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CCDR

CANADA COMMUNICABLE DISEASE REPORT

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Summary of the National Advisory Committee on Immunization (NACI) Seasonal Influenza Vaccine Statement for 2026–2027

Angela Sinilaite¹, Winnie Siu^{1,2}, Kristin Klein^{3,4}, Jesse Papenburg^{5,6,7}, on behalf of the National Advisory Committee on Immunization (NACI)*

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Abstract

Background: The National Advisory Committee on Immunization (NACI) reviews evolving evidence on influenza immunization annually and updates vaccine recommendations. The NACI *Statement on seasonal influenza vaccines for 2026–2027* updates recommendations from the 2025–2026 season.

Objective: To highlight new and updated information since the 2025–2026 statement and to summarize the 2026–2027 NACI seasonal influenza vaccine recommendations.

Methods: The NACI Influenza Working Group applied the NACI evidence-based process to assess available evidence and formulate recommendations, which were evaluated and approved by NACI. Throughout the process, NACI's peer-reviewed Ethics, Equity, Feasibility, and Acceptability (EEFA) framework, along with its evidence-informed tools (Ethics Integrated Filters, Equity Matrix, Feasibility Matrix, and Acceptability Matrix) were applied.

Results: The overarching recommendation for seasonal influenza vaccination remains unchanged. Key updates for the 2025–2026 statement include: 1) integration of a new evidence review on optimal timing of seasonal influenza vaccination, including consideration of intraseasonal waning, and 2) integration of guidance on seasonal influenza vaccination in the context of avian influenza, with supporting resources.

Conclusion: This guidance reaffirms NACI's recommendation that influenza vaccine should be offered annually to anyone six months of age or older who does not have a contraindication to the vaccine.

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Introduction

Canada experiences annual seasonal influenza epidemics, primarily in the late fall and winter. The burden of influenza-associated illness and death varies each year due to factors such as circulating virus type, vaccine match to circulating strains and affected populations (1). Influenza activity in Canada is usually low in the late spring and summer, begins to increase over the fall, and peaks in the winter months. Multiple influenza

strains typically circulate each season, but one strain often predominates. There are also often differences in the timing, intensity of influenza activity observed across regions in Canada.

Globally, approximately 3–5 million cases of severe influenza illness and 290,000 to 650,000 deaths from influenza occur annually (2). In Canada, prior to the COVID-19 pandemic



(i.e., 2010–2011 to 2018–2019 influenza seasons), influenza caused approximately 15,000 hospitalizations annually, more than any other seasonal respiratory virus (3). Vaccination remains the most effective form of protection against influenza and its complications, underscoring the importance of annual vaccination programs.

Given the dynamic nature of influenza, the National Advisory Committee on Immunization (NACI) reassesses its guidance on influenza immunization on an annual basis and provides the Public Health Agency of Canada (PHAC) with recommendations on the use of authorized seasonal influenza vaccines. Annual updates reflect changes in influenza epidemiology, vaccine-related evidence (including safety, effectiveness, and programmatic considerations), immunization practices, and available products in Canada. The NACI Influenza Working Group leads the annual update of the NACI statement on seasonal influenza vaccines, which involves a thorough literature review and evaluation through deliberation at the scientific, clinical practice and population health levels. In May 2026, PHAC released updated NACI guidance on seasonal influenza vaccines for 2026–2027, based on current evidence and expert opinion.

This article provides a concise summary of NACI's recommendations and supporting information for the 2026–2027 influenza season, with emphasis on new or updated information since the 2025–2026 statement on seasonal influenza vaccines. For detailed information, refer to NACI's *Statement on seasonal influenza vaccines for 2026–2027* (4).

Methods

In preparation for the *Statement on seasonal influenza vaccines for 2026–2027*, the NACI Influenza Working Group identified the need for evidence reviews on new topics and analyzed available evidence following NACI's evidence-based process, which included developing updated recommendations as needed (5). Strength of NACI recommendations is defined in **Table A1** in the **Appendix**. NACI's peer-reviewed framework and evidence-informed tools (including the Ethics Integrated Filters, Equity Matrix, Feasibility Matrix, and Acceptability Matrix) were applied to systematically assess issues of ethics, equity, feasibility and acceptability (6).

Results

The overarching recommendation for seasonal influenza vaccination remains unchanged (see Summary of the NACI recommendations for the use of influenza vaccines for the 2026–2027 influenza season, below). The following sections summarize the key updates for the 2026–2027 statement.

Intraseasonal waning of influenza vaccine effectiveness and optimal timing for seasonal influenza vaccination

The 2026–2027 seasonal influenza guidance includes an updated summary of the available evidence and key considerations regarding the optimal timing of seasonal influenza vaccine administration. This evidence review addresses the seasonality of influenza activity across Canada, intraseasonal waning of influenza vaccine-induced immunity and key programmatic considerations (7). While the current evidence is insufficient to establish optimal timing for specific populations, vaccination in early fall provides sustained protection for most of the season. Therefore, significant changes to the timing of existing annual influenza vaccination programs are neither warranted nor feasible at this time, and achieving high coverage remains the most critical determinant of program success.

Seasonal influenza vaccination in the context of avian influenza

In February 2025, NACI published preliminary guidance on human vaccination against avian influenza in a non-pandemic context, offering a framework to inform Canadian provinces and territories' decision-making on the use of human vaccines against avian influenza.

The seasonal influenza guidance has now been updated to align with this guidance on human vaccines against avian influenza, stating that although seasonal influenza vaccines do not protect against avian influenza A(H5N1) viruses, they may mitigate the severity of seasonal influenza and reduce the risk of co-infection with seasonal and avian influenza strains. Individuals whose occupational or recreational activities increase their risk of exposure to avian influenza A(H5N1) viruses are a group for whom influenza vaccination is particularly important.

For more information, refer to NACI's *Rapid response: Preliminary guidance on human vaccination against avian influenza in a non-pandemic context as of December 2024* (8).

Other updates

The seasonal statement for 2026–2027 also includes the following additional updates to the previous year's statement: highlights of 2024–2025 influenza trends in Canada from new national surveillance data; vaccine products authorized and available for use in Canada for the coming season; a refined presentation of safety content to help ensure streamlined access to essential information on contraindications and precautions; and streamlined and updated appendices to improve usability and clarity.



Summary of the NACI recommendations for the use of influenza vaccines for the 2026–2027 influenza season

NACI recommends that influenza vaccine should be offered annually to anyone six months of age and older who does not have a contraindication to the vaccine. Influenza vaccine should be prioritized for the groups for whom influenza vaccination is particularly important indicated in **List 1**. Refer to **Table 1** for the recommended influenza vaccine products and **Table 2** for the recommended dose and administration route according to each age group.

List 1: Groups for whom influenza vaccination is particularly important

People at high risk of influenza-related complications or hospitalization: - All children 6 to 59 months of age - Adults and children with the following chronic health conditions^a: - Cardiac or pulmonary disorders (including bronchopulmonary dysplasia, cystic fibrosis, and asthma) - Diabetes mellitus and other metabolic diseases - Cancer, immune compromising conditions (due to underlying disease, therapy, or both, such as solid organ transplant or hematopoietic stem cell transplant recipients) - Renal disease - Anemia or hemoglobinopathy - Neurologic or neurodevelopmental conditions (includes neuromuscular, neurovascular, neurodegenerative, neurodevelopmental conditions, and seizure disorders [and, for children, includes febrile seizures and isolated developmental delay], but excludes migraines and psychiatric conditions without neurological conditions) - Class 3 obesity (defined as body mass index of 40 kg/m² and over) - Children 6 months to 18 years of age undergoing long-term treatment with acetylsalicylic acid, because of the potential increase of Reye's syndrome associated with influenza - All pregnant women and pregnant individuals - All individuals of any age who are residents of nursing homes and other chronic care facilities - Adults 65 years of age and older - Individuals in or from First Nations, Inuit, or Métis communities as a result of intersecting determinants of health rooted in historic and ongoing colonization and systemic racism People capable of transmitting influenza to those at high risk: - Healthcare and other care providers in facilities and community settings who, through their activities, are capable of transmitting influenza to those at high risk - Household contacts, both adults and children, of individuals at high risk, whether or not the individual at high risk has been vaccinated: - Household contacts of individuals at high risk - Household contacts of infants less than 6 months of age, as these infants are at high risk but cannot receive influenza vaccine - Members of a household expecting a newborn during the influenza season - Those providing regular childcare to children 0 to 59 months of age, whether in or out of the home - Those who provide services within closed or relatively closed settings to people at high risk (e.g., crew on a cruise ship) Others: - People who provide essential community services - People whose occupational or recreational activities increase their risk of exposure to avian influenza A(H5N1)

^a Refer to immunization of persons with chronic diseases and immunization of immunocompromised persons Part 3 (9) of the *Canadian Immunization Guide* for additional information about vaccination of people with chronic diseases

Table 1: Recommendations on choice of influenza vaccine type for individual and public health program-level decision making by age group

Recipient by age group	Vaccine types authorized ^a and available for use	Recommendations on choice of influenza vaccine
6–23 months	IIV-Adj IIV-SD IIV-cc	- Any age-appropriate influenza vaccine should be used for infants and young children who do not have contraindications, noting the following considerations: - Influvac® (IIV3-SD) is authorized for use in children six months of age and older; however, additional NACI evidence review is required before recommending its use in children younger than three years. Updated guidance will be provided once this review is complete.
2–17 years ^b	IIV-SD IIV-cc LAIV	- Any age-appropriate influenza vaccine should be used for children and adolescents who do not have contraindications including those with chronic health conditions, noting the following considerations and exceptions: - Influvac® (IIV3-SD) is authorized for use in children six months of age and older; however, additional NACI evidence review is required before recommending its use in children younger than three years. Updated guidance will be provided once this review is complete. LAIV is contraindicated in children or adolescents with: - Severe asthma (defined as currently on oral or high-dose inhaled corticosteroids) - Active wheezing, or medically attended wheezing in the 7 days prior to vaccination - Immune compromising conditions, with the exception of stable HIV infection, i.e., if the child is currently being treated with ART for at least four months and has adequate immune function - Current receipt of long-term aspirin or aspirin-containing therapy - Pregnancy
18–59 years	IIV-SD IIV-cc LAIV	- Any age-appropriate influenza vaccine should be used for adults 18 to 59 years of age who do not have contraindications, noting the following considerations and exceptions: - There is some evidence that IIV may provide better efficacy than LAIV in adults

**Table 1: Recommendations on choice of influenza vaccine type for individual and public health program-level decision making by age group (continued)**

Recipient by age group	Vaccine types authorized ^a and available for use	Recommendations on choice of influenza vaccine
18–59 years	IIV-SD IIV-cc LAIV	- LAIV is contraindicated in adults with: - Severe asthma (defined as currently on oral or high-dose inhaled corticosteroids) - Active wheezing, or medically attended wheezing in the 7 days prior to vaccination - Immune compromising conditions - Pregnancy - LAIV is not recommended for: - Adults with any of the chronic health conditions identified in List 1 - Healthcare workers
60–64 years	IIV-SD IIV-cc	Any age-appropriate influenza vaccine should be used for adults 60–64 years of age who do not have contraindications.
65 years and older ^c	IIV-Adj IIV-SD IIV-HD IIV-cc	IIV-HD, IIV-Adj, or RIV should preferentially be offered, when available, over IIV-SD or IIV-cc for adults 65 years of age and older without contraindications. If no preferred product is available, any available influenza vaccines authorized for this age group should be used.

Abbreviations: ART, antiretroviral therapy; IIV, inactivated influenza vaccine; IIV-Adj, adjuvanted inactivated influenza vaccine; IIV-cc, mammalian cell–culture-based inactivated influenza vaccine; IIV-HD, high-dose inactivated influenza vaccine; IIV-SD, standard-dose inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; LAIV, live attenuated influenza vaccine; RIV, recombinant influenza vaccine

^a Authorized products may or may not be marketed and available in Canada in a given season

^b Refer to Table 5 in NACI's *Statement on seasonal influenza vaccines for 2026–2027* (4) for a summary of vaccine characteristics of LAIV compared with IIV in children 2–17 years of age

^c Refer to the NACI supplemental statement on influenza vaccination in adults 65 years of age and older (10) for rationale, supporting evidence appraisal and additional details on the evidence reviews that were conducted to support this recommendation

Conclusion

Annual influenza vaccination continues to be recommended by NACI for all individuals aged six months and older, noting product-specific age indications and contraindications. Adults 65 years of age and older should receive a high-dose or adjuvanted influenza vaccine, when available. Influenza vaccination is particularly important for groups identified in List 1.

Authors' statement

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WS — Writing—review & editing

KK — Writing—review & editing

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The NACI *Statement on seasonal influenza vaccines for 2026–2027* was prepared by A Sinilaite, W Siu and J Papenburg, on behalf of the NACI Influenza Working Group, and was approved by NACI.

Competing interests

None.

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Table 2: Recommended dose and route of administration, by age, for influenza vaccine types authorized for the 2026–2027 influenza season

Age group	Influenza vaccine type (Route of administration)					Number of doses required
	IIV-SD ^a (IM)	IIV-cc ^b (IM)	IIV-Adj ^c (IM)	IIV-HD ^d (IM)	LAIV ^e (Intranasal)	
6–23 months	0.5 mL ^f	0.5 mL	0.25 mL	N/A	N/A	1 or 2 ^g
2–8 years	0.5 mL	0.5 mL	N/A	N/A	0.2 mL (0.1 mL per nostril)	1 or 2 ^g
9–17 years	0.5 mL	0.5 mL	N/A	N/A	0.2 mL (0.1 mL per nostril)	1
18–59 years	0.5 mL	0.5 mL	N/A	N/A	0.2 mL (0.1 mL per nostril)	1
60–64 years	0.5 mL	0.5 mL	N/A	N/A	N/A	1
65 years and older	0.5 mL	0.5 mL	0.5 mL	0.7 mL	N/A	1

Abbreviations: IIV-Adj, adjuvanted inactivated influenza vaccine; IIV-cc, mammalian cell–culture-based inactivated influenza vaccine; IIV-HD, high-dose inactivated influenza vaccine; IIV-SD, standard-dose inactivated influenza vaccine; IM, intramuscular; LAIV, live attenuated influenza vaccine; N/A, not applicable

^a Fluzone® (6 months and older), Influvac® (6 months and older), Fluviral (6 months and older)

^b Flucelvax® Quad (6 months and older)

^c Flud Pediatric™ (6 to 23 months) or Flud® (65 years and older). Although authorized, Flud® Pediatric has not been available in Canada since 2019

^d Fluzone® High-Dose Quadrivalent (65 years and older)

^e FluMist® Quadrivalent (2 to 59 years)

^f Evidence suggests moderate improvement in antibody response in infants, without an increase in reactogenicity, with the use of full vaccine doses (0.5 mL) for unadjuvanted inactivated influenza vaccines. This moderate improvement in antibody response without an increase in reactogenicity is the basis for the full dose recommendation for unadjuvanted inactivated vaccine for all ages. For more information, refer to the *Statement on Seasonal Influenza Vaccine for 2011–2012* (11)

^g Children six months to less than nine years of age receiving seasonal influenza vaccine for the first time in their life should be given two doses of influenza vaccine, with a minimum interval of four weeks between doses. Children six months to less than nine years of age who have been vaccinated with one or more doses of seasonal influenza vaccine in the past should receive one dose of influenza vaccine per season thereafter



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Appendix

Table A1: Strength of the National Advisory Committee on Immunization recommendations

Strength of NACI recommendation (Based on factors not isolated to strength of evidence, e.g., public health need)	Strong	Discretionary
Wording	"should/should not be offered"	"may be considered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should") OR known/anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages closely balanced with known/anticipated disadvantages OR uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present	A discretionary recommendation may be considered for some populations/individuals in some circumstances Alternative approaches may be reasonable

Abbreviation: NACI, National Advisory Committee on Immunization



Berry contagious: Use of post-exposure prophylaxis to respond to an outbreak of hepatitis A associated with frozen imported berries in Canada

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Abstract

Background: In April 2016, the Public Health Agency of Canada received reports of three locally-acquired cases of hepatitis A in one province who reported consuming frozen berries sold by a common retail chain. Subsequently, cases of hepatitis A with frozen berry consumption in other provinces were reported, and all illness onsets were within an eight-week period.

Objective: To conduct a national outbreak investigation with provincial and federal partners to identify the source, and determine appropriate public health measures.

Methods: Epidemiological data were collected through case interviews and purchase history records were obtained from the retailer. Hepatitis A virus (HAV) genotyping and ribonucleic acid (RNA) fingerprinting identified outbreak-related cases. The food safety investigation included traceback, traceforward, and testing of the suspected product.

Outcome: Of the 25 confirmed cases, 21 were genotyped, revealing a multi-strain outbreak: 16 were genotype 1B with identical RNA fingerprints; and five cases were genotype 1A with nearly identical RNA fingerprints. Epidemiologic evidence implicated a frozen berry blend (Product A). Hepatitis A virus was detected in a closed retail sample, an open sample from a case's home and a blackberry input. Product A was recalled, and post-exposure prophylaxis was offered. More than 11,000 people were vaccinated by the retailer and public health units. In September 2016, a new cluster of hepatitis A cases matching the outbreak strain was identified; the index case had consumed recalled product.

Conclusion: Rapid epidemiologic investigation, purchase history records, traceback evidence, retailer cooperation and collaboration between public health partners facilitated rapid identification and product recall.

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Introduction

Hepatitis A is a nationally notifiable disease in Canada, where endemicity is low and has been reported at a rate at or below one per 100,000 individuals since 2007 (1). It is not part of

the regular vaccination schedule except in the province of Québec (2). From 2014 to 2018, reported hepatitis A infections in Canada were predominantly genotype 1A (59%) or



genotype 1B (26%), with fewer cases identified than genotypes 3A (15%) and 2A (0.3%) (*personal communication, A. Andonov, 2019*).

In Canada, local and regional public health authorities investigate cases of hepatitis A and report to the respective province or territory who then report age, sex and case counts to the nationally notifiable diseases surveillance system. Timely notification of increases in hepatitis A, based on a five-year rolling average, are provided on a weekly basis through the National Enteric Surveillance Program (3) or through notification from provincial or territorial public health partners. Provincial laboratories are encouraged to submit all hepatitis A virus (HAV) specimens to the National Microbiology Laboratory (NML) for genotyping and ribonucleic acid (RNA) fingerprinting. The NML maintains an extensive molecular database of primarily locally-acquired HAV strains in Canada, enabling cluster detection and notification when identical RNA fingerprints are detected in two or more cases (1,2).

Foodborne outbreaks of hepatitis A in North America and Europe have been linked to fresh and frozen produce, including sun-dried tomatoes, green onions, frozen berries and pomegranate seeds (4). Notably, in 2012 and 2013, two outbreaks of hepatitis A in Europe associated with contaminated berries affected over 1,400 individuals (5). One of these outbreaks was linked to two similar, but genetically distinct, strains of HAV in epidemiologically-linked outbreak cases (6). Subsequent hepatitis A outbreaks associated with frozen berries have been reported in Europe (7–10).

Between March 31 and April 5, 2016, two local health units in a single Canadian province identified three locally-acquired cases of hepatitis A who reported consuming frozen berries purchased

from a single retail chain. Subsequently, other provinces reported hepatitis A cases with frozen berry consumption and all illness onsets were within an eight-week period. A national outbreak investigation was initiated in collaboration with provincial and federal partners to identify a common source of the illnesses and determine appropriate public health measures. This retrospective outbreak report describes the epidemiological, microbiological and food safety findings of the investigation, and the associated public health response to Canada’s first known multi-strain outbreak of HAV associated with frozen imported berries.

