
Adult (18 years and older)	30.9	29.6–32.3	42.6	39.1–46.2	32.9	31.0–35.0	21.9	19.9–24.1	33.1	25.1–41.9
Sex[b] (%)										
Children: female	47.3	45.5–49.0	48.7	43.9–53.5	46.8	44.2–49.3	47.8	45.0–50.7	41.4	30.9–52.4
Children: male	52.7	50.9–54.4	51.3	46.5–56.1	53.2	50.6–55.7	52.2	49.3–55.0	58.6	47.6–69.1
Adults: female	96.0	94.9–97.0	96.3	93.6–98.1	95.9	94.2–97.2	97.0	94.5–98.6	88.4	75.0–96.1
Adults: male	3.9	3.0–5.1	3.7	1.9–6.4	4.0	2.7–5.7	3.0	1.4–5.5	11.6	3.9–25.1

Table 3: Characteristics of cases linked to any childcare facility outbreak during each wave of the COVID-19 pandemic, based on the date the case was reported[a] (*continued*)

Characteristic of cases	All	95% CI	Waves 1 & 2 May 10, 2020–Feb 25, 2021		Wave 3 Feb 26, 2021–Jul 1, 2021		Wave 4 Jul 2, 2021–Dec 15, 2021		Wave 5 Dec 16, 2022–Dec 31, 2022	
			n	95% CI	n	95% CI	n	95% CI	n	95% CI
Genotype (%)										
Alpha	23.9	22.7–25.1	2.6	1.6–4.0	49.0	46.9–51.1	0	N/A	0	N/A
Beta	0.2	0.1–0.3	0	N/A	0.3	0.1–0.7	0	N/A	0	N/A
Gamma	0.5	0.3–0.7	0	N/A	1.0	0.6–1.5	0	N/A	0	N/A
Delta	23.4	22.2–24.6	0	N/A	1.3	0.9–1.9	67.3	64.9–69.7	20.8	14.2–28.8
Omicron	1.1	0.8–1.4	0	N/A	0	N/A	0.3	0.1–0.8	33.8	25.8–42.7
Not genotyped	39.0	37.5–40.4	95.0	93.2–96.4	29.4	27.5–31.3	25.0	22.9–27.3	37.7	29.3–46.6
Unresolved or wild type	12.1	11.2–13.1	2.4	1.4–3.7	19.0	17.4–20.7	7.3	6.1–8.7	7.7	3.8–13.7
Vaccine doses at SOD (%)[c]	**N=1,433**		**N=325**		**N=731**		**N=344**		**N=43**	
1 dose	5.1	4.0–6.4	0	N/A	5.6	4.1–7.6	9.6	6.6–13.3	0	N/A
2 doses	12.1	10.4–13.9	0	N/A	-	N/A	40.4	35.1–45.9	86.0	72.1–94.7
3 doses	-	N/A	0	N/A	0	N/A	-	N/A	-	N/A
No doses	82.6	80.6–84.6	100.0	98.9–100[d]	94.3	92.3–95.8	49.7	44.2–55.2	-	N/A
Vaccine doses as of March 2022 (%)[c]	**N=1,433**		**N=325**		**N=731**		**N=344**		**N=43**	
1 dose	2.0	1.4–2.9	1.5	0.5–3.6	1.1	0.5–2.1	4.8	2.8–7.7	0	N/A
2 doses	57.4	54.8–60.0	54.5	48.9–60.0	58.1	54.4–61.7	59.6	54.1–64.9	51.2	35.5–66.7
3 doses	31.5	29.1–34.0	35.7	30.5–41.2	35.4	32.0–39.0	17.4	13.5–21.9	44.2	29.1–60.1
4 doses	-	N/A	0	N/A	0	N/A	-	N/A	-	N/A
No doses	8.9	7.4–10.5	8.3	5.5–11.9	5.3	3.8–7.2	18.0	14.0–22.5	-	N/A
Severe outcomes in children (%)	**N=3,187**		**N=435**		**N=1,480**		**N=1,185**		**N=87**	
Hospitalized	0.3	0.1–0.5	-	N/A	-	N/A	-	N/A	-	N/A
Intensive care unit	0	N/A	0	N/A	0	N/A	0	N/A	0	N/A
Death	0	N/A	0	N/A	0	N/A	0	N/A	0	N/A
Severe outcomes in adults (%)	**N=1,426**		**N=323**		**N=727**		**N=333**		**N=43**	
Hospitalized	2.2	1.5–3.2	1.5	0.5–3.6	2.2	1.3–3.5	3.3	1.7–5.8	0	N/A
Intensive care unit	0.4	0.1–0.8	-	N/A	-	N/A	-	N/A	-	N/A
Death	0	N/A	0	N/A	0	N/A	0	N/A	0	N/A

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; N/A, not applicable; SOD, symptom onset date; -, proportion was being suppressed because the count was <5
[a] Proportions based on case counts that are fewer than five are suppressed (indicated with a dash)
[b] There were fewer than 1% of individuals who did not disclose or for whom biological sex was missing in the database
[c] This section only includes the 1,433 cases that were 12 years of age and older
[d] This is a one-sided test, 97.5% confidence interval

Outbreak case examples

Our case examples are detailed in **Table 4**. We did not include some potentially identifying information, such as the geographic zone the facility is in, precise dates of the outbreak, precise facility size or counts of severe outcomes. The "Day 1" for each outbreak is the earliest symptom onset set. These eight outbreaks included 143 cases that attended childcare facilities and an additional 44 who lived in the same household and had symptoms after those of the childcare case. These 187 total cases included fewer than five hospitalizations and intensive care unit admissions and no deaths.

Table 4: Details of example childcare facility outbreaks from each wave of the pandemic

Wave	Size of facility and number of cohorts with cases	Genotypes	Public health measures described	Information about index case	Number of cases at the facility	Subsequent cases in households of childcare attendees	# of cases who attended facility while infectious/ on SOD/ after SOD	Other information[a]
Wave 1 & 2A	Unknown Three cohorts	Likely wild type (no genotyping)	Staff reported the centre follows sanitization, distancing, staff masking, and a limit of two staff in break rooms at a time.	A staff member who worked while infectious (but symptoms developed after work) in the cohort that later had child cases.	22 from 21 households; 16 children, 6 adults	Three households with child index (4 cases). One household with adult index (1 case).	19/8/0	By the time the outbreak was reported on Day 8, almost all cases had already developed symptoms. Cases in children seem limited to a single cohort, while staff cases span at least three. The facility was closed on Day 6 due to cases.
Wave 1 & 2B	Fewer than 50 Two cohorts	Likely wild type (no genotyping)	Staff at the facility reported continuously masking, cohorting children, increased cleaning, and limiting the number of children at activities.	Two staff who both could be index cases were tested while asymptomatic, but worked while infectious and pre-symptomatic.	Five from 4 households; 2 children, 3 adults	One household with child index (1 case).	4/1/0	Cases in children were limited to a single cohort. The facility closed on Day 9, but exposed staff and children were quarantined prior to this.
Wave 3A	More than 100 ~90% of cohorts	66/74 genotyped were Alpha variant 1/74 is presumptive wild type 7/74 were unresolved	The facility conducted symptom and temperature screening, enhanced cleaning and staff wore face masks when not in their cohort. Staff had a shared bathroom and lunchroom; however, the lunchroom was reported to be in use by only one person at a time.	A child who attended on but not after SOD. Second case was a staff member working in multiple cohorts while symptomatic.	69 from 61 households; 46 children, 23 adults	Six households with child index (7 cases). One household with child and adult index (1 case). Nine households with adult index (15 cases).	29/12/4	Many of the earlier cases did not get tested quickly after symptom onset, including a staff who worked after their SOD and in multiple cohorts. The outbreak was not flagged for tracking until 10 days after the first case developed symptoms, at which point to 17 individuals at the facility had already developed symptoms.
Wave 3B	Fewer than 50 One cohort	12/13 genotyped were Alpha variant 1/13 was unresolved	Staff reported measures in place including hand hygiene, masking, frequency surface cleaning and physical distancing. Staff are limited to only two at a time in the lunchroom.	The likely index is a staff member, who did not get tested for six days after symptom onset.	Six from 6 households; 3 children, 3 adults	Two households with child index (3 cases). Two households with adult index (6 cases).	3/2/0	The facility closed on Day 7 of the outbreak. Vaccines were not yet widely available and none of the staff cases had received any doses yet, nor had vaccine-eligible household cases.
Wave 4A	More than 100 Two cohorts of children, unknown staff cohorts	19/20 genotyped were Delta variant 1/20 was unresolved	Facility reports public health measures including distancing the children, when possible, enhanced surface cleaning, daily health checks and continual staff masking.	The earliest case was a child with no known household exposures who did not get tested until four days after symptom onset.	20 from 18 households; 17 children, 3 adults	Three households with child index (3 cases).	20/9/3	The outbreak seems to have spread from one cohort to the other via siblings. The staff cases all had at least one vaccine dose, with 2/3 having had two doses. 5/9 vaccine-eligible household cases had two doses. The remaining had no doses. The facility closed on the evening of Day 7.

Table 4: Details of example childcare facility outbreaks from each wave of the pandemic (*continued*)

Wave	Size of facility and number of cohorts with cases	Genotypes	Public health measures described	Information about index case	Number of cases at the facility	Subsequent cases in households of childcare attendees	# of cases who attended facility while infectious/ on SOD/ after SOD	Other information[a]
Wave 4B	50–100 Two cohorts	5/5 genotyped were Delta variant	Staff reported using enhanced surface cleaning and hand hygiene, and daily symptom checks. Staff had not been masking prior to the outbreak but began masking again.	Likely index was a child who attended after their symptoms began and who did not get tested until four days later.	Five from 5 households; 3 children, 2 adults	No observation of transmission from a daycare case to a household member.	5/1/2	One staff case had no vaccine doses, and the other had two. No indication that the facility closed at any point during the outbreak.
Wave 5A	50–100 Two cohorts	7/8 genotyped were Omicron variant 1/8 was unresolved	Both staff and children were reported to wear masks, and staff conducted enhanced cleaning throughout the facility. Children and staff ate together in their cohorts.	Child who did attend just before but not on or after SOD, but did not get tested until four days after SOD.	Eight from 6 households; 7 children, 1 adult	One household with a child index (1 case).	8/3/4	All vaccine-eligible child cases had received one dose of the vaccine, although two had received that dose just a few days prior to their SOD. The one staff case had two doses. Vaccine-eligible household cases had 1–2 doses. The facility closed on Day 5.
Wave 5B	50–100 One cohort	5/7 genotyped were Omicron variant 2/7 were Delta variant	No information about public health measures at the facility were documented in available records.	The Delta index case was a staff who attended after their SOD. The Omicron index case was a staff who attended after their SOD. The staff member's household was exposed at an event, but the staff did not believe their core symptom[b] related to COVID-19 and did not get tested for four days.	Eight from 7 households Delta: 1 child, 1 staff Omicron: 4 children, 2 staff	One household with a child index (2 cases).	8/4/4	Staff cases all had two vaccine doses. Three children had one dose, and two had no doses. Vaccine-eligible household members had two doses. The facility closed on Day 26.

Abbreviations: COVID-19, coronavirus disease 2019; SOD, symptom onset date
[a] Here we included additional information gathered somewhat unsystematically from the outbreak investigation or comments from staff and parents
[b] Core symptom refers to fever, cough, sore throat or shortness of breath

Discussion

Our surveillance of COVID-19 outbreaks in Alberta throughout the first two years of the pandemic is an important contribution to knowledge of transmission in this setting. Previously, reporting in Alberta was limited to lists of childcare outbreaks that reached a specific threshold, or cases in age groups that would also include children in care. Additionally, the existing literature on outbreaks in childcare focuses on specific facilities or time periods. Here, we discuss differences across time periods and age groups, the evidence of the impacts of vaccination in this setting, and the factors that appeared to drive the large outbreaks we examined in detail.

We found that the outbreak and associated case characteristics we examined often differed for each time period. The number of index cases tested within one day of symptom onset dropped steadily through the time periods (51.4%, 40.6%, 34.6% and

30.8%, from May 2020 to December 31, 2021), which could be due to cases either choosing not to seek testing or cases not being able to access timely testing. Wave 3 had the lowest proportion of outbreaks with limited secondary transmission (i.e. transmission beyond the first case(s) who were identified and initiated outbreak tracking). The attack rates in adults dropped from 28.5% in waves 1 and 2 and 28.7% in wave 3 (when vaccines were largely unavailable), to 12.1% and 14.3% in waves 4 and 5, respectively. The attack rates in children varied somewhat less across time periods and was highest in wave 3 (16.3%) and 8.9%, 9.1% and 5.8% in waves 1 and 2, 4 and 5, respectively. Notably, in wave 4, when vaccination coverage in the adult population was high and immune-evasive variants like Omicron had not yet begun to dominate in Alberta, the percent of outbreaks with children-index cases was highest (70% vs. the pandemic average of 55.1%) and the attack rate in adults was also the lowest (12.1% vs. the pandemic average of 21.4%). The highest proportion of cases in children (77.3%) was also in wave 4. The only scenario when the attack rate was higher in children than adults was when the probable index was also a child in wave 4.

Our data analysis suggests that, at least in the childcare setting, spread from children to adults and adults to children is less common than spread within each of these groups. The proportion of cases in children is at its highest when children are the probable index (85.4%), compared to only 46.8% when an adult is the index case. This contrasts with a 2020 article, where Ehrhardt *et al.* described child-to-child transmission in schools/childcare facilities as "very uncommon" (10). Link-Gelles *et al.* noted limited secondary transmission in childcare, finding that 69% of programs had a single case with no apparent secondary transmission (17). While we were only able to look at the proportion of outbreaks with limited spread (only 1–2 total cases), as facilities with only a single case were not tracked after August 2020, it is still striking that we found only 30.2% of outbreaks with limited spread. Adults are generally overrepresented in the case counts as well. Our work found that the average outbreak cases were 68.6% children and 31.4% adults, which is likely an over-representation of adult cases as, due to required ratios of staff to children in childcare, adults providing care are generally 25% or less a childcare cohort (one staff per three infants) and as low 6% in older groups (one staff per 15 children). Kim *et al.* also reported a high proportion of cases in adults (13). Adults often had a much higher attack rate than children, averaging 21.4% across the pandemic vs. 11.8% in children. The highest average attack rate for adults was in waves 1 and 2 when 37.3% of adults were infected when there was an adult index case at the facility. In the same scenario, the attack rate in children was only 8.5%. The highest attack rate children experienced was in wave 3 (18.3%, when a child was the index case). In 2022, Li *et al.* reported that staff had a much higher attack rate than children (47% vs. 11%), in line with our observations (14), although in 2021 Loenenbach *et al.* reported more similar attack rates in children vs. adults (23% vs. 30%) (15). Lopez *et al.* identified similarly low attack rates for facilities in 2020, between 17% and 18% for the entire facility (27).

Our observations also point to the value of vaccination in these settings. While wave 4 was dominated by the more contagious and more virulent Delta variant, 40% of vaccine-eligible cases had two doses of the vaccine, which may have helped limit spread. Wave 4 had a lower number of average cases/outbreak than wave 3 (when vaccines were still largely unavailable) and the lowest attack rate in adults. There is a stark contrast between outbreaks in waves 1 and 2 when an adult was the index case and no one was vaccinated (attack rate is 37.3%) and wave 4 when a child was the index case and much of the adult population was vaccinated (6.4%), suggesting that the most transmission in the childcare setting happens when unvaccinated adults introduce the virus into an unvaccinated population, and the least transmission happens when a child introduces the virus into a population where adults are at least mostly vaccinated. Wave 4 had a much higher proportion of outbreaks with a probable child index case (70.1% in wave 4 compared to 48.5% in wave 3), indicating that when vaccination coverage was high, adults were transmitting in these settings less frequently. At the beginning of wave 4 in early July 2021, the coverage of one dose of the vaccine in the Alberta population aged 12–19 years was 62.7%, 20–39 years was 63.9% and 40–59 years was 75.6%, and this rose to 85.4%, 83.9% and 88.9%, respectively, by December 15. The percent of childcare cases in wave 4 who had no doses of vaccine appears higher than the general Alberta population. While we found that 49.7% of cases 12 years of age and older in wave 4 had no doses of vaccines at their SOD, the percent of those aged 12–19, 20–39 and 40–59 years in the general population with no vaccine doses was 37.3%, 36.1% and 24.4%, respectively. This dropped by the end of wave 4 to 14.6%, 16.1% and 11.1%, respectively. While we cannot directly compare the Alberta general population vaccination rates to our observation that 49.7% of cases were unvaccinated, which is for the entire time period, combining all of those 12 years and older and are specific to SOD. There still appears to be an over-representation of individuals with no vaccine doses in our cases compared to what would have been expected at the time, which indicates that unvaccinated adults were more susceptible to infection.

As expected from previously published articles, most COVID-19 cases in our adult population were female, which aligns with typical staffing at childcare centres. Again, as with previously published articles, our work also noted that cases in childcare facilities trend with cases in the community (13,17) and the most common variants identified via genotyping aligned with what was circulating in the community at the time.

There are a few things to note from the more detailed contextual factors in the case examples described in Table 4. The largest outbreaks involved either individuals attending while symptomatic (waves 3, 4 and 5) or, in the case of waves 1 and 2,

individuals delaying testing for several days after symptom onset, which prevented contact tracing and isolation, and prevented parents from being able to make informed decisions about risks of sending their child. There are no data on when specific symptoms began, so it is not possible to identify if children were attending their childcare facilities with symptoms that were mandated to require testing. We do not have information available about air quality at the facilities and cannot determine what role ventilation may have had in increasing or decreasing spread in each outbreak. While contextual information, such as our case examples provide, can be difficult to interpret and enable few conclusions to be drawn, the experiences of what occurs on the ground in an outbreak situation can be important lessons for policy-makers and operators alike.

While our data cannot be used to estimate how often a child or adult infected in childcare settings infects their household members, they do demonstrate that household transmission occurs from both adults and children. Of the 127 households that had cases linked to any of the case examples, 30 had confirmed cases with symptoms that started after the case linked to a childcare facility (17 child household index cases, 12 adult index cases and one household with both an adult and a child index case). This contrasts with studies that suggest no secondary transmission from school-aged children (28) and reduced transmission from children to their households (29). Our findings of increased cases in children when a child is the index case contrast with the Silverberg *et al.* article (29) which reported that children transmit to other children less readily but is consistent with an article by Paul *et al.* (30) that suggested that children aged 0–3 years were the most at risk for transmitting to their households.

