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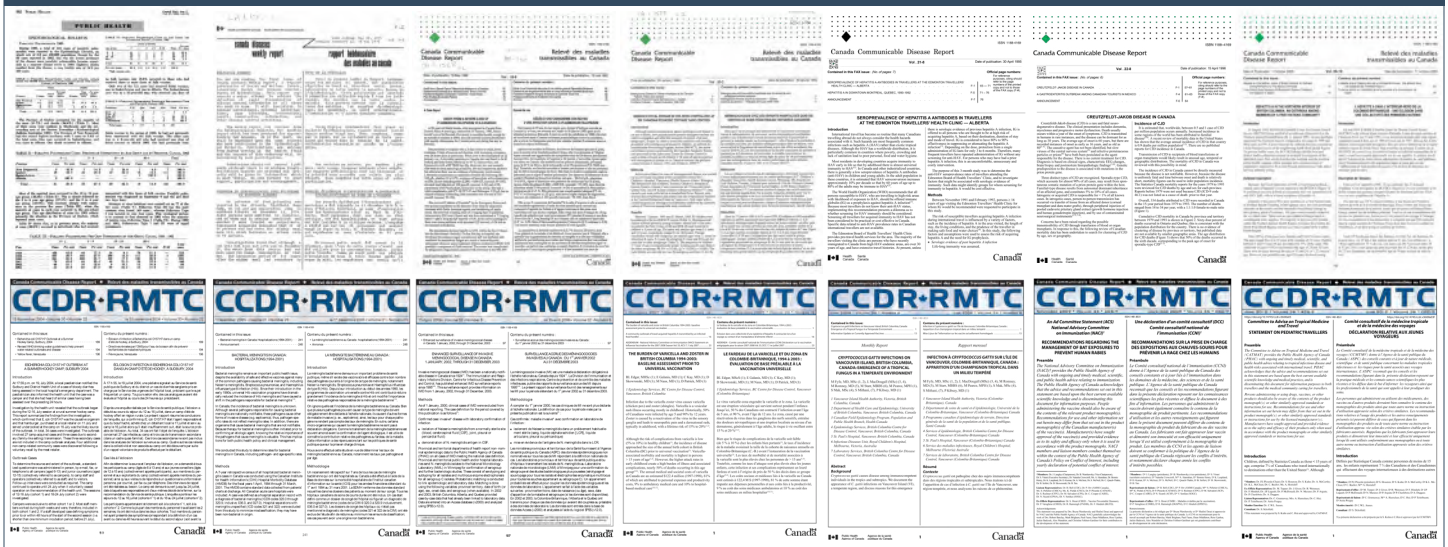

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SURVEILLANCE

Invasive pneumococcal disease 2021–2022

SURVEILLANCE

Invasive group A streptococcal disease

OUTBREAK REPORT

Human Trichinellosis – Arizona, Minnesota, and South Dakota

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CCDR
CANADA COMMUNICABLE DISEASE REPORT

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

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CANADA COMMUNICABLE DISEASE REPORT

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EDITORIAL

Canada Communicable Disease Report—50 years later

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The first issue of *Canada Diseases Weekly Report* was published on May 10, 1975. The first article was entitled, "Outbreak report of staphylococcal, food poisoning in Northern Alberta." I was about 14 years old when I filled out a subscription to the weekly report. Every week, I received in the mailbox an envelope with three folded, printed pages. I kept those pages in a binder which I carried with me over many, many decades. I could have never imagined then that 50 years later, I would be in the seat of the Editor-in-Chief of the *Canada Communicable Disease Report* (CCDR).

At its inception, the *Canada Diseases Weekly Report* was published by the Laboratory Centre for Disease Control, at Health and Welfare Canada. The report represented a major attempt to rapidly disseminate disease control information to Canadians across the country. It was rooted in the Epidemiological Bulletin, a monthly report introduced and published in the mid-fifties by the *Canadian Medical Association Journal*. The *Canada Diseases Weekly Report* specialized in disease surveillance, epidemiological investigations, case histories, international health, immunization information, and other activities in the realm of disease control.