Methods

Case definitions

A confirmed case was defined as a resident of or visitor to Canada with laboratory-confirmed HAV infection with 1) genotype 1B and identical RNA fingerprint or 2) genotype 1A and identical RNA fingerprint or 3) genotype 1A with a single nucleotide difference to the RNA fingerprint (**Table 1**); and where infection was likely acquired in Canada with a date of onset or laboratory collection date on or after January 1, 2016.

A probable case was defined as a resident of or visitor to Canada with laboratory-confirmed HAV infection using the Immunoglobulin M (IgM) antibody to HAV test (and who had not been vaccinated against HAV in the four weeks before onset), who reported consumption of the implicated frozen berry product within their illness incubation period (15–50 days before symptom onset) with genotype information pending or unavailable, and where infection was likely acquired in Canada with a date of onset or laboratory collection date on or after January 1, 2016.

Table 1: Nucleotide sequences of ribonucleic acid fingerprints associated with the hepatitis A virus genotypes 1B and 1A outbreak strains

Outbreak strain genotype	Nucleotide sequence
1B	GATTGCAAATTACAATCACTCTGATGAATATTTGTCCTTTAGTTGTTATTTGTCTGTTAC AGAACAATCAGAGTTTTATTTTCCCAGAGCTCCATTGAATCAAATGCCATGTTATCCA CTGAATCAATGATGAGCAGAATTGCAGCTGGAGACTTGGAGTCATCAGTGGATGATC CCAGATCAGAGGAGGACAGAAGATTTGAGAGTCACATAGAATGTAGGAAGCCATAC AAAGAATTGAGATTAGAAGTTGGGAAACAAAGACTCAAGTATGCTCAGGAAGAATTG TCAAATGAAGTACTTCCACCTCCTAGGAAAATGAAGGGACTGTTTTACAAGCCAAAA TTTCTCTTTTTTATACTGAGGAGCAT
1A	GATTGCAAATTACAATCATTCTGATGAATATTTGTCCTTTAGTTGTTATTTGTCTGTCAC AGAACAGTCAGAGTTCTATTTTCTAGAGCTCCATTAAATCAAATGCTATGCTGTCCA CTGAGTCTATGATGAGTAGAATTGCAGCTGGAGATTTGGAGTCATCGGTGGATGATC CTAGATCAGAGGAGGACAGAAGATTTGAGAGTCATATAGAATGTAGGAAACCATACA AAGAATTGAGATTGGAGGTTGGCAAACAAAGACTCAAATATGCTCAGGAAGAGTTGT CAAATGAAGTGCTTCCACCTCCTAGGAAAATGAAGGGGCTATTTTACAAGCTAAGAT TTCTCTTTTTTATACTGAAGAGCAT



Laboratory analysis

Clinical specimens were screened for IgM anti-HAV at local community or private laboratories, or at provincial public health laboratories. Since 2013, the Public Health Agency of Canada (PHAC) has recommended that all IgM anti-HAV reactive clinical specimens be forwarded to the NML for genotyping and RNA fingerprinting. A 373-nucleotide fragment in the VP1-2A junction region was amplified to determine genotype and analysed for RNA fingerprinting as previously described (11). Due to the small size of the VP1/2A junction region, the complete VP1 gene was amplified whenever possible to improve the phylogenetic analysis of closely related HAV strains (12).

Testing for the presence of HAV in food samples collected from retail, the Product A manufacturing facility, and from case homes was completed by the Canadian Food Inspection Agency (CFIA) in Saint-Hyacinthe, Québec. The viral RNA was extracted from frozen food samples using a magnetic silica bead-based method (13) and detected by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) (14). The HAV strain LSH/S (VR-2266, ATCC, Gaithersburg, Maryland, United States) was used as RT-qPCR positive control. The assay used for HAV detection targets and amplifies a conserved region of the viral genome located in the non-structural cysteine proteinase and RNA polymerase junction (3C/3D region) (15). This short, conserved region is a preferred target for a detection assay; however, it does not allow for further HAV typing since genotype 1A and 1B differ by only one or two nucleotides from the positive amplicon sequence in that region (Table 2). Presumptive positive HAV RT-qPCR amplicons were cloned, and five bacterial colonies per sample were selected for amplification and sequenced by Sanger sequencing (16) to confirm the results; however, food products that tested positive for HAV were neither further typed nor sequenced.

Epidemiological investigation

Cases were interviewed by local health authorities using either a routine provincial hepatitis A questionnaire or the national hepatitis A hypothesis generating questionnaire. All questionnaires were collected and analyzed centrally at PHAC

to identify common exposures. Consent was requested from cases who reported consuming the suspected food product to obtain their individual purchase history from the relevant retail chain. Since Product A was a frozen product with a two-year shelf life, purchase histories of up to six months were requested. The information was used to confirm purchase of Product A in the weeks/months prior to illness onset.

Data analysis

Descriptive analyses were conducted to describe cases by case definition category (confirmed or probable), HAV sequence, age, sex, hospitalization, frozen berry exposure and symptom onset date.

Food safety investigation

Food samples from case homes were collected by local investigators, and the CFIA collected five closed food samples of the item of interest, Product A, from different retail locations. The CFIA conducted traceback, traceforward and food safety investigation activities related to Product A. The input import dates, and the Product A purchase dates captured in the case purchase histories were used to guide the Product A sampling plan at the manufacturing facility. To identify other potentially contaminated products, nine different lots of inputs (three blackberry, two cherry, four strawberry) and four different lots of finished products (retention samples) were collected by CFIA at the manufacturing facility.

Results

Case characteristics

Twenty-five lab-confirmed cases of hepatitis A were identified across three provinces in eastern Canada (Figure 1), where 21 cases met the confirmed case definition and four were classified as probable. Symptom onset dates ranged from February 26 to May 16, 2016. The median age of cases was 48 years (range: 10–70 years), and 56% were male (n=14/25). Ten cases (42% or 10/24) were hospitalized and no deaths were reported.

Table 2: Amplicon and reference sequences of the hepatitis A virus 3C/3D region used for detection in Product A and frozen blackberry input

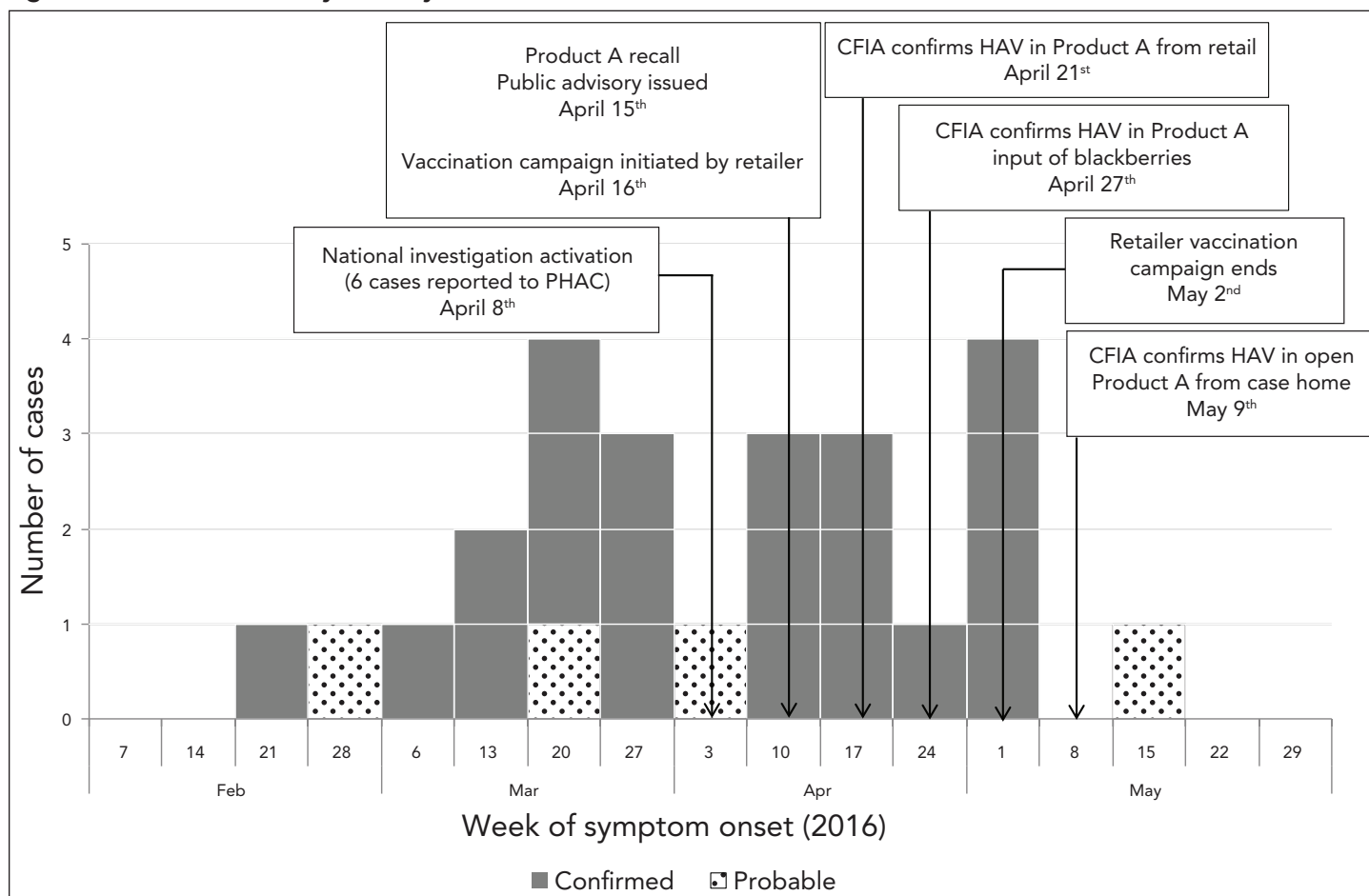
Description	Sample and reference identification number	Amplicon and reference sequences ^a
NCBI reference genotype 1B	M16632	GGTCTCCAAAACGCTTTTGTAGAAAGAGTCCCATTATCATCACATTGATAAAACCATGATT
NCBI reference genotype 1A	Q425480	A.....C.....C.....
Reference RT-qPCR control	AH003953	A.....C.....C.....
Food Product A	VI_020_2	A.....C.....
	VI_0042_001	A.....C.....R.....
Frozen blackberry input	VI-0031-5	A.....C.....

Abbreviations: NCBI, National Center for Biotechnology Information; RT-qPCR, reverse transcription-quantitative polymerase chain reaction

^a R=A or G



Figure 1: Distribution of confirmed and probable hepatitis A cases (n=25) by symptom onset and timeline of significant events, February 26–May 16, 2016^a



Abbreviations: CFIA, Canadian Food Inspection Agency; HAV, hepatitis A virus; PHAC, Public Health Agency of Canada
^a Each box denotes a case

Laboratory analysis

Genotyping and RNA fingerprinting were completed for 21 of the 25 outbreak cases. Sixteen cases were genotype 1B with identical RNA fingerprints, and five cases were genotype 1A with an identical RNA fingerprint match or an RNA fingerprint that differed by a single nucleotide. Genotype was not determined for four cases; these isolates were either not forwarded to the NML for genotyping, could not be typed or were PCR-negative.

Epidemiological investigation

Twenty-three of 25 outbreak cases (92%) reported consuming or probably consuming Product A during their incubation period. The remaining two cases did not report consuming Product A but matched the primary 1B outbreak strain. Given HAV's long incubation period (15–50 days), cases may not have recalled consuming Product A or may have unknowingly consumed the product outside the home (e.g., at a social gathering, restaurant or as a free sample offered by the retailer).

Thirteen purchase histories were retrieved from the 23 cases that confirmed shopping at the retail chain where Product A was sold. Product A was identified in 12 of the 13 retrieved purchase

histories; where eight cases were HAV genotype 1B, two cases were HAV genotype 1A and two cases' HAV genotype was not determined. Product A was not identified in the purchase history of the remaining case (HAV genotype 1A), due to a lost membership card, but the case verbally confirmed the purchase. Additionally, one case (HAV genotype 1B) confirmed consumption of the product at a friend's home. Purchase dates of Product A were obtained from the friend, but no purchase history was retrieved.

Food safety investigation

Product A was a mixture of frozen strawberries, blackberries, cherries, blueberries and raspberries sold at a single retail chain across five provinces in Eastern Canada. The individual berry inputs for this product were sourced from various suppliers in multiple countries and the final berry blend product was packaged at the manufacturer in Eastern Canada. Strawberries came from suppliers in Mexico and Turkey, blackberries from suppliers in Serbia and Bulgaria, cherries from suppliers in Turkey, blueberries from multiple suppliers in Argentina and Chile and raspberries from suppliers in Chile, Serbia and Bulgaria. Inputs from South America were not investigated as the



predominant outbreak strain, genotype 1B, is more prevalent in eastern Europe and Mediterranean countries (17). Inputs from the previous six months were considered; older inputs were known to be unavailable at retail as finished product during the timeframe of interest.

One closed sample of Product A (best before date: March 15, 2018) from retail was positive for the presence of HAV. Of the 13 input ingredients and retention samples tested, one was positive for HAV: an input of blackberries imported from Bulgaria in February 2016, used only in Product A (best before date: March 15, 2018). There were no other Canadian importers of blackberries from this same Bulgarian exporter; however, Product A (best before date: March 15, 2018) contained four additional lots of blackberries, all from Bulgaria. These four additional lots were also used to make Product A (best before date: December 9, 2017), and a retention sample tested negative for HAV. One opened sample of Product A (best before date: February 2, 2018) from a case home was also positive for the presence of HAV. The sequencing results of the positive open and closed sample of Product A and the frozen blackberry input are shown in Table 2.

Public health measures

A voluntary product recall was issued by the manufacturer for Product A (best before date: up to and including March 15, 2018) on April 15, 2016, seven days after the outbreak investigation was initiated. Public Health Agency of Canada, CFIA, provincial and local health authorities issued public messaging alongside accompanying social media messaging regarding the outbreak, the Product A recall, links to the retailer's website and post-exposure prophylaxis (PEP) initiatives. The retailer posted information on their website regarding the product recall, including advice to customers and information on vaccination clinics. A timeline illustrating illness onsets and when significant events in the outbreak investigation occurred is shown in Figure 1.

Following the recall notice, the retailer used its membership program to issue two automated phone calls to members that had purchased Product A. The first call advised the member to not to consume Product A due to the recall, and the second informed the member of immunization being offered to eligible individuals and directed members to contact their local public health unit for more information. As per the guidelines for prophylaxis administered early in the HAV incubation period (18), all individuals who had consumed Product A in the previous two weeks were eligible for PEP offered by public health units in provinces where Product A was distributed, and by nurses and pharmacists at the retail locations where the product was purchased. The vaccination campaign was initiated by the retailer on April 16, 2016, the day after the product was recalled, and concluded on May 2, 2016. Approximately 2,578 individuals were vaccinated at local health units in three provinces, and 9,405 individuals were vaccinated at the retailer clinics. Numbers

of vaccinations provided by public health in two of the five provinces were not available.

Discussion

This was Canada's first known multi-strain outbreak of HAV associated with widely distributed frozen imported berries. Multi-strain outbreaks linked to frozen berries have been reported in the United States (19) and Northern Europe (6,20). A common element of the frozen berry products implicated in these multi-strain outbreaks is the inclusion of inputs from multiple countries, as well as potential contamination of inputs by sewage. In this investigation, strong epidemiological evidence implicated two HAV strains associated with Product A. All but two cases with the predominant 1B outbreak strain and all cases with the 1A outbreak strain reported consuming Product A, with no other common food exposures identified. Although lab confirmation of both outbreak strains in Product A was not possible due to limitations in HAV detection methods, the epidemiological link was strong. This investigation demonstrates that multi-strain outbreaks associated with frozen berries are possible. Investigators should consider the possibility of a multi-strain event, especially if strong epidemiological evidence supports the hypothesis.

Purchase histories associated with store membership records, including product names and purchase dates provided the necessary specificity for action by public health and food safety partners. Supermarket receipts, store membership or purchase history data has been used to identify common exposures and confirm purchase of products in hepatitis A outbreak investigations in Canada (11) and Europe (6,20). In this investigation, prompt collection of purchase history data enabled quick identification of Product A, which was removed from the market seven days after the start of the national investigation. The collection of detailed food history of early cases, a clearly identified product distributed to a single retailer, and timely availability of purchase history information, contributed to the success of this investigation. Public health investigators should consider obtaining consent for loyalty/membership card or purchase histories early in an investigation, as they have proven useful in both hypothesis generation and product confirmation (21,22).

As a result of the outbreak investigation findings and subsequent product recall, the retailer initiated an extensive vaccination campaign. The availability of pharmacies within most of the retailer locations, direct calls to members who purchased the recalled product, and willingness of the retailer allowed for the prompt provision of prophylaxis. The same retail chain used a similar approach in a 2013 outbreak of hepatitis A associated with frozen pomegranate arils, with 165 affected individuals (19). Retailer membership data were used to identify and contact customers who had purchased the implicated product(s) to offer



PEP, and more than 10,000 affected customers were vaccinated through in-store clinics.

Although the retailer was able to offer vaccination, jurisdictions reported challenges, including availability of vaccine, public and inter-agency communications and determining leadership of the PEP campaign. Coordination was complicated by varying provincial recommendations and criteria to guide decision-making around vaccine eligibility. This outbreak highlighted uncertainty about the role of public health authorities in decision-making regarding PEP for HAV, when retailers have desire and capacity to provide vaccinations. As a result, a protocol to support PEP decision-making in multi-jurisdictional foodborne hepatitis A illness outbreaks was developed to outline the roles and responsibilities of stakeholders, including public health authorities and the retail industry. It has been adapted and published as Annex 2 in Ontario's Foodborne Illness Outbreak Response Protocol (23).

Several months after the outbreak concluded, a cluster of nine HAV cases matching the primary outbreak strain by RNA fingerprinting were identified in an eastern Canadian province where the implicated product had been sold. The index case had no travel history and had consumed the recalled Product A, confirmed by membership card information. Inadequate product recall communication was cited by investigators as a possible factor, as some individuals may not have been aware or complied with the recall. Case interviews revealed that several adult cases in the second cluster had contact with children who attended the same daycare, with no other commonalities identified. Investigation of the eight cases associated with the daycare indicated secondary transmission, and PEP was used as a means to prevent tertiary transmission. One case with no connection to the daycare reported travel to Bulgaria during their exposure period, providing evidence that this outbreak strain was circulating in that country. This later cluster, involving both foodborne and person-to-person transmission in a daycare, underscores the importance of broad communication of public health advice related to recalled products, especially those with a long shelf life.

A study has shown that in model experiments, frozen storage for three months had limited effects on HAV survival in frozen berries (24). This was observed in this outbreak, and was well described in a previous HAV outbreak investigation where frozen strawberries consumed by cases in February and March 1997 were traced back and their date of processing was April–May 1996, almost a year prior to the outbreak (25). During this event, broad and timely public communications were necessary to ensure that all consumers, including those exposed through shared food or in-store samples, were notified of the recall and availability of PEP. The identification of the second outbreak reinforced the importance of PEP campaigns to prevent additional illness associated with widely distributed retail foods, especially those like Product A with a long shelf life, and given the ability of HAV to persist under freezing conditions.

Conclusion

This investigation adds to the evidence that frozen imported berries can be a source of HAV for countries with low endemicity. Rapid detection by the local health unit and detailed epidemiologic and purchase history information resulted in the rapid identification and recall of Product A from the market. The public health action including the PEP campaign provided by the retailer in collaboration with public health authorities likely prevented further illnesses. The second outbreak associated with consumption of recalled product highlights the importance of broad consumer communications, as recall notices may not reach all consumers.

Authors' statement

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The data from this article are not publicly available due to privacy concerns and legislative requirements.

Competing interests

None.