Strength and limitations

A major strength of our analysis is the inclusion of all cases linked to outbreaks at childcare facilities in the Province of Alberta. There are, however, still several limitations to our work. The eligibility for PCR testing, the definition of outbreak and the nature of contact tracing changed over time. Our analysis includes cases who chose to seek testing and this sample may have missed cases who did not wish to get tested. In examining individual outbreaks, there are several major limitations that require great caution in any attempts to correlate outcomes of the outbreak with any specific behaviours or public health interventions. The specific public health measures implemented in each facility were not systematically captured and there was no way to verify that the measures are being implemented consistently. Some descriptions of measures were provided by individual staff members and not the official outbreak investigation, which sometimes did not indicate what measures were in place. Index cases were identified through self-reported symptom onset data and individuals might not have accurately remembered when mild symptoms started, might have disregarded symptoms that do not seem to fit and (with very young children) might have had earlier symptom onset than when they were able to communicate them to their care providers. We identified household cases of childcare cases through contact tracing data, which may be incomplete. We only have information on those who tested positive via PCR testing—there may have been additional cases who tested positive via rapid test and therefore did not seek PCR testing. We do not know if exposed individuals got PCR testing and were negative, or if they did not get any PCR testing and may have been infected. We also do not know the vaccination status of exposed individuals, except for comments on vaccination coverage of staff in outbreak reports.

The total cases linked to wave 5 outbreaks are likely underestimated because testing in wave 5 became limited just a week into the wave due to testing capacity issues. Many childcare facilities closed shortly after wave 5 began, due to the Christmas holiday, and childcare outbreak tracking ended shortly after. Our estimates for wave 5 are also imprecise due to the resulting low number of outbreaks and associated cases. It is possible that patterns observed with earlier outbreaks would have changed with the introduction of the Omicron variant.

Conclusion

While attack rates were lower in children than in adults in childcare facilities, children were at risk of COVID-19 infection in this setting and could transmit to caregivers and each other. The average attack rates in adults and the high proportion of cases in adults indicated that spread happened more readily among adults than children. Measures known to prevent spread among adults may be an important factor in preventing spread across childcare cohorts, and in keeping facilities open during outbreaks. Almost half of all childcare cases have been in children under five years of age; a population that has only recently been eligible for vaccination, will likely be delayed due to ineligibility for future variant-specific boosters, and is unable to mask properly or physically distance from caregivers and peers. As community transmission continues in Alberta and around the globe, so does the potential for emergence of new variants. It is unclear what role the public health measures, such as masking among staff, played in preventing spread to children and how important such measures will be in future pandemic waves. However, measures shown to be effective in other settings will likely be effective here, and childcare facilities can implement protections such as encouraging vaccination among their staff, eligible children and their families, strictly enforcing the exclusion of symptomatic staff and children, and facilitating rapid testing of those who become symptomatic. As each wave in our analysis had unique characteristics, facility managers should be aware that as new variants/subvariants emerge, there may be changes in transmission dynamics and therefore changes in which measures are most effective.

Authors' statement

JG — Conceptualized the project, conducted analysis, interpreted the data and results, drafted the paper, and revised the paper
SPR — Conducted analysis, interpreted the data and results, revised the paper
AS — Conducted analysis, interpreted the data and results, revised the paper

Competing interests

None.

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Supplemental material

These documents can be accessed on the Supplemental material file.

Figure S1: Epidemic curve of cases related to childcare outbreak wave 1 & 2A based on symptom onset date
Figure S2: Epidemic curve of cases related to childcare outbreak wave 1 & 2B based on symptom onset date
Figure S3: Epidemic curve of cases related to childcare outbreak wave 3A based on symptom onset date
Figure S4: Epidemic curve of cases related to childcare outbreak wave 3B based on symptom onset date
Figure S5: Epidemic curve of cases related to childcare outbreak wave 4A based on symptom onset date
Figure S6: Epidemic curve of cases related to childcare outbreak wave 4B based on symptom onset date
Figure S7: Epidemic curve of cases related to childcare outbreak wave 5A based on symptom onset date
Figure S8: Epidemic curve of cases related to childcare outbreak wave 5B based on symptom onset date

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Appendix

Overview of public health measures relevant to childcare in Alberta

While the general audience may not be interested in some of the details outlined in the Appendix, they provide important context to understand the outbreaks. For instance, these details provide context for interpreting the proportion of the population with no vaccines, or help the reader understand who was eligible for polymerase chain reaction (PCR) testing at different times. Documenting policy changes will assist future outbreak epidemiologists in understanding why we found the transmission patterns we did.

The first measure to protect children was implemented in Alberta on March 16, 2020, when childcare facilities including daycares, out-of-school care, and preschools in the province were ordered to close. A limited number of childcare facilities were allowed to re-open on March 23, 2020, to care for children of healthcare and critical infrastructure workers, and this was expanded to include all essential workers on April 1, 2020. Childcare facilities were permitted to open on May 14, 2020, provided facilities could follow guidelines including cohorts of 10 individuals, including staff and children. In Alberta, the staff-to-child ratios in childcare facilities range from 1:3 for infants, to 1:15 for children six years and older, and day homes are limited to six children (not including the day home provider's children), with not more than three children under three years of age (21). The cohort limit was expanded to 30 on June 12, 2020, and removed entirely on August 21, 2020. Guidelines issued also included enhanced screening, hygiene, facility cleaning, staff distancing when possible, and masking when a child became ill. Vaccine requirements were never imposed on childcare staff or eligible children, however, childcare staff were able to book vaccine appointments on May 4, 2021, two days earlier than the general public over age 30, and six days earlier than the general public aged 12 and older. Children aged five to 11 were not eligible for vaccinations until November 26, 2021, and children under five became eligible August 2, 2022.

The PCR testing available for children and childcare workers varied throughout the pandemic. On April 9, 2020, the testing eligibility was expanded to include essential workers who were symptomatic, anyone living with someone 65 years and older, and all Calgary Zone residents. This was quickly expanded to include anyone with symptoms on April 13, 2020. On May 29, 2020, two weeks after childcare facilities were starting to open, testing was expanded to anyone without restrictions. Testing shifted again September 17, 2020, and was focused on only symptomatic cases, known contacts of cases, those linked to outbreaks, and asymptomatic cases in priority locations (which did not include childcare). On December 23, 2021, symptomatic Albertans were asked to use rapid tests and were no longer eligible for PCR testing (with exceptions for those eligible for specific treatments and those in specific high-risk settings). Childcare guidelines were soon shifted to include reference to rapid test results.

Comprehensive screening for COVID-19 variants of concern (VOC) began in early February 2021, coinciding with the arrival of the B.1.1.7 Alpha, and B.1.351 Beta variants in the province (31). However, this comprehensive screening was paused when cases were at their peak in waves 3 to 5, and instead VOC screening was prioritized to outbreak-associated cases, hospitalized cases, and a random sample of community cases. Overall, from February 2021 when large scale screening began to the end of our reported period (December 31, 2021), 67% of cases were screened for VOCs (internal data).

Initially, outbreak investigations in childcare settings in Alberta were opened when there was one case confirmed to have COVID-19 (32). This shifted to two confirmed cases within 14 days, or two epidemiologically linked cases, in August 2020 (33). This definition was updated to only include cases who were at the childcare setting while communicable or who likely acquired there in June 2021 (34), and again in September 2021 to include outbreaks based on two cases meeting respiratory illness case definition (35). Childcare COVID-19 outbreaks stopped being opened on December 31, 2021, and the February 2022 update to the Public Health Management Guidelines did not mention childcare settings beyond that cases should not attend (36).

For much of the pandemic, facilities were put on alert and tracking began with a single confirmed case, and publicly reported when there were five or more cases. This changed on March 17, 2021, when public reporting of cases moved to 10 cases. Cases were only included as part of the outbreak if they have a primary connection to the facility (for example, if they work there or attend). For most of the COVID-19 pandemic, when a case was confirmed at a childcare facility in Alberta, the case was referred to a specialist outbreak investigation team to conduct contact tracing.

RAPID COMMUNICATION

SARS-CoV-2 vaccine acceptance among caregivers of children younger than five years of age: A cross-sectional survey in Toronto

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Abstract

Background: Despite severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccine approval in Canada for children six months to five years old, vaccine acceptance for this age group remains low compared with other age groups. This study aimed to assess vaccine acceptance among caregivers of children younger than five years old and to identify factors associated with SARS-CoV-2 vaccine hesitancy in Toronto.

Methods: A multi-language self-administered survey was sent to caregivers of children attending 660 Toronto schools and two community health centres between April 5 to July 4, 2022. Data on socio-demographic characteristics, acceptance of routine childhood and influenza vaccines and current SARS-CoV-2 vaccine status for parents and older siblings were collected.

Results: A total of 253 caregivers of children younger than five years old answered the survey. Although 234 (94%) of the responding caregivers were fully vaccinated against SARS-CoV-2 and more than 90% had their children older than five years receiving one dose of the vaccine, only 148 (59%) had intentions to vaccinate their child younger than five years old.

Conclusion: These findings highlight the importance of interventions to increase vaccine confidence among caregivers of children aged younger than five years old.

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Keywords: SARS-CoV-2, COVID-19, caregivers, children, vaccine acceptance, vaccine hesitancy, survey

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Introduction

In Ontario, from January 15, 2020, to March 11, 2023, there have been 1,695 children younger than five years old hospitalized for coronavirus disease 2019 (COVID-19) and 23 deaths from COVID-19 (1). National data from Canada found that among children younger than 18 years old hospitalized because of COVID-19, the highest proportion of severe disease was in children aged 2–5 years old (2). On July 14, 2022, Health Canada first approved severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) vaccines for children six months to five years of age (3). However, the uptake of SARS-CoV-2 vaccines in this age group has been low in all provinces and remains below 10% in Canada, compared with 52% in the 5–11 years old age group and 83.9% in the 12–17 years old age group (4). Although vaccine uptake rates (which refer to the actual behaviour of getting a vaccine) are lower than reported rates of vaccine acceptance (which refer to the intent to receive a vaccine, or attitude), understanding the COVID-19 vaccine acceptance rates in caregivers of young children and their reasons for hesitancy would allow for the development of targeted interventions to increase confidence and uptake in this age group (5,6). This study addresses time-sensitive and urgent public health matters: 1) the assessment of vaccine acceptance (intent to receive a vaccine or to vaccinate) in caregivers of children younger than five years of age and 2) identification of factors associated with vaccine hesitancy (delay in acceptance or refusal of vaccines) in Ontario prior to the national approval of vaccines for this age group (6).

Methods

A multi-language self-administered cross-sectional survey was sent to caregivers of children and/or pre-school children at 660 public and private schools affiliated with the Hospital for Sick Children COVID-19 Testing Centre and two community health centres in Toronto. The survey was distributed from April 5 to July 4, 2022—immediately before the approval of the vaccine for children six months to five years of age. Caregivers who reported caring for children younger than five years old were asked about their intention to vaccinate their child(ren) against SARS-CoV-2 upon approval of the vaccine for this age group, and their reasons for being hesitant to accept COVID-19 vaccines. Caregivers were considered vaccine-acceptant when they intended (very likely/likely) to vaccinate their children against SARS-CoV-2 in the future, and vaccine-hesitant when had little or no intention (very unlikely/unlikely/unsure) to vaccinate their children in the future. The survey collected information on socio-demographic characteristics (including age, relationship to the child, education status, country of birth and ethnicity) and current vaccine status for caregivers and older siblings of the school-aged group. The questionnaire can be found in the **Supplemental material**. Data were analyzed using χ^2 or Fisher's exact tests and *p*-values of <0.05 were considered to be statistically significant. Responses to the open-ended questions were coded and clustered using thematic analysis.

Results

A total of 253 caregivers of children younger than five years old answered the survey. Although 234 (94%) of the responding caregivers had received at least two doses of COVID-19 vaccine and more than 90% had their children older than five years receiving at least one dose of the vaccine, only 148 (59%) intended to vaccinate their child(ren) younger than five years old. The level of COVID-19 vaccine acceptance differed among caregivers of different ethnic backgrounds, with lowest acceptance reported in Black (25%) and Middle Eastern (37.5%) (p=0.006). Other characteristics associated with differences in vaccine acceptance included caregiver's age (p=0.039, lowest in those over 40 years of age), education level (p=0.011, lowest in university graduates) and vaccination status (p<0.001, lowest in unvaccinated caregivers) (**Table 1**). Caregivers reported seeking information on COVID-19 vaccines primarily from public health resources (79%), government organizations (62%), social media (58%) and family doctors or paediatricians (45%). When comparing caregivers with different ethnic backgrounds, there were significant differences in the number of those seeking information from public health resources (p<0.001) and family doctors or paediatricians (p<0.001). Compared with caregivers with White background, all other ethnic backgrounds had lower reports of seeking information from public health resources (p<0.001) and family doctors or paediatricians (p<0.001). Additionally, seeking information from family doctors or paediatricians (p=0.029), public health resources (p<0.001), government organizations (p<0.001), professional groups (p=0.012) and social media (p=0.001) differed among caregivers with different levels of education. Caregivers with higher levels of education had higher reports of getting information from family doctors or paediatricians (except for those less than high school), public health resources, government organizations, professional groups and social media (except for a community college diploma) than those with lower levels of education (**Table 2**).

Table 1: SARS-COV-2 vaccine acceptance among caregivers of children younger than five years of age

Characteristic of caregiver	All participants (N=253)		Vaccine acceptance[a]				*p*-value
			Acceptant (N=148, 58.5%)		Hesitant (N=105, 41.5%)		
	n/N	%	n/N	%	n/N	%	
Relationship to child							
Father	52/253	20.6	35/52	67.3	17/52	32.7	0.34
Mother	199/253	78.7	112/199	56.3	87/199	43.7	
Grandparent	2/253	0.7	1/2	50.0	1/2	50.0	
Ethnicity[b]							
White	105/244	43.0	68/105	64.8	37/105	35.2	0.006
East/Southeast Asian	49/244	20.1	35/49	71.4	14/49	28.6	
South Asian	28/244	11.5	16/28	57.1	12/28	42.9	
Black	24/244	9.8	6/24	25.0	18/24	75.0	
Mixed and other race category	17/244	7.0	10/17	58.8	7/17	41.2	
Latino	13/244	5.3	7/13	53.8	6/13	46.2	
Middle Eastern	8/244	3.3	3/8	37.5	5/8	62.5	

Table 1: SARS-COV-2 vaccine acceptance among caregivers of children younger than five years of age (*continued*)

Characteristic of caregiver	All participants (N=253)		Vaccine acceptance[a]				*p*-value
			Acceptant (N=148, 58.5%)		Hesitant (N=105, 41.5%)		
	n/N	%	n/N	%	n/N	%	
Age group							
Younger than 30 years	5/253	2.0	0/5	0.0	5/5	100.0	0.039
30–39 years	148/253	58.5	86/148	58.1	62/148	41.9	
40–49 years	95/253	37.5	58/95	61.1	37/95	38.9	
50 years or older	5/253	2.0	4/5	80.0	1/5	20.0	
Education status							
Less than high school	5/243	2.1	3/5	60.0	2/5	40.0	0.011
High school or equivalent	23/243	9.5	11/23	47.8	12/23	52.2	
Community college	42/243	17.3	17/42	40.5	25/42	59.5	
University graduate	173/243	71.2	114/173	65.9	59/173	34.1	
Country of birth							
Canada	127/249	51.0	80/127	63.0	47/127	37.0	0.24
Other countries	122/249	49.0	68/122	55.7	54/122	44.3	
Country of birth income level[c]							
Low/lower middle income	50/247	20.2	29/50	58.0	21/50	42.0	0.81
High/upper middle income	197/247	79.8	118/197	59.9	79/197	40.1	
Has family doctor or paediatrician							
Yes	240/251	95.6	139/240	57.9	101/240	42.1	0.766
No	11/251	4.4	7/11	63.6	4/240	36.4	
Number of children							
1	27/250	10.8	17/27	63.0	10/27	37.0	0.595
2	143/250	57.2	85/143	59.4	58/143	40.6	
3	58/250	23.2	35/58	60.3	23/58	39.7	
4 or more	22/250	8.8	10/22	45.5	12/22	54.5	
Caregiver's SARS-CoV-2 vaccination status							
Received at least one dose	236/252	93.7	147/236	62.3	89/236	37.7	<0.001
Has not received any dose	16/252	6.4	1/16	6.3	15/16	93.8	
Sibling's (aged 12–18 years) SARS-CoV-2 vaccination status							
Received at least one dose	33/46	71.7	21/33	63.6	12/33	36.4	0.007
Has not received any dose	13/46	28.3	2/13	15.4	11/13	84.6	
Sibling's (aged 5–11 years) SARS-CoV-2 vaccination status							
Received at least one dose	136/195	69.7	109/136	80.1	27/136	19.9	<0.001
Has not received any dose	59/195	30.3	6/59	10.2	53/59	89.8	
Current sources of information on SARS-CoV-2 vaccines[d]							
Family doctor or paediatrician	113/251	45.0	71/113	62.8	42/113	37.2	0.21
Public health resources	197/251	78.5	122/197	61.9	75/197	38.1	0.038
Government organizations	156/251	62.3	96/156	61.5	60/156	38.5	0.21
Professional groups[e]	56/251	22.3	37/56	66.1	19/56	33.9	0.19
Social media[f]	145/251	57.8	88/145	60.7	57/145	39.3	0.41
Social network[g]	81/251	32.3	49/81	60.5	32/81	39.5	0.66
Other sources[h]	17/251	68.0	3/17	17.6	14/17	82.4	<0.001

Abbreviation: SARS-COV-2, severe acute respiratory syndrome coronavirus 2
[a] Caregivers were considered vaccine-acceptant when they intended (very likely/likely) to vaccinate their children against SARS-CoV-2 in the future, and vaccine-hesitant when had little or no intention (very unlikely/unlikely/unsure) to vaccinate their children in the future
[b] Caregivers were able to choose multiple responses for their ethnicity, the Indigenous ethnic group was classified as "mixed and other" due to small group size
[c] Caregivers' country of birth income level was defined based on the World Bank classification 2021 (7)
[d] Caregivers were able to choose multiple answers for the current source of information
[e] Professional groups such as Canadian Medical Association, Canadian Nurses Association, etc.
[f] Social media includes Twitter, Facebook, WhatsApp, WeChat, radio/television/newspapers or news websites
[g] Social networks such as family, friends, neighbours or co-workers. Percentages were calculated based on the cases with complete data
[h] Other sources reported in open-ended questions include scientific articles, workplaces, schools, statistics on government websites, World Health Organization and Centers for Disease Control and Prevention reports, and a friend (a virologist)