Dr. Franklin M. M. White was appointed its first Editor and Eleanor Paulson Assistant Editor. In 1979, Ms. Paulson became the Managing Editor and finally, almost 10 years later, she became the Editor. In January 1992, the first issue of CCDR, formerly entitled *Canada Diseases Weekly Report* was published, always specializing in "disease surveillance, outbreak investigation, tropical health, and quarantine information, childhood immunization, infection control, sexually transmitted disease, and other disease control activities." By 2001, having spent close to 30 years working for the journal, Eleanor Paulson became the Editor-in-Chief. Over the following years, several people took on the roles or duties of Editor-in-Chief or Managing Editor. Between 2009 and 2012, however, the journal became moribund, publishing supplements and a few Advisory Committee Statements (ACS) sporadically. Following the SARS outbreak, Dr. Ken Scott, senior medical advisor at the Infectious Disease Prevention and Control Branch, was appointed by Dr. Rainer Engelhardt to revive CCDR after several healthcare professionals and even a journalist inquired why the Public Health Agency of Canada was not publishing CCDR anymore. Dr. Scott took on the assignment and since he knew that Dr. Patricia Huston had previous experience in publishing, they both tackled this special project aiming to revive CCDR. During that time, all centres provided funding to support the journal. Dr. Engelhardt contributed with the working hours of one of his executive assistants for CCDR and that's how it began!

In November 2013, Dr. Huston was appointed Scientific Editor with a short article entitled, "CCDR is changing", announcing that the Public Health Agency of Canada's flagship publication on infectious diseases was being revitalized as a biweekly issue with "Briefs" and useful links. In 2015, CCDR became a monthly issue interspersed with six supplements. The journal had also introduced a masthead and a 12-member Editorial Board by June 2015. A year later, the journal was completely redesigned, going from a Word PDF to a formal desktop-published version with a journal cover. In the following years, the quality of the journal kept improving both in design and content. In September 2018, the journal was accepted into PubMed, and in 2020, into the Directory of Open Access Journals, certified with a "DOAJ Seal." In October 2019, I became the Editor-in-Chief and Dr. Huston became the Editor Emeritus, in recognition of all her exceptional contributions after almost six years at the helm of CCDR.

Today, the journal provides a platform to showcase and publish the work of the very diverse and specialized programs of the Public Health Agency of Canada, from the various branches at the Agency involved in infection prevention and control, including ACS from the National Advisory Committee on Immunization and reports from the Canadian Public Health Laboratory Network. CCDR publishes epidemiologic studies, eyewitness reports, implementation science research, outbreak reports, overviews, qualitative studies, rapid communication, surveillance reports, commentaries and several other types of articles. CCDR also publishes selected articles from the provincial, regional and local public health units, Canadian universities, and infectious disease departments from various hospitals across the country.

Today, CCDR and the *Health Promotion and Chronic Disease Prevention in Canada: Research, Policy and Practice* (HPCDP Journal) are the two main, bilingual, peer-reviewed and open access scientific journals of the Public Health Agency of Canada. Together, we are proud to disseminate top quality Canadian data and findings to support evidence-informed discussions. We sincerely hope that our daily efforts contribute to informing, guiding and shaping public health actions, for the benefit of Canada and beyond.

Acknowledgements

Several people have been part of the editorial team over the years and we would like to pay them tribute (in alphabetical order): Dr. S. E. Acres, Jacob Amar, Dr. Fraser Ashton, Debbie Baker, Nicole Beaudoin, Daniel Beck, Francine Boucher, A. Carter, Dr. Alejandra Dubois, Caroline Ethier, Diane Finkle-Perazzo, Annie Fleurant-Ceelen, Rachel Geitzler, Joshua Hachey, Anton Holland, Kim Hopkinson, Dr. Patricia Huston, Charu Kaushal, Katy Keeler, Jocelyn Lee, Joanna Odrowaz, Toju Ogunremi, Wendy Patterson, Eleanor Paulson, Albina Peled, Pascale Plante-Defoy, Marion Pogson, Mylène Poulin, Dr. Hilary Robinson, Laura Rojas Higuera, K. Rozee, Lyal Saikaly, Dena Schanzer, Dr. John Spika, Diane Staynor, Dr. Laura Stewart-Davis, Kyla Tyson, Dr. Franklin M. M. White, Liang (Richard) You, and several students under the Federal Student Work Experience Program (FSWEP).

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Invasive pneumococcal disease surveillance in Canada, 2021–2022

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Abstract

Background: Invasive pneumococcal disease (IPD, *Streptococcus pneumoniae*) has been a nationally notifiable disease in Canada since 2000. The use of conjugate vaccines has caused a shift in the distribution of serotypes over time. This report is a summary of the demographics, serotypes and antimicrobial resistance of IPD isolates collected in Canada in 2021 and 2022.