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Outbreak of *Escherichia coli* O157 associated with pork products linked to colonized swine in Alberta, 2018

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Abstract

Background: In March 2018, an outbreak of *Escherichia coli* (*E. coli*) O157 infections was identified in Alberta. The objective of this article is to describe the outbreak, including the epidemiological, food safety and laboratory investigations that contributed to the identification of the outbreak source.

Methods: Outbreak cases were identified through notifiable disease surveillance. Exposure (including food consumption) information was collected from outbreak cases. Onsite investigations were conducted at food facilities linked to outbreak case exposures, including collection of environmental swabs and food samples for *E. coli* O157 analysis and traceback investigation.

Results: There were 43 outbreak cases identified; 33% of cases were hospitalized and one case was fatal. Dates of illness onset ranged between March and May 2018. An *E. coli* O157 outbreak strain was identified in outbreak case isolates and in 20 samples collected as part of this investigation (pork, swine feces and environmental swab). Implicated pork was traced back to a provincially licensed abattoir and meat processing facility. Outbreak cases were linked to six food facilities; 51% of cases were linked to one restaurant facility. Interventions included recall of implicated pork products, and temporary closure and implementation of food handling process improvements at implicated facilities.

Conclusion: This investigation demonstrates a direct link between colonized swine, contaminated pork products and human *E. coli* O157 illnesses. The findings highlight the importance of consumer guidance for safe pork handling, as well as interventions during animal husbandry, biosecurity, slaughter, processing and handling to reduce the risk of human *E. coli* O157 illnesses.

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Keywords: *E. coli* O157, outbreak, pork, swine, foodborne illness

Introduction

Shiga-toxin-producing *Escherichia coli* (STEC), including *E. coli* O157, is a major cause of foodborne illness in humans and is associated with morbidity and mortality worldwide. In 2019, there were 397 laboratory-confirmed *E. coli* O157 illnesses in Canada, a rate of 1.06 illnesses per 100,000 population; in Alberta, the rate was 2.17 per 100,000 population (1). In Canada,

approximately 60% of *E. coli* O157 illnesses have been attributed to foodborne transmission (2). Furthermore, it is estimated that beef and raw produce are the source of 47.4% and 19.5% of foodborne *E. coli* O157 illnesses, respectively; for pork, the estimate is 2.0% (3). Pork-associated *E. coli* O157 outbreaks are relatively uncommon in Canada (4); in Alberta, however,



there have been two previously reported *E. coli* O157 outbreaks attributed to pork products in 2014 (5) and 2016 (6). Between March and May 2018, an outbreak of 43 *E. coli* O157 infections associated with pork products was investigated in Alberta, Canada. The objective of this article is to describe the outbreak, including the epidemiological, food safety and laboratory investigations that contributed to the identification of pork products from infected swine as the source, describe the public health interventions implemented to prevent further illnesses, and highlight that pork should be considered as a vehicle of transmission of *E. coli* O157 infections.

Methods

Overview and outbreak detection

Shiga-toxin-producing *E. coli* is a notifiable disease in Alberta and the rest of Canada. The outbreak investigation began on March 27, 2018, when Alberta Health Services (AHS) identified a sudden increase above baseline incidence of *E. coli* O157 cases in one AHS Zone through notifiable disease surveillance, with two cases reporting consumption of food from the same restaurant. The outbreak was declared over on June 1, 2018, following two maximum *E. coli* O157 incubation periods (20 days) without a new case linked to the outbreak.

Outbreak case finding and data collection

The case definition for the outbreak was as follows: a resident of, or visitor to, Alberta with laboratory-confirmed *E. coli* O157 infection matching the outbreak pulsed-field gel electrophoresis (PFGE) pattern combination, and illness onset on or after March 1, 2018. Outbreak cases were identified through notifiable disease surveillance and subsequent PFGE characterization of case isolates. Individuals meeting the case definition for *E. coli* O157 were interviewed using a standard AHS public health follow-up questionnaire to collect relevant clinical, demographic and exposure information. When this approach did not reveal the outbreak source, open-ended re-interviews were conducted, including face-to-face discussion in case homes and at area hospitals.

Epidemiologic and statistical analysis

Frequency of outbreak case exposures from completed questionnaires were analyzed, including consumption of specific foods and purchase of food from specific food facilities. Microsoft Excel was used to analyze the data, generate descriptive statistics and create charts. An epidemiological study (e.g., case-control) was not conducted; case series analysis yielded compelling source attribution data.

Food safety investigation

The outbreak was investigated by member agencies of the Canada-Alberta Partners in Food Safety Alberta Foodborne Illness and Risk Investigation Protocol (FIRIP) (7) after initial case investigation revealed illnesses were likely foodborne. The FIRIP

partner agencies conducted inspections and onsite investigations at implicated food facilities. They collected environmental swabs and food samples from those facilities, as well as food samples from outbreak case homes. Employees of an implicated restaurant submitted clinical specimens for analysis, as required by the local Medical Officer of Health (MOH). Swine and cattle fecal samples were also collected from the implicated abattoir, meat processing facility and live animal production areas. Samples were submitted to Alberta Precision Laboratories, Public Health Laboratory (ProvLab), Alberta Agriculture and Irrigation (AGI; formerly Alberta and Forestry), and the Canadian Food Inspection Agency (CFIA) laboratories for *E. coli* O157 isolation and characterization.

Laboratory investigation

Environmental and food samples were analyzed following methods published in the Health Canada Compendium of Analytical Methods (8), namely, MFLP-30 and/or MFHPB-10 (with and without modifications), as well as MFLP-22, in some cases. All *E. coli* O157 isolates (clinical, food and environmental) were characterized by PFGE and subsequently by whole-genome multilocus sequence typing (wgMLST) using the standardized PulseNet International Protocol. For PFGE, all isolates were digested by *Xba*I and *Bln*I restriction enzymes followed by analysis using BioNumerics 6.01 and a comparison of representative PFGE profiles was prepared using the Dice coefficient and Unweighted Pair Group Method with Arithmetic Mean (UPGMA) cluster analysis. Pulsed-field gel electrophoresis patterns were uploaded to the PulseNet Canada (PNC) database located at the Public Health Agency of Canada National Microbiology Laboratory (NML), Winnipeg; a national pattern was designated. As for wgMLST, the analysis was performed using BioNumerics 7.6.

Public health interventions

Public health interventions initiated to control the outbreak included:

- Recall of raw pork products possibly contaminated with *E. coli* O157
- Exclusion of *E. coli* O157-infected employees working at an implicated restaurant identified through MOH-required screening and voluntary closure of the restaurant pending screening results
- Implementation of food handling process improvements at implicated facilities, under the supervision of FIRIP partners
- Public notification via news releases regarding the outbreak and *E. coli* O157 prevention measures

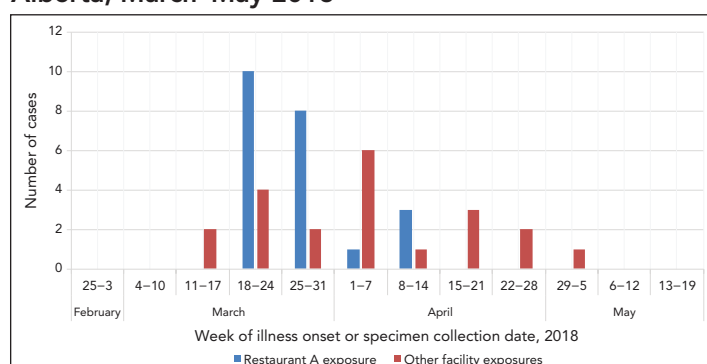
Results

There were 43 outbreak cases identified. Outbreak case mean and median ages were 27 and 23 years, with a range of 1–85; 16 cases (37%) were aged six years or less. Twenty-five (58%) cases were male. Predominant symptoms reported were diarrhea (97%),



bloody stool (89%), and abdominal pain (54%). Fourteen (33%) cases were hospitalized, and five (12%) developed hemolytic uremic syndrome. One case was fatal. Four (9%) were secondary cases (i.e., household contact of another outbreak case). Most cases resided in one metro region of Alberta (35, 81%); six cases resided elsewhere in Alberta, and two cases were non-Alberta residents. Dates of illness onset or specimen collection dates ranged between March and May 2018 (Figure 1). Mean incubation period was 3.3 days with a range of 2–5 days (among cases with a known suspected exposure date).

Figure 1: Case distribution by week of illness onset or specimen collection date and facility exposures, pork-associated outbreak of *Escherichia coli* O157, Alberta, March–May 2018



Note: The epidemiologic curve shows the number of outbreak cases illustrated by month and week of symptom onset or specimen collection date. Cases occurred between March and May of 2018. During the weeks of March 11–April 29, 2018, there were 1 to 14 cases. There were two cases during the week of March 11, and in the two-week period March 18 to 31, there was a peak of 24 outbreak cases. The number of weekly cases steadily declined in the remaining weeks of the outbreak. Outbreak cases are also illustrated by facility exposures. Cases with exposure to Restaurant A occurred between the weeks of March 18 to April 8, with 1 to 10 cases reported each week. Cases with other facility exposures took place between the weeks of March 11–April 29, 2018, with 1 to 6 cases reported each week.

Case exposure investigation and traceback revealed that 35/43 cases had direct or indirect exposure to food from a provincially licensed meat facility (Facility A) via an Alberta restaurant, Restaurant A (22/35), and other facilities in Alberta that processed pork from Facility A (13/35, Table 1). Seven cases consumed pork products purchased from Retail Establishment A, four of whom consumed mettwurst, a sausage product understood to contain raw pork not cured or smoked and sold as ready-to-eat. Production records revealed that during the timeframe of interest, Facility A supplied pork to Retail Establishment A. Further investigation identified four additional

facilities (Retail Establishment B, Retail Establishment C, Retail Establishment D, Restaurant B) that produced pork products consumed by outbreak cases, which received pork from Facility A, directly or through secondary points of sale. Eight cases had indeterminate or no known exposure to pork originating from Facility A.

Food safety investigation—Restaurant A

Twelve cases reported consuming food from Restaurant A as direct or indirect patrons of the restaurant. Meal consumption dates ranged between March 16 to March 24. Seven cases reported consumption of pork in the restaurant meal. Complete and detailed food histories were challenging to collect: six cases reported consumption of food served in the “Boodle” style (assorted cooked meats, rice and vegetables served on banana leaves and eaten by group dining parties (9)), two cases consumed leftover food provided by restaurant patrons and two cases were vague historians. Three cases that reported no consumption of food from Restaurant A were household contacts of Restaurant A patrons that developed diarrhea within seven days of the meal but were not tested for *E. coli* O157.

Investigators visited the restaurant on and between March 27 and April 18. During inspections, the following were noted: several containers of meats kept at room temperature, unsanitary conditions in food preparation areas, and evidence of a rodent infestation in the facility. Violations were corrected and included completion of an online food safety course by restaurant employees.

Restaurant A staff (18 in total) submitted stool specimens for *E. coli* O157 screening as required by the MOH; specimens from seven employees were *E. coli* O157 culture positive (see Table 1). All employees identified as *E. coli* O157-infected via stool screening worked at the restaurant during the implicated meal date period. Six cases reported having no diarrhea at any time between March 1 and the date their specimen was collected; one employee reported onset of diarrhea on March 31 that lasted one day. Ready-to-eat food handled by infected employees was discarded upon request. Infected employees were excluded by MOH order from food handling occupations pending submission of two consecutive *E. coli* O157-negative stool specimens. The restaurant voluntarily closed on April 2 and reopened on April 18.

Table 1: Case exposures to facilities that received pork from Facility A, pork-associated outbreak of *Escherichia coli* O157, Alberta, March–May 2018

Facility	Number exposed ^a	Reported pork consumption (cooked, raw/undercooked)	Facility employee	Secondary case
Restaurant A	22	7 ^b (7, 0)	7	3
Retail Establishment A	7	7 (3, 4 ^c)	N/A	N/A
Other facilities ^d	6	5 (4, 1 ^e)	N/A	1

Abbreviation: N/A, not applicable

^a Not shown: six cases with indeterminate exposure, two cases with no known exposure to pork originating from Facility A

^b Among 12 restaurant patron cases

^c Consumed ready-to-eat sausage product containing raw pork

^d Includes Retail Establishment B, Retail Establishment C, Retail Establishment D, Restaurant B

^e Consumed pork intentionally undercooked



Food safety investigation—Facility A

Facility A is a provincially licensed abattoir located in Alberta that slaughters swine and processes various beef and pork products for retail, restaurants and direct sale. This facility also includes a 100-sow farrow to finish swine barn, and a 1,500-cattle feedlot operation on the same premises in close proximity to the abattoir. Swine slaughtered and processed in Facility A were all from the premises. Beef cattle from the premises were slaughtered off-site at a federally licensed plant, and some beef product was brought back and processed on site.

Alberta Agriculture and Irrigation staff conducted root cause analyses in the meat processing area at Facility A that revealed three general areas for improvement: a lack of record-keeping to verify process controls, inadequate handling of the ready-to-eat product, and inadequate slaughter procedures. Further investigation demonstrated that the operators and staff needed further training and explanation on how pathogens can enter the food chain during slaughter, dressing, and processing. The operator and staff were very responsive to AGI's recommendations.

On April 18, at AGI request, all products at Facility A were held pending further investigation. On April 24, Facility A voluntarily recalled all raw pork products produced at the facility on or between February 19 and April 24. This resulted in over 100 recalled pork products produced or sold by eight facilities, as communicated in CFIA recall notices on or between April 24 and May 2. Foodborne Illness and Risk Investigation Protocol partners collaborated on recall effectiveness checks for the affected products.

Alberta Agriculture and Irrigation conducted further investigation at Facility A in May 2018. The swine barn was located within a few hundred metres of the cattle feedlot. The cattle in the feedlot were sourced directly from a small number of farms. No illness was reported or observed in either the swine or the cattle during the outbreak period, although *E. coli* O157 infection in these species is typically asymptomatic. Both operations were well maintained. Extensive sampling of the swine barn and feedlot was conducted and continued in the swine barn once a month for the following five months.

Laboratory investigation

Escherichia coli O157 was detected in 20/50 pork product samples collected from various premises as part of this investigation. *Escherichia coli* O157 was also detected in swine feces from the barn on the premises, in cattle feces from the feedlot on the premises, and a production area environmental swab (Table 2). Repeated swine barn sampling identified *E. coli* O157 each month in 7% to 15% of samples, indicating that the organism was persisting in the barn. A predominant PFGE cluster pattern was identified among clinical *E. coli* O157 outbreak isolates, which matched all food, environmental, swine and cattle fecal isolates. Isolates with this PFGE cluster pattern

Table 2: Food and environmental samples with *Escherichia coli* (*E. coli*) O157 detected, pork-associated outbreak of *E. coli* O157, Alberta, March–May 2018

Food facility	Sample results ^a with <i>E. coli</i> O157 detected
Facility A	Raw pork parts ^b (n=2), environmental samples: cattle feces (n=8), swine feces (n=4), environmental swab (n=1)
Restaurant A	Raw pork parts ^b (n=2)
Retail Establishment A	Raw pork parts ^b (n=1), raw sausage (n=1), ready-to-eat sausage containing raw pork (n=1)
Retail Establishment B	Raw pork parts ^b (n=1), raw sausage ^c (n=7)
Retail Establishment C	Raw ground pork ^d (n=2)
Retail Establishment D	Raw pork parts ^b (n=1)

Abbreviation: *E. coli*, *Escherichia coli*

^a Among 50 samples collected containing pork originating from Facility A, and 180 environmental samples collected at Facility A: environmental swab (n=128), swine feces (n=26), cattle feces (n=26)

^b Includes pork hock, leg, shoulder and/or chop

^c Collected from homes of outbreak cases (n=3) and from retail establishment (n=4)

^d Collected from home of outbreak case

had not been seen in Alberta since 2017, when three isolates were identified.

The NML reported no other occurrences of the PFGE cluster pattern in the 60-day window prior to the outbreak. The wgMLST results indicate that the outbreak isolates (clinical, food and environmental) were closely related (a less than 10 allele difference among them) except one isolate (clinical) that differed by 12 alleles.

Discussion

Between March 2018 to May 2018, an outbreak of 43 *E. coli* O157 infections in Alberta was identified through notifiable disease surveillance. The epidemiological, laboratory and food safety evidence collected during the investigation supported pork from a single meat facility as the primary source of this outbreak. The identified linkage was used to inform interventions aimed at limiting further illness transmission, including a recall of pork products from the implicated facility and improvements to its food handling processes. This investigation demonstrates a direct link between colonized swine, contaminated pork products, and human illness with *E. coli* O157.

At time of publication, this was the third significant pork-associated *E. coli* O157 outbreak in Alberta since 2014. Pork consumption patterns of Albertans would not seem to be a factor; weekly pork consumption frequency by Albertans (53.1%) is less than in most other Canadian provinces (10). Mishandling and/or undercooking of pork by several establishments in the distribution chain was a contributing factor for all three outbreaks. Consumer knowledge of the risks of consuming



raw or undercooked pork may also have been a contributing factor, given that four outbreak cases consumed raw pork in a sausage sold as ready-to-eat, and one outbreak case consumed intentionally undercooked pork.

While *E. coli* O157 is considered endemic in beef cattle in Alberta, there has been limited research on its presence in swine in the province. A previous provincial abattoir survey did not detect *E. coli* O157 in pork carcasses (11), however, a more recent Alberta survey in 2017 (12) indicated that the bacteria is present in swine colon contents at a low level (1.4%). Control or eradication of infection in livestock has proven challenging and no effective practical methods have been developed.

In the same 2017 Alberta survey, *E. coli* O157 was not detected in pork carcass or swine colon content samples collected from Facility A, indicating a possible recent introduction to the swine barn. The presence of the organism in the cattle suggests the adjacent feedlot as a possible source. The swine barn had undergone an extensive renovation just prior to the outbreak, which may have increased the risk of exposure to *E. coli* O157 due to increased human traffic into the barn and reduced biosecurity during this period. However, since samples from both cattle and swine were taken during the same time period, no conclusion can be made about the cattle being infected first.

More than half of outbreak cases were epidemiologically linked to Restaurant A. This restaurant received pork from Facility A prior to and during the outbreak, but conditions and practices identified at the restaurant may also have contributed to transmission. Only seven of 12 restaurant patron cases reported pork consumption in their meals, which is suggestive of cross-contamination between raw pork received by the restaurant and other foods. This may have resulted from improper food handling practices observed during the investigation. For cases that reported consumption of food served in the “Boodle” style, the proximity of pork (if undercooked) to other foods served in this manner could result in cross-contamination. More than a third of employees were found to be infected with the *E. coli* O157 outbreak strain during the investigation, all but one of whom were reportedly asymptomatic. The period of communicability of the infected employees could not be confirmed, but it is plausible that they contributed to transmission.

Limitations

A key limitation of this investigation was the inability to confirm the root cause of the colonization of swine and the contamination of pork products. Furthermore, this investigation and similar recent investigations in Alberta have not yielded information to determine why pork products are a recurring vehicle of transmission of human *E. coli* O157 in Alberta, and not in other jurisdictions in Canada.

Conclusion

This outbreak investigation, combined with the two previous pork-associated *E. coli* O157 outbreaks in Alberta since 2014, provide evidence that pork should be considered to be a vehicle of transmission of *E. coli* O157 infections and should be included in consumer guidance for safe pork handling. The investigation findings also demonstrate that swine colonization with the pathogen may occur and contribute to risk of human illness, highlighting the importance of interventions during animal husbandry, biosecurity, slaughter, processing and handling to reduce the risk of *E. coli* O157 in pork products, especially when swine are raised in close proximity to beef cattle.