Table 2: Current sources of information on SARS-CoV-2 vaccines among caregivers of children younger than five years of age

Characteristic of caregiver	All participants (N=251)[a]		Current sources of information on SARS-CoV-2 vaccines													
			Family doctor or paediatrician (N=113, 45.0%)		Public health resources (N=197, 78.5%)		Government organizations (N=156, 62.2%)		Professional groups (N=56, 22.3%)		Social media (N=145, 57.8%)		Social network (N=81, 32.3%)		Other sources (N=17, 6.8%)	
	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%	n/N	%
Ethnicity (*p*-value)	**N/A**		**<0.001**		**<0.001**		**0.658**		**0.54**		**0.059**		**0.902**		**0.233**	
White	105/242	43.4	64/105	61.0	97/105	92.4	71/105	67.6	30/105	28.6	64/105	61.0	31/105	29.5	9/105	8.6
East/Southeast Asian	48/242	19.8	12/48	25.0	39/48	81.3	30/48	62.5	8/48	16.7	35/48	72.9	17/48	35.4	1/48	2.1
South Asian	28/242	11.6	10/28	35.7	20/28	71.4	15/28	53.6	4/28	14.3	13/28	46.4	8/28	28.6	0/28	0.0
Black	24/242	9.9	11/24	45.8	15/24	62.5	16/24	66.7	4/24	16.7	13/24	54.2	6/24	25.0	2/24	8.3
Mixed and other race category	16/242	6.6	4/16	25.0	9/16	56.3	9/16	56.3	4/16	25.0	8/16	50.0	7/16	43.8	2/16	12.5
Latino	13/242	5.4	6/13	46.2	8/13	61.5	7/13	53.8	2/13	15.4	5/13	38.5	5/13	38.5	0/13	0.0
Middle Eastern	8/242	3.3	3/8	37.5	5/8	62.5	4/8	50.0	1/8	12.5	2/8	25.0	2/8	25.0	1/8	12.5
Age group (*p*-value)	**N/A**		**0.597**		**0.48**		**0.64**		**0.655**		**0.299**		**0.41**		**0.42**	
Younger than 30 years	4/251	1.6	1/4	25.0	4/4	100.0	3/4	75.0	1/4	25.0	3/4	75.0	2/4	50.0	0/4	0.0
30–39 years	148/251	59.0	64/148	43.2	118/148	79.7	87/148	58.8	31/148	20.9	84/148	56.8	52/148	35.1	11/148	7.4
40–49 years	94/251	37.5	46/94	48.9	70/94	74.5	62/94	66.0	24/94	25.5	53/94	56.4	25/94	26.6	5/94	5.3
50 years and older	5/251	2.0	2/5	40.0	5/5	100.0	4/5	80.0	0/5	0.0	5/5	100.0	2/5	40.0	1/5	20.0
Education status (*p*-value)	**N/A**		**0.029**		**<0.001**		**<0.001**		**0.012**		**0.001**		**0.323**		**0.445**	
Less than high school	5/241	2.1	3/5	60.0	2/5	40.0	2/5	40.0	0/5	0.0	0/5	0.0	0/5	0.0	1/5	20.0
High school or equivalent	122/241	50.6	10/22	45.5	13/22	59.1	7/22	31.8	1/22	4.5	7/22	31.8	5/22	22.7	1/22	4.5
Community college	42/241	17.4	11/42	26.2	25/42	59.5	23/42	54.8	6/42	14.3	27/42	64.3	15/42	35.7	3/42	7.1
University graduate	172/241	71.4	87/172	50.6	150/172	87.2	120/172	69.8	49/172	28.5	106/172	61.6	57/172	33.1	11/172	6.4

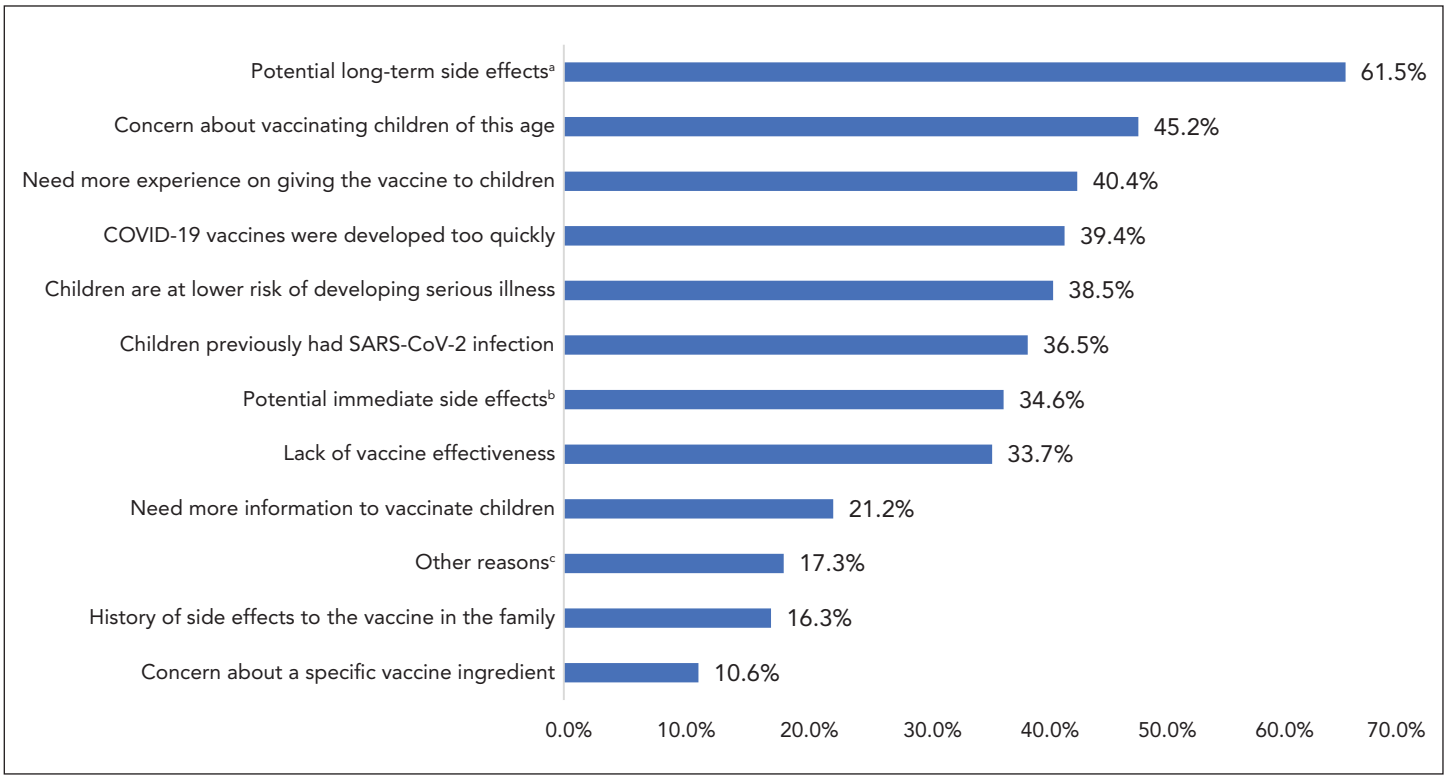
Abbreviations: N/A, not applicable; SARS-COV-2, severe acute respiratory syndrome coronavirus 2
[a] For the question on current sources of information, there were two missing answers

Among caregivers who were vaccine hesitant (105 caregivers with one participant not providing a reason), the most common reason for vaccine hesitancy was the concern about long-term side effects (n=64/104; 62%). A third of caregivers who were hesitant to vaccinate their child(ren) reported concerns around the lack of data and evidence on COVID-19 vaccines, reported immediate side effects from vaccines and the potential for new unspecified side effects. Additional concerns included children being too young to be vaccinated (n=47/104; 45%) and wanting to wait until there is more experience with vaccinating children in this age group (n=42/104; 40%). Among caregivers with concerns about long-term side effects reported in open-ended questions, 11 (17.2%) were concerned about cardiovascular side effects, six (9.4%) about neurological or developmental side effects, four (6.3%) about infertility, three (4.7%) about inflammation and autoimmune disease and 16 (25.0%) about other long-term side effects (**Figure 1**).

Conclusion

In this study, conducted prior to approval in Canada for COVID-19 vaccination in children between six months and five years of age, we found that caregivers' intent to vaccinate their child younger than five years old was low. Although vaccine acceptance and uptake may not necessarily be identical concepts, interestingly, the proportion of caregivers who were found to be acceptant of COVID-19 vaccines for their child was found to be much lower than the proportion of caregivers who reported to be vaccinated or who had an older child that was already vaccinated against COVID-19 (6). These findings highlight that targeted interventions are needed to support caregivers with education and opportunities for enhanced discussion supporting COVID-19 vaccination decisions for their young children, especially in groups that were found to have lower vaccine acceptance. Healthcare and public health professionals play a crucial role in fostering SARS-CoV-2 vaccine confidence in parents and relaying up-to-date and accurate information on the benefits and risks of vaccination to caregivers of young children.

Figure 1: Reasons for SARS-CoV-2 vaccine hesitancy in caregivers of children younger than five years of age[a,b,c]



Abbreviations: COVID-19, coronavirus disease 2019; SARS-COV-2, severe acute respiratory syndrome coronavirus 2

[a] Long-term side effects reported in open-ended questions include cardiovascular (11/64 or 17.2%; e.g. myocarditis, pericarditis, bleeding and other cardiovascular effects), neurological or developmental (6/64 or 9,4%; e.g. developmental or cognitive issues, stroke and aneurism and other neurological side effects), uncertain due to lack of data, evidence for and potential unspecified new side effects (20/64 or 31.3%), infertility (4/64 or 6.3%), inflammation and autoimmune disease (3/60 or 4.7%) and other long-term side effects (6/64 or 25.0%)

[b] Immediate side effects include cardiovascular (11/36 or 30.6%; e.g. myocarditis/pericarditis, thrombosis and other cardiovascular effects), neurological (3/36 or 8.3%; e.g. stroke, Bell's palsy or other forms of paralysis and seizure), vaccine reactogenicity (7/36 or 19.4%; e.g. fever and pain), allergic reactions (2/36 or 5.6%); inflammation and autoimmune disease (2/36 or 5.6%) and other immediate side effects (11/36 or 31%)

[c] Other reasons include vaccination being unnecessary (4/18 or 22.2%), lack of effectiveness (3/18 or 16.7%) and other reasons (5/18 or 27.8%; e.g. other specific concerns and other general and unspecified concerns)

Authors' statement

PPPR — Co-first author, conceptualization, writing–original draft, writing–review and editing
EKS — Co-first author, writing–original draft, data analysis, writing–review and editing
SKM — Conceptualization, writing–review and editing
DSF — Data analysis, writing–review and editing
SAF — Project administration, data curation, writing–review and editing
JO — Methodology, resources, writing–review and editing
MES — Methodology, resources, 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

PPPR has been a co-investigator on an investigator-led project funded by Pfizer that is unrelated to this study. SKM has received honoraria for lectures from GlaxoSmithKline and Johnson and Johnson China, was a member of ad hoc advisory boards for Pfizer Canada and Sanofi Pasteur, and is a co-investigator on an investigator led grant from Pfizer, all unrelated to this study. All other authors report no conflicts of interest.

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Supplemental material

These documents can be accessed on the Supplemental material file.

Survey instrument

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COVID-19 outbreak trends in Canada, 2021

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Abstract

Background: In January 2021, the Public Health Agency of Canada launched an outbreak surveillance system, the Canadian COVID-19 Outbreak Surveillance System (CCOSS), with the goal of monitoring incidence and severity of coronavirus disease 2019 (COVID-19) outbreaks across various community settings and complementing case surveillance.

Methods: Seven provinces were included in this report; these provinces submitted weekly cumulative COVID-19 outbreak line lists to CCOSS in 2021. Data includes administrative variables (e.g. date outbreak declared, date outbreak declared over, outbreak identifier), 24 outbreak settings, and number of confirmed cases and outcomes (hospitalization, death). Descriptive analyses for COVID-19 outbreaks across Canada from January 3, 2021, to January 1, 2022, were performed examining trends over time, severity, and outbreak size.

Results: Incidence of outbreaks followed similar trends to case incidence. Outbreaks were most common in school and childcare settings (39%) and industrial/agricultural settings (21%). Outbreak size ranged from 2 to 639 cases per outbreak; the median size was four cases per outbreak. Correctional facilities had the largest median outbreak size with 18 cases per outbreak, followed by long-term care facilities with 10 cases per outbreak. During periods of high case incidence, outbreaks may be under-ascertained due to limited public health capacity, or reporting may be biased towards high-risk settings prioritized for testing. Outbreaks reported to CCOSS were dominated by jurisdictions with the largest populations.

Conclusion: The trends illustrate that COVID-19 outbreaks in 2021 were reported most frequently in community settings such as schools; however, the largest outbreaks occurred in congregate living settings. The information gathered from outbreak surveillance complemented case incidence trends and furthered understanding of COVID-19 in Canada.

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Keywords: COVID-19, Canada, outbreak, surveillance, outbreak trends, SARS-CoV-2 transmission, public health, respiratory virus

Introduction

Context

On January 25, 2020, the first severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection was detected in Canada (1). The World Health Organization (WHO) declared coronavirus disease 2019 (COVID-19), the disease caused by SARS-CoV-2 infection, a pandemic on March 11, 2020 (2) and COVID-19 rapidly spread across Canada with many cases and deaths associated with outbreak events (3,4). Outbreaks can result in many infections over a short period of time, which has the potential to rapidly increase community transmission through secondary exposures and strain healthcare services (4).

The Public Health Agency of Canada (PHAC) determined that outbreak surveillance could provide additional data on the COVID-19 epidemic in Canada to help guide the public health response; as a result, PHAC created the Canadian COVID-19 Outbreak Surveillance System (CCOSS) following consultations with provincial and territorial partners. In January 2021, CCOSS launched with seven provinces contributing data: British Columbia (BC), Alberta (AB), Manitoba (MB), Ontario (ON), Québec (QC), Nova Scotia (NS) and Prince Edward Island (PE). These provinces represent 93% of the Canadian population (5). The remaining Canadian provinces and territories indicated their support for national outbreak surveillance but were unable

to participate at that time. Ongoing efforts are underway to integrate interested partners.

Outbreak surveillance has not been commonly conducted for established pathogens at the national level. Very few countries, such as Ireland and the United Kingdom, reported trends on COVID-19 outbreaks (6,7). The implementation of an event-based surveillance system to capture COVID-19 outbreak trends in Canada is novel and different from existing event-based surveillance systems in its timeliness and the level of detail captured.

Objectives

Systematic monitoring of COVID-19 outbreak trends allows for the improved understanding of settings and populations most at risk of experiencing outbreaks and of the relative impact of outbreaks on the burden of COVID-19 in Canada. This federal/provincial/territorial initiative allowed for national outbreak trends to be monitored during the pandemic. Knowledge gained from CCOSS informs public health response in Canada for prevention and control of SARS-CoV-2 transmission in various settings. This report provides a retrospective descriptive analysis of COVID-19 outbreak trends in Canada observed over a one-year period from January 2021 to January 2022.

Methods

Information sources

Data were extracted from the CCOSS database and enhanced with case-level data from the National COVID-19 Case Dataset, both stored in a Postgres database and maintained by PHAC. The CCOSS is a passive event-based surveillance system implemented in January 2021 that aims to systematically monitor the incidence and severity of COVID-19 outbreak events by setting type. Seven provinces were included in this analysis (BC, AB, MB, ON, QC, NS and PE); these provinces submitted cumulative COVID-19 outbreak line lists electronically to CCOSS on a weekly basis in 2021. The surveillance system captures aggregate outbreak-level data on administrative variables (e.g. date outbreak declared, date outbreak declared over, outbreak identifier), 24 outbreak settings and number of confirmed cases and outcomes (hospitalization, death). In 2021, provinces submitted records of outbreaks for a variety of outbreak settings, including but not limited to the following settings of interest: long-term care facilities (LTCF), acute care, school and childcare settings, correctional facilities, congregate living, and industrial settings (**Table 1**) (8,9).

Table 1: Condensed grouping of outbreak settings in Canadian COVID-19 Outbreak Surveillance System

Condensed settings	CCOSS outbreak settings
Acute care	Acute care setting
Congregate living	Congregate living setting (e.g. assisted living, shelters, group homes), retirement residence
Correctional facility	Correctional facility
Industrial/agricultural	Industrial setting, agri-food processing facility
Long-term care facility	Long-term care facility
School and childcare	School, daycare, or day camp
Other	Community healthcare setting, emergency services, mass gathering event, office, personal care setting, recreational facility, restaurant/bar, retail, social event, transportation, travel/tourism, other specify, workplace unspecified, unknown

Abbreviation: CCOSS, Canadian COVID-19 Outbreak Surveillance System

The National COVID-19 Case Dataset is a non-nominal case-based surveillance system capturing data on case demographics, clinical status and outcomes, exposures, risk factors, vaccination, and variant lineages of COVID-19 cases in Canada. For provinces that provided permission for linkage of outbreak and case data, CCOSS data were linked to the COVID-19 case dataset using unique outbreak identifiers. This linkage allowed PHAC to obtain additional information on outbreak case counts and severe outcomes for outbreaks with missing information and variant lineages.

Definitions

The national definition for COVID-19 outbreaks is as follows: two or more confirmed cases of COVID-19 (10) epidemiologically linked to a specific setting and/or location, excluding households since household cases may not be declared or managed as an outbreak if the risk of transmission is contained. This definition also excludes cases that are geographically clustered (e.g. in a region, city, or town) but not epidemiologically linked, and cases attributed to community transmission (10).

To contextualize the impact of each variant of concern (VOC), we utilized the period from VOC introduction to the end of the dominant period. Using data from the National COVID-19 Case Dataset, the case with the earliest episode date was used to define the date of introduction. The date corresponding to the end of the dominant period was identified based on the last date that the proportion of VOC cases accounted for at least 75% of sequenced cases reported. March 2021 to May 2021 corresponded to a period of mixed VOC (Alpha, Beta, Gamma) dominance as no single VOC represented over 75%.