Methods: The National Microbiology Laboratory (NML) of the Public Health Agency of Canada in Winnipeg, Manitoba collaborates with provincial and territorial public health laboratories to conduct national surveillance of IPD. There were 1,999 isolates reported in 2021 and 3,775 isolates in 2022. Serotype was determined by the Quellung reaction or whole-genome sequencing (WGS). Antimicrobial susceptibilities were determined by WGS methods, broth microdilution, or data shared by collaborators in the Canadian Antimicrobial Resistance Alliance program at the University of Manitoba. Population-based IPD incidence rates were obtained through the Canadian Notifiable Disease Surveillance System.

Results: The incidence of IPD in Canada was 5.62 cases per 100,000 population in 2021, decreasing from the peak of 10.86 cases per 100,000 population in 2018. Serotypes with increasing trends ($p<0.05$) between 2018 and 2022 included: 4 (6.1%–12.4%), 9V (1.0%–5.1%) and 12F (4.8%–5.4%). The overall prevalence of PCV13 serotypes increased over the same period (31.2%–41.5%, $p<0.05$) while the prevalence of non-vaccine types decreased significantly (27.3%–21.5%, $p<0.0001$). The highest rates of antimicrobial resistance in 2021 and 2022 were seen with clarithromycin (21%, 2021; 24%, 2022) and erythromycin (22%, 2021; 24%, 2022). Multidrug-resistant IPD continued to increase from 2018 to 2022 (6.7%–12.6%, $p<0.05$).

Conclusion: The number of cases of IPD continued to decrease in 2021 in comparison to previous years, however, 2022 saw a return to pre-COVID-19 levels. Disease due to PCV13 serotypes 3, 4, 9V and 19F, as well as non-PCV13 serotypes 12F and 20, is increasing in prevalence. Surveillance of IPD to monitor changing serotype distribution and antimicrobial resistance is essential.

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Keywords: invasive pneumococcal disease, IPD, Canada, *Streptococcus pneumoniae*, PCV13, pneumococcus, serotype, surveillance, antimicrobial resistance

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Introduction

Streptococcus pneumoniae, the causative agent of invasive pneumococcal disease (IPD), is responsible for severe infections worldwide, such as meningitis and bacteremia, with children, the elderly and immunocompromised individuals being at greatest risk (1). The majority of cases can be attributed to a small subset of serotypes despite there being over 100 distinct types; vaccination strategies have been successful in reducing the incidence of these types (1,2). Pneumococcal conjugate vaccines (PCV), PCV7 (containing serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F), PCV10 (PCV7 serotypes plus 1,5 and 7F), and PCV13 (PCV10 serotypes plus 3,6A and 19A) were introduced in Canada between 2002 and 2011 (3–7). These vaccines have been successful in decreasing the incidence of their constituent serotypes, however, subsequent increases in non-vaccine serotypes continue (3,4,8). PPV23, a 23-valent pneumococcal polysaccharide vaccine (which includes all PCV13 serotypes except 6A, plus serotypes 2, 8, 9N, 10A, 11A, 12F, 15B/C, 17F, 20, 22F and 33F) has been available for use in Canada since 1989 for adults and people over two years of age at high risk of IPD (6,9).

In 2023, the National Advisory Committee on Immunization (NACI) recommended the use of a 15-valent vaccine (PCV15: PCV13 serotypes plus 22F and 33F) for all ages older than six weeks (10,11). A 20-valent vaccine (PCV20: PCV15 serotypes plus 8, 10A, 11A, 12F and 15B/C) has been recommended for use in seniors over 65 years and for adults between 18 and 64 years with underlying medical conditions (12,13).

The objective of this annual surveillance report is to provide a summary of the serotypes and antimicrobial resistance associated with IPD in Canada in 2021 and 2022.

Methods

Surveillance program

Canadian surveillance of IPD consists of a passive laboratory-based system where invasive isolates from the provincial and territorial public health laboratories are sent to either the National Microbiology Laboratory (NML) in Winnipeg, Manitoba, the Alberta Public Health Laboratory (ProvLab), or the *Laboratoire de santé publique du Québec* (LSPQ) for serotyping. There were 1,999 IPD isolates reported in 2021 and 3,775 isolates reported in 2022 (**Table 1** and **Table 2**), including isolates serotyped by LSPQ (n=353, 2021; n=708, 2022) and ProvLab (n=302, 2021; n=643, 2022). An expansion of IPD surveillance in Québec occurred in 2019 to include all invasive strains. Sterile clinical isolation sites include blood, cerebrospinal fluid, peritoneal, pericardial or joint fluid, internal body sites, and deep tissue, including surgical or biopsy samples. For this report, isolates from pleural fluid (empyema) are included, despite not meeting the current national case definition for invasive disease, as they are widely considered as invasive in other jurisdictions (3).