Authors' statement

LH — Investigation, conceptualization, formal analysis and interpretation of data, writing—original draft, writing—review & editing

JK — Investigation, conceptualization, formal analysis and interpretation of data, writing—review & editing

SE — Investigation, formal analysis and interpretation of data, writing—review & editing

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NH — Investigation, writing—original draft, writing—review & editing

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KH — Investigation, writing—review & editing

CK — Investigation, writing—review & editing

GG — Investigation, writing—review & editing

VM — Investigation, writing—review & editing

TK — Investigation, conceptualization, interpretation of data, writing—review & editing

Competing interests

No conflicts of interests to declare.

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None.

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Canada's progress in implementing poliovirus containment

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Abstract

Background: The goal of the Global Polio Eradication Campaign is to eliminate the remaining poliovirus circulating in human populations. Once eradicated, polio immunization rates are expected to decline and the only source of poliovirus will be in laboratory facilities, which poses a risk for re-introducing poliovirus into susceptible human populations.

Objective: To develop and implement a robust poliovirus containment and monitoring program in Canada to support global polio eradication efforts.

Methods: The Public Health Agency of Canada's Centre for Biosecurity (PHAC-CB) established the National Authority for Containment (NAC Canada) to oversee World Health Organization (WHO)'s Global Action Plan (GAP) for Poliovirus Containment. Facilities that entered into the GAP Containment Certification Scheme were designated as Poliovirus Essential Facilities. With the goal of reducing poliovirus material storage in Canada, and for containing the existing poliovirus stocks, the NAC Canada established inventories, audited and certified Poliovirus Essential Facilities, completed GAP training and qualified auditors and performed stakeholder outreach.

Results: Canada was among the first countries to qualify GAP auditors under the Containment Certification Scheme and was the first country in the world to move onto the second stage of poliovirus containment, when a Canadian Poliovirus Essential Facility was awarded the first Interim Certificate of Containment (ICC). The Canadian national poliovirus inventory, maintained by NAC Canada, leveraged the PHAC-CB Biosecurity Portal and stakeholder outreach (including surveys, website, newsletters, webinars) to identify sources of poliovirus and potentially infectious materials. From 2018–2024, the number of facilities in Canada storing wild type and Sabin poliovirus were reduced by 82% and 89%, respectively. In 2022, a multi-jurisdictional emergency exercise was conducted to evaluate coordinated response mechanisms for a simulated laboratory release of poliovirus. The Risk Group classification of human polioviruses in Canada was increased to Risk Group 3 (RG3) in 2023, to better align with the WHO GAP containment requirements.

Conclusion: Canada's NAC is collaborating with national stakeholders and international partners towards the goal of poliovirus eradication. Containment and monitoring efforts to reduce poliovirus in storage and to verify that Canadian Poliovirus Essential Facilities meet both federal legislative requirements and GAP biorisk management elements are key to health security in the current and post-polio eradication worlds. Canada's NAC activities will continue working towards decreasing the risk associated with poliovirus to safeguard the health and safety of Canadians.

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Keywords: poliovirus, containment, polio, eradication, health security, Canada, Global Action Plan, World Health Organization, *Human Pathogens and Toxins Act*, regulations



Introduction

The international campaign to eradicate polio has achieved significant progress since the Global Polio Eradication Initiative (GPEI) was initiated in 1988 (1). Since then, the number of polio cases has been reduced by 99.9% and two of the three wild poliovirus types (wildtype poliovirus types 2 and 3; WPV2 and WPV3) have been eradicated from circulation in human populations (2,3). Among these successes come new challenges, as wild poliovirus type 1 (WPV1) persists in two endemic countries (Afghanistan and Pakistan) and circulating vaccine-derived polioviruses (cVDPV) can emerge from oral poliovirus vaccine (OPV) use in under-vaccinated populations (2). Once WPV1 circulation has been stopped and OPV use has been discontinued, polio immunization rates are expected to decline and the only source of human polioviruses will be in laboratory facilities in the form of samples and culture collections (4). Canada, along with World Health Organization (WHO) member states, has recognized the importance of minimizing the risk of facility-associated release of polioviruses into susceptible human populations in a post-eradication world.

Under *World Health Assembly resolution 71.16*, Canada has committed to the containment of polioviruses (5). The WHO set a target date of 2026 for all poliovirus and poliovirus materials to be under the full containment requirements set out in the Global Action Plan (GAP) for Poliovirus Containment IV (GAPIV) (4). The GAPIV sets out strict biorisk management elements to contain polioviruses in Poliovirus Essential Facilities (PEFs), which are designated by the National Authority for Containment (NAC) on the basis that the facility serves a critical national or international function in vaccine production, research or public health diagnostics. The GAPIV considers containment for all poliovirus materials under a common biorisk standard, replacing the former Global Action Plan III (GAPIII), which focused on immediate containment of WPV2 materials (6). Poliovirus Essential Facilities acquire certification through the rigorous Containment Certification Scheme (CCS) process, which defines the roles and responsibilities, oversight and audit requirements for storing and working with polioviruses (7). Ongoing monitoring of Canadian facilities for compliance against the GAP is critical, as accidental poliovirus containment breaches have occurred at vaccine manufacturers, such as in the Netherlands (2017 and 2022), Belgium (2014) and France (2018 and 2024) (8–12). Importation of poliovirus from endemic countries has led to outbreaks in other global health regions, such as in WHO African Region (Malawi and Mozambique) (13), and Canada remains at risk for travel-associated importation of poliovirus (14). In 2022, poliovirus shedding linked to international travel was detected through genomic wastewater surveillance; however, no cases of poliomyelitis were identified in Canada (15,16). In parallel, the ongoing development of engineered attenuated poliovirus strains (e.g., OPV and S19) (17,18) reinforces the need for sustained public health surveillance and stringent containment of poliovirus materials in Canada.

The Public Health Agency of Canada's Centre for Biosecurity (PHAC-CB), serving as Canada's NAC, is working to reduce the number of facilities storing polioviruses in Canada and to ensure only certified facilities hold poliovirus materials under GAP containment requirements (4,6). This article presents Canada's progress in implementing poliovirus containment, working towards the goal of a polio-free world and keeping Canadians healthy, safe and secure.

Intervention

Establishment of the National Authority for Containment of Poliovirus (Public Health Agency of Canada's Centre for Biosecurity)

In 2015, NAC Canada was established within PHAC-CB to provide oversight on poliovirus containment in Canada and coordinate GAP certification with WHO's Global Certification Commission-Containment Working Group (WG). The PHAC-CB is mandated to protect the health and safety of Canadians against the risks posed by human pathogens and toxins by administering *Human Pathogens and Toxins Act* (HPTA) (19) and *Human Pathogens and Toxins Regulations* (HPTR) (20). The PHAC-CB Office of Biosafety and Biocontainment Operations Director serves as the National Poliovirus Containment Coordinator to coordinate with WHO and international NACs on containment issues. There are six members of NAC Canada who are employees of PHAC-CB, whose primary roles are in administering the HPTA by working in Canada's national biosafety and biocontainment inspection program.

Containment certification scheme process: National poliovirus inventory, Global Action Plan audits and certification plan

As the national regulator, PHAC-CB inspectors verify compliance with the HPTA, HPTR and the *Canadian Biosafety Standard*, 3rd edition (21) in Canadian facilities performing controlled activities with human pathogens and toxins. Through the inspection and licensing process, PHAC-CB maintains records on known poliovirus storage in Canada. An initial survey captured information on polioviruses as part of the HPTA registration process and outreach for import permits (2009–2015), followed by further surveys during the HPTA application process (2016). Additional outreach to non-HPTA regulated facilities was conducted (2016–2022) to identify other possible locations for poliovirus and potentially infectious material (PIM) storage, such as anthropology departments, water treatment facilities and pharmaceutical companies.



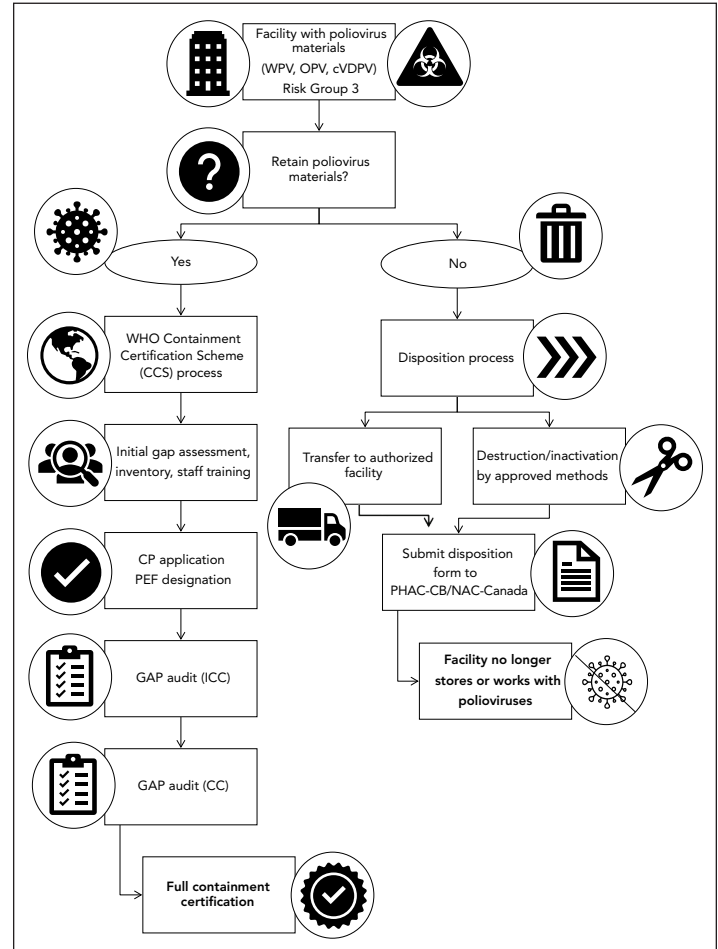
Facilities were encouraged to destroy existing poliovirus materials, transfer materials to approved facilities or begin the process to become a certified PEF (**Figure 1**). Facilities that chose to retain materials, and that were deemed by NAC Canada to serve an essential function (e.g., public health or research laboratories, vaccine manufacturers), were endorsed by the NAC and designated as PEFs to enter into the CCS process. Canada's NAC conducted an initial gap assessment (2018–2019) of these designated PEFs, including extensive site interviews, document reviews and physical verifications of the facilities. Applications were submitted for a Certificate of Participation to WHO-Global Certification Commission-Containment WG in 2019 and were approved in 2020. Canadian PEFs underwent full audits against the third edition of the GAP (GAPIII) in 2021, as NAC auditors focused on elements including safety management systems, biorisk management, research, diagnostics, production environments, engineering principles and concepts, emergency preparedness and security. Canadian NAC auditors identified corrective actions for designated PEFs to complete before they could be fully compliant with GAPIII. Upon confirmation that identified deficiencies were corrected, NAC Canada and PEFs prepared the Interim Certificate of Containment application packages and submitted to WHO-Global Certification Commission-Containment WG in 2022–2023.

Outcomes

National Authority for Containment Canada and the national poliovirus inventory

Establishing NAC Canada under the PHAC-CB was a key step in rapidly advancing poliovirus containment in Canada, as the existing regulatory structure for laboratory facilities was already in-place. Under the HPTA, Canada has the legal framework to require the containment of polioviruses which have been classified as Risk Group 3 (RG3) pathogens since November 2023 (see below in Outreach and communications). Canada's poliovirus activities (**Table 1**) include PHAC-led initiatives to accelerate the full implementation of the GAP containment requirements, complete polio inventories and destroy unnecessary materials and continue to reduce the number of facilities storing polioviruses. Canada's RG3 classification and *Canadian Biosafety Standard*, 3rd edition requirements align with WHO's GAPIV biorisk management elements for poliovirus containment (4). The national poliovirus inventory is updated using information entered by regulated parties into the secure PHAC-CB Biosecurity Portal when licence applications under the HPTA are submitted. Between 2015–2023, there was an 82% decrease in the number of Canadian facilities with wild type poliovirus materials and an 89% decrease in facilities with OPV Sabin materials. Initially from 2015, GAPIII containment requirements were focused on poliovirus type 2 infectious materials (WPV2, cVDPV2, oral polio vaccine type 2 [OPV2]) and type 3 materials were under containment

Figure 1: Poliovirus containment certification process for a Poliovirus Essential Facility



Abbreviations: CC, Containment Certificate; CP, Certificate of Participation; cVDPV, circulating vaccine-derived polioviruses; GAP, Global Action Plan; ICC, Interim Certificate of Containment; OPV, oral polioviruses; PEF, Poliovirus Essential Facility; PHAC-CB/NAC Canada, Public Health Agency of Canada's Centre for Biosecurity/National Authority for Containment Canada; WHO, World Health Organization; WPV, wild-type poliovirus

Note: Canadian facilities entering into the poliovirus Containment Certification Scheme process would require a Risk Group 3 licence under the *Human Pathogens and Toxins Act*. Poliovirus materials can include WPV, OPV and cVDPV

requirements since 2019. Canada was proactive in developing the inventory, capturing all poliovirus materials through surveys and outreach in-advance of WHO's type-specific requirements. Approximately 350 applications are received annually in Canada for new licences, renewals and amendments. No new facilities have planned to enter the poliovirus CCS process since HPTA licensing was implemented in 2016.

Attenuated poliovirus strains which are not included by WHO under GAP containment requirements (novel oral poliovirus [nOPV], S19 strains, polio-rhinovirus chimera [PVSRIPO]) are still regulated by PHAC-CB under the HPTA and *Canadian Biosafety Standard*, 3rd edition and are tracked as part of Canada's national poliovirus inventory. In particular, nOPV vaccine strains, which were engineered to be more genetically stable and less likely to revert to WPV-like cVDPV polioviruses, have continued to cause polio outbreaks (22) and require

**Table 1: Canada's activities and successes in poliovirus containment**

Activity	Description	Status
Establishing a National Authority for Containment of Poliovirus	Created within PHAC-CB as part of Canada's commitments to polio eradication and <i>World Health Assembly Resolution 71.16</i>	Completed, 2015
	Approving qualified GAP auditors	Completed; training on-going
Certifying Poliovirus Essential Facilities in Canada	Auditing facilities that store polioviruses to GAP requirements	Interim Certificates of Containment awarded under GAPIII; audits planned for GAPIV
	Periodic audits; monitoring and reporting	Ongoing
National poliovirus inventory	Creating a national inventory of all polioviruses and poliovirus materials (nOPV, S19, potentially infectious material)	Completed, surveys and outreach 2017–2022
	Tracking through Biosecurity Portal and disposition forms	Ongoing
Risk Group and Containment Level classification	Review RG/CL for polioviruses and conduct risk assessments	Increased to RG3/CL3 in November 2023
International partnerships and reporting	Annual report to WHO/PAHO on poliovirus containment as part of the Global Polio Eradication Campaign	Ongoing
	International NAC meetings to share best practices and implementation on GAP containment requirements	Ongoing
Emergency preparedness exercise	Conduct a Polio Outbreak Simulation. Exercise to test the multi-jurisdictional response to an accidental poliovirus containment event; involved over 40 participants from federal, provincial and municipal levels	Completed, November 2022
Outreach to regulated parties and the Canadian public	Publish in the PHAC-CB <i>Biosafety and Biosecurity for Pathogens and Toxins News</i>	Completed July 2021 and February 2022; ongoing
	PHAC-CB webinar	Planning in-progress
	Creating a NAC website	Completed

Abbreviations: GAP, Global Action Plan; NAC, National Authority for Containment; nOPV, novel oral poliovirus; PHAC-CB, Public Health Agency of Canada's Centre for Biosecurity; RG/CL, Risk Group/Containment Level; RG3/CL3, Risk Group 3/Containment Level 3; WHO/PAHO, World Health Organization/Pan American Health Organization

ongoing compliance monitoring and verification in laboratory facilities by PHAC-CB. Furthermore, PIM may be a source of polioviruses and WHO has published a guidance document to mitigate the risk of these materials (23). Potentially infectious material includes human fecal or respiratory samples, sewage samples, or their derivatives, that were collected at a time and place where poliovirus was in circulation (including use of OPV Sabin vaccines). Polioviruses in clinical or environmental samples can survive indefinitely in laboratory freezers, or months stored in the refrigerator (24). The PHAC-CB/NAC Canada's survey for PIM contacted 1060 organizations over a period of five years. This outreach identified no additional facilities possessing poliovirus PIM, or facilities had destroyed any potential materials.

Poliovirus Essential Facility audits and containment certification scheme results

Canada was among the first countries in the world to qualify auditors and perform audits under the 2015 published edition of the GAPIII in 2021 (6). All Canadian GAP auditors are members of NAC Canada, are experts in microbiology, biosafety and engineering, and were qualified based on their extensive education, training, experience and security clearance. As of 2024, the four qualified NAC Canada GAP auditors have over 278 estimated days of collective laboratory auditing experience,

plus specific training in biorisk management and GAP auditing of PEFs. For facilities indicating they planned to continue activities with polioviruses post-eradication, gap assessments were conducted and identified areas for improvement before full GAPIII certification audits were planned. Two facilities went through to the Certificate of Participation application stage of the CCS, while other facilities communicated the intention to dispose of poliovirus materials. At the time (2021), facilities were audited under GAPIII elements (6), but NAC Canada plans to conduct new audits to verify compliance to the revised GAPIV international standard (4) in advance of the final Containment Certification stage of the CCS. In general, audits discovered only minor nonconformities in training, documentation and general processes, which were remedied by corrective actions.

Following this GAPIII audit and application process, Canada was the first country to advance to the second stage of poliovirus containment, when a designated PEF was awarded an Interim Certificate of Containment in October 2022 (25,26). This key milestone exemplified Canada's substantial progress in poliovirus containment, while WHO has noted delays in other countries establishing NACs and creating poliovirus inventories (27,28). At the time of the preparation of this manuscript, PHAC-CB/NAC Canada was initiating the GAPIV audit process in Canada.



Outreach and communications

Canada's increase to Risk Group 3 and Containment Level 3 for human polioviruses

After a review and updating the pathogen risk assessment on human polioviruses, PHAC-CB recommended increasing the RG classification to RG3 and Containment Level (CL) classification to CL3. This recommendation was considered by the HPTA Advisory Committee (29) and approved in 2023. The HPTA-regulated parties were informed of the change in October 2023 and provided with three options if they performed controlled activities with polioviruses: 1) transfer materials to a certified PEF; 2) destroy materials through approved methods; and 3) apply for a RG3 licence under the HPTA and begin the CCS process to become a PEF. Outreach surrounding the increase in classification to RG3/CL3 resulted in a reduction of facilities retaining polioviruses, as well as identifying additional materials which were destroyed by approved protocols.

Additional outreach and reporting

In addition to survey activities, PHAC-CB communicates with HPTA-regulated parties in Canada regarding poliovirus containment activities through a website (30), a quarterly newsletter (24), webinars and by offering training. Canada's NAC engages international partners in discussing best practices on facility audits, including serving as the Chair of the International NAC group in 2023–2024. Annually, WHO member states report on their progress towards polio eradication goals through their respective WHO regional arm. Canada's report is prepared through a collective effort of multiple Health Portfolio areas and submitted to the Pan American Health Organization. The PHAC-CB is responsible for the poliovirus containment section and reports on overall inventories. In addition, NAC Canada provides input into international documents and initiatives, including the World Health Assembly, reviewing resolutions and poliovirus containment-related processes (such as the revision of the GAP). Nationally, PHAC-CB also coordinated with Health Canada to remove polioviruses from the list of surrogate organisms prescribed for testing the efficacy of chemical disinfectants (31).