To provide context for the role of COVID-19 vaccines on outbreak incidence, we added a vaccination timeline for the start of the vaccination campaign in priority groups (December 2020) and the dates Health Canada authorized vaccines for individuals aged 12–17 years (May 5, 2021) and 5–11 years (November 19, 2021) and first booster doses (November 9, 2021), understanding that there are variations in the timing of the vaccine rollout in different jurisdictions (11–14).

Data quality and missing data

The national COVID-19 outbreak definition was applied to CCOSS data. Denominators for outbreak settings (e.g. number of schools or populations at risk within these settings) were not available; thus, it was not possible to calculate which settings are most at risk of outbreaks from these data, only which settings most commonly report outbreaks. Therefore, calculated proportions of outbreaks by setting are relative to the overall number of outbreaks. The completeness of variables reported in the outbreak line list varied by jurisdiction. In a jurisdiction that did not report on industrial setting outbreaks separately, where possible "workplace unspecified" outbreaks were mapped to "industrial/agricultural" based on information from location names. Case fatality was defined as the proportion of confirmed COVID-19 cases associated with an outbreak that died due to COVID-19. Case fatality was missing for approximately 5% of outbreaks. Duplicate records identified using unique outbreak identifiers were removed.

Data analysis

The CCOSS outbreak settings were grouped for analyses according to Table 1. Settings that represented less than 2% of outbreaks or that were inconsistently reported across provinces were grouped into the "other" category. For reporting purposes, data were aggregated by epidemiological week (Sunday to Saturday) in which the outbreak was declared; therefore, this report covers outbreaks declared during the period of January 3, 2021, to January 1, 2022. Data were extracted on April 29, 2022. Data were cleaned and analyzed using R Statistical Software version 4.0.4. Descriptive statistics on outbreak trends by setting, over time and by case characteristics, such as outbreak size and severe outcomes, were computed.

Results

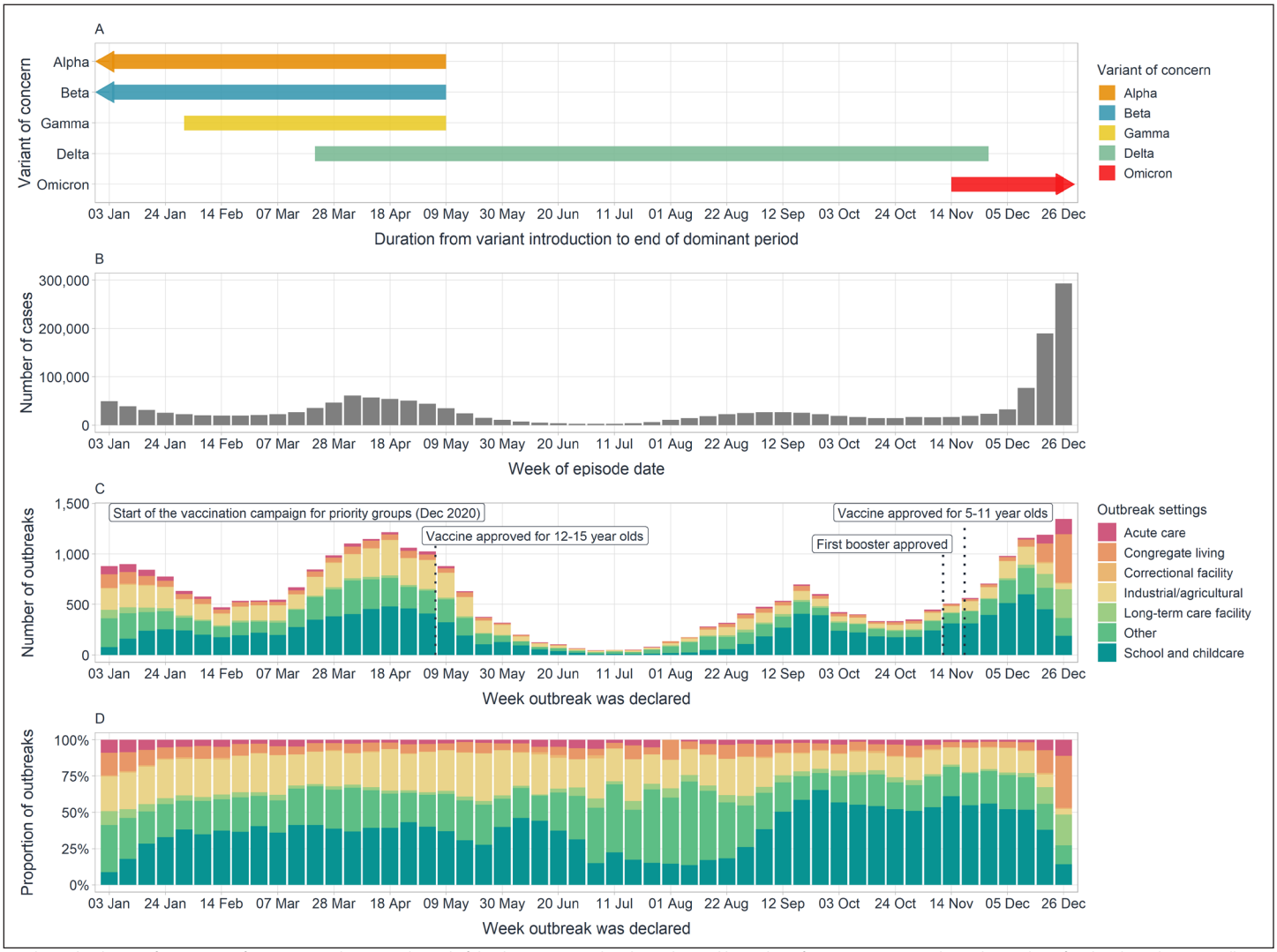
Outbreak trends by settings

From January 3, 2021, to January 1, 2022, a total of 30,078 outbreaks were reported to CCOSS from the seven contributing provinces (**Table 2**). Outbreaks were most common in school and childcare settings (39%), followed by industrial/agricultural settings (21%), congregate living settings (8%), LTCF (4%), acute care facilities (4%), and correctional facilities (1%). Twenty-four percent of outbreaks occurred in "other" settings. In Canada, schools are in session from January to June and September to mid-December, and during these periods, school and childcare settings consistently accounted for the largest weekly proportion of outbreaks (**Figure 1**). This was especially evident from September to December 2021, when children younger than 12 years of age were not yet eligible for COVID-19 vaccination; the proportion of outbreaks with vaccine-eligible populations was smaller during fall of 2021. In school and childcare settings, primary schools accounted for the largest proportion of outbreaks, followed by childcare centres, K–12 schools (combined primary and secondary schools), and secondary schools. In the "other" setting, outbreaks occurring in workplaces of an unspecified type accounted for the largest proportion of outbreaks (**Figure 2**). In congregate living settings, retirement residences and assisted living/group homes accounted for the largest proportion of outbreaks.

Table 2: Number and proportion of outbreaks, outbreak-associated cases, hospitalizations, deaths, and summary statistics of outbreak size by setting

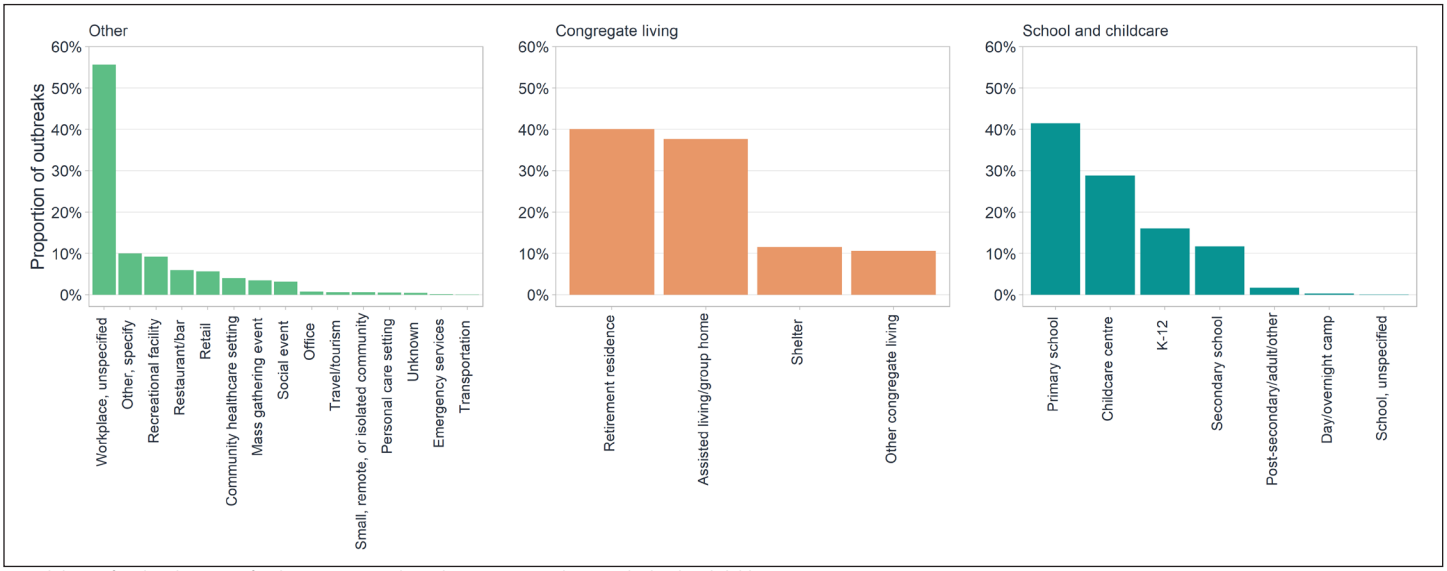
Setting	Outbreaks n=30,078		Cases n=241,335		Hospitalizations n=10,252		Deaths n=3,988		Median size	
	n	%	n	%	n	%	n	%	n	Range
School and childcare	11,699	39	73,311	30	294	3	7	<1	4	2–236
Other	7,069	24	39,912	17	1,031	10	157	4	3	2–364
Industrial/agricultural	6,262	21	38,777	16	939	9	103	3	3	2–300
Congregate living setting	2,508	8	34,641	14	2,960	29	1,098	28	6	2–374
Long-term care facility	1,267	4	34,703	14	885	9	1,554	39	10	2–342
Acute care	1,120	4	12,051	5	4,073	40	1,061	27	7	2–112
Correctional facility	153	1	7,940	3	70	1	8	<1	18	2–639

Figure 1: The evolution of COVID-19 trends from January 3, 2021, to January 1, 2022[a]



[a] A shows the duration from variant of concern introduction to the end of the dominant period, B shows the weekly number of COVID-19 cases, C shows the number of outbreaks and vaccine rollout timelines and D shows the proportion of outbreaks

Figure 2: Proportion of outbreaks for specific settings[a], January 3, 2021, to January 1, 2022



[a] Breakdown of outbreak settings for those categorized as other, congregate living and school and childcare settings

Temporal outbreak trends

The incidence of outbreaks followed similar trends in reported cases (Figure 1). Waves denoting increasing and decreasing rates of declared outbreaks were largely driven by the introductions of VOCs and the subsequent stabilization of transmission within Canada. The increase in outbreaks in March 2021 was heavily driven by the Alpha variant, although there were also outbreaks involving Beta and Gamma variants. The Delta variant drove the resurgence in the incidence of outbreaks in August 2021, which peaked in late September 2021. The introduction of the Omicron variant in November 2021 led to a significant increase in the incidence of outbreaks but was not proportional to the magnitude of the increase observed in case incidence.

Outbreak trends by case characteristics

A total of 241,335 outbreak-associated cases were reported to CCOSS between January 3, 2021, and January 1, 2022 (Table 2). The distribution of cases by setting was similar to trends in outbreak incidence, with most cases reported in school and childcare settings (30%). Most outbreak-associated hospitalizations were associated with acute care facilities (40%) or congregate living setting (29%) outbreaks. The highest proportions of outbreak-associated deaths were in LTCF (39%), congregate living settings (28%) and acute care facilities (27%). The highest outbreak case fatality was in acute care facilities, with a mean case fatality of 10.7%, followed by LTCF (4.3%) and congregate living settings (2.9%).

The size of outbreaks ranged from 2 to 639 cases per outbreak with a median of four cases per outbreak (Table 2). Correctional facilities (18 cases per outbreak) had the highest median outbreak size followed by LTCF (10 cases per outbreak), acute care facilities (seven cases per outbreak) and congregate living settings (six cases per outbreak). **Figure 3** shows that the largest outbreaks were reported in correctional facilities, with more than 18% of outbreaks reporting more than 100 cases, followed by LTCFs (6%).

Within LTCF, there was a sharp decline in the incidence of outbreak-associated deaths in January 2021 shortly after the COVID-19 vaccine rollout began, for which LTCF was one of the priority settings (**Figure 4**). Subsequently, incidence of outbreak-associated deaths remained low and relatively stable until the introduction of the Omicron variant in late 2021 which resulted in a rapid increase in cases and deaths (Figure 1, Figure 4).

Figure 3: Proportion of outbreaks by outbreak size and setting

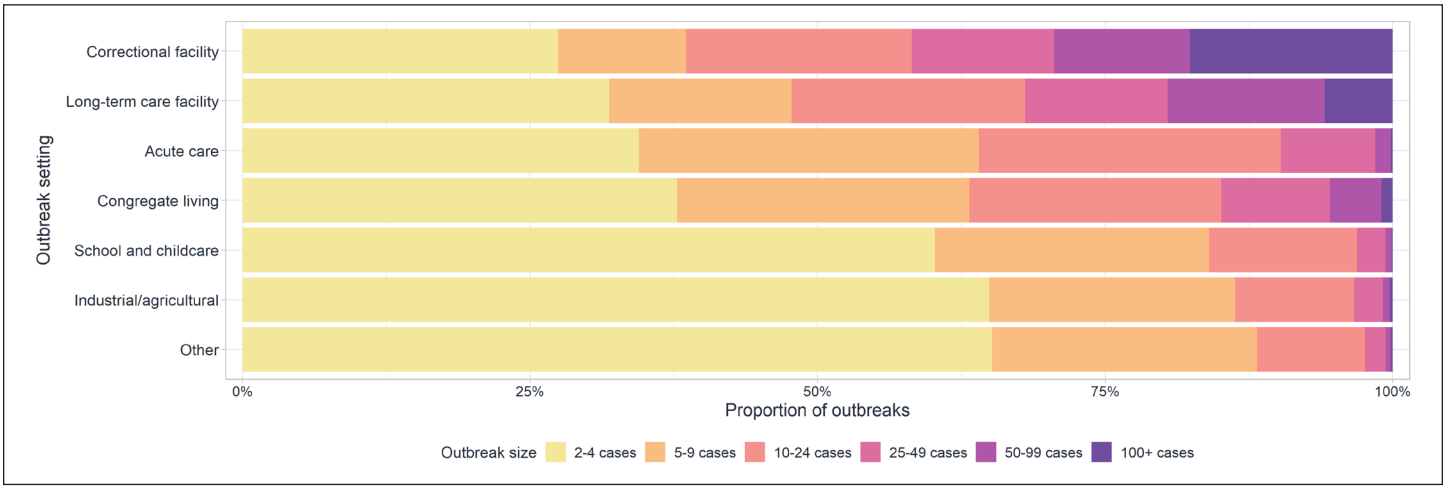
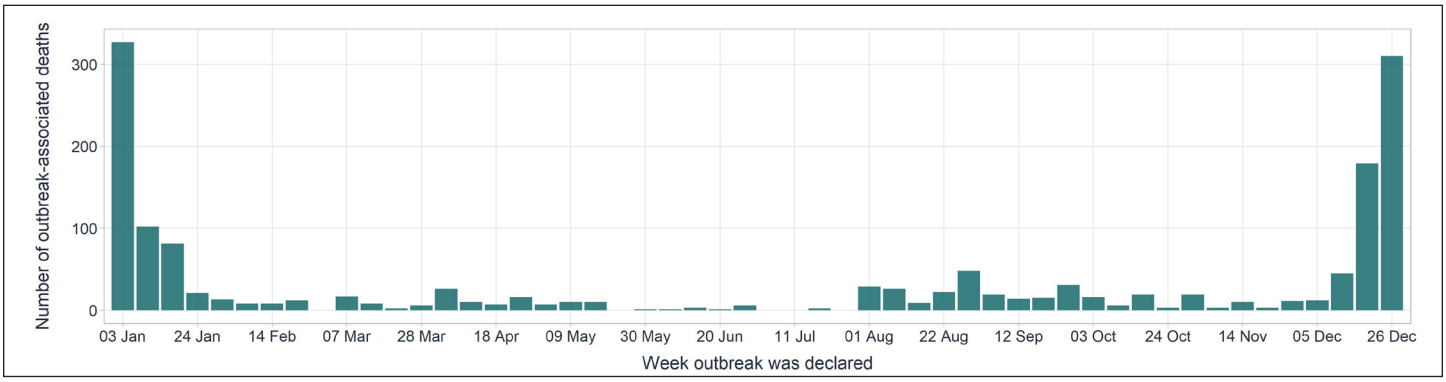


Figure 4: Weekly number of long-term care facility outbreak-associated deaths, January 3, 2021, to January 1, 2022



Discussion

In 2021, 30,078 outbreaks were reported to CCOSS, with the highest proportions being in school and childcare, industrial/agricultural and congregate living settings. Temporal trends for outbreak and case incidence generally aligned; however, a larger relative increase was noted in cases compared to outbreaks in December 2021, following the introduction of the Omicron variant. Settings that experienced the highest severity were acute care and LTCF. The largest outbreaks were reported in correctional facilities and LTCFs, both of which are congregate living settings.

In 2021, the majority of outbreaks reported to CCOSS were in settings considered to be essential services and functions (15,16). The most reported setting was school and childcare settings (39%). There are approximately 15,500 schools in Canada (17), representing almost 5.7 million students (18) and 766,200 educators (17) resulting in a large population at risk. During the Delta-driven resurgence of cases from September to November 2021, when those under 12 years of age were not yet eligible for COVID-19 vaccinations, primary schools experienced the largest increase in the incidence of outbreaks relative to other settings (19). Despite their large representation, the size of school and childcare outbreaks remained small compared to other settings, with 60% of outbreaks reporting fewer than four cases; severity in this setting remained low throughout 2021, which is consistent with what has been reported in the literature (20,21). Studies conducted globally reported similar findings, whereby outbreak cases were small and transmission risk was low when public health measures were in place (e.g. masking, vaccination, cohorting, physical distancing, screening, testing) (22,23).