Isolate testing

Invasive pneumococcal disease isolates were screened using bile solubility and optochin disc susceptibility at NML until October 2022, when bile solubility was discontinued (Oxoid) (14). Serotyping of IPD at LSPQ and ProvLab Alberta was performed by the Quellung reaction using commercial antisera (SSI Diagnostica; Statens Serum Institut, Copenhagen, Denmark) (15). Serotyping at NML was performed by the Quellung reaction until October 2022; from November 2022 to December 2022, whole-genome sequencing (WGS) was carried out on all isolates submitted to NML using the Illumina platform, with serotypes identified directly using the WGS Analysis and Detection of Molecular Markers (WADE) pipeline, as described

Table 1: Number of invasive *Streptococcus pneumoniae* isolates submitted by province, 2021

Province	Age group (years)						Not given	Total
	<2	2–4	5–14	15–49	50–64	≥65		
British Columbia[a]	4	4	5	90	93	82	0	278
Alberta	4	9	3	131	87	65	3	302
Saskatchewan	2	4	1	45	28	24	0	104
Manitoba	9	8	3	58	38	25	0	141
Ontario	51	22	13	153	162	204	5	610
Québec	45	23	8	90	120	165	0	451
Atlantic[b]	4	1	0	17	33	30	3	88
Northern[c]	0	1	0	11	13	0	0	25
Total	**119 (6%)**	**72 (4%)**	**33 (2%)**	**595 (30%)**	**574 (29%)**	**595 (30%)**	**11 (1%)**	**1,999**

[a] Includes isolates from Yukon
[b] Includes isolates from New Brunswick, Prince Edward Island, Nova Scotia, and Newfoundland and Labrador
[c] Includes isolates from the Northwest Territories and Nunavut
Note: Population-based incidence of disease data for 2009 to 2021 were obtained through the Canadian Notifiable Disease Surveillance System (CNDSS). Population data for incidence rates were obtained from Statistics Canada's annual population estimates

Table 2: Number of invasive *Streptococcus pneumoniae* isolates submitted by province, 2022

Province	Age group (years)						Not given	Total
	<2	2–4	5–14	15–49	50–64	≥65		
British Columbia[a]	10	10	12	172	134	176	2	516
Alberta	22	15	17	272	177	135	2	640
Saskatchewan	8	9	5	109	60	47	0	238
Manitoba	10	2	8	97	61	55	0	233
Ontario	64	59	48	260	340	395	4	1,170
Québec	46	25	22	156	183	365	0	797
Atlantic[b]	6	3	10	26	44	65	5	159
Northern[c]	0	0	1	8	9	4	0	22
Total	**166 (4%)**	**123 (3%)**	**123 (3%)**	**1,100 (29%)**	**1,008 (27%)**	**1,242 (33%)**	**13 (0.3%)**	**3,775**

[a] Includes isolates from Yukon
[b] Includes isolates from New Brunswick, Prince Edward Island, Nova Scotia, and Newfoundland and Labrador
[c] Includes isolates from the Northwest Territories and Nunavut

elsewhere (16). Isolates that were non-typeable by WGS were confirmed by the Quellung reaction and the National Center for Biotechnology Information (NCBI)'s Basic Local Alignment Search Tool (BLAST) analysis of the rpoB gene (15,17). For this study, serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to differentiate between the two types (18,19).

Antimicrobial susceptibility testing (AST) was performed on most 2021 IPD isolates submitted to NML for serotyping by the provincial public health laboratories (Saskatchewan, Manitoba, Ontario, Québec, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, and six of eight health regions in New Brunswick). In collaboration with the University of Manitoba and the Canadian Antimicrobial Resistance Alliance, minimum inhibitory concentrations were determined using in-house broth microdilution in accordance with Clinical & Laboratory Standards Institute (CLSI) guidelines (20,21). Minimum inhibitory concentrations for 2022 isolates were determined using a combination of WGS-predicted susceptibility and in-house broth microdilution (20–22). Antimicrobials included in this report are penicillin, ceftriaxone, chloramphenicol, clarithromycin, clindamycin, doxycycline, erythromycin, trimethoprim/sulfamethoxazole, linezolid, and vancomycin. Minimum inhibitory concentration interpretive standards were defined according to CLSI breakpoints (21). Multidrug resistance (MDR) was defined as resistance to three or more classes of antimicrobials for this report.