Polio outbreak simulation exercise

Although Canada is rated as a low-risk country for polio according to the Pan American Health Organization (32), planning and vigilance are important in preparing for potential poliovirus events. In 2022, PHAC held a Polio Outbreak Simulation Exercise (POSE) table-top exercise based on a simulated, unintentional laboratory containment breach involving poliovirus. Over 40 exercise participants from multiple Canadian jurisdictions discussed the coordination, response roles, governance and operational structures that would be involved in an accidental poliovirus event. As part of the table-top exercise, participants reviewed Canada's national polio response protocol, *Guidance for the response and management*

of a poliovirus event or outbreak in Canada (33), the Federal/Provincial/Territorial Public Health Response Plan for Biological Events (34) and WHO's *Public health management of facility related exposure to live polioviruses* (35). Emphasis was placed on rapid detection, notification and investigation made to support timely implementation of public health controls, limiting potential spread and promoting knowledge-sharing among Canadian partners.

Conclusion

Canada is a world leader in biosafety and biosecurity, as recognized in the 2018 International Health Regulations—Joint External Evaluation Report (36,37) and has reached important milestones in poliovirus containment as part of the global campaign to eradicate polio. Between 2017–2024, through engagement (outreach, training, education and regulatory oversight), Canada reduced the number of facilities with poliovirus materials by approximately 80%–90%, depending on the type. Despite the challenges, work continues to identify potential sources of poliovirus, promote containment and biorisk management, audit facilities for compliance with the GAP and national legislation and collaborate with our international partners. The ongoing circulation of WPV1 and cVDPVs in human populations threatens re-emergence of polio unless complete eradication is achieved. The use of polioviruses in vaccine production, as well as the development of new strains of poliovirus (novel OPV, S19 strains, PVSRIPO), requires ongoing vigilance by PHAC-CB inspections to verify all Canadian facilities remain HPTA compliant. In both the current and post-eradication world, containment is critical to mitigate the risk of polioviruses accidentally being re-introduced into the human population. Canadian organizations are encouraged to contact PHAC-CB regarding questions on poliovirus PIM, or any biosafety or biosecurity issue. This paper has detailed Canada's substantial progress and successes in poliovirus containment. The PHAC-CB/NAC Canada looks forward to continuing working with national and international partners in biosafety and biosecurity to keep Canadians healthy and safe.

Authors' statement

DT — Conceptualization, formal analysis, visualization, writing—original draft, writing—review & editing
LM — Writing—review & editing, investigation, formal analysis, supervision
DL — Writing—review & editing, investigation, formal analysis
DB — Writing—review & editing, investigation, formal analysis
CR — Writing—review & editing, investigation
AB — Writing—review & editing, investigation, project administration

Competing interests

None.



ORCID numbers

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Associations between the number of self-reported SARS-CoV-2 infections and the diagnosis of new health conditions among adults in Canada, January 2020–June 2023

Dianne Zakaria^{1*}, Xue feng Hu², Samina Aziz¹, Lisa Oliver², Janine Clarke²

Abstract

Background: Preexisting health conditions increase the risk of severe outcomes after SARS-CoV-2 infection. Emerging evidence suggests this relationship may be bi-directional with infection potentially increasing the risk of new health condition diagnoses.

Objective: To examine the association between number of SARS-CoV-2 infections and the subsequent diagnosis of new health conditions, excluding longer-term symptoms after SARS-CoV-2 infection, and to examine associations between infection and vaccination characteristics, including longer-term symptoms, and new diagnoses among the infected.

Methods: Population-based self-report cross-sectional survey data with longitudinal follow-up collected from Canadian adults was used to examine new diagnoses of 21 health conditions (and combinations thereof) since the first SARS-CoV-2 infection or, for uninfected adults, since the start of the pandemic. Multivariable binomial logistic regression was used to estimate adjusted odds ratios (aOR) controlling for sex, age, education, income, obesity, smoking status, preexisting health conditions and time at risk.

Results: Relative to adults reporting no SARS-CoV-2 infections, those reporting two or more had significantly greater odds of being diagnosed with a new condition (aOR=1.76, 95% confidence interval [CI]: 1.12–2.76, $p=0.0133$), respiratory condition (aOR=5.03, 95% CI: 1.72–14.73, $p=0.0114$), and back problems (aOR=3.79, 95% CI: 1.12–12.89, $p=0.0056$). Among infected adults, acute symptoms that limited daily life during the first infection (aOR=1.63, 95% CI: 1.08–2.48, $p=0.0206$) and longer-term symptoms (aOR=3.35, 95% CI: 2.24–5.03, $p<0.0001$) were also associated with being diagnosed with a new condition.

Conclusion: Repeated SARS-CoV-2 infections may increase the risk of reporting newly diagnosed health conditions. Findings regarding acute infection severity and longer-term symptoms should be interpreted cautiously. Both of these factors may have increased care seeking and opportunities for diagnoses and may be the consequence of a new health condition (reverse causation).

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Keywords: SARS-CoV-2, COVID-19, health conditions, population-based survey, Canada, adults

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Introduction

Research shows that preexisting chronic conditions increase the risk of more severe outcomes (e.g., hospitalization, death) after a SARS-CoV-2 infection, including the development of longer-term symptoms (1–6). Lesser known, however, is emerging research suggesting this relationship may be bi-directional, as SARS-CoV-2 infection may increase the risk of new health condition diagnoses, with more severe infections associated with greater increases in risk (7–10). In addition, reinfections, pre-Omicron era infections, and not being vaccinated prior to infection have also been identified as potential risk factors for new health conditions (11–13). Hypothesized underlying mechanisms include persistent SARS-CoV-2 reservoirs in tissues, immune dysregulation, autoimmunity, microbiota disruption, clotting and endothelial abnormalities, dysfunctional neurological signalling and organ damage (14,15). The proposed bi-directional relationship is confounded by the indirect effects of the COVID-19 pandemic, which decreased health service use, thereby delaying the diagnosis of health conditions (16,17) and potentially increasing the risk of their development due to compromised preventive health care. This highlights the importance of incorporating a control group when estimating the risk of new health conditions due to SARS-CoV-2 infection.

Research examining the association between SARS-CoV-2 infection and the risk of new health condition diagnoses has limitations. Studies may be primarily based on people attending healthcare institutions (8,9,11–13) or specific subpopulations such as children and adolescents (11) or veterans (12,13), they may not assess the impact of vaccinations and/or infection characteristics (7–9,11) or they may not examine specific health conditions (7).

Currently, there is limited research that uses representative, population-based data to examine associations between SARS-CoV-2 infection and the diagnosis of new health conditions, and risk estimates for the general Canadian population are lacking. Considering the average infection-acquired SARS-CoV-2 seroprevalence in Canada's 10 provinces was 81.8% as of the end of October 2023 (18), even modest increases in the risk of new health condition diagnoses can translate to substantial additional cases depending on the background risk among the uninfected. The greater the background risk, the greater the additional cases. In this study, population-based survey data collected from Canadian adults was used to conduct exploratory analyses examining associations between the number of self-reported confirmed or suspected SARS-CoV-2 infections and newly diagnosed health conditions, excluding longer-term symptoms after SARS-CoV-2 infection. The secondary objective was to explore whether the time of first SARS-CoV-2 infection, vaccination status prior to first infection, severity of acute symptoms during first infection and longer-term symptoms after any SARS-CoV-2 infection were associated with the diagnosis of new health conditions among adults reporting one or

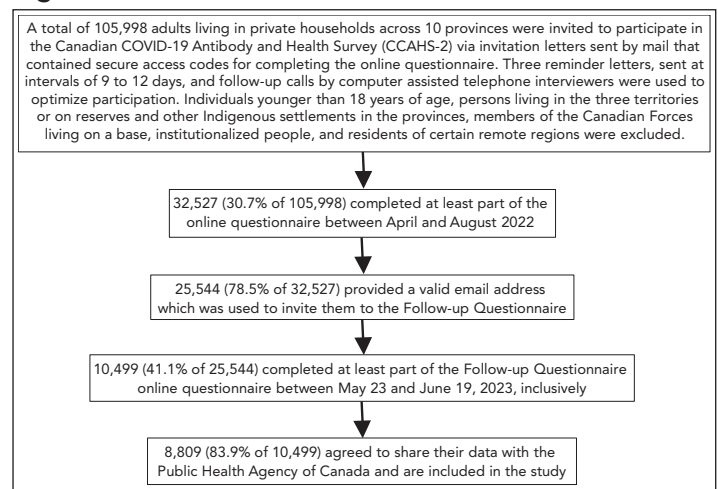
more SARS-CoV-2 infections. The findings from this study will contribute to an evidence base that can inform future public health practice, clinical decision-making, healthcare resource needs and future research.

Methods

Data source and questionnaires

Data was used from the second cycle of the Canadian COVID-19 Antibody and Health Survey (CCAHS-2), a population-based cross-sectional survey that employed probability sampling, and Follow-up Questionnaire (FQ), which collected additional information on a subsample of adults who participated in the earlier CCAHS-2. The analytical sample consists of 8,809 respondents who participated in both the CCAHS-2 and FQ, and agreed to share their data with the Public Health Agency of Canada (Figure 1). Detailed information on the surveys and questionnaires is publicly available (19).

Figure 1: Recruitment and inclusion flowchart



Primary outcome—new diagnosed health conditions

The CCAHS-2 questionnaire asked all respondents whether a healthcare professional had diagnosed them with any of 21 specified health conditions (see Table 1 footnote a for list of conditions), along with the date of first diagnosis of each condition. In the FQ, respondents reporting a confirmed or suspected SARS-CoV-2 infection were asked whether a healthcare provider had diagnosed them with these conditions for the first time since their first infection. Those not reporting an infection were asked about new diagnoses since the start of the pandemic. The FQ did not capture the date of diagnosis, only its occurrence in time relative to the first SARS-CoV-2 infection or start of the pandemic, respectively. In the FQ, respondents were instructed to exclude preexisting conditions or conditions



Table 1: Self-reported sociodemographic, health and SARS-CoV-2 infection characteristics for adults in Canada by new diagnosis of select health conditions^a, January 2020–June 2023

Characteristics	All n=8,717		New condition diagnosed n=1,137		No new condition diagnosed n=7,580		p-value
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	
Sex at birth							
Male	48.9	47.8–50.0	43.7	38.2–49.4	49.6	48.4–50.7	0.0659
Female	51.1	50.0–52.2	56.3	50.6–61.8	50.4	49.3–51.6	. ^b
Age at questionnaire completion (years)							
18 to 34	24.8	23.9–25.7	13.9	9.6–19.3	26.2	25.1–27.4	<0.0001
35 to 49	25.7	24.7–26.7	19.8	15.7–24.3	26.5	25.3–27.7	-
50 to 64	24.5	23.6–25.4	30.3	25.4–35.7	23.8	22.8–24.8	-
65 and older	24.9	24.0–25.8	36.0	31.3–40.9	23.5	22.5–24.5	-
Sexual orientation							
Heterosexual	92.7	91.5–93.9	94.7	92.0–96.7	92.5	91.1–93.7	0.1208
Ethnicity							
White only	72.3	70.2–74.3	75.1	68.4–81.1	71.9	69.6–74.2	0.0708
Racialized, non-Indigenous	25.5	23.5–27.5	20.6	15.1–27.1	26.1	23.9–28.4	-
Indigenous	2.3	1.6–3.1	x ^c	x	2.0	1.4–2.8	-
Education							
Post-secondary education attained in household	84.0	82.4–85.5	75.5	69.6–80.7	85.1	83.5–86.6	<0.0001
Neighbourhood household income quintile							
Lowest quintile	18.6	16.9–20.4	25.1	19.7–31.1	17.8	16.0–19.7	0.0526
2 nd	19.1	17.6–20.6	17.9	13.9–22.4	19.3	17.7–20.9	-
3 rd	17.7	16.1–19.4	15.7	12.3–19.5	17.9	16.2–19.8	-
4 th	23.0	21.1–24.9	20.9	16.1–26.3	23.2	21.2–25.3	-
Highest quintile	21.6	20.0–23.4	20.5	16.4–25.2	21.8	20.0–23.7	-
Residence							
Rural residence	14.4	13.5–15.4	12.4	9.3–16.1	14.7	13.7–15.8	0.2363
Smoking status							
Current smoker	5.1	4.3–6.0	8.3	5.1–12.4	4.7	3.9–5.6	0.0177
Body mass index (kg/m ²) ^d							
Underweight or normal (BMI less than or equal to 24.99	29.6	27.6–31.7	23.5	18.7–28.9	30.4	28.2–32.7	0.0264
Overweight (BMI greater than 24.99 and less than or equal to 29.99	36.8	34.8–38.8	36.9	31.1–43.0	36.8	34.7–38.9	-
Obese (BMI more than 29.99	33.6	31.5–35.6	39.6	34.2–45.1	32.8	30.6–35.1	-
Disability							
Identifies as having a disability	7.2	6.1–8.4	14.5	10.7–19.1	6.2	5.1–7.5	<0.0001
COVID-19 vaccine							
Received 2 or more COVID-19 vaccine doses	94.2	91.4–96.3	96.5	92.4–98.8	93.8	90.7–96.2	0.1910
Number of SARS-CoV-2 infections							
0	33.2	31.2–35.2	52.8	46.9–58.6	30.6	28.5–32.8	<0.0001
1	46.7	44.5–48.8	23.6	18.8–29.0	49.6	47.3–51.9	-
2 or more	20.2	18.6–21.9	23.6	18.7–29.0	19.7	18.0–21.6	-
Time at risk (mean number of years	2.0	1.9–2.0	2.6	2.5–2.8	1.9	1.9–2.0	<0.0001

Abbreviations: BMI, body mass index; CI, confidence interval; n, unweighted sample

^a Select health conditions include chronic lung condition, asthma, chronic heart disease, high blood pressure, effects of a stroke, chronic neurological disorder, Alzheimer disease or other dementia, arthritis, back problems, osteoporosis, cancer, weakened immune system, chronic blood disorder, diabetes, chronic kidney disease, bowel disorder, liver disease, urinary incontinence, sleep apnea, chronic fatigue syndrome or fibromyalgia, and mental health condition

^b p-value relates to the variable as a whole, not categories of the variable

^c Suppressed for confidentiality or poor reliability

^d Body mass index is defined as a person's weight in kilograms divided by the square of their height in metres

Note: Estimates for Canada exclude the territories. All estimates are weighted and are percentages unless otherwise indicated. Adults with missing information on newly diagnosed health conditions are excluded from the analysis

Data source: Canadian COVID-19 Antibody and Health Survey—Cycle 2 and Follow-up Questionnaire



under investigation prior to the first infection or start of the pandemic, respectively, and there was no duration requirement for reported new health condition diagnoses. In order to capture health conditions diagnosed since the CCAHS-2 was conducted, for which a date of diagnosis was not captured, information reported in both the CCAHS-2 and FQ was used to classify respondents into one of three mutually exclusive categories for each health condition: no condition; condition present prior to first infection or the start of the pandemic for those not reporting an infection; or, condition diagnosed for the first time after first infection or since the start of the pandemic for those not reporting an infection.

Primary explanatory variable—number of self-reported confirmed or suspected SARS-CoV-2 infections

In the FQ, all respondents were asked “Since the start of the COVID-19 pandemic, how many different COVID-19 infections did you think or know you had?”. Respondents were instructed to include infections with a positive test result and infections suspected to be COVID-19 because of the symptoms experienced or recent contact with a COVID-19 case. The date of the first SARS-CoV-2 infection was also captured. To investigate the potential cumulative effect of repeated SARS-CoV-2 infections, the number of self-reported infections was categorized as 0, 1, or 2 or more.

Additional explanatory variables

Time at risk for diagnosis of new conditions varied by self-reported SARS-CoV-2 infection status. Respondents reporting a confirmed or suspected infection were at risk as of the date of their first infection, while all others were considered at risk beginning January 1, 2020. This date was chosen to align with earliest infections reported by respondents. All respondents continued to be at risk for new diagnosed health conditions until they completed the FQ.

Time period of first SARS-CoV-2 infection was dichotomized as occurring either before or during the less virulent Omicron wave, defined here as beginning December 2021 (20).

Vaccination status prior to first SARS-CoV-2 infection was determined using the number and dates of receipt of COVID-19 vaccine doses, captured in both the CCAHS-2 and FQ, along with the date of first SARS-CoV-2 infection. Respondents were categorized as having received either one or fewer, or two or more doses (i.e., fully vaccinated) prior to the month of first infection. Respondents receiving one dose prior to infection were too few to examine separately.

Severity of acute symptoms during first SARS-CoV-2 infection was determined using information from both the CCAHS-2 and FQ and categorized as either impacting daily activities or not. Longer-term symptoms related to SARS-CoV-2 infection

were defined as symptoms three or more months after a SARS-CoV-2 infection that could not be explained by anything else. Finally, because of their potential association with the diagnosis of new health conditions and/or number of SARS-CoV-2 infections, socioeconomic and health characteristics captured in the CCAHS-2 were also considered (Table 1).

A supplementary file, including details on imputations applied to COVID-19 vaccination dates collected in CCAHS-2 and to the self-reported date of first SARS-CoV-2 infection, as well as key questionnaire content, is available from the corresponding author.

Statistical analyses

Statistical procedures that acknowledge the complex survey design were used in combination with final and bootstrap weights supplied by Statistics Canada. Descriptive statistics (mean, percentage) and corresponding 95% confidence intervals (CIs) were used to characterize the Canadian adult population overall, as well as by diagnosis of a new health condition. The CIs for weighted means use the *t*-distribution, and the *t*-test was used to test for differences between group means ($\alpha=0.05$, two-tailed). Confidence intervals for weighted proportions were calculated using the Clopper-Pearson exact method, and the design-based first-order Rao-Scott chi-square test of association was used to test for group differences.

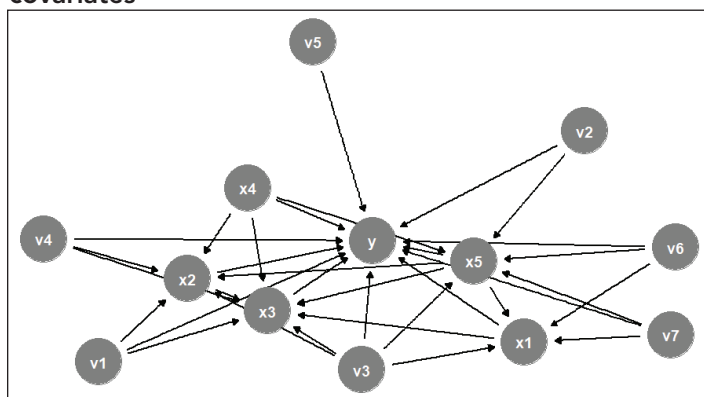
Binomial logistic regression was used to assess whether the number of SARS-CoV-2 infections was independently associated with the diagnosis of new conditions after adjusting for sex at birth, age at start of time at risk, highest educational attainment among household members, national neighbourhood household income quintile, obesity, smoking status, number of preexisting health conditions and time at risk. Given the relatively small number of new diagnoses during time at risk, a parsimonious modelling approach was essential to ensure convergence and stable estimates. Older age (21) and preexisting chronic conditions have been shown to increase the risk of diagnosis of a new condition (22–24). Additionally, longer time at risk increases the opportunity for new diagnoses, regardless of infection status. To determine which socioeconomic and health characteristics to include in all models and how to model them, binomial logistic regression was employed to identify those characteristics significantly ($p<0.05$, two-tailed) associated with a new diagnosis of at least one of the specific health conditions, examined separately, after adjusting for number of SARS-CoV-2 infections, sex, age, number of preexisting health conditions and time at risk.