The second most reported outbreak setting was "other," which consists of multiple settings aggregated for reporting purposes. "Unspecified workplaces" accounted for the majority of outbreaks in "other" settings. The remaining settings included restaurants, bars, retail and recreational facilities. Outbreak trends in these settings often follow case incidence trends and can contribute to community transmission given the potential for exposure from multiple networks (24,25). However, the reported outbreaks in these settings were lower than may have been expected, potentially as a result of extended lockdown orders for nonessential settings through the course of 2021 and/or lower levels of symptom surveillance and testing compared to essential and high-risk settings (25,26).

Although the incidence of outbreaks was highest in community-type settings (e.g. schools, retail, restaurants), outbreak size was the largest in settings with congregate living, likely due to the communal nature of these settings (9). Larger outbreak sizes may reflect increased transmissibility in high-risk populations, configuration of settings (e.g. shared bedrooms, communal areas), population dynamics (e.g. rotating staff, transient population, visitors) and outbreak management strategies (e.g. case cohorting, inability to vacate populations) within those settings. Attack rates in dormitories and shelters, both congregate settings, ranged from 1.9%–41.7% (27,28). Denominators were not available for outbreaks submitted to CCOSS; however, high case counts in congregate settings such as retirement residences and shelters suggest attack rates may have been high.

Industrial/agricultural outbreaks accounted for the third-largest proportion of outbreaks (21%). Early in the pandemic, several large outbreaks were reported in industrial/agricultural settings (e.g. meat processing facilities, oil refineries, warehouses), many of which involved temporary foreign workers, immigrant populations and rotational workers (29–34). Poor ventilation, difficulties maintaining physical distancing, shared transportation and housing, lack of paid sick leave and the rotational nature of the work can lead to rapid transmission of SARS-CoV-2 in certain industrial/agricultural settings—often overlapping with wider marginalized employee populations (35,36). Additionally, many industrial and/or work camp settings involve workers from jurisdictions across Canada, which creates an elevated risk of importation of COVID-19 into the workplace, as well as back into communities in various parts of the country as workers return following rotations. Following broader vaccination rollout in May 2021, including mandatory vaccine policies in some settings, there was a dramatic reduction in the incidence of outbreaks in industrial/agricultural settings; however, this may have been in part due to revised testing strategies and outbreak management. Incidence remained relatively low until the introduction of the Omicron variant in November, which has been shown to escape immunity (37). The case fatality in this setting was 0.2%, though this could be biased by the healthy worker effect (38).

The LTCF are settings that experienced devastating impacts as a result of COVID-19 outbreaks (39,40). In Canada, 80% of COVID-19 deaths during the first pandemic wave occurred in LTCF, when COVID-19 vaccines were not yet available (40). In November 2020, the National Advisory Committee on Immunization (NACI) recommended that the first stage of the COVID-19 vaccine rollout be prioritized to residents and staff of LTCF, among other high-risk settings such as retirement residences and acute care facilities (41). Jurisdictions across Canada reported high vaccine uptake among this population (42–45). As vaccine coverage increased among the LTCF population in early 2021, there was a notable and rapid decrease in the incidence of COVID-19 deaths in this setting, aligning with evidence demonstrating vaccine protection against severe outcomes (46–48). In December 2021, we observed an increase in the incidence of deaths associated with outbreaks in LTCF, reflecting evidence of a shift in the immunity profile following the introduction of the immuno-evasive Omicron variant in fall of 2021 (49).

Outbreaks can result in high morbidity and mortality—adding strain to the healthcare system in addition to individual suffering (50). For COVID-19, the following populations have been identified as higher risk for severe outcomes: older adults (especially those living in congregate settings); people with medical conditions; pregnant people; and communities that experience disproportionate burdens of disease (People of Colour, Indigenous Peoples, refugee populations) (51). However, details on communities disproportionately impacted by COVID-19 were not available through CCOSS or case data. Within the CCOSS data, congregate living settings and LTCF experienced high case burdens; however, acute care settings had the highest case fatality (10.7%). The highest numbers of deaths were reported in LTCF, followed by congregate living settings and acute care facilities. Other countries, such as France, the United Kingdom, Belgium and Australia, have also noted severe outcomes in these high-risk populations (52). Mortality rates in LTCF have been higher than those of older adults in community dwellings (53). An international review found that 19%–72% of deaths during the pandemic occurred in LTCF (52). High mortality in acute care settings may be due to patients having comorbidities that impacted their clinical outcome (54). Approximately 90% of deaths in acute care outbreaks were among individuals older than 60 years of age (54). Interpreting severity for acute care is challenging, as individuals are already hospitalized and death rates may be influenced by underlying health conditions. Similarly, residents of LTCF who become ill have access to care in the facility rather than being hospitalized, complicating the interpretation of nonfatal severity outcomes in this setting. Continuing to monitor COVID-19 outbreaks in LTCF and acute care settings is recommended and aligns with current surveillance practices for other respiratory viruses (e.g. influenza).

Strengths

The CCOSS was rapidly and effectively implemented as a novel initiative in collaboration with federal, provincial and territorial partners in the middle of an emerging infectious disease emergency. PHAC recently conducted an evaluation of CCOSS and found that the surveillance system had good representation, with participating jurisdictions representing 93% of the Canadian population (5). Data providers consistently submitted outbreak line lists to CCOSS on a weekly basis and as a result, data were very timely. The system is flexible and was able to adapt to the needs of jurisdictions (e.g. multiple methods of data sharing, file types) and changes to data elements and format. Additionally, data were mapped to CCOSS variables by PHAC, which reduced reporting burden on provinces and improved acceptability. Outbreak data from CCOSS can also be linked to case data from the National COVID-19 Case Dataset to obtain information on outbreak-associated cases which further reduced reporting burden for certain jurisdictions, although linkage was not possible for all participating provinces. Variable completeness was excellent for the basic variables (i.e. outbreak identifier, setting, start date, number of cases) required for describing outbreak trends.

The CCOSS processes were efficient, which allowed for the timely dissemination of trends from CCOSS to various audiences in its short weekly surveillance cycle. Outbreak trend data, including outbreak setting, outbreak size and severity, have been used by the Office of the Chief Public Health Officer to provide context to the case incidence and for epidemic planning and modelling (55). The outbreak data collected from CCOSS has helped inform decisions by NACI around additional vaccine doses for LTCF residents. Epidemiologists from PHAC examined LTCF outbreak trends for several months following the implementation of the second dose of vaccine in LTCF residents (i.e. June to September 2021) to identify any increases in the incidence and size of outbreaks that could indicate waning immunity and the need for an additional vaccine dose.

Outbreaks have not been experienced equally across Canada. Smaller provinces and territories experienced fewer and less varied types of outbreaks compared with more densely populated provinces with large urban centres and/or concentrations of large industrial operations. Field epidemiologists mobilized to assist with the control and investigation of COVID-19 outbreaks in some provinces and territories, and used nationally aggregated outbreak statistics in the context of public health measures to make recommendations suitable to novel yet similar contexts.

Limitations

The accuracy and validity of the data reported to CCOSS by provinces for each outbreak setting are unknown and dependent on public health capacity to identify cases, contact trace, and establish epidemiological links. During periods of high case incidence, outbreaks may be under-ascertained due to limited public health capacity, or where high-risk settings were prioritized for testing. Outbreak size was underestimated in certain settings such as industrial settings, correctional facilities and acute care, where separate outbreaks were administratively recorded by smaller groupings for public health management (e.g. by floor, units, or another identifier). Furthermore, enhanced outbreak management implemented by some jurisdictions during periods with high surges in cases (i.e. the introduction of the Omicron variant) may impact the incidence of outbreaks reported, outbreak size and outbreak declared/end dates.

Only seven provinces of 13 provinces/territories were included in this analysis. The national outbreak analysis presented in this report was highly influenced by three of the most populous provinces in Canada (ON, QC and AB), which submitted the highest number of outbreaks (99%) and covered the greatest number of outbreak settings. Smaller participating jurisdictions and non-participating provincial and territorial jurisdictions may experience outbreak trends that differ from the national picture presented here, which was heavily influenced by the more populous provinces.

In October 2021, AB changed their outbreak definition to between two and 10 cases for certain settings (56). This would have led to an underreporting of smaller outbreaks in these settings and biased the outbreak size towards larger outbreaks.

Denominators for a number of facilities within a province or health region were not available, and even if they were, it would be difficult to identify how many facilities were affected by outbreaks since some facilities might report multiple outbreaks over time or report outbreaks by units/floors/classes, etc. The lack of denominators by setting and population at risk made it impossible to calculate attack rates for a setting or within a facility.

The data mapping of "workplace unspecified" to industrial/agricultural for jurisdictions that did not report on industrial settings separately may have contributed to non-industrial/agricultural workplaces being included. This could have contributed to an artificial increase in the number of outbreaks reported in this setting.

Conclusion

Nationally aggregated provincial outbreak data permitted trend and additional descriptive analyses to inform our understanding of where COVID-19 outbreaks occur in Canada and support ongoing efforts to reduce transmission in high-risk settings. Outbreak trends illustrated that outbreaks were reported more frequently in certain settings, specifically schools and workplaces; however, congregate living settings were prone to larger outbreaks and acute care settings experienced the highest case fatality. The information gathered from outbreak surveillance complemented case incidence trends and furthered understanding of COVID-19 in Canada. Monitoring COVID-19 outbreaks in high-risk settings such as LTCF, acute care and congregate living aligns with current surveillance practices for other respiratory viruses and continues to be a priority.

Authors' statement

DD — Conceptualization, methodology, software, formal analysis, writing–original draft, writing–review and editing, visualization
EM — Conceptualization, methodology, writing–original draft, writing–review and editing
AB — Conceptualization, writing–review and editing
CC — Conceptualization, writing–review and editing
JE — Conceptualization, writing–review and editing
RM — Conceptualization, supervision, writing–review and editing
KP — Conceptualization, supervision, writing–review and editing

Competing interests

None.

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National epidemiological analysis of the association of COVID-19 vaccination and incidence of COVID-19 cases in Canada, January to August 2021

Public Health Agency of Canada, COVID-19 Surveillance*, Vaccine Coverage and Information System, Vaccine Effectiveness Surveillance Program, and Public Health Risk Science/National Microbiology Laboratory Teams[1]

Abstract

Background: In December 2020, Canada began its coronavirus disease 2019 (COVID-19) vaccine rollout campaign. Canadians were vaccinated with differing time intervals between doses, vaccine products and vaccine schedules, based on age, timing of vaccination and jurisdiction. The objective of this study is to describe the epidemiology and association between the incidence of COVID-19 cases following vaccination, time since completion of primary series, time between doses and/or product combination and probability of developing severe outcomes.

Methods: The national COVID-19 case data and vaccination coverage data were extracted from the National COVID-19 Surveillance System, and the Canadian COVID-19 Vaccination Coverage Surveillance System. Population estimates from Statistics Canada were used as denominators for rates and for number of people "not fully vaccinated". Two binomial generalized linear models were constructed for analysis.

Results: Within the analysis period, fully vaccinated (i.e. completed primary series) cases (n=17,206) were more commonly female and older, and had fewer reported severe outcomes relative to not fully vaccinated cases (n=615,999). Episode date of fully vaccinated cases most frequently occurred two months after receiving their second dose, and time-between doses of 29–49 and 50–77 days were most common. The probability of becoming a detected COVID-19 case in not fully vaccinated individuals was higher than those fully vaccinated. Those receiving two doses of AstraZeneca and those with shortest time intervals between doses had higher probabilities of becoming COVID-19 cases.

Conclusion: Findings from Canada's national surveillance systems support that being fully vaccinated against COVID-19, having a longer time interval between doses and receiving a messenger ribonucleic acid (mRNA) COVID-19 vaccine schedule compared to other vaccines reduce the probability of becoming a case, using data from January to August 2021.

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Introduction

On January 30, 2020, the World Health Organization (WHO) announced the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (coronavirus disease 2019; COVID-19) outbreak as a Public Health Emergency of International Concern, and a pandemic was declared on March 11, 2020. Since then, the pandemic has resulted in significant morbidity, mortality, and threat to the overall well-being of Canadians (1,2). Individual and collective actions were heavily relied on, while safe and effective vaccines were under development.

On December 14, 2020, Canada began its COVID-19 vaccine rollout campaign against SARS-CoV-2 infection following the approval of Pfizer-BioNTech Comirnaty, Moderna-Spikevax, AstraZeneca Vaxzevria and Janssen Jcovden (Johnson & Johnson) COVID-19 vaccines (3). Due to the anticipated constraints on vaccine supply, initial doses of COVID-19 vaccination were prioritized for key populations. The vaccination campaign began with residents in long-term care facilities, health workers and adults residing in the territories or living in remote and isolated communities. As vaccine supply changed, Canada's National Advisory Committee on Immunization (NACI) COVID-19 vaccination program's recommendations evolved. At the time of interest of this article (January 1 to August 31, 2021, i.e., during the Alpha, Gamma and Delta variants' waves) receiving a second dose of a two-dose vaccine schedule (completing the primary series) was recommended to provide better and longer-term protection against COVID-19 (4). The recommended time interval between doses was extended to four months by March 2021, from the initial recommendation of 21 to 28 days; however, intervals differed across jurisdictions based on their vaccination strategies. Vaccine eligibility expanded and, along with recommendations for extending the time interval between doses, all Canadian residents 12 years of age and older were eligible for a first dose by May 2021 (5–7). In June 2021, NACI recommended interchangeability of available vaccines and preferential use of messenger ribonucleic acid (mRNA) vaccines to complete primary vaccination series due to the safety concerns that arose with AstraZeneca use (thrombosis with thrombocytopenia) (6). As a result, Canadian residents were vaccinated with differing time intervals between doses, vaccine products and vaccine schedules, based on age, timing of vaccination and Province/Territory (P/T) of residence. A timeline of national recommendations is available in **Supplemental material, Figure S1**.

The COVID-19 vaccines have demonstrated high effectiveness against severe outcomes such as hospitalization and death. Assessing the variations in vaccine series and their impact on transmission dynamics within Canada contributes to the growing body of evidence to better define the long-term COVID-19 vaccine performance and future vaccine development policies (8–18).

The objective of this article is to describe the epidemiology and explore the association between the incidence of COVID-19 cases following vaccination and time since completion of primary series. The analysis includes a descriptive summary of vaccination coverage and cases following vaccination, and an analysis model of cases following vaccination to investigate whether time since last dose, time between doses, and/or product combination are associated with becoming a COVID-19 case or developing severe outcomes, following adjustments for relevant covariates.

Methods

Definitions

Based on NACI recommendations during the period of analysis (January 1 to August 31, 2021), vaccination programs prioritized delivery of primary vaccination series, whereby individuals with a completed primary vaccination series were denoted as "fully vaccinated". As Canadian vaccination programs evolved in the latter half of 2021, with the rollout of additional and booster doses, the following definitions reflect the vaccine rollout up to August 2021 focusing on primary series completion.

For this analysis, vaccination status of laboratory-confirmed cases was only based on approved vaccines for use by Health Canada for the period of analysis [Pfizer-BioNTech Comirnaty (Pfizer); Moderna Spikevax (Moderna); AstraZeneca Vaxzevria or COVISHIELD (AstraZeneca)] and was defined in the following categories:

- "Fully vaccinated" cases (i.e. case with a complete primary series): episode date 14 days or more after receipt of the second dose in a two-dose series. For this analysis, only those with a complete primary series are included, as the period of analysis predates the Canadian rollout of additional and booster doses.
- "Not fully vaccinated" cases included the following:
  - Unvaccinated cases included those who were unvaccinated at the time of their episode date.
  - Cases not yet protected from vaccination included those whose episode date occurred less than 14 days after their first vaccine dose.
  - Partially vaccinated cases included those whose episode date occurred 14 days or more after their first vaccine dose or less than 14 days after their second vaccine dose.

Month of last dose refers to the month the second dose of a two-dose COVID-19 vaccine was administered. It was used to calculate the number of months since last dose to infection (based on episode date), referred to in this analysis as "months since last dose".

Episode date was used to temporally classify confirmed cases and refers to symptom onset date. When symptom onset date was unavailable or the case was asymptomatic, episode date refers to either laboratory specimen collection date or laboratory testing date.

Data sources

Vaccination coverage data were obtained from P/T immunization registries through the Canadian COVID-19 Vaccination Coverage Surveillance System. Data aggregated by 10-year age group, sex, month of last dose, vaccine product received (i.e. Pfizer-Pfizer, Moderna-Moderna, AstraZeneca-AstraZeneca, mixed mRNA, AstraZeneca-mRNA) and time interval between doses, which reflected the varying recommendations on dose intervals throughout the period of interest (see Supplemental material, Figure S1) (0–28 days, 29–49 days, 50–77 days, 78 or more days) were only available for individuals fully vaccinated as of August 14, 2021.

The national COVID-19 case data was extracted from the National COVID-19 Case dataset, which includes detailed case-level information received from all P/Ts and is maintained by the Public Health Agency of Canada (PHAC). For this analysis, COVID-19 case data included basic demographic data, episode dates, severe outcomes, vaccine products received and date of vaccination for each dose administered. Twelve out of 13 P/Ts (excluding Québec) reported case-level vaccination data for the analysis period (January 1, 2021, to August 31, 2021), with data extracted from the COVID-19 case dataset on February 18, 2022.

The July 1, 2021, population estimates provided by Statistics Canada for Provinces and Nunavut, and population estimates provided by the Yukon and Northwest Territories governments, were used as the denominator for the vaccination coverage rate and to calculate the number of people not fully vaccinated (19).

Analysis

Laboratory-confirmed cases 12 years and older, with episode dates between January 1, 2021, and August 31, 2021, were included in the analyses (20).

For statistical modelling analyses, cases were aggregated by P/T, age group, sex, vaccination status, and month of episode date. To establish denominators, the coverage data and population estimates were used to determine the number of individuals in each P/T, age group, sex and vaccination status group eligible to become a case each month. Counts of cases were linked to coverage denominators to calculate proportion of individuals that became a COVID-19 case in each aggregate group. Coverage data contained discrete counts of fully vaccinated individuals, meaning vaccination status was classified as either fully vaccinated or not fully vaccinated. Counts of not fully vaccinated individuals were derived by subtracting the number of fully vaccinated from Statistics Canada's population estimates. For modelling analyses of fully vaccinated individuals, cases were stratified and aggregated by vaccine product series, time interval between doses, and number of months since last dose. In the coverage data, individuals were considered fully vaccinated on the month they completed their primary vaccination series. With respect to number of months since last dose, fully vaccinated individuals were assigned a value of zero months during this month of series completion.