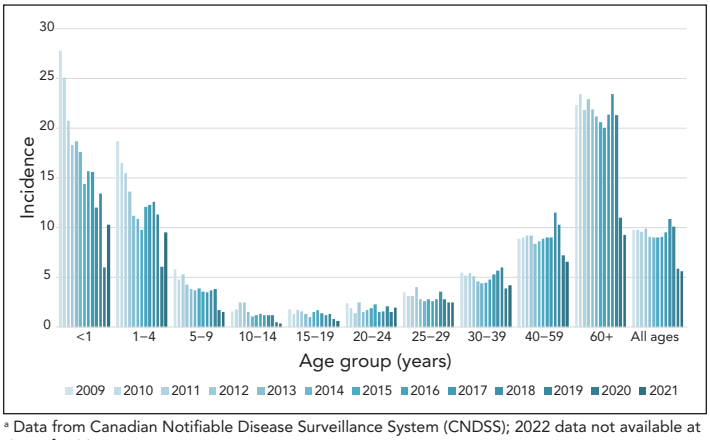
Data analysis

As previously described (23), data submitted with bacterial isolates included patient age, sex, clinical source, province, and date of collection. Duplicate isolates collected from the same patient within 14 days were counted once if they were the same serotype, with the most invasive isolation site assigned. Meningitis-related isolates were regarded as most invasive, followed by blood and then other sterile sites. Data was aggregated by age into <2, 2–4, 5–14, 15–49, 50–64, and ≥65-year-old age groups, and regionally into Western (British Columbia, Alberta, Saskatchewan, Manitoba), Central (Ontario, Québec), Eastern (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador) and Northern (Yukon, Northwest Territories and Nunavut) regions of Canada. Statistical significance of trends was assessed using the Cochran-Armitage test of trend, with a *p*-value of <0.05 considered to be statistically significant.

Results

Overall IPD incidence rates in Canada remained stable from 2009 to 2019 (9.8–10.1), after which there was a decline in 2020 and 2021 to fewer than six cases per 100,000 population (**Figure 1**, **Appendix, Supplemental Table S1**).

Figure 1: Annual incidence of invasive pneumococcal disease cases per 100,000 population in Canada by age group, 2009–2021[a]



[a] Data from Canadian Notifiable Disease Surveillance System (CNDSS); 2022 data not available at time of writing