Separate models assessed the new diagnosis of any of the 21 conditions, any condition within defined categories (cardiovascular, respiratory, neurological and musculoskeletal) and each specific condition. Respondents with a preexisting condition were excluded from the corresponding



condition-specific model. For condition categories, respondents reporting all conditions within the category as preexisting were excluded from the category's model. To examine associations between infection and vaccination characteristics and new diagnoses, the analytical sample was limited to adults reporting at least one SARS-CoV-2 infection and the same models were rerun with the addition of the characteristic; separate models were run for each characteristic. When examining the effect of longer-term symptoms after SARS-CoV-2 infection, respondents reporting their first infection within 82 days of completing their FQ were excluded from the model due to insufficient follow-up to ascertain the presence of longer-term symptoms three or more months after infection. An 82-day threshold was used rather than 89 days, to account for the imprecision in self-reported infection dates recorded as occurring in the early (assigned 5th day), middle (15th) or late (25th) part of the month. Due to potential multicollinearity between time at risk and both "period of infection" and "number of vaccine doses received prior to first infection", sensitivity analyses were conducted excluding time at risk when assessing the effects of these two characteristics. For all modelling, analyses were limited to adults with complete data for all the variables included in the model. The complexity of hypothesized relationships between the variables examined reinforces the exploratory nature of the study (Figure 2).

Figure 2: Directed acyclic graph displaying hypothesized relationships between new health condition diagnoses, main explanatory variables of interest, and additional covariates



Note: y=new health condition diagnosis; x1=number of self-reported confirmed or suspected SARS-CoV-2 infections; x2=severity of acute SARS-CoV-2 infection symptoms; x3=continuing symptoms 3 or more months after SARS-CoV-2 infection; x4=time period of first SARS-CoV-2 infection; x5=vaccination status prior to first SARS-CoV-2 infection; v1=sex at birth; v2=age at start of time at risk; v3=number of preexisting health conditions; v4=obesity; v5=smoking status; v6=highest education achieved by household members; and v7=national neighbourhood household income quintile

Since a minimum of five events (i.e., new diagnoses) per model parameter is desirable for modelling purposes (25), outcomes (e.g., respiratory condition, chronic lung condition, weakened immune system, etc.) with fewer than 60 new diagnoses were not modelled separately.

To ensure confidentiality, all descriptive estimates based on fewer than 30 respondents or having fewer than five respondents in the numerator of a proportion (unweighted) are suppressed. To ensure adequate reliability, descriptive estimates with coefficients of variation greater than 33.3% are also suppressed. In addition, multivariable models are not presented when the overall likelihood ratio test for the model is non-significant, any categorical variable includes fewer than 30 respondents or five new diagnoses in a specific category (unweighted), or any bootstrap replicate samples are excluded from variance estimation due to absent response levels or non-convergence.

SAS Enterprise Guide 7.1 (SAS 9.4TM) was used for all analyses, and R version 4.3.2 was used to produce the forest plots (forestploter package) and directed acyclic graph (dagitty and ggdag packages).

The study was exempt from research ethics board review under article 2.2 of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans–TCPS 2 (2022) (26).

Results

Adults who reported being diagnosed with a new condition during their time at risk were more likely to be older, current smokers and obese, to identify as having a disability, to have greater time at risk for diagnosis of a new condition and to report at least one preexisting health condition (Table 1 and Table 2). They were also less likely to report a SARS-CoV-2 infection or to live in a household where someone had completed post-secondary education.

Among adults reporting at least one infection, those diagnosed with a new condition were more likely to have been first infected prior to the Omicron wave; to report that acute symptoms during their first infection affected daily life; and to report longer-term symptoms three or more months after infection. They were also less likely to have been fully vaccinated prior to their first infection (Table 3).

Compared to adults reporting no infections, those reporting two or more had significantly ($p < 0.05$) greater odds of being diagnosed with a new condition (adjusted odds ratio [aOR]=1.76, 95% CI: 1.12–2.76, $p = 0.0133$), a respiratory condition (aOR=5.03, 95% CI: 1.72–14.73, $p = 0.0114$), and back problems (aOR=3.79, 95% CI: 1.12–12.89, $p = 0.0056$) (Figure 3). Although not statistically significant, strong associations (i.e., $aOR > 2$) were also observed between one infection and respiratory conditions, as well as between both one and two or more infections and sleep apnea.



Table 2: Self-reported health conditions for adults in Canada by new diagnosis of select health conditions, January 2020–June 2023

Characteristics	All n=8,717		New condition diagnosed n=1,137		No new condition diagnosed n=7,580		p-value
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	
Preexisting conditions							
Select conditions							
Any of select conditions ^a	49.4	47.4–51.5	61.1	55.3–66.7	47.9	45.7–50.2	<0.0001
Respiratory	7.7	6.7–8.9	10.0	7.0–13.8	7.5	6.4–8.6	0.1085
Chronic lung condition	1.6	1.2–2.1	3.1	1.5–5.4	1.4	1.1–1.9	0.0178
Asthma	6.6	5.7–7.7	8.1	5.3–11.6	6.5	5.5–7.6	0.2740
Cardiovascular	18.4	17.1–19.9	18.7	15.0–22.7	18.4	16.9–20.0	0.9005
Chronic heart disease	2.4	1.9–3.0	3.6	1.8–6.3	2.3	1.8–2.9	0.1616
High blood pressure	17.0	15.6–18.4	16.1	12.9–19.8	17.1	15.6–18.6	0.6211
Effects of a stroke	0.4	0.3–0.7	x ^b	x	0.4	0.2–0.6	x
Neurological	1.9	1.4–2.5	x	x	1.7	1.2–2.2	x
Chronic neurological disorder	1.8	1.4–2.4	x	x	1.5	1.1–2.0	x
Alzheimer disease or other dementia	x	x	x	x	x	x	x
Musculoskeletal	20.7	19.3–22.1	30.2	25.5–35.2	19.5	18.0–21.0	<0.0001
Arthritis	12.6	11.5–13.8	19.7	15.5–24.4	11.7	10.6–12.9	<0.0001
Back problems	11.0	10.0–12.2	18.3	14.6–22.4	10.1	9.0–11.3	<0.0001
Osteoporosis	3.1	2.5–3.8	5.0	2.9–8.0	2.8	2.2–3.6	0.0452
Other conditions							
Cancer	7.3	6.4–8.2	12.1	9.1–15.6	6.7	5.7–7.7	0.0001
Weakened immune system	3.2	2.6–4.0	5.0	3.0–7.8	3.0	2.4–3.7	0.0459
Chronic blood disorder	0.6	0.4–1.0	x	x	0.5	0.3–0.8	x
Diabetes	6.5	5.5–7.6	9.2	6.4–12.8	6.2	5.1–7.3	0.0348
Chronic kidney disease	0.8	0.5–1.1	1.0	0.5–1.9	0.7	0.4–1.1	0.3419
Bowel disorder	4.1	3.4–4.9	7.3	4.9–10.3	3.7	3.0–4.5	0.0006
Liver disease	0.7	0.4–1.1	x	x	0.7	0.4–1.1	x
Urinary incontinence	2.2	1.7–2.7	4.4	2.8–6.5	1.9	1.4–2.5	0.0009
Sleep apnea	6.3	5.5–7.2	7.7	5.6–10.4	6.2	5.3–7.1	0.1773
Chronic fatigue syndrome or fibromyalgia	1.1	0.8–1.5	1.4	0.8–2.2	1.1	0.8–1.5	0.3997
Mental health condition	11.0	9.7–12.4	14.3	10.6–18.8	10.6	9.2–12.1	0.0525
Newly diagnosed conditions							
Select conditions							
Any of select conditions	11.4	10.2–12.7	100.0	undefined	N/A	N/A	N/A
Respiratory	1.1	0.8–1.5	9.5	6.9–12.8	N/A	N/A	N/A
Chronic lung condition	0.6	0.4–1.0	5.3	3.2–8.1	N/A	N/A	N/A
Asthma	0.5	0.3–0.8	4.5	2.9–6.7	N/A	N/A	N/A
Cardiovascular	3.1	2.4–3.9	26.8	21.8–32.4	N/A	N/A	N/A
Chronic heart disease	0.6	0.3–1.1	5.3	2.6–9.5	N/A	N/A	N/A
High blood pressure	2.3	1.8–2.9	19.9	15.8–24.7	N/A	N/A	N/A
Effects of a stroke	0.3	0.1–0.5	2.3	1.1–4.2	N/A	N/A	N/A
Neurological	0.3	0.2–0.5	2.6	1.3–4.4	N/A	N/A	N/A
Chronic neurological disorder	0.2	0.1–0.4	1.9	0.9–3.5	N/A	N/A	N/A
Alzheimer disease or other dementia	x	x	x	x	N/A	N/A	N/A



Table 2: Self-reported health conditions for adults in Canada by new diagnosis of select health conditions, January 2020–June 2023 (continued)

Characteristics	All n=8,717		New condition diagnosed n=1,137		No new condition diagnosed n=7,580		p-value
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	
Newly diagnosed conditions (continued)							
Musculoskeletal	3.1	2.4–3.9	26.7	21.5–32.3	N/A	N/A	N/A
Arthritis	1.6	1.2–2.1	13.8	10.3–17.8	N/A	N/A	N/A
Back problems	1.3	0.9–1.9	11.4	7.6–16.3	N/A	N/A	N/A
Osteoporosis	0.6	0.3–1.0	5.1	2.7–8.5	N/A	N/A	N/A
Other conditions							
Cancer	0.8	0.4–1.3	6.7	3.8–10.7	N/A	N/A	N/A
Weakened immune system	0.6	0.3–0.9	4.9	2.9–7.7	N/A	N/A	N/A
Chronic blood disorder	x	x	x	x	N/A	N/A	N/A
Diabetes	0.9	0.5–1.4	7.4	4.4–11.4	N/A	N/A	N/A
Chronic kidney disease	x	x	x	x	N/A	N/A	N/A
Bowel disorder	0.7	0.4–1.1	6.1	3.9–9.1	N/A	N/A	N/A
Liver disease	x	x	x	x	N/A	N/A	N/A
Urinary incontinence	0.3	0.2–0.4	2.3	1.4–3.5	N/A	N/A	N/A
Sleep apnea	1.3	0.9–1.9	11.2	7.6–15.8	N/A	N/A	N/A
Chronic fatigue syndrome or fibromyalgia	0.4	0.2–0.6	3.2	1.7–5.5	N/A	N/A	N/A
Mental health condition	1.6	1.1–2.1	13.7	10.1–18.1	N/A	N/A	N/A

Abbreviations: CI, confidence interval; n, unweighted sample; N/A, not applicable

* Includes the 21 conditions detailed in the table

† Suppressed for confidentiality or poor reliability

Note: Estimates for Canada exclude the territories. All estimates are weighted percentages. Adults with missing information on newly diagnosed health conditions are excluded from the analysis

Data source: Canadian COVID-19 Antibody and Health Survey—Cycle 2 and Follow-up Questionnaire

Table 3: Self-reported infection and vaccination characteristics for adults reporting a SARS-CoV-2 infection in Canada by new diagnosis of select health conditions, January 2020–June 2023

Characteristics	All n=5,575		New condition diagnosed n=468		No new condition diagnosed n=5,107		p-value
	Estimate	95% CI	Estimate	95% CI	Estimate	95% CI	
Period of first SARS-CoV-2 infection							
January 2020 to November 2021	21.9	19.7–24.2	43.7	35.0–52.8	20.0	17.7–22.4	<0.0001
December 2021 to June 2023	78.1	75.8–80.3	56.3	47.2–65.0	80.0	77.6–82.3	-
Number of COVID-19 vaccine doses received before first SARS-CoV-2 infection							
One or no dose	23.8	21.1–26.7	43.1	34.2–52.4	22.1	19.3–25.1	<0.0001
Two or more doses	76.2	73.3–78.9	56.9	47.6–65.8	77.9	74.9–80.7	-
Severity of acute symptoms during first SARS-CoV-2 infection							
Did not affect daily life	46.0	43.2–48.7	36.4	27.6–46.1	46.8	43.9–49.7	0.0347
Affected daily life	54.0	51.3–56.8	63.6	53.9–72.4	53.2	50.3–56.1	-
Symptoms three or more months after SARS-CoV-2 infection							
Yes	19.6	17.6–21.8	46.0	37.5–54.8	17.4	15.3–19.6	<0.0001
No	80.4	78.2–82.4	54.0	45.2–62.5	82.6	80.4–84.7	-

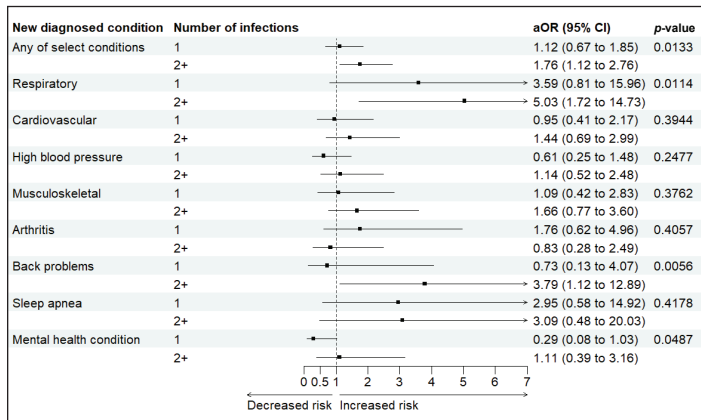
Abbreviations: CI, confidence interval; n, unweighted sample

Note: Estimates for Canada exclude the territories. All estimates are weighted percentages. Adults with missing information on newly diagnosed health conditions are excluded from the analysis. See Table 2 for list of select health conditions

Data source: Canadian COVID-19 Antibody and Health Survey—Cycle 2 and Follow-up Questionnaire



Figure 3: Adjusted relative odds of reporting new diagnosis of select conditions for number of SARS-CoV-2 infections among adults in Canada, January 2020–June 2023



Abbreviations: aOR, adjusted odds ratio; CI, confidence interval

Note: Estimates for Canada exclude the territories. All estimates are weighted and adjusted for sex at birth, age at start of follow-up, highest education achieved by household members, neighbourhood household income quintile, obesity, smoking status, number of preexisting health conditions, and time at risk. For all health condition outcomes, the reference category is 0 infections. "Any of select conditions" includes the 21 conditions listed in Table 2. P-values are for the type 3 analysis of effect for number of SARS-CoV-2 infections after adjusting for other variables in the model

Data source: Canadian COVID-19 Antibody and Health Survey—Cycle 2 and Follow-up Questionnaire

Among adults reporting a SARS-CoV-2 infection, being first infected prior to the Omicron wave (vs. during) or having received fewer than two COVID-19 vaccine doses prior to the first infection (vs. two or more doses) was not significantly associated with new diagnoses (Figure 4). However, sensitivity analyses showed that after removing time at risk from the model, being infected prior to the Omicron wave was significantly associated with greater odds of being diagnosed with a new condition (aOR=2.17, 95% CI: 1.46–3.23, $p=0.0001$) and cardiovascular condition (aOR=2.64, 95% CI: 1.34–5.19, $p=0.0051$), with a borderline significant association for high

blood pressure (aOR=1.88, 95% CI: 0.89–4.00, $p=0.0987$). Similarly, after removing time at risk from the model, not being fully vaccinated prior to the first infection was significantly associated with greater odds of being diagnosed with a new condition (aOR=1.92, 95% CI: 1.30–2.84, $p=0.0010$), cardiovascular condition (aOR=2.67, 95% CI: 1.50–4.77, $p=0.0009$), and high blood pressure (aOR=2.38, 95% CI: 1.22–4.61, $p=0.0105$).

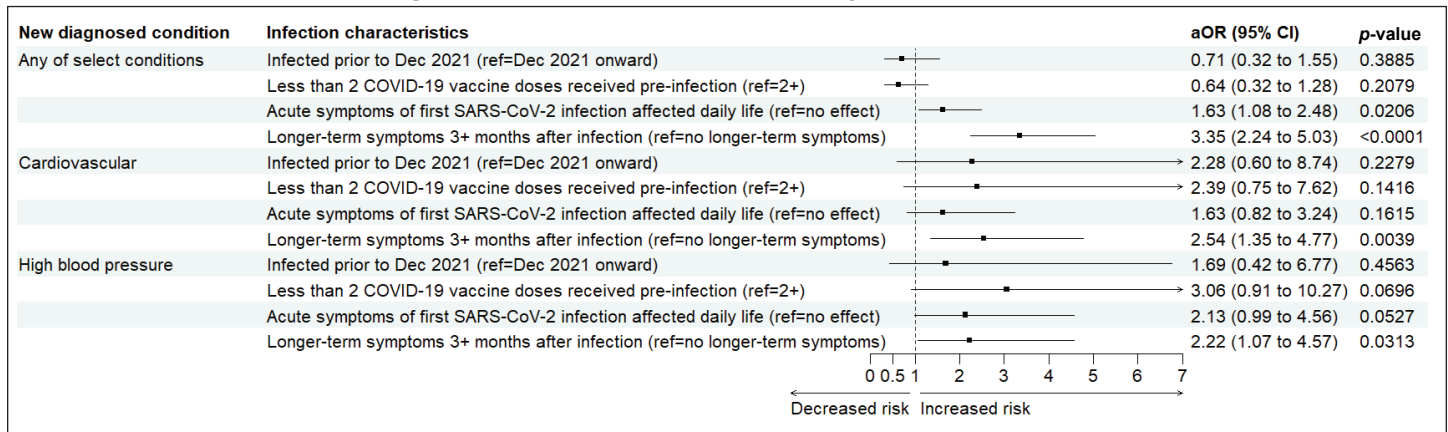
Adults reporting that their daily life was impacted by acute symptoms during their first SARS-CoV-2 infection (vs. not impacted) had significantly greater odds of reporting a newly diagnosed condition (aOR=1.63, 95% CI: 1.08–2.48, $p=0.0206$), with a borderline significant association for high blood pressure (aOR=2.13, 95% CI: 0.99–4.56, $p=0.0527$) (Figure 4).

Adults reporting longer-term symptoms three or more months after any SARS-CoV-2 infection (vs. no longer-term symptoms) had significantly greater odds of reporting a newly diagnosed condition (aOR=3.35, 95% CI: 2.24–5.03, $p<0.0001$), cardiovascular condition (aOR=2.54, 95% CI: 1.35–4.77, $p=0.0039$), and high blood pressure (aOR=2.22, 95% CI: 1.07–4.57, $p=0.0313$) (Figure 4). Additional details regarding all modelling results are available from the corresponding author.

Discussion

Our exploratory analyses using population-based self-report survey data indicated that reporting two or more SARS-CoV-2 infections (vs. no infection) was significantly associated with greater odds of being diagnosed with a new health condition, respiratory condition and back problems. Among adults reporting at least one SARS-CoV-2 infection, having daily life negatively impacted by acute symptoms during the first infection (vs. not impacted) was significantly associated with

Figure 4: Adjusted relative odds of reporting new diagnosis of select conditions for SARS-CoV-2 infection and vaccination characteristics among infected adults in Canada, January 2020–June 2023



Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; ref, reference

Note: Estimates for Canada exclude the territories. All estimates are weighted and adjusted for sex at birth, age at start of follow-up, highest education achieved by household members, neighbourhood household income quintile, obesity, smoking status, number of preexisting health conditions, time at risk, and number of SARS-CoV-2 infections. "Any of select conditions" includes the 21 conditions listed in Table 2. P-values are for the type 3 analysis of effect for each SARS-CoV-2 infection and vaccination characteristic after adjusting for other variables in the model

Data source: Canadian COVID-19 Antibody and Health Survey—Cycle 2 and Follow-up Questionnaire



greater odds of being diagnosed with a new health condition, while longer-term symptoms (vs. no longer-term symptoms) after any SARS-CoV-2 infection was significantly associated with greater odds of being diagnosed with a new health condition, cardiovascular condition and high blood pressure.

The lack of association between being diagnosed with a new condition and both period of first SARS-CoV-2 infection and vaccine doses received prior to first infection could have been the result of correlations with time at risk, as evidenced by the sensitivity analyses. The findings with respect to more severe acute infections or prolonged symptoms after infection should be interpreted cautiously. Both situations may have increased care seeking and opportunities for diagnoses and may be the consequence of a new health condition rather than a risk factor (i.e., reverse causation).