Cases with missing or invalid vaccination date or product, demographic data (age and sex), or episode date were excluded from the analysis (fewer than 0.5% of cases). To align COVID-19 case data with the coverage dataset, cases that received more than two doses of a COVID-19 vaccine, the Janssen COVID-19 vaccine, or a non-Health Canada authorized COVID-19 vaccine were excluded, along with fully vaccinated cases that completed their primary series after August 14, 2021.

Statistical models

Two binomial generalized linear models were constructed to assess associations between COVID-19 vaccination, vaccination characteristics (i.e. vaccine products received, time interval between doses and time since last dose), and COVID-19 case incidence. In each model, the main response variable was the proportion of individuals that became COVID-19 cases in a month, among their respective cohort. The total number of individuals in each aggregate group was included as weights in the models, and all predictor variables were included as categorical variables. Atlantic Provinces (Newfoundland and Labrador, New Brunswick, Prince Edward Island and Nova Scotia) were grouped as an "Atlantic" jurisdiction, while all Territories were excluded due to low case counts.

A main model (model 1) was fit to data aggregated by jurisdiction, age group, sex, month of episode date and vaccination status. A second model (model 2) was fit to only fully vaccinated groups, aggregated by jurisdiction, age group, sex, month of episode date, vaccine product series, time interval between doses and month of last dose. The variables used to aggregate data were included as predictor variables in each model.

Using both fit models, predicted effects of each level of each variable were calculated. When calculating the effect of a level, all other variable levels were controlled at their average value. For each level, point estimates and 95% confidence intervals were generated for the probability of an individual becoming a detected COVID-19 case. Variable-level p values were calculated to assess statistical significance of all predictor variables.

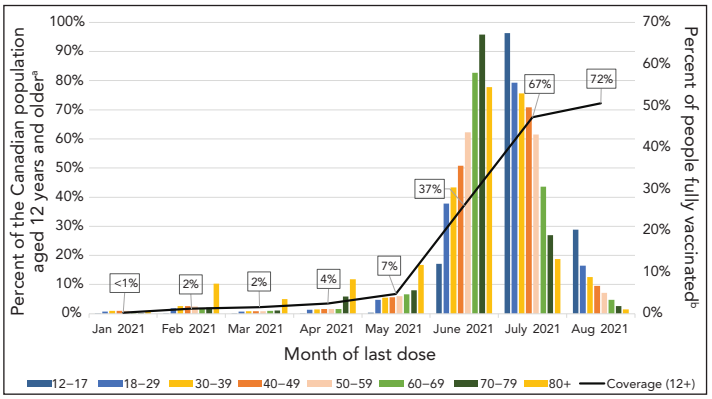
Data cleaning, manipulation, and visualizations were performed in Excel MS Office and SAS V9.4. Statistical analyses were performed in R version 4.0.2.

Results

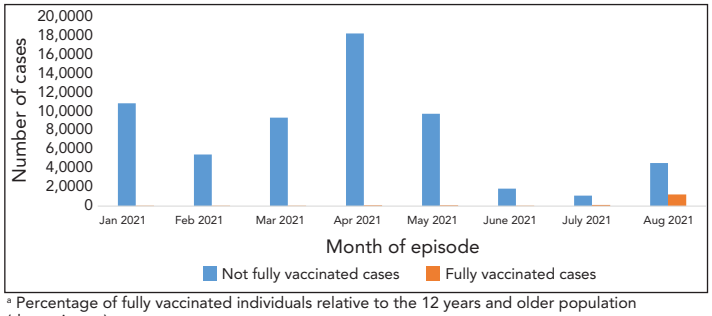
As of August 14, 2021, 72% (n=24,209,666) of individuals 12 years of age and older were fully vaccinated in Canada. Of these, 9% completed their primary series between January and May 2021, and 84% completed their primary series between June and July 2021, given the vaccine rollout in Canada. Among those 50 years of age and older who were fully vaccinated, most completed their series in June 2021 (ranging from 44% in those aged 50–59 years to 67% in those aged 70–79 years). The majority of younger age groups who completed their primary series did so in July 2021 (ranging from 50% in those aged 40–49 years to 67% in those aged 12–17 years) (**Figure 1**).

Figure 1: (A) Percent of people fully vaccinated by month of last dose[a,b] and (B) confirmed cases[c] in Canada, January to August 2021

(A)



(B)



[a] Percentage of fully vaccinated individuals relative to the 12 years and older population (denominator)
[b] Percent distribution of fully vaccinated individuals within each age group, by month of last dose (denominator is fully vaccinated individuals within each age group)
[c] By month of episode and vaccination status

Across jurisdictions, those in the Territories completed their series earlier than those in the Provinces. Among the Territories, 62% to 75% of those aged 12 years and older completed their primary series by April 2021, compared to 2% to 11% among the Provinces (Supplemental material, **Figure S2**).

There were 633,205 confirmed cases of COVID-19 reported to the national COVID-19 case dataset with episode dates between January 1, 2021, and August 31, 2021, that met analysis inclusion criteria. Of these, 17,206 (2.8%) cases were fully vaccinated at episode date, compared to 615,999 (97.2%) not fully vaccinated at episode date (**Table 1**). See Supplemental material **Figure S3** for description of case population for analysis. As vaccine campaigns prioritized key populations, including long-term care facility residents, healthcare workers and older adults by decreasing age over time, fully vaccinated cases were older (median age of 45 years compared to 37 years among not fully vaccinated cases) and more commonly female than for the not fully vaccinated cases. The majority of not fully vaccinated cases occurred in April 2021 (n=183,085; 29.7%), while most fully vaccinated cases occurred in August 2021 (n=12,642; 73.5%; Figure 1). There were fewer hospitalizations and deaths reported among fully vaccinated cases compared to not fully vaccinated cases during the period of analysis (Table 1). See Supplemental material **Table S1** for number and percent of those 12 years of age and older who were fully vaccinated by jurisdiction, age group and sex in Canada.

Table 1: Descriptive table of national COVID-19 cases in Canada between January 1, 2021, and August 31, 2021

Characteristics	Total (n=633,205)				
	"Not fully vaccinated" cases (n=615,999)		"Fully vaccinated" cases (n=17,206)		Total cases, n
	n	%	n	%	
Age group (years)					
12–17	49,733	8.1%	275	1.6%	50,008
18–29	171,734	27.9%	3,533	20.5%	175,267
30–39	121,332	19.7%	3,194	18.6%	124,526
40–49	98,259	16.0%	2,829	16.4%	101,088
50–59	85,091	13.8%	2,504	14.6%	87,595
60–69	50,873	8.3%	2,136	12.4%	53,009
70–79	23,039	3.7%	1,220	7.1%	24,259
80 and older	15,938	2.6%	1,515	8.8%	17,453
Sex					
Male	314,935	51.1%	7,185	41.8%	322,120
Female	301,064	48.9%	10,021	58.2%	311,085
Month of episode					
January	109,387	17.8%	6	0.0%	109,393
February	54,899	8.9%	87	0.5%	54,986
March	94,244	15.3%	319	1.8%	94,543
April	183,085	29.7%	1,022	5.9%	184,107
May	98,459	16.0%	1,119	6.5%	99,578
June	18,782	3.0%	574	3.3%	19,356
July	11,411	1.8%	1,437	8.4%	12,848
August	45,752	7.4%	12,642	73.5%	58,394
Province/Territory					
British Columbia	98,201	15.9%	3,575	20.8%	101,776
Alberta	125,909	20.4%	5,425	31.5%	131,334

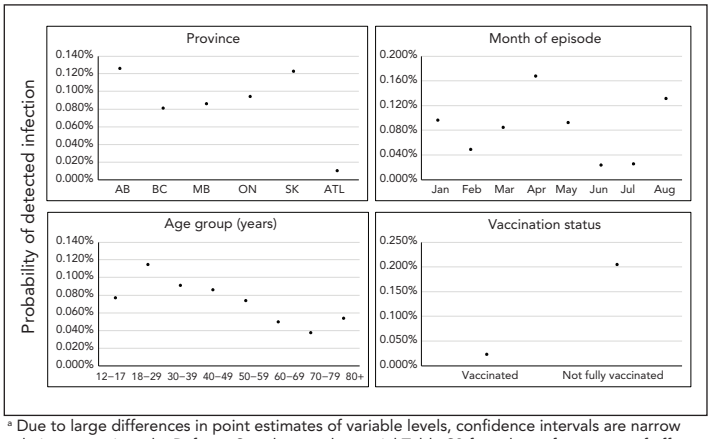
Table 1: Descriptive table of national COVID-19 cases in Canada between January 1, 2021, and August 31, 2021 (*continued*)

Characteristics	Total (n=633,205)				
	"Not fully vaccinated" cases (n=615,999)		"Fully vaccinated" cases (n=17,206)		Total cases, n
	n	%	n	%	
Province/Territory (*continued*)					
Saskatchewan	32,072	5.2%	1,330	7.7%	33,402
Manitoba	26,296	4.3%	607	3.5%	26,903
Ontario	326,645	53.0%	5,923	34.4%	332,568
Atlantic	6,009	1.0%	142	0.8%	6,151
New Brunswick	1,115	0.2%	37	0.2%	1,152
Nova Scotia	3,783	0.6%	72	0.4%	3,855
Newfoundland and Labrador	993	0.2%	25	0.1%	1,018
Prince Edward Island	118	0.0%	8	0.0%	126
Territories	867	0.1%	204	1.2%	1,071
Yukon	441	0.1%	88	0.5%	529
Northwest Territories	213	0.0%	111	0.6%	324
Nunavut	213	0.0%	5	0.0%	218
Severe outcome					
Hospitalization	33,523	5.4%	809	4.7%	34,332
Mortality	6,353	1.0%	272	1.6%	6,625
Months since last dose[a]					
0 months	N/A	N/A	449	2.6%	449
1 month	N/A	N/A	4,564	26.5%	4,564
2 months	N/A	N/A	7,002	40.7%	7,002
3 months	N/A	N/A	1,994	11.6%	1,994
4 months	N/A	N/A	1,173	6.8%	1,173
5 months	N/A	N/A	623	3.6%	623
6 months	N/A	N/A	1,190	6.9%	1,19
7 months	N/A	N/A	211	1.2%	211
Time interval between doses[a]					
0–28 days	N/A	N/A	3,192	18.6%	3,192
29–49 days	N/A	N/A	6,313	36.7%	6,313
50–77 days	N/A	N/A	5,967	34.7%	5,967
78 or more days	N/A	N/A	1,734	10.1%	1,734

Abbreviation: N/A, not applicable
[a] Data on time since primary series completion, and time interval between doses are only available for fully vaccinated cases

The most common vaccine schedule to complete primary series was the Pfizer-Pfizer (63.2%), followed by the Moderna-Moderna (17.5%). Among fully vaccinated cases, the majority received two doses of Pfizer-Pfizer vaccine (n=11,608; 67.5%). Episode date of fully vaccinated cases was most frequent two months after receiving their second dose to complete primary vaccination series (n=7,002; 40.7%), and time-between doses of 29–49 days (n=6,313; 36.7%) and 50–77 days (n=5,967; 34.7%) were most common. See Supplemental material **Table S2** for number and percent of those 12 years of age and older who were fully vaccinated, by dose interval, month of last dose and vaccine schedule in Canada, as of August 14, 2021. From model 1, variable-level *p* values indicated statistical significance at $p<0.001$ for all predictor variables except sex ($p=0.18$; Supplemental material **Table S3**; see Supplemental material **Figure S4** for predicted effects of sex). Predicted effects demonstrated that the probability of becoming a detected COVID-19 case was higher among not fully vaccinated individuals than fully vaccinated individuals, after adjustment for P/T, age, sex and month of episode date (**Figure 2**). The probability of becoming a detected COVID-19 case of a not fully vaccinated individual was estimated to be 0.204% (95% CI, 0.203–0.206; Supplemental material Table S3). Comparatively, the estimated probability for a fully vaccinated individual was 0.023% (95% CI, 0.023–0.024).

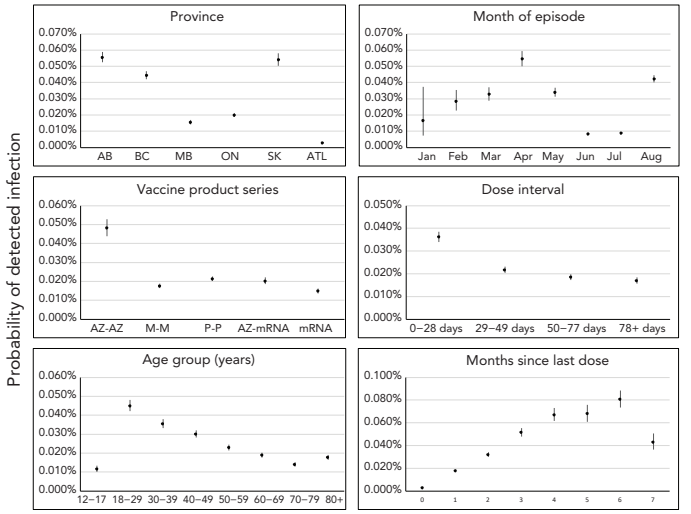
Figure 2: The effect of covariates included in model 1 on predicted probability of an individual becoming a detected COVID-19 case[a,b]



[a] Due to large differences in point estimates of variable levels, confidence intervals are narrow relative to y-axis scale. Refer to Supplemental material Table S3 for values of measures of effect and confidence intervals
[b] Solid points and vertical solid lines show the effect and 95% prediction interval, where visible. Covariates where effects did not differ significantly among levels (only sex) are not shown

From model 2, variable-level *p* values indicated statistical significance at $p<0.001$ for all predictor variables except sex ($p=0.22$; Supplemental material **Table S4**). Predicted effects demonstrated that, after controlling for predictor variables, fully vaccinated individuals receiving two doses of AstraZeneca and fully vaccinated individuals with the shortest time interval between doses (0–28 days) had higher probabilities of becoming a detected COVID-19 case, compared to individuals receiving other vaccine series and time interval between doses, respectively (**Figure 3**). Overall, there is a clear signal of increasing probability in becoming a detected case as time since primary series completion increased from zero to six months (Figure 3).

Figure 3: The effect of covariates included in model 2 on predicted probability of "fully vaccinated" individuals becoming a detected COVID-19 case[a]



Abbreviations: AB, Alberta; ATL, Atlantic; AZ-mRNA, AstraZeneca-messenger ribonucleic acid; AZ-AZ, AstraZeneca-AstraZeneca; BC, British Columbia; MB, Manitoba; M-M, Moderna-Moderna; mRNA, messenger ribonucleic acid; ON, Ontario; P-P, PfizerPfizer

[a] Solid points and vertical solid lines show the effect and 95% prediction interval, where visible. Covariates where effects did not differ significantly among levels (only sex) are not shown. Refer to Supplemental material Table S4 for values of measures of effect and confidence intervals

Discussion

Key results

At the national level, the results demonstrate that the majority of fully vaccinated 12-year-olds and older completed their series between June and July 2021, with most 50-year-olds and older completing their series in June and those 12–49-year-olds in July. Additionally, cases residing in the Territories completed their series earlier than those residing in Provinces. These observations coincide with the Canada's vaccine rollout program, which initially targeted the oldest age demographics, high-risk populations and adults residing in the Territories or living in remote and isolated communities. As vaccine eligibility expanded over time with decreasing age, Canadian residents 12 years of age and older were eligible for a first dose by May 2021 (5). These results highlighted that the majority of not fully vaccinated cases occurred in April 2021. This is consistent with the timing of the third wave of COVID-19 cases driven by the Alpha variant, as well as the lower vaccination coverage for those 12-year-olds and older (only 4% of this age group was fully vaccinated at the time). The first vaccine dose was being rolled out and eligibility was in the midst of expanding, resulting in lower number of individuals protected against COVID-19 at this time (21–23). Of the cases that met analysis criteria, not fully vaccinated individuals had higher case probability compared to fully vaccinated, consistent with international analyses (15,24,25). Fully vaccinated cases were more likely to be female and older than not fully vaccinated, as vaccine eligibility initially targeted older populations and people working in healthcare settings—where females are outnumbered (26,27).

This analysis further investigated vaccine programmatic factors and whether time since last dose, time interval between doses and/or product combination are associated with becoming a COVID-19 case. Among fully vaccinated individuals, those with a shorter time interval between doses (0–28 days), those receiving two doses of AstraZeneca and those with increased time since last dose from zero to six months, had an elevated probability of becoming a COVID-19 case. Individuals who were vaccinated seven months after their last dose had a lower probability of becoming a case; however, results must be interpreted with caution as the cohort of individuals eligible to become a case seven months after series completion was small (n=211, August 2021), due to the length of the analytic period.

Comparison

Studies suggest that age (6,9–14,16,24,25,28–31), type of vaccine products used (6,10,12,14,16,24,25,29,31,32), time interval between doses, time since last dose (6,9,11–16,18,25,28–34), vaccination status (8,12,24,25,29,31) and predominance of emerging and evolving variants (9,15,25,31,33) may impact the duration of protection against COVID-19 and its severity (6,8–16). This national analysis is consistent with analyses performed interprovincially and internationally, supporting that vaccine effectiveness against infection decreased across all age groups one to six months after full vaccination (12). Results suggest that decreases in vaccine effectiveness may be in part due to waning immunity, as demonstrated by a study conducted in Israel, where those who completed their vaccination series in January and February 2021 were at a 2.26-fold increased risk of developing COVID-19 compared to those who completed their series in March and April 2021 (18). A similar trend was observed in a study conducted in England, where greater waning in vaccine effectiveness was observed among older adults, specifically those 65 years and older, and in those who were clinically vulnerable (6). Canadian studies conducted in Ontario, British Columbia and Québec highlighted vaccine effectiveness against infection was greater with an mRNA containing schedule compared to two doses of AstraZeneca Vaxzevria vaccine (31,35). As for the time interval between doses, studies conducted in the United States and Israel found that time elapsed between the last dose and becoming a case was significantly longer among those with a longer time interval between doses than those with a time interval less than 90 days, with attenuation increasing by month (28,33).