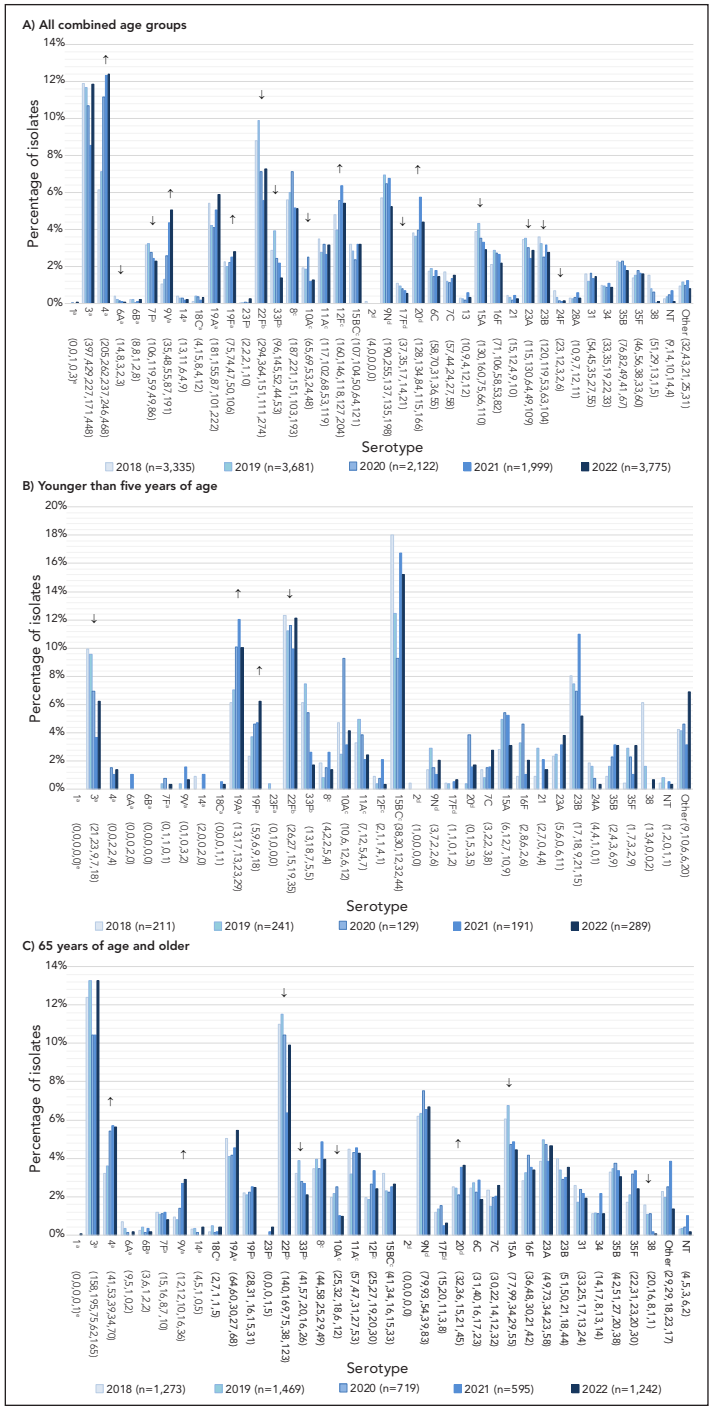
There was a large increase in the number of isolates submitted in 2022 (n=3,775) compared to 2021 (n=1,999), particularly in the first and last quarters of 2022 (Appendix, **Figure S1**). The distribution among age groups was consistent year-to-year. Infants <2 years of age accounted for 4%–6% of isolates, toddlers aged 2–4 years for 3%–4%, children aged 5 to 14 years for 2%–3%, patients aged 15 to 49 years for 29%–30%, older adults aged 50 to 64 years for 27%–29% and seniors aged ≥65 years for 30%–33% (Table 1 and Table 2). Of the isolates with gender information available, isolates from male patients represented 58.2% (n=1,152) and 57% (n=2,152) of isolates collected in 2021 and 2022, respectively. Blood was the most frequent clinical isolation site, accounting for 94% (n=1,877) of isolates in 2021 and 92% (n=3,460) in 2022. Additional information on specimen source by age and serotype are available in Appendix, **Figures S2 to S5**.

The most commonly collected serotypes overall in both 2021 and 2022 were 4 (12.3%, n=246 and 12.4%, n=468) and 3 (8.6%, n=171 and 11.9%, n=448) (**Figure 2**, A). Other common serotypes included 22F, 19A, 12F and 9N. Serotypes that demonstrated significant increasing trends in prevalence from 2018 to 2022 include PCV13 serotypes 4 (6.1%−12.4%, $p<0.001$), 9V (1.0%−5.1%, $p=0.011$) and 19F (2.2%−2.8%, $p=0.0422$), as well as 12F (4.8%–5.4%, $p=0.0068$) and 20 (3.8%–4.4%, $p=0.0143$) (Figure 2A). Vaccine serotypes that significantly decreased in prevalence from 2018 to 2022 include 22F, 33F ($p<0.0001$) and 6A, 7F, 10A and 17F ($p\leq0.007$) (Figure 2A).

The three most common serotypes in children <2 years during 2021 and 2022, respectively, included 15B/C (10.9%, 15.1%), 22F (12.6%, 10.8%), and 19A (12.6%, 9.6%), while the most common for 2 to 4-year-olds was serotype 15B/C (26.4%, 15.4%), followed by 22F (5.6%, 13.8%). Serotypes 22F (18.2%, 17.1%), 3 (3.0%, 12.2%) and 19F (15.2%, 11.4%) were the most common in 5 to 14-year-olds. Serotype 4 was the most prevalent serotype in 15 to 49-year-olds (22.7%, 21.8%) followed by serotypes 12F (9.1%, 10.5%) and 3 (7.4%, 9.3%). Serotypes 4 (12.7%, 14.9%) and 3 (9.9%, 14.6%) were the most common in 50 to 64-year-olds, while serotypes 3 (10.4%, 13.3%) and 22F (6.4%, 9.9%) were dominant in adults over 65 years of age. See Figure 2 and Appendix, **Figures S6 to S7**.