The findings align, in part, with previous studies and contribute to available research on the general population. Regarding the diagnosis of a new condition, while the aOR for two or more infections relative to no infection (aOR=1.76, 95% CI: 1.12–2.76) is consistent with De Ridder *et al.*'s (7) aOR for any confirmed infection (aOR=2.15, 95% CI: 1.43–3.23), no significant association for one infection was found. Bowe *et al.* (12) found that, relative to adults with no confirmed SARS-CoV-2 infections, the risk of at least one sequelae across multiple organ systems increased with the number of confirmed SARS-CoV-2 infections from 37% (hazard ratio [HR]=1.37, 95% CI: 1.36–1.38) for one infection, to 107% (HR=2.07, 95% CI: 2.03–2.11) for two infections, to 135% (HR=2.35, 95% CI: 2.12–2.62) for three or more infections.

Based on a meta-analysis, Gaudet *et al.* (9) reported moderate increases in the risk of diagnosis of respiratory disorders (HRs: 1.83–1.89) and sleep apnea (HRs: 1.5–1.7) in adult outpatient/mixed outpatient and inpatient samples. Gaudet *et al.* also found that the risk of diagnosis of new conditions was often higher among inpatients than outpatients or mixed samples, highlighting the importance of infection severity. Although research has demonstrated an association between infection and musculoskeletal disorders (12), no studies were found that specifically examined back problems.

Consistent with the findings during sensitivity analyses, Xie *et al.* (13) found that the risk of new post-acute SARS-CoV-2 infection sequela across multiple organ systems during the first year after infection was about 34% and 23% greater in the pre-Delta and Delta era relative to the Omicron era among unvaccinated adults, respectively; and, that the risk of sequela among unvaccinated adults was 78% and 122% greater than in vaccinated adults in the Delta and Omicron era, respectively, although Xie *et al.* did not acknowledge the sequencing of vaccination and infection.

The CCDSS, which includes data to fiscal year 2023–2024 for select chronic conditions, did not indicate notable sustained increases in the overall age-standardized incidence rate of asthma, chronic obstructive pulmonary disease, ischemic heart disease, stroke, osteoarthritis and rheumatoid arthritis relative to the pre-pandemic period (21). Although there was no significant association between number of SARS-CoV-2 infections and new high blood pressure diagnoses, the CCDSS documented an 8.1% increase in the overall age-standardized incidence rate for high blood pressure between fiscal year 2019–2020 (2,093 per 100,000, 95% CI: 2,085–2,101) and fiscal year 2022–2023 (2,262 per 100,000, 95% CI: 2,254–2,270); however, population-based surveillance data should be interpreted cautiously. True changes in incidence may be confounded by the indirect effects of the pandemic, including changes in the availability and likelihood of accessing health services during the pandemic, or changes in coding practices in administrative health data. The CCDSS indicated declines in the incidence of many conditions during the pandemic, and more recent increases could be the result of diagnostic “catch-up”.

Strengths and limitations

The primary strengths of this study are that it is population-based, considers a wide range of health conditions and allows for the examination of infection and vaccination characteristics. Its primary limitations are its reliance on participation and self-reporting, which make it susceptible to survivor, selection, misclassification, recall and surveillance biases. The most severely affected adults, who did not survive their SARS-CoV-2 infection(s), were excluded from the study. Of those adults invited to participate in the CCAHS-2, 8.3% (n=8,809 of 105,998) were included in the analytical sample. Although weights were adjusted for non-response and calibrated using auxiliary information to reflect the target population, biased estimates may still occur if participants differed systematically from the target population in ways not corrected through weighting. Some suspected infections may have been due to conditions or infections unrelated to SARS-CoV-2, while others who did not report an infection may have actually been infected, potentially biasing the true underlying association toward the null (27). There was no serology data on FQ participants as of June 2023 to incorporate it into the analyses. The FQ data collected between May 23 and June 19, 2023 indicated that about 67% of adults reported at least one SARS-CoV-2 infection (Table 1), which is comparable to infection-acquired SARS-CoV-2 seroprevalence in Canada's 10 provinces as of June 6, 2023 (78%), considering the latter estimate included children and youth: age groups with the highest seroprevalence (18,28). Although self-report is imperfect, other measures such as seroprevalence cannot provide information about the timing or number of infections and is affected by issues like non-seroconversion and seroreversion (14). Adults reporting an infection may have been more likely to recall a new diagnosis or visit their healthcare provider, increasing



the chances of receiving a diagnosis. Similarly, seeking care for a health condition may have increased the likelihood of having a SARS-CoV-2 infection diagnosed. There was no information to adjust for pre-pandemic health seeking behaviour, which could bias the findings if health-seeking behaviour differed by self-reported SARS-CoV-2 infection status. Although adjustment was made for time at risk, differences in the start of follow-up between adults reporting and not reporting a SARS-CoV-2 infection may have biased the results; adults reporting an infection had less time at risk for new health condition diagnoses and had a greater proportion of their time at risk distributed later in the calendar-time period of follow-up. Adjustment was not made for all potential confounders, such as province of residence and healthcare service availability, which may be associated with both number of SARS-CoV-2 infections and diagnosis of new health conditions. Considering the FQ was conducted more than three years ago, the findings may not apply today given the evolving viral, vaccine, and population immunity landscape. The relatively small number of newly diagnosed conditions decreased the power of the analyses and limited the number of specific conditions modelled. Finally, since *p*-values were not adjusted for the number of analyses performed, some of the findings may be due to chance (i.e., type I error).

Conclusion

The exploratory analyses found several significant associations between new condition diagnoses and SARS-CoV-2 infection and vaccination characteristics. Compared to adults reporting no SARS-CoV-2 infections, those reporting two or more infections had significantly greater odds of being diagnosed with a new health condition, reinforcing the continued importance of public health efforts to prevent infection. Although more population-based research is needed to disentangle the effects of infection characteristics, vaccination status and surveillance bias, the exploratory analyses indicated that being first infected early in the pandemic, not being fully vaccinated prior to first infection, experiencing acute symptoms that limit daily life during the first infection, and reporting prolonged symptoms after any infection may be associated with an increased risk of diagnosis of new health conditions. Continued investigation into the long-term sequelae of SARS-CoV-2 infections, particularly reinfections, and the biological, behavioural and systemic factors that may mediate the effects of these infections is needed. Such investigations could assist healthcare practitioners in tailoring COVID-19 vaccine recommendations and post COVID-19 monitoring for new health conditions and guide public health practice and messaging when promoting COVID-19 vaccine uptake and personal protective measures (e.g., masking) to prevent and minimize the severity of infections, as well as the potential development of new health conditions.

Authors' statement

DZ — Conceptualization, methodology, writing—original draft, writing—review & editing, formal analysis, visualization

XH — Conceptualization, methodology, writing—original draft, writing—review & editing, formal analysis

SA — Conceptualization, methodology, writing—original draft, writing—review & editing

LO — Conceptualization, methodology, writing—original draft, writing—review & editing

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Competing interests

None.

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Appendix

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Foodbook 2.0: A mixed method for survey data collection

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Abstract

Background: Foodbook 2.0 is a population-based food consumption study that was administered in all provinces and territories in Canada from January 2023 to January 2024. It was the second iteration of the study, the first having been conducted in 2014–2015. This iteration of the study provides updated data on food consumption in Canada. This article describes the study methods and compares respondent demographic information between modes of recruitment.

Methods: The study utilized a dual-method recruitment approach, with 75% of the sample coming from a national list of mailing addresses, and 25% from a national list of telephone numbers. Respondents completed the study online or over the telephone. The study examined food, animal, and water exposures during the seven days preceding the interview, as well as consumer food safety knowledge and practices, recent acute gastrointestinal illness, and demographic characteristics.

Results: There were 21,744 participants in the study, with 73% (15,843) of the sample completing the study online, and 27% (5,901) completing the study over the telephone. The dual-method approach to recruitment was successful in reaching the target sample size. Certain demographic groups had higher response rates for one recruitment method over the other.

Conclusion: The data collected in this study on food, animal and water exposures among people in Canada provide essential population reference information for comparison during enteric illness outbreak investigations. This information will inform risk assessments and public health research, supporting interventions aimed at preventing enteric illness in Canada. Evaluation of the modes of recruitment will help inform future iterations of the Foodbook study.

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Keywords: Foodbook, enteric illness outbreak, foodborne outbreak, food safety, acute gastrointestinal illness

Introduction

Foodbook 2.0 is a population-level food consumption study that was administered in all provinces and territories (P/Ts) in Canada from January 2023 to January 2024 (1). The study collected data on food exposures, water exposures, animal-related exposures, consumer food safety knowledge and practices, recent acute gastrointestinal illness, and demographic factors. The first iteration of the study was conducted in 2014–2015 (2). Foodbook 2.0 captured updated data on food exposures and data on new exposures of interest since 2015.

The study was the first nationally representative Canadian food consumption study to collect data over a seven-day period. It

has provided valuable data that have been used to inform food safety and public health in Canada (3–18). Foodbook has also been used as a hypothesis generation method during outbreak investigations to help identify the source of illness (5,19–31).

While the first iteration of the study still provides meaningful data, food consumption patterns change over time, and it is important for outbreak investigators to have accurate population reference data. In addition, new food items have been identified as potential sources of enteric illness since the study's completion in 2015. As a result, Foodbook 2.0 provides updated population reference data for comparison during outbreak



investigations. The data will also inform risk assessments and public health research to support public health interventions aimed at preventing enteric illness in Canada.

The original Foodbook study was completed entirely via telephone surveys. Data collection for Foodbook 2.0 employed both telephone and online surveys to reflect changing patterns in survey response in Canada. Because Foodbook 2.0 used different recruitment and survey completion methodology compared to the original study, it is important to evaluate the utility of the mixed methods approach in order to inform the methods of future surveys. This article describes these study methods and compares respondent demographic information between modes of recruitment.

Methods

To ensure the precision of Foodbook 2.0 data, a minimum sample size was calculated using a 95% confidence level and a 5% margin of error, resulting in a total target of 19,968 completed surveys. The minimum sample size was calculated to be 384, based on a 95% confidence interval and a 5% margin of error. The minimum sample size was allotted to each P/T, with the remaining sample assigned proportionally based on population size using Statistics Canada estimates. These targets were designed to provide sufficient power to accurately estimate proportions. This is particularly important for the burden of acute gastrointestinal illness estimates, which are rare in the population.

Foodbook 2.0 was first piloted internally to ensure that the questions were interpreted as intended. The survey was then adjusted based on feedback. Following this, the study underwent an initial pilot test from November 1, 2022 to November 14, 2022, and a second pilot test from December 1, 2022 to December 19, 2022. These pilot tests ensured that skip patterns functioned appropriately, that proper consent was obtained, and that respondents correctly and accurately understood both the questions and the nature of the survey. Based on feedback from interviewers and survey respondents, adjustments were made to improve the survey tool. Adjustments included clarifying the wording of questions, shortening the interviewer script, and removing the consumer food safety module from the telephone version of the survey to reduce survey length and optimize response rates. The finalized version of the survey was launched on January 2, 2023, and the study continued until January 7, 2024. The survey tool is available online (32).

The questionnaire asked about food, animal and water exposures during the seven days preceding the interview, aligning with the average incubation period of common enteric pathogens. Food categories included vegetables, fruits, nuts, seeds, meats, seafood, eggs, dairy, other foods, and country foods (only asked to respondents residing in the territories). The

questionnaire also asked about food purchasing habits, special diets, water exposures, animal and animal food exposures, food safety knowledge and behaviours (online only), and recent gastrointestinal illness. To avoid respondent fatigue, skip patterns were built into the questionnaire. For example, if a respondent indicated they did not eat any beef in the past seven days, they were not asked any of the subsequent questions about consuming specific beef products.

Sampling technique

The study employed a dual sampling frame approach. Specifically, 75% of the sample was drawn from a national list of mailing addresses, while the remaining 25% came from a national list of telephone numbers. Households were contacted either by mailed letter or by telephone. One participant was randomly selected from each household to participate in the study, based on the age and number of household members (Figure 1).

Figure 1: Invitation letter mailed to households selected to participate in Foodbook 2.0

«CCI_Address»
«CCI_City» «CCI_Province» «CCI_PC»

The Public Health Agency of Canada is conducting a research study called Foodbook. Your household, along with 20,000 other Canadian households, has been randomly chosen to participate in this study. The survey should only take 25 minutes, and your responses are completely anonymous.

You will be asked about what foods you eat and other activities you do that may affect your health. This will help us improve how we respond to foodborne illness outbreaks. Your answers are important to us and will ultimately help us improve the health of Canadians.

Which member of my household can take part in the study?

Only one member of your household can take part in the study. Please note that people of all ages, including infants and children, are also eligible to complete this survey.

- If you are the **only person** in your household, **you** have been chosen to take part in the study.
- If your household has **two members**, the «M_2Per_en» member has been chosen.
- If your household has **three or more members**, list the **three** «M_3PerFil1_en» in order from «M_3PerFil2_en»:

1. _____ 2. _____ 3. _____

The «M_3PerFil3_en» member has been chosen.

If the chosen person is unable to complete the questionnaire (e.g., a child who is too young to provide their informed consent or unable to read the survey questions), someone else who knows their eating habits and activities can fill out the questionnaire for them.

How does the selected person take part in the study?

Please visit: <https://cci-survey.ca/foodbook>, and enter your Survey Code to complete the questionnaire, or call (toll-free): 1-888-313-8927 Monday to Friday between 9 am and 9 pm, or Saturday to Sunday 10 am to 6:30 pm local time to complete the survey by phone.

Your Survey Code is: «PIN»

If you encounter any technical problems with accessing or completing the online survey, please call (toll-free) 888-313-8927, or email us at foodbook@cci-research.com.

Thank you for taking part in this study!

- The Foodbook Research Team

To find out more about this study, please visit the following website:
www.canada.ca/en/public-health/services/food-borne-illness-canada/foodbook-study.html, or reach out to the Foodbook Research Team at: foodbook.atlasalimentaire@phac-aspc.gc.ca

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To enhance youth recruitment, a child was selected to complete the survey in 50% of households with children under 18 years of age. Despite this, youth recruitment remained low (the proportion of youth respondents was compared to the proportion of youths in the Canadian population). To increase youth participation, beginning in the fifth month of data



collection in households with children, a child was selected to complete the survey 100% of the time.

The survey was completed independently by the respondent via an online survey tool (Voxco; Montréal, Québec), or through a telephone interview with a trained interviewer. The survey was offered in English, French, and Inuktitut. All data were entered into Voxco and were housed within Canada.

Participants who had traveled outside their P/T of residence overnight within the seven days before completing the survey were excluded from the food, animal, and water modules of the survey, and only completed the food safety knowledge and practices and recent acute gastrointestinal illness modules.

Informed consent

Informed consent was obtained from all participants. If an individual was under the age of 16 (18 in Québec), consent to participate was sought from their parent or legal guardian. Proxy respondents were utilized for children and individuals with medical or activity limitations. Participants were informed of the objective of the study, the time required to complete the study, and that the study was managed and funded by the Public Health Agency of Canada (PHAC). There was no direct benefit to the participants taking part in the study, but they were informed that the study would help improve enteric disease research and outbreak response in Canada. The study was approved by the Health Canada Research Ethics Board (REB 2021-007P), as well as the Newfoundland and Labrador Health Research Ethics Authority (HREB 2021.145), the Nunavut Research Institute (05 005 23R-M), and the Nunatsiavut Government Research Advisory Committee (NGRAC-14558480).

Optimization of response rate

To optimize response rates, the researchers offered clear explanations of the study to respondents, scheduled call-backs at more convenient times, and offered both online and telephone survey options to all respondents.

Measurement and analyses

Results were weighted using design weights to account for the sampling design, including disproportional sampling frames, probability of selection, and non-response. Post-stratification weights were then applied to align the sample's demographic distribution (i.e., age group, sex, and household size) with 2021 Canadian census data. Weighted proportions were computed using Stata 15.1 (StataCorp, Texas Station, Texas).

The survey was considered complete once the respondent reached the end of the survey and submitted it. Due to survey skip patterns, respondents may not have answered all questions. For instance, those who answered 'No' to consuming 'Any beef' skipped the rest of the beef section. During data cleaning, those respondents were marked as 'No' for all subsequent questions about beef consumption. These adjustments were

made to accurately reflect the proportion of the population that consumed each item. All survey questions were optional; respondents who left any questions unanswered were still considered to have provided a complete response upon submitting the survey.

A sub-analysis was conducted to compare demographic characteristics between respondents that were recruited by mail versus those recruited by telephone call. The proportions of each demographic characteristic for mail-recruited versus telephone-recruited respondents were analyzed using a Wald chi-square test of equal proportions. For example, the proportion of respondents recruited by mail that fell into the 0–9 age group was compared to the proportion of respondents recruited by phone that fell into the 0–9 age group. The Bonferroni correction was applied to ensure the *p*-value was a conservative estimate and that the results were not inflated, resulting in a *p*-value of 0.0011. This was used to minimize Type 1 errors. Additional analyses were performed to compare those that switched methods (i.e., were recruited by mail but responded by telephone or vice versa), to those that responded to the survey using the same stream in which they were recruited.

Results

A total of 145,914 valid landline and mobile telephone numbers were contacted, with 4,965 individuals completing the survey over the telephone, yielding a response rate of 3%. Another 196 individuals contacted by telephone completed the study online.

Mail invitations to participate in the study were sent to 189,801 households. Of those, 15,647 individuals completed an online survey, yielding a response rate of 8%. An additional 936 individuals contacted by mail called the survey company to complete the survey via telephone.

In total, 21,744 individuals participated in the study. Sampling targets were met for all P/Ts except for Nunavut (125/400; 31%) and Northwest Territories (321/402; 80%). Interviews were distributed evenly across all 12 calendar months. Among all respondents, 1,424 (7%) reported traveling outside their P/T of residence within the seven days preceding completion of the survey. Overall, data completeness was much better for phone respondents.