Strengths and limitations

Given Canada's unique vaccine rollout, this is the first analysis to nationally assess the associations between COVID-19 vaccination status, vaccination characteristics (i.e. vaccine products received, time interval between doses and time since last dose) and case incidence based on these factors. This analysis has high representation across Canada, with 12 of 13 P/Ts providing vaccine information on COVID-19 cases and all P/Ts providing vaccination coverage information; however, variability in reporting across P/Ts may impact interpretation. There are

several limitations to acknowledge in this analysis, one of which is that vaccination data were not available for cases from all P/Ts, which may result in an overgeneralization of national results. The expanding vaccine eligibility criteria in Canada over the analysis period (January to August 2021) also presented additional contextual challenges for the interpretation of results, specifically with varying representativeness of Canadian population through analysis period.

Second, this analysis was notably limited by the vaccination coverage dataset providing only counts of fully vaccinated individuals by month of last dose. As a result, only two vaccination status categories could be analyzed—fully vaccinated and not fully vaccinated individuals—as granularity was lost in this latter unconventional classification group. As partial vaccination has demonstrated to reduce the risk of SARS-CoV-2 infection, the inclusion of partially vaccinated individuals in the not fully vaccinated group may impact the estimated effects when comparing by vaccination status (36–38). Counts by month of last dose also prevented analyses from precisely accounting for the 14 days to achieve full-vaccination protection in the coverage dataset. Individuals were considered fully vaccinated the month they received their last dose, inflating fully vaccinated coverage estimates for this month (zero months since last dose) and to a lesser extent the following month.

Additionally, this analysis included only cases from the eight-month period following the beginning of vaccine rollout in Canada, limiting the generalizability and size of fully vaccinated coverage groups with longer months since last dose. The limited period of analysis also prevented assessment of severe outcomes, as hospitalizations among fully vaccinated cases were infrequent (n=809) and insufficient for the stratification required for model building.

Lastly, this analysis did not explicitly investigate impacts by public health measures and variants due to limited cases with whole genome sequencing. The period of analysis was performed during the Alpha and Delta waves, which are not explicit effect modifiers on vaccine breakthrough and vaccine effectiveness, as several studies have suggested that vaccine effectiveness and viral burden were reduced with Delta circulation (6,11,25,30).

Interpretation and generalizability

The jurisdictions included in the generalized linear models represent 77% of the Canadian population (9/13 P/Ts) and the jurisdictions included in the descriptive analysis represent 78% of the Canadian population (12/13 P/Ts). Vaccination program rollout and vaccine availability varied across P/Ts and over time; therefore, interpretation at the national level should be done with caution.

Conclusion

Findings from Canada's national surveillance systems support that being fully vaccinated against COVID-19, a longer time interval between doses and mRNA COVID-19 vaccines schedule reduce the probability of becoming a COVID-19 case following vaccination. National analyses inform guidance on booster doses and contribute to the growing body of evidence on COVID-19 vaccine performance and vaccine recommendations. Further national analysis on variants, severe outcomes and public health measures may strengthen vaccine effectiveness research and recommendations.

Authors' statement

SB — Model analysis lead, data curation, formal analysis, review and editing
BHMF — Formal analysis of vaccination coverage datasets, review and editing
JR — Conceptualization and analysis of vaccination coverage datasets and review
SM — Formal analysis of case dataset, review and editing
FB — Formal analysis of case dataset
JM — Original draft, review and editing
NL — Manuscript lead, review and editing
ML — Methodological guidance, review and editing
BC — Literature review
AF — Review and editing
LW — Review and editing

Competing interests

None.

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Supplemental material

These documents can be accessed on the Supplemental material file.

Figure S1: Timeline of relevant vaccine program in Canada for those 12 years of age and older, December 2020 to August 2021
Figure S2: Cumulative percent distribution of "fully vaccinated" individuals by month of last dose and Province/Territory, January 1, 2021 to August 14, 2021
Figure S3: Description of case population for analysis
Table S1: Number and percent of those 12 years of age and older who were "fully vaccinated" by jurisdiction, age group and sex in Canada, as of August 14, 2021
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Extensive SARS-CoV-2 testing reveals BA.1/BA.2 asymptomatic rates and underreporting in school children

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Abstract

Background: Case underreporting during the coronavirus disease 2019 (COVID-19) pandemic has been a major challenge to the planning and evaluation of public health responses. School children were often considered a less vulnerable population and underreporting rates may have been particularly high. In January 2022, the Canadian province of Newfoundland and Labrador (NL) was experiencing an Omicron variant outbreak (BA.1/BA.2 subvariants) and public health officials recommended that all returning students complete two rapid antigen tests (RATs) to be performed three days apart.

Methods: To estimate the prevalence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), we asked parents and guardians to report the results of the RATs completed by K–12 students (approximately 59,000 students) using an online survey.

Results: When comparing the survey responses with the number of cases and tests reported by the NL testing system, we found that one out of every 4.3 (95% CI, 3.1–5.3) positive households were captured by provincial case count, with 5.1% positivity estimated from the RAT results and 1.2% positivity reported by the provincial testing system. Of positive test results, 62.9% (95% CI, 44.3–83.0) were reported for elementary school students, and the remaining 37.1% (95% CI, 22.7–52.9) were reported for junior high and high school students. Asymptomatic infections were 59.8% of the positive cases. Given the low survey participation rate (3.5%), our results may suffer from sample selection biases and should be interpreted with caution.

Conclusion: The underreporting ratio is consistent with ratios calculated from serology data and provides insights into infection prevalence and asymptomatic infections in school children; a currently understudied population.

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Keywords: SARS-CoV-2, COVID-19, testing, asymptomatic, children, underreporting, Newfoundland and Labrador

Introduction

During a pandemic, surveillance is essential for forecasting health care demand and to inform public health decisions. Infection underreporting and inadequate surveillance can lead to unreliable predictions, undermining effective risk assessment (1). Underreporting of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which causes coronavirus disease 2019 (COVID-19), has been a major challenge to the analysis of epidemiological data and the implementation of preventive and control measures (2). During the pandemic, COVID-19 prevalence has been inconsistently underreported for a variety of reasons, including challenges in maintaining a high-testing capacity (3), discouraged testing of non-symptomatic individuals (4) and many mild or asymptomatic infections, particularly in children and youth (5). Challenges to providing accurate COVID-19 case counts have increased throughout the epidemics. Reasons have been the establishment

of more transmissible variants (6), the promotion of self-testing alongside no requirement that these results be reported (7,8) and increased vaccination coverage, decreasing the likelihood of severe outcomes and the resultant need to seek health care (9). All these factors have led to inconsistent variation of case reporting over time, challenging epidemic forecasting.

The Omicron variant of SARS-CoV-2 (formerly BA.1 or B.1.1.529.1, with sister lineage BA.2 or B.1.1.529.2) was first detected in South Africa on November 8, 2021. It was declared a variant of concern by the World Health Organization on November 28, 2021 (10). The Omicron variant spread extremely rapidly around the world. In Canada, the first Omicron variant case was reported in Ontario on November 28, 2021, (11) and in Newfoundland and Labrador (NL), the first Omicron variant case was reported on December 15, 2022 (12). Before the spread of the Omicron variant, there was only limited spread of SARS-CoV-2 in the NL community (13). Until that time, NL had implemented a containment strategy, consistent with an elimination (or zero-COVID) strategy (14,15). This containment strategy limited SARS-CoV-2 spread through strict border control, contact tracing, self-isolation requirements and non-pharmaceutical interventions aimed to end community transmission whenever outbreaks occurred (16).

When Omicron variant infections began spreading in the community, NL reported its highest COVID-19 case counts since the beginning of the pandemic. On January 17,2022, 239 new cases were reported (17), which was 0.45% of the provincial population. After January 17, the province no longer publicly reported cases by age group. Until then, 19.7% of the reported cases were for those younger than 20 years of age. A more detailed overview of the epidemiological situation in NL has been published previously ((16); see also **Supplemental material A**).

With the Omicron variant's higher transmissibility, its potential to escape the human immune response (meaning that vaccinated individuals and individuals that have already had COVID-19 may be susceptible for reinfection (18)), and, at the time, unknown health risks, these high-case counts raised concerns of health care capacity overload. The NL elementary (grades K–6), junior high (grades 6–7) and high schools (grades 8–12) closed early for winter break on December 20, 2021 (19). To reduce infection spread and protect the health care system, the return to in-person teaching for these students was postponed to January 25, 2022 (20).

In addition to the delayed return to school, public health officials strongly recommended that K–12 students (approximately 59,000 individuals) complete rapid antigen tests (RATs; (4,21)). The Department of Health and Community Services distributed BTNX Rapid Response COVID-19 antigen test kits to schools, and the schools distributed the kits to their students. A first RAT was to be completed on January 22, three days before the return to in-person school. Students testing negative were asked to complete another test the morning of January 25 just before returning to school. Students that recorded positive test results were to self-isolate for 7–10 days, depending on their vaccination status (22). At the time, 89.1% of the NL population aged five years and older and 85.7% of the total population were fully vaccinated (defined as two doses) (23). Students were to complete these RATs to "reduce the risk of someone attending school while infected" (16). There was no requirement to report these RAT results, but positive results could be submitted using the provincial COVID Assessment and Reporting Tool.

The wide distribution of RATs throughout the province, and the recommendation from public health officials for school students to complete these RATs on specific dates, allowed us to study the underreporting of the Omicron variant (BA.1/BA.2 subvariant) and infection prevalence in NL school students. Between February 3 and February 19, 2022, we deployed an internet survey that enabled parents and guardians to voluntarily report the number of positive and negative results for RATs completed by school students (grades K–6 or 7–12) on January 22 and 25. Our survey was unrelated to the provincial COVID Assessment and Reporting tool. Parents were asked to specify whether positive cases were symptomatic or asymptomatic, and to provide the Forward Sortation Area (FSA)—a truncated postal code—and the Regional Health Authority (RHA) where the tests were completed. Results for students in one household were to be reported together (**Supplemental material B**).

The recommendation for school children to complete these RATs first occurred on January 13. However, February 3 was the earliest we could begin the internet survey due to the time it took to obtain the necessary approvals. To ensure informed consent, as many students were younger than 19 years of age (the age of majority in NL (24)), parents and guardians were asked to report the RAT results, but the reported test results were only for K–12 students. We asked participants to report their FSA (the first three letters/digits of a postal code) so we could determine if spatially adjacent infection spread was occurring, and if there was substantial variation in infection prevalence within and between RHAs. We requested that results be reported together for one household because the Omicron variant is highly transmissible within a household (25). Household positivity (rather than individual positivity) is a more reliable measure of prevalence, given that test results from individual students living in the same household are not independent. Furthermore, to estimate underreporting, we compared the results of the RATs with COVID-19 cases reported by the provincial testing system. This comparison was made at the household level because beginning on January 24, 2022, it was stated that household members of COVID-19 cases in NL should not undergo testing at the provincial testing sites (17).

Until 2021, COVID-19 testing in Canada occurred mostly for symptomatic individuals, and testing of asymptomatic individuals

occurred in vulnerable populations, which included the elderly, residents of long-term care, hospital admissions and, sometimes, contacts of cases. As a less vulnerable population, asymptomatic school children were unlikely to be tested for COVID-19, thus, K–12 students may represent an understudied population. Our analysis aimed to estimate underreporting from the NL provincial testing system, the prevalence and distribution of Omicron variant cases among school students, and the percentage of infections that were asymptomatic for school students that reported positive RAT results.

Methods

Survey

Parents and guardians of students in grades K–12 that had completed at least one rapid test on January 22 or January 25 were given the opportunity to answer a web survey to report the test results of their household. Participation was voluntary and consent was required before the survey questions were released. Parents and guardians were told that providing the RAT results would help to understand COVID-19 prevalence and underreporting in NL.

The survey was advertised through broadcast media (two radio morning shows covering eastern NL, two radio morning shows covering central and western NL, and two evening television news shows covering NL) and on social media (Facebook and Twitter). All principals of private and of elementary, junior high and high schools in the NL English School District were emailed requesting that survey participation details be provided to parents and guardians. All Indigenous groups in the province were emailed information describing how to participate in the study. Exceptions were Innu Nation and Sheshatshiu Innu First Nation School, which returned to school later, and requested that their students complete the RATs on different dates.

The survey consisted of four questions, taking approximately five minutes to complete (Supplemental material B). Parents and guardians were asked to provide the following information: 1) the first three letters/digits of their postal code, corresponding to the FSA (e.g. A1A); 2) their RHA (i.e. Eastern Health, Central Health, Western Health or Labrador-Grenfell Health); 3) the number of rapid tests from their household completed on January 22 and January 25, indicating how many rapid tests were negative, positive symptomatic or positive asymptomatic, and 4) whether the students were in grades K–6 or 7–12.

The survey was completed by a total of 1,278 households, where 52% of the households counted more than one student. A total of 2,055 test results were reported (with mostly two-test results per student reported), out of an estimated 59,452 students returning to school, which indicates participation of approximately 3.5%.

Test accuracy: sensitivity, specificity, and confidence intervals

The observed number of positive test results N^+ is the sum of observed positive test results from infected individuals and false positive test results from uninfected individuals, such that:

Equation 1:

$$N^+ = \underbrace{pN\sigma^+}_{true\ positives} + \underbrace{(1-p)N(1-\sigma^-)}_{false\ positives} = N\theta \quad with \quad p,\sigma^+,\sigma^- \in [0,1],$$

where p is the true proportion of infected individuals, N is the total number of tests, θ is the probability of an individual testing positive, and σ^+ and σ^- are sensitivity (i.e. the probability of testing positive if infected) and specificity (i.e. the probability of testing negative if uninfected), respectively.

By rearranging equation 1, we obtain an estimator p^* for the true proportion of K–12 students infected with COVID-19:

Equation 2:

$$p* = \begin{cases} 0 & if \quad \frac{N^+}{N} < 1-\sigma^-, \\ \frac{1-\sigma^- - \frac{N^+}{N}}{1-\sigma^- - \sigma^+} & if \quad 1-\sigma^- < \frac{N^+}{N} < \sigma^+ \leq 1, \\ 1 & if \quad \frac{N^+}{N} > \sigma^+, \end{cases}$$

and the estimator θ^* for the probability of testing positive:

Equation 3:

$$\theta* = p*\sigma^+ + (1-p*)(1-\sigma^-)$$

Notice that $N^+ \sim \text{Bin}(N, \theta)$. Therefore, $\text{Bin}(N,\theta^*)$ can be resampled to obtain a parametric bootstrap confidence interval estimate.

Sensitivity was estimated as σ^+=0.9044. This estimate was based on sensitivity values at different viral loads, and on estimates of viral load during infection (26). Specificity was assumed to be σ^-=0.994, based on the study of Parvu *et al.* (27). Testing positive if uninfected is very unlikely (with a mean of six out of every 1,000 tests completed), while testing negative if infected can occur with a mean of one out of every 10 cases. A complete derivation of the sensitivity and specificity estimates is provided in **Supplemental material C**.

The observed number of positive asymptomatic cases includes true positive asymptomatic cases and false positive asymptomatic cases, which could be false positive cases (with very low probability, as discussed above (27)) or positive symptomatic cases falsely reported as asymptomatic. We could not estimate the proportion of symptomatic cases that may

be falsely reported as positive asymptomatic, as this is based on participants' self-assessment; therefore, our analysis of asymptomatic cases is based on the raw reported cases, for which no confidence intervals can be provided.

Data analysis

Anonymized survey results and the code used for the analysis is publicly available. Each row of the data corresponds to the reporting of a single household, where column entries correspond to the number of positive tests (distinguishing between symptomatic and asymptomatic cases), and negative tests in grades K–6 and grades 7–12.

Our analysis provided insights into the following: 1) the rates of underreporting of COVID-19 cases (Omicron variant, BA.1/BA.2 subvariant) in NL at the population level and at the household level; 2) the proportion of positive tests occurring in elementary (primary) schools (grades K–6) and in junior high and high schools (grades 7–12), and the corresponding proportions of asymptomatic cases; and 3) the spatial distribution of positive households in the province.

Test accuracy was taken into account by considering test sensitivity and specificity. Data were analyzed using the programming language R and the Postal Code Conversion File (28).

Underreporting

To gain insights into COVID-19 underreporting, we compared estimates of the percentage of positive tests among K–12 students (obtained using the survey-reported RAT results) with provincial case counts (Supplemental material A, **Figure S1**). Provincial case counts were based on the Public Service Advisory COVID-19 announcements from the Department of Health and Community Services, which reported the daily number of new cases (29).

In NL, publicly available daily age-structured provincial case counts ended on January 17, 2022, after which only the total number of new cases was provided. By considering age-structured active cases reported till January 17 we derive the percentage of active cases among the younger age group, consisting of individuals aged 0–19 years old (Supplemental material A, **Figure S2**). We use this percentage to obtain an estimate for reported COVID-19 prevalence among the age group 0–19 years when the rapid antigen testing occurred on January 22 and January 25 (Supplemental material A). We estimated that 0.49% of the NL population and 0.45% of the age group 0–19 years (averaged across January 20 to January 27, 2022) were reported infected with COVID-19. Finally, we use these estimates to quantify the reported household positivity, estimated to be 1.2%. A discussion of the comparison between reported COVID-19 prevalence and estimated percent positivity in K–12 students and prevalence of COVID-19 in households, derived from the rapid antigen testing results is provided in a later section of this article.

Analysis of positive cases

The total number of positive tests was calculated from the number of positive tests on January 25 and the number of positive tests on January 22 that were not subsequently reported on January 25. We defined negative tests as the number of negative tests on January 25. This decision was made because parents and guardians were instructed by public health officials not to carry out a second test if the first test was positive, and we decided this after noting that 69 households (out of 1,278) reported different entries on the first and the second testing date (**Supplemental material D**). Positive cases are reported at the provincial level and were divided into symptomatic and asymptomatic cases. The proportion of reported positive cases in elementary (grades K–6) and junior high and high schools (grades 7–12) was also reported.

Spatial distribution of cases

We defined positive households as households reporting at least one positive result on either January 22 or January 25. The percentage of positive households was computed at the level of the RHA and for each FSAs, as described later in this article. We performed Moran's I statistics (30) to investigate the correlation between spatial proximity and COVID-19 prevalence rates in different FSAs.

Results

Underreporting

When considering the survey-reported RAT results for K–12 students, we estimated that 5.0% (95% CI, 3.8–6.5) of households were positive for COVID-19. When considering the provincial COVID-19 data, we estimate that 1.2% of all households were positive for COVID-19, if we assume that only one test per household was reported in a single day. When comparing our estimates with the provincial estimates we determined that the number of underreported positive households was 4.3 (95% CI, 3.1–5.3) times higher than the counts reported by the NL testing system.