Significant increases of serotypes 19A (7.1%–10.0%, $p=0.04$) and 19F (3.7%–6.2%, $p=0.035$) were observed in children <5 years of age from 2018 to 2022 (Figure 2B). Serotype 19F also increased significantly for children 5 to 14 years (4.4%–11.4%, $p=0.0265$). Patients 15 to 49 years of age saw significant increases in serotypes 4 (11.7%–21.8%, $p<0.0267$) and 9V (1.4%–7.6%, $p<0.0001$). Adults 50 to 64 years of age saw similar increases in serotypes 4 (7.8%–14.9%, $p<0.0001$) and 9V (1.4%–6.1%, $p<0.0001$). Significant increases for seniors ≥65 years were noted for serotype 4 (3.2%−5.6%, $p=0.0003$), 9V (0.9%–2.9%, $p<0.0001$) and 20 (2.5%–3.6%, $p=0.0039$) (Figure 2C). Serotypes 6A, 7F, 22F, 33F, 10A, 17F, 15A 23A, 23B, 24F and 38 all showed significant decreases from 2018 to 2022 for all combined age groups ($p\leq0.047$) (Figure 2A).

Figure 2: Invasive *Streptococcus pneumoniae* serotype prevalence trends by age, 2018–2022[a,b,c,d,e,f,g]



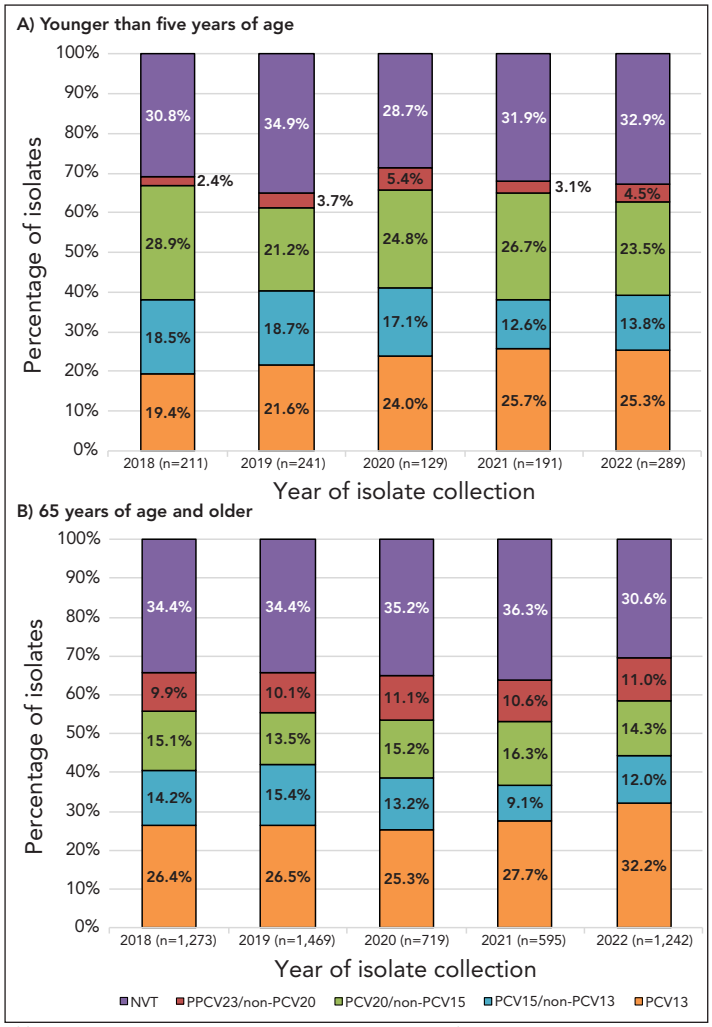
[a] Component of PCV13
[b] Component of PCV15
[c] Component of PCV20
[d] Component of PPV23
[e] Number of isolates for 2018, 2019, 2020, 2021 and 2022, respectively
[f] For serotypes with an overall (2018–2022) N≥30: up or down arrows indicate statistically significant trends toward increasing or decreasing prevalence for the 2018–2022 timespan, using the chi-squared test for trend. Serotypes with no arrow either did not demonstrate a statistically significant trend, or did not have an overall N≥30
[g] Serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to precisely differentiate between the two types (18,19). Trends for more detailed age groups can be found in the Appendix, Figures S8 to S12