Comparison of the demographic characteristics of respondents recruited by mail versus those recruited by telephone is provided in **Table 1**. Respondents in the 10–19 age group and those 65 years and older were more often recruited by telephone, whereas those in the 20–64 age group were more often recruited by mail. Those reporting East/Southeast Asian, Middle Eastern, or South Asian ethnicities were more likely to be recruited by mail than by telephone. Alternatively, Indigenous people, White

**Table 1: Demographic characteristics of study respondents by mode of recruitment, Foodbook 2.0, Canada, January 2023–January 2024**

Baseline characteristics	Mode of recruitment		p-value ^a
	Mail (%)	Telephone (%)	
Age group (years)	N=16,256	N=5,114	N/A
0–9	665 (4.1%)	242 (4.7%)	0.056
10–19	679 (4.2%)	300 (5.7%)	<0.001 ^b
20–64	8,813 (54.2%)	2,195 (42.9%)	<0.001 ^b
65+	6,099 (37.5%)	2,377 (46.4%)	<0.001 ^b
Gender	16,419	5,150	N/A
Male	6,668 (40.6%)	2,042 (39.7%)	0.219
Female	9,664 (58.9%)	3,077 (59.7%)	0.257
Transgender or another gender	87 (0.5%)	31 (0.6%)	0.554
Language	16,583	5,191	N/A
English	13,661 (82.4%)	4,296 (83.2%)	0.151
French	2,922 (17.6%)	861 (16.7%)	0.117
Inuktitut	0 (0%)	4 (0.08%)	0.045
Ethnicity	16,065	5,107	N/A
Black	197 (1.2%)	89 (1.7%)	0.011
East/Southeast Asian	1,156 (7.2%)	145 (2.8%)	<0.001 ^b
Indigenous	188 (1.2%)	101 (2.0%)	<0.001 ^b
Latino	185 (1.2%)	40 (0.8%)	0.0137
Middle Eastern	237 (1.5%)	35 (0.7%)	<0.001 ^b
More than one ethnicity	515 (3.2%)	276 (5.4%)	<0.001 ^b
South Asian	341 (2.1%)	65 (1.3%)	<0.001 ^b
White	13,070 (81.4%)	4,321 (84.6%)	<0.001 ^b
Other	176 (1.1%)	35 (0.7%)	0.004
Income	14,524	4,589	N/A
Less than \$40,000	2,407 (16.6%)	997 (21.7%)	<0.001 ^b
\$40,000 or more, but under \$80,000	4,248 (29.2%)	1,303 (28.4%)	0.264
\$80,000 or more, but under \$120,000	3,592 (24.7%)	1,068 (23.3%)	0.043
\$120,000 or more	4,277 (29.4%)	1,221 (26.6%)	<0.001 ^b
Education	14,662	4,437	N/A
Less than high school diploma or its equivalent	514 (3.5%)	261 (5.9%)	<0.001 ^b
High school diploma or a high school equivalency	2,361 (16.1%)	900 (20.3%)	<0.001 ^b
Registered apprenticeship or other trade certificate or diploma	1,002 (6.8%)	308 (6.9%)	0.842
College, CEGEP or other non-university certificate or diploma	3,308 (22.6%)	1,061 (23.9%)	0.062
University certificate, diploma or degree	7,477 (51.0%)	1,907 (43.0%)	<0.001 ^b
Urban or rural community	16,130	5,105	N/A
Urban	13,933 (86.4%)	4,013 (78.6%)	<0.001 ^b
Rural	2,197 (13.6%)	1,092 (21.4%)	<0.001 ^b
Provinces/territories	16,583	5,161	N/A
Alberta	1,766 (10.6%)	539 (10.4%)	0.674
British Columbia	2,185 (13.2%)	639 (12.4%)	0.133
Manitoba	845 (5.1%)	269 (5.2%)	0.742
New Brunswick	573 (3.5%)	174 (3.4%)	0.771
Newfoundland and Labrador	438 (2.6%)	158 (3.1%)	0.120
Nova Scotia	709 (4.3%)	223 (4.3%)	0.888
Northwest Territories	200 (1.2%)	121 (2.3%)	<0.001 ^b
Nunavut	90 (0.5%)	35 (0.7%)	0.289
Ontario	4,985 (30.1%)	1,604 (31.1%)	0.167
Prince Edward Island	408 (2.5%)	116 (2.2%)	0.373
Québec	3,155 (19.0%)	954 (18.5%)	0.383
Saskatchewan	830 (5.0%)	222 (4.3%)	0.033
Yukon	399 (2.4%)	107 (2.1%)	0.150

Abbreviations: CEGEP, College of General and Vocational Education; N/A, not applicable

^a p-values were derived from a Wald chi-square test of equality of proportions^b A significant p-value was determined using a Bonferroni correction. The significant p-value of 0.05 was divided by the number of tests (i.e., 43), resulting in a significant p-value of 0.0011

Note: The numbers of respondents recruited by mail/telephone are not consistent across variables. These values represent the numbers of respondents recruited by mail/telephone that provided a response to that question. Respondents could reply 'unsure/prefer not to answer' to any question and still be included in the analyses (excluding language of completion and province/territory of residence)



people or those reporting more than one ethnicity were more likely to be recruited by telephone. Individuals with a university certificate, diploma or degree; those earning \$120,000 or more; and those living in urban areas were more likely to be recruited by mail. In contrast, individuals with less than a high school diploma or with a high school diploma or its equivalent, were more likely to be recruited by telephone. Finally, respondents with a household income less than \$40,000, as well as respondents residing in the Northwest Territories or rural areas were more likely to be recruited by telephone.

Respondents were able to choose their preferred response mode, completing the survey online or by telephone regardless of how they were recruited. Overall, 1,132 respondents switched between modes (Table 2). The demographic characteristics of those who were recruited by mail but chose to complete the survey over the telephone was compared to those that were recruited by mail and completed the survey online. Those that were recruited by telephone but chose to complete the survey online were compared to those that were recruited by telephone and completed the survey over the telephone. Those that were recruited by mail but completed the survey over the telephone were significantly more likely to be older adults aged 65 years or older. This group was also significantly more likely to be female, to reside in New Brunswick, to be White, and to have a high school diploma or its equivalent, or less than a high school education. Respondents that were recruited by mail but completed the survey over the telephone were significantly more likely to be in the 65+ age group.

Table 2: Survey method of completion by contact method, Foodbook 2.0, Canada, January 2023–January 2024

Method of completion	Method of contact		
	Mail	Telephone	Total
Online	15,647	196	15,843
Telephone	936	4,965	5,901
Total	16,583	5,161	21,744

Discussion

Foodbook 2.0 used a mixed-mode sampling frame designed to collect updated data on food, water, and animal exposures from a representative sample of people in Canada. By combining mail-based and telephone-based recruitment and offering both online and telephone response options, the study aimed to increase participation and reach diverse segments of the population. This approach reflects current best practices in survey methodology and acknowledges the declining efficacy of single-mode surveys (33,34).

The mail-based mode recruited the most participants (73%), particularly adults aged 20–64, and offered a cost-effective mechanism to recruit a large number of households. The mail-

recruited, online-completed version of the survey could be completed on the respondent's own schedule, making it more accessible to many. However, mail invitations could not be personally addressed, potentially lowering the response rate. In addition, respondents were instructed to select a household member based on age order; however, the extent to which these instructions were followed is unclear. Data completeness was lower for surveys completed online, as respondents could leave questions unanswered.

In contrast, telephone recruitment was more effective in engaging older adults who may be less comfortable using online platforms, as well as individuals with lower income or educational attainment (35–38). This difference in demographic representation across modes highlights the importance of maintaining multiple recruitment and response channels to ensure inclusivity. Furthermore, offering a telephone version of the survey removed technical barriers (such as those associated with the online survey), making it more accessible to some demographic groups. Having the interviews completed by trained interviewers also ensured the survey was navigated correctly, and that questions were not skipped. However, recruitment and survey completion by phone was extremely time- and resource-intensive, with many calls required to get a single completed survey. Because of the time required to complete the telephone survey, one module of the survey was only asked to online respondents.

Although respondents were able to choose their preferred response mode, switching between modes was uncommon. A larger proportion of mail-recruited respondents chose to complete the survey over the telephone versus telephone-recruited respondents choosing to complete the survey online. Individuals choosing to complete the survey over the telephone were more commonly older adults (65+) or individuals with less formal education (36–39). This ability to switch modes underscores the value of flexible data collection approaches (33,34). Offering both methods may have increased the overall survey response rate, as those that switched methods between recruitment and survey completion may not have completed the survey otherwise. A mixed methods approach ensures the study population is more representative of the Canadian population, which is important for a study like Foodbook, which aims to be nationally representative.

Limitations

Despite the large sample size and national reach, certain limitations remain. Response rates were low, at approximately 8% for mail-recruited online respondents and 3% for telephone recruitment and completion. While the response rate is in line with that of the first iteration of Foodbook (2.7%), this raises concerns about non-response bias (40). Individuals who chose not to participate may differ systematically in their exposure patterns, which could impact generalizability. Comparing to census values shows that demographic groups, including older



adults, White participants, university-educated individuals, and those from higher-income households were over-represented in the study population. While weighting adjustments were applied to correct for these imbalances, residual biases may persist. Excluded populations, such as those without a fixed home address or telephone access, or those that are not fluent in English, French, or Inuktitut, may also have affected national representation. Furthermore, despite selection methods intended to increase youth participations, youth remained under-represented relative to the Canadian population.

The mixed-mode design introduces potential inconsistencies in how questions were interpreted or answered. For example, online respondents could pause and verify their answers, whereas telephone respondents may have relied on memory alone. Conversely, surveys completed by telephone with an interviewer allowed the interviewer to clarify ambiguous questions and encourage completion, potentially reducing item non-response.

Recruitment in Nunavut and the Northwest Territories was challenging. Given the small population size of the two territories, additional sample and outreach was limited. The sampling plan also had to accommodate restrictions on how many contacts could be recruited in a week, to ensure data collection could be spread throughout the year. These populations are also commonly over-sampled in surveys, which could lead to survey fatigue. Face-to-face interviews and community engagement are recommended approaches for outreach in these areas; however they were not feasible for this study given its national scope (41,42).

Despite these challenges, Foodbook 2.0 represents a significant achievement in large-scale population surveillance. It provides timely, detailed, and geographically comprehensive data on exposures relevant to enteric illness risk in Canada. These data will serve as essential reference points for outbreak investigations, risk assessments, and public health research. The flexibility and scalability of the survey design offer a promising framework for future national health surveillance initiatives.

Future iterations of Foodbook should aim to improve representation of under-sampled populations, including Indigenous communities, recent immigrants, and individuals with limited access to traditional communication channels. Enhanced personalization of recruitment materials, expanded language offerings, and engagement with community organizations may help to address these gaps. Increasing response rates through targeted follow-up strategies and continued innovation in survey delivery will also be important.

Conclusion

Foodbook 2.0 successfully provided updated data on food, water, and animal exposures among people in Canada. It demonstrates the value of flexible, mixed-mode data collection for public health surveillance, particularly in the context of evolving communication preferences and demographic diversity. Although some limitations in reach and representation remain, the survey provides a critical foundation for informing enteric disease prevention and response in Canada.

Authors' statement

MT — Data curation, writing—original draft, writing—review & editing

MR — Data curation, writing—original draft

MKT — Writing—review & editing

AN — Writing—review & editing

VM — Conceptualization, data duration, writing—review & editing

Competing interests

The authors have no conflicts of interest to declare.

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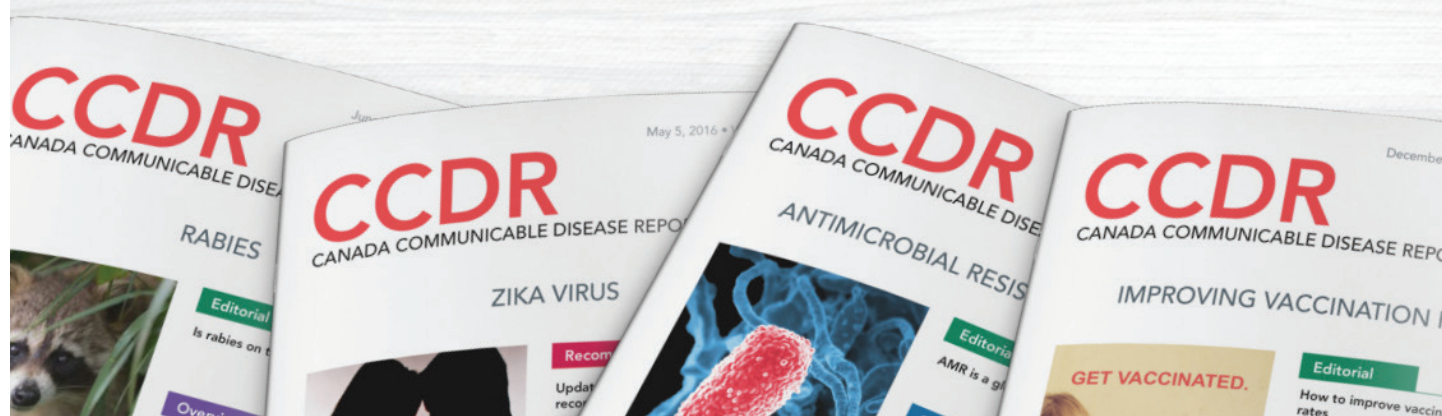
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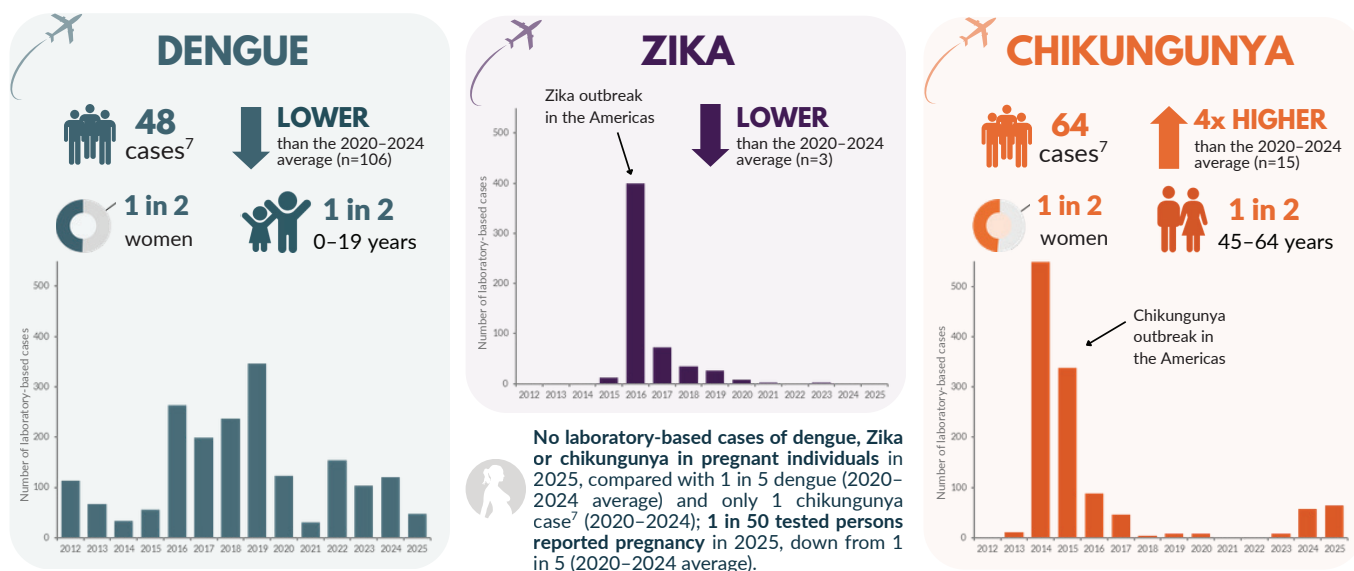


Travel-related dengue, Zika and chikungunya in Canada, 2025

Update to results from a feasibility pilot study on laboratory-based surveillance

Dengue, Zika and chikungunya are vector-borne diseases (VBD) spread by mosquitoes that people living in Canada may encounter during travel abroad¹. These diseases are **not currently endemic in Canada** and are not reportable and/or nationally notifiable; yet **hundreds of travelers returning from endemic regions are diagnosed** in Canada each year²⁻⁴.

Laboratory-based surveillance uses routine laboratory requisition and testing data to identify and monitor disease activity. The **Retro 3 feasibility pilot**⁵ applied this approach to retrospectively analyze travel-related dengue, Zika, and chikungunya in Canada from 2012 to 2024^{3,4}, with the dataset subsequently updated to include 2025. **Results reflect testing conducted at the National Microbiology Laboratory (NML) only**, including confirmatory serology for all provinces and territories and molecular testing for all except British Columbia, Alberta, Ontario and Québec, and therefore underestimate the total disease burden⁶.



Latin America and the Caribbean⁸ remained the top travel region linked to laboratory-based cases in 2025. Guadeloupe was the top country linked to dengue and Cuba, Réunion and Mauritius to chikungunya laboratory-based cases⁹.

- A total of 48 dengue, 1 Zika and 64 chikungunya laboratory-based travel-related cases were identified among a total of 660 persons whose samples were tested for these diseases at the NML in 2025¹⁰.
- In 2025, dengue cases⁷ seemed to occur at slightly younger ages compared to 2020–2024 (median, IQR¹¹: 34, 10–50 vs. 37, 26–54), with higher proportions aged 0–19 years (1 in 2 vs. 1 in 5), whereas chikungunya cases⁷ shifted toward older ages compared to 2024¹² (median, IQR¹¹: 50, 38–59 vs. 36, 28–46), with most cases aged 45–64 (1 in 2 vs. 1 in 4).
- The Caribbean region was linked to about 1 in 3 dengue and 3 in 5 chikungunya cases⁷ with available travel information⁸ in 2025, the same as the 2020–2024 average for dengue, but higher than in 2024¹² for chikungunya (1 in 8 cases). Destinations in South-Eastern Asia were linked to one quarter of dengue and Eastern Africa to one fifth of chikungunya cases⁹.

In 2025, pilot laboratory-based surveillance identified higher counts of chikungunya laboratory-based travel-related cases than the 2020–2024 historical average and for 2024, consistent with increased transmission reported globally. Dengue counts were lower. Leveraging laboratory data for epidemiological analysis can provide valuable, timely insights to support monitoring of evolving trends and inform public health response.



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1. Public Health Agency of Canada. Mosquitoes and mosquito-borne diseases. Ottawa, ON: PHAC; 2023. 2. Public Health Agency of Canada. Dengue fever. Ottawa, ON: PHAC; 2024. 3. Public Health Agency of Canada, BCCDC Public Health Laboratory, Alberta Health Services Laboratory Services, Public Health Ontario Laboratory. Travel-related dengue, Zika and chikungunya in Canada, 2012–2023. Results from a feasibility pilot study on laboratory-based surveillance. Can Commun Dis Rep 2025;51(5):212. 4. Public Health Agency of Canada, BCCDC Public Health Laboratory, Alberta Precision Laboratories, Public Health Ontario Laboratory. Travel-related dengue, Zika, and chikungunya in Canada, 2024: Update to results from a feasibility pilot study on laboratory-based surveillance. Can Commun Dis Rep 2025;51(9):174. 5. Public Health Agency of Canada, BCCDC Public Health Laboratory, Alberta Health Services Laboratory Services, Public Health Ontario Laboratory. Retro 3: A feasibility pilot study for the development of a laboratory-based surveillance system for vector-borne diseases. Can Commun Dis Rep 2023;51(5):213. 6. As of 2025, the National Microbiology Laboratory (NML) conducts all dengue, Zika and chikungunya testing for Saskatchewan, Manitoba, Newfoundland and Labrador, Nova Scotia, New Brunswick, Prince Edward Island, Yukon, Northwest Territories and Nunavut. It also performs confirmatory serology for these diseases for British Columbia, Alberta, Ontario and Québec, and additionally conducts all chikungunya serology for British Columbia and all Zika serology for Alberta. Initial serology and molecular testing for dengue, Zika and chikungunya are occasionally also referred to the NML from all four provinces (British Columbia, Alberta, Ontario and Québec) during periods of local testing disruption. High-volume temporary referrals were excluded from analyses and laboratory-based case counts to avoid inflating trends. 7. Laboratory-based cases. 8. Travel regions are based on the United Nations' Statistical Division's M49 classification system. Travel within Canada was excluded. Highlighted box is an approximation of countries/areas within the Latin America and Caribbean subregion. Travel information was available for 40% of individuals whose samples were tested for dengue, Zika or chikungunya at the NML in 2025. 9. In 2025, country of recent travel was available for 1 in 4 dengue (n=12 of 48), approximately 1 in 2 chikungunya (n=29 of 64) laboratory-based cases and for the single Zika case, and may have included multiple destinations. Dengue: Guadeloupe (n=3); Brazil, Dominican Republic, Ecuador, Honduras, Indonesia, Mexico, Philippines, Sierra Leone and Thailand (n=1 each). Zika: India (n=1). Chikungunya: Cuba (n=14), Réunion (n=3), Mauritius (n=2), Cameroon, Colombia, Dominican Republic, Ethiopia, France, India, Mexico, Philippines and Sri Lanka (n=1 each). 10. Year is defined as the year of the earliest available date among sample collection, sample receipt or symptom onset. 11. IQR, interquartile range (age in years). 12. Previous years (2020–2023) had few cases, thus not supporting comparison.

Public Health Agency of Canada, BCCDC Public Health Laboratory, Alberta Precision Laboratories, Public Health Ontario Laboratory. Travel-related dengue, Zika and chikungunya in Canada, 2025: Update to results from a feasibility pilot study on laboratory-based surveillance. Can Commun Dis Rep 2026;52(9):377



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