The RAT results that we collected at the individual level indicate a percent positivity of 3.7% (95% CI, 2.9–4.7) among children and youth (**Table 1**). Provincial reporting was lower, at 0.45% (Supplemental material A) indicating that on average only one out of every 8.4 (95% CI, 6.4–10.4) infections has been reported, although we note that this calculation overlooks that infections spread more readily to other household members than to members of the wider community.

Table 1: Rapid antigen test results at the provincial level and at the level of the four Regional Health Authorities of Newfoundland and Labrador

Region	Total reported positive tests	Total tests	Percent estimated true positives (95% CI)	Total reported positive households	Total reporting households	Percent estimated positive households (95% CI)
Newfoundland and Labrador	82	2,055	3.7% (2.9–4.7)	66	1,278	5.0% (3.8–6.5)
Eastern Health (EH)	61	1,648	3.5% (2.5–4.5)	46	1,019	4.4% (3.0–5.8)
Central Health (CH)	5	105	4.6% (3.9–9.9)	5	63	8.2% (1.1–17.0)
Western Health (WH)	11	221	4.9% (1.9–8.4)	10	143	7.1% (2.4–11.8)
Labrador-Grenfell Health (LG)	5	81	6.2% (0.7–13.1)	5	53	9.8% (1.4–18.2)

Abbreviation: CI, confidence interval

Analysis of positive cases

A total of 82 out of 2,055 tests were reported positive, giving an estimate of the true prevalence as 3.7% (95% CI, 2.9–4.7) (**Table 2**). A larger proportion of these positive tests, namely 62.9% (95% CI, 44.3–83.0), was reported in elementary school students, while the remaining 37.1% (95% CI, 22.7–52.9) was reported in junior high and high school students (grades 7–12). More than half of the cases were reported as asymptomatic (59.8%), with no significant difference in the proportion of asymptomatic cases in grades K–6 and in grades 7–12 (i.e. 60.8% and 58.1% respectively).

Table 2: Rapid antigen test results and estimates of Omicron variant positivity and percent asymptomatic infections[a], Newfoundland and Labrador

Definition	Results (95% CI)
Total reported positives	82
Total reported tests	2,055
Percent estimated true positives	3.8% (2.9–4.7)
Total reported positives (grades K–6)	51
Total reported positives (grades 7–12)	31
Total reported (grades K–6)	1,192
Total reported (grades 7–12)	863
Positives in grades K–6 (percent of total estimated true positives)	62.9% (44.3–83.0)
Positives in grades 7–12 (percent of total estimated true positives)	37.1% (22.7–52.9)
Total reported asymptomatic	49
Total reported asymptomatic (grades K–6)	31
Total reported asymptomatic (grades 7–12)	18
Asymptomatic (percent of total reported positives)	59.8%
Asymptomatic (percent of reported positives in grades K–6)	60.8%
Asymptomatic (percent of reported positives in grades 7–12	58.1%

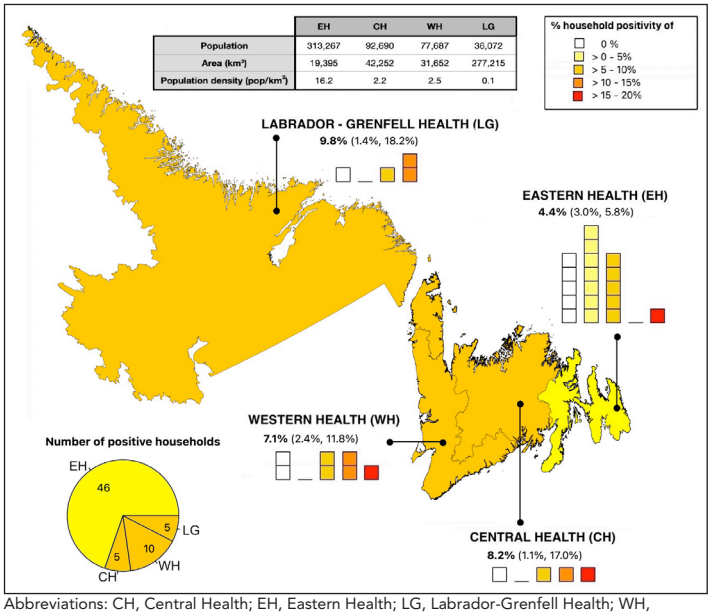
Abbreviation: CI, confidence interval
[a] In elementary schools (grades K–6) and in junior high and high schools (grades 7–12)

Spatial distribution of cases

A total of 66 out of 1,278 households reported at least one positive test on January 22 or January 25, with corresponding household positivity of 5.0% (95% CI, 3.8–6.5). Reports of positive tests were distributed across all four RHAs. **Figure 1** represents a map of NL, divided by RHAs, from left to right, Labrador-Grenfell Health, Western Health, Central Health, and Eastern Health. The household positivity (i.e. the percentage of households which reported positive test results from K–12 students) reported by each of its FSAs is shown for each RHA, where each square corresponds to a single FSA within the RHA and the colour of the square represents the reported household positivity. We include only results of FSAs for which test results of students of six or more households have been reported. All RHAs reported household positivity higher than 10% in one or more FSAs, as well as low or zero positive tests in other FSAs. The FSAs were not identified, because we do not have consent from the participants to release this information. The population size, area and population density of each RHA is provided in Figure 1. The total number of households reporting is provided in Table 1.

Participants from Eastern Health, as the smallest but most populated health region of the province, reported results for 17 out of 18 FSAs. This region reported 46/1,019 positive households (out of 66 total positive households in the whole province), but lower COVID-19 prevalence rates with respect to other health regions, with the percentage of positive households being 4.4% (95% CI, 3.0–5.8). Participants from Central Health reported 5/63 positive households and a household positivity of 8.2% (95% CI, 1.1–17.0), based on the RAT results of four out of seven FSAs. Participants from Western Health reported results from seven out of seven FSAs, with 10/143 positive households and household positivity of 7.1% (95% CI, 2.4–11.8). Participants from Labrador-Grenfell Health reported results from four out of four FSAs, with 5/53 positive households, with a household positivity estimated as 9.8% (95% CI, 1.4–18.2). The number of FSAs reporting low versus high percentage household positivity for each RHA is provided in Figure 1. Because of lower reporting

Figure 1: Map of Newfoundland and Labrador, divided by Regional Health Authorities[a]



Abbreviations: CH, Central Health; EH, Eastern Health; LG, Labrador-Grenfell Health; WH, Western Health

[a] Percent values represent the percentage of positive households in each region, with 95% confidence intervals. The pie chart represents the number of reported positive households for each health region as a fraction of the total number of positive households in the province. The population, area, and population density of each RHA are provided in the table in the top of the figure

rates and possible sampling biases, there is high uncertainty associated with household positivity in the regions of Labrador-Grenfell Health, Central Health and Western Health, and, more generally, with prevalence at the FSAs level.

We obtained a Moran's I coefficient of -0.08, and a *p*-value of 0.35, indicating no correlation between spatial proximity and COVID-19 prevalence rates among FSAs.

Discussion

Underreporting has been a major challenge for COVID-19 pandemic monitoring and response planning. These challenges have increased with the establishment of the highly transmissible Omicron variant (7,31) and the expanded use of rapid tests, the results of which are not officially reported in some jurisdictions (7,8). Underreporting rates may have been particularly high among children and youth, given their relatively low risk of experiencing severe outcomes (32). In NL, public health officials recommended that all K–12 students complete RATs on January 22 and 25, 2022. We conducted an online survey where parents and guardians of K–12 students could report these RAT results. Self-administered rapid tests were not reported in the NL provincial case counts, and characteristics of the NL population eligible for testing under the provincial system (4), were very different than the characteristics of the population that completed the RATs on January 22 and 25, 2022. We estimated that only one out of every 8.4 (95% CI, 6.4–10.4) cases occurring in children and youth or one out of every 4.3 (95% CI, 3.1–5.3) positive households, were reported by provincial case counts.

The COVID-19 Immunity Taskforce uses serological analysis of blood donations to estimate the percentage of provincial populations that have been infected with SARS-CoV-2 (33). When interpreted relative to the number of cases reported by the NL testing system, these serology data imply that from January to February 2022, one in every 2.3 cases were reported (Supplemental material C, **Table S1**). For comparison, in other Canadian provinces from January to February 2022, the underreporting ratio ranged from one in every 17.2 cases reported (British Columbia) to an equal number of cases reported and detected by serology (Prince Edward Island; **Supplemental material E, Table S2**). Underreporting ratios are generally highest in children (34). The underreporting ratio that we estimate from our study of rapid antigen testing in K–12 students is broadly consistent with COVID-19 Immunity Taskforce data. Eligibility for testing, such that the results of the testing could be reported in the provincial case counts, was relatively unrestricted in NL at the time of our study, while in all other provinces except for Prince Edward Island, most individuals were ineligible for testing under the provincial systems due to age restrictions on eligibility (Supplemental material E).

Most of the positive cases occurred in elementary schools (62.9%, 95% CI, 44.3–83.0), while previously published articles found higher COVID-19 prevalence in junior high and high schools (secondary schools) relative to elementary schools (35–37), presumably due to student cohorting. Elementary school students tend to remain with the same classmates throughout the day, while older students have different classmates in different classes. However, for the RAT results collected in our study, testing was conducted after schools had been closed for five weeks; therefore, student cohorting or other public health measures aimed to reduce COVID-19 spread in schools would not have impacted our results. Potentially, a major factor influencing our results was the vaccination status of the students. Vaccination rates for 5–11-year-olds in NL were the highest in Canada, with 75% having received one dose of the vaccine on January 19, 2022 (38). However, youth aged 12 years or older became eligible for vaccination starting May 23, 2021, while children aged five years and older became eligible for vaccination only on November 23, 2021. At the time of our study (specifically, on January 22, 2022), nearly all junior and high school-aged youths were fully vaccinated (96.7% of NL residents aged 12–17 years), while nearly all elementary school-aged children had not completed a full-vaccination series (only 3.3% of NL residents aged 5–11 years had completed a full-vaccination series (39)).

Whether children and youth are more susceptible than adults to SARS-CoV-2 infection has been a matter of debate (40). Understanding the role that children play in the transmission of the virus is key to inform public health policies for the implementation of non-pharmaceutical interventions, such as

school closures. Given the consequences of school closures on mental and social health (41,42), it is important to understand the effect that closing schools has on COVID-19 transmission. Understanding the role of school children in SARS-CoV-2 spread may also help inform vaccine prioritization strategies. Possible vaccination strategies include prioritizing essential workers (e.g. teachers or other workers with a large number of social contacts), which would reduce transmission and the total number of infections (43).

We estimate that 59.8% of the positive tests were asymptomatic, where asymptomatic rates were similar among elementary school students (60.8%) and students in junior high and high schools (58.1%). Previous studies have reported asymptomatic rates associated with the Omicron variant to be between 32% and 44% (44), where asymptomatic rates tend to be higher in younger age groups (44–46). Our high asymptomatic rates could be due to reporting errors. In some instances (Supplemental material D) participants reported asymptomatic infection on February 22 and symptomatic infection on February 25, which indicates a possible confusion between asymptomatic and pre-symptomatic infections. Infections asymptomatic at the time of the testing, but with symptoms appearing some days later, should have been reported as symptomatic, but may have been reported as asymptomatic instead, which would lead to an overestimation of the percentage of asymptomatic infections. On the other hand, the survey was conducted two weeks after the RATs were taken, such that participants were given enough time to realize whether symptoms occurred during the infectious period, and correctly report whether infections were symptomatic or not. It could be possible that asymptomatic rates in children and youth are effectively high or that the estimate is unreliable due to low sample size.

The RAT survey results also allowed us to investigate the spatial distribution of COVID-19 cases. We found high heterogeneity in the percentage of positive cases reported across the province, and no relationship between regional proximity and COVID-19 prevalence. Although a positive correlation between COVID-19 prevalence and population density may have been expected (47,48), we find that Eastern Health, the RHA with the highest population density, reported the lowest infection prevalence. Due to our small sample size, we could not determine whether the low counts registered for Eastern Health are an artifact of higher reporting rates, and whether using a finer spatial scale or having a larger dataset for certain FSAs could have revealed more insights into the spatial pattern of cases. Previous studies have also found marked heterogeneity in the spatial distribution of COVID-19 cases (49,50), where household size, rather than population density, has been recognized to be a better indicator of COVID-19 hotspots (51,52).

Given the low participation rate in the survey (3.5%) and small sample sizes, and given that participation in the survey was voluntarily, our results may suffer from sample selection biases, and should be interpreted with caution. It may be that those households with positive tests were more likely to report results, which may have inflated positive case counts in comparison to provincial estimates. Additionally, different social and psychological stresses may have resulted in certain social groups (such as pro or anti-vaccine groups) being more likely to report results than others, leading to additional biases. Finally, sources of bias also occur in the provincial testing system; for example, higher testing rates of vulnerable individuals, hospital admissions and long-term care residents, many of whom are elderly.

Conclusion

Our analysis of reported data on extensive SARS-CoV-2 testing in NL reveals possible pattern of BA.1/BA.2 prevalence among children and youth, a currently understudied population. We found that in February 2022 only one out of every 4.3 (95% CI, 3.1–5.3) positive households were captured by provincial case count, with asymptomatic infections being 59.8% of the positive cases. Given the low survey participation rate, our results should be interpreted with caution. Nonetheless, our study provides an overview on the epidemiological situation in NL at the time the tests were conducted and discusses the difficulty in obtaining epidemiological data in the context of volatile public health care measures and rampant disease spread.

Authors' statement

MM — Conceptualization, methodology, validation, formal analysis, investigation, writing (original draft), writing (review & editing)
AH — Conceptualization, methodology, validation, investigation, writing (review & editing), supervision, project administration, funding acquisition
JL-O — Methodology
ZM — Conceptualization, methodology, writing (review & editing)

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Competing interest

None.

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Supplemental material

These documents can be accessed on the Supplemental material file.

Supplemental material A: Newfoundland and Labrador provincial case counts
Supplemental material B: Survey
Supplemental material C: Sensitivity and specificity
Supplemental material D: Data handling
Supplemental material E: Estimating underreporting from COVID-19 Immunity Task Force serology data

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Summary In Labrador Inuktitut

SakKiKattasimajut Kaujititautsiasimangitunut KanimmasiKaniammat COVID-19 silatsuamut siammasimajumut apomautigijautsiasimavuk pannaigutiliugiamut ammalu Kimiggugiamut inulimânut ânniasiutiligijet kamagiamut. Malitsiasimangitut Kaujititausimangitunut apviataugajattuk atuniKatsiatumik ulugianattunik Kimiggugiamut nalunagajammat sivunittini atuttaugiaKagajakKotunut. Kaujititsilualungitut puttujugalausimajuk piluattumik akungani sugusinut ammalu inosuttunut, tamannauluattuk KanimmasiKajunut ilinniavimmejut suguset isumagijauKattamata attutausagaisot, ammalu ottugattauluasimangitut KanimmasiKammangâmmik COVID-19. Januarami 2022, Newfoundland ammalu Labrador (Canada) pitaKalaummijut taijamik Omicron Kanimmasigiallak siammasimajuk (BA.1/BA.2 Kanimmasigiallait) ammalu ânniasiutiligijet kiggatuttaligijingit pikKujilauttut ilonnait ilinniavimmejut utigasuajut nukatlinut, ammalu puttujunnejunut ilinniavimmi (kititangit Kanitangani 59,000 ilinniavimmejut) pijagegialet maggonik tuavittumik Kaujisonik KanimmasiKajuKammangât ottugautennik atugialet pingasuit ullunik avittusimajonnik. Kanitanganut kitigasuagiangit piusigijaujunut ilinganiKajumut SARS-CoV-2, apigilaukKugut angajukKânik ammalu kamajinnik KaujititsiKattagiamut sakKijunut tuavittumik ottugattaujunut KanimmasikKakKomangâmmik pijagettaugialet taikkununga K–12 ilinnavmmejunut atutillugit Kagitaujakkut Kaujisajunut, ammalu nalunaitsilutillu ilinniavimmejumut inigijanga ammalu tainna ilinniavimmejuk KanimmasiKappat nalunaigutiKasimammangât. kamagijauniammata Kaujisattausimajut taikkununga numaranut KanimmasiKajunut ammalu ottugattausimajut Kaujijausimatlutik taikkutigona Newfoundland ammalu Labrador ottugattet piusinginnut, KaujilaukKugut atautsik atunik 4.3 (3.1–5.3) Kanimmasilet illuni tigujaulaukKut taikkununga pravinsikkunut kitijausimajunut, una 5.1% Kanimmasilet kititangit pisimajunit tuavittumik KanimmasiKammangâmmik ottusimajunut sakKisimajut, ammalu 1.2% KanimmasiKasimajut Kaujititautlutik taikkutigona atusimajunut prâvinsimi ottugautet piusingatigut.

Tânna Kaujisannik Kaujijausimajut nalunaitsilaukKuk puttunippângusimajut ilinganiKajunut SARS-CoV-2 Kanimmasilet Kaujijausimajut iluani nukatlinut ilinniavimmejunut, pitaKatillugit 62.9% KanimmasimaKajunut (95% CI, 44.3–83.0) Kaujijausimajut pisimajunit K–6 ilinniavimmejunut, ammalu amiakkungit 37.1% (95% CI, 22.7–52.9) Kaujijausimajut nukatlinut ammalu puttunippânejunik ilinniavimmejunut. Kanimmasilet nalunagutinik imailingasimavut 59.8% KanimmasiKajunut, angijongitumik atjigelugatik akungani nalunaigutiKajunut mikinippânut ilinniavimmejunut (60.8%) upvalu nukatlinut ammalu puttunippânejunut ilinniavinni (58.1%). Unuttolaungimata ilauKataujut Kaujisannimit (3.5%), Kaujisimajavut pitaKagajattut ottugattausimajunut annigijausimajunut apomautiKatlutik, ammalu tukisijaugalik kamatsiagutigijaulluni. Tamannaugaluatluni, kititavut KaujititautsiaKattangitunut malittigetsiatut numarangit kititangit pisimajunit Kaujisattilagijinnit Kaujigatsanginnut, ammalu Kaujisasimajavut sakKititsivuk tukisinitsaugiamut ilinganiKajumut COVID-19 Kaujimattitautsiangitunut ammalu nalunaigutiKajunut ununnigijangit ilinniavimmejunut sugusinut, mânnaluatsiak Kaujisattausiasiangitut tamakkua inuKutingit.

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