Regionally, the top two serotypes associated with Western Canada, 4 (18.2%, 2021; 18.0%, 2022) and 3 (8.0%, 2021; 11.5%, 2022), remained the same as in previous years. In Central Canada, serotype 3 continued to be the most prevalent (9.1%, 2021; 12.1%, 2022), followed by 19A (7.4%, 2021; 8.4%, 2022). In Eastern Canada, serotypes 20 (15.9%) and 22F (11.4%) were the most common in 2021, while serotypes 4 (15.7%) and 3 (14.5%) were predominant in 2022. Serotype 4 continues to dominate in Northern Canada (81%, 2021; 34%, 2022) (Appendix, **Figures S13 to S17**).

Serotypes belonging to the currently recommended PCV13 vaccine have significantly increased in prevalence overall from 2018 to 2022 (31.2%–41.5%, p=0.0269); this increase was seen in all age groups except children from 2 to 14 years. The proportion of PCV15-unique serotypes decreased significantly overall (11.7%–8.7%, p<0.0001), however, there was no significant change in the under 15-year age group. Proportions of PCV20-unique and PPV23-unique serotypes have not significantly changed from 2018 to 2022 among the age groups. The number of non-vaccine serotypes overall has decreased from 2018 to 2022 (27.3%–21.5%, p<0.001) (**Figure 3**, Appendix, **Figures S18 to S23** and **Tables S2 to S8**).

Due to the different AST methods used for 2021 and 2022, the total number of isolates tested for each antimicrobial varied. The highest rate of resistance for both 2021 and 2022 was for clarithromycin (20.9%, 2021; 24.1%, 2022) (**Table 3**). Penicillin resistance increased significantly from 3.4% in 2018 to 8.3% in 2022 (p<0.0001), as did doxycycline resistance (8.5%–17.15%, p<0.0001) and trimethoprim-sulfamethoxazole resistance (7.5%–14.9%, p<0.0001). Significant decreases were seen for chloramphenicol resistance (5.4%–2.7%, p=0.01) and erythromycin resistance (25.8%–24.0%, p<0.0001). Resistance to ceftriaxone remains low, ranging from a high of 1.0% to a low of 0.3% between 2018 and 2022 (Table 3). All isolates were susceptible to linezolid and vancomycin. Resistance rates for specific serotypes are listed in **Table 4** and **Table 5**.

Figure 3: Invasive *Streptococcus pneumoniae* serotype trends by vaccine and age[a], 2018–2022



Abbreviations: NVT, non-vaccine serotype; PCV, pneumococcal conjugate vaccine; PPCV, pneumococcal polysaccharide vaccine
[a] Vaccine serotypes include PCV13 (1, 3, 4, 5, 6A/C, 6B, 7F, 9V, 14, 19A, 19F, 18C, 23F); PCV15 (all PCV13 serotypes plus 22F and 33F); PCV20 (all PCV15 serotypes plus 8, 10A, 11A, 12F, 15B/C) and PPV23 (PCV20 serotypes except 6A, plus 2, 9N, 17F, 20); NVT=all serotypes not included in PCV13, PCV15, PCV20 and PPV23. Trends for more detailed age groups can be found in the Appendix, Figures S18 to S23 and Tables S2 to S8

Table 3: Proportion of antimicrobial resistant invasive *Streptococcus pneumoniae* isolates by year, 2018–2022

Antimicrobial	Year (n, %)				
	2018	2019	2020	2021	2022
AXO	12 (0.7%)	6 (0.3%)	3 (0.3%)	10 (1.0%)	4 (0.4%)
CHL	100 (5.4%)	59 (3.2%)	43 (4.0%)	32 (3.2%)	29 (2.7%)
CLA	465 (26.2%)	473 (26.1%)	243 (23.7%)	195 (20.9%)	249 (24.1%)
CLI	128 (6.9%)	166 (8.9%)	86 (8.0%)	79 (8.0%)	88 (8.1%)
DOX	152 (8.5%)	216 (11.9%)	126 (12.2%)	135 (14.5%)	177 (17.2%)
ERY	31 (25.8%)	75 (43.9%)	54 (44.3%)	110 (21.6%)	260 (24.0%)
LEV	5 (0.3%)	9 (0.5%)	1 (0.1%)	0 (0.0%)	2 (0.2%)
PEN	63 (3.4%)	48 (2.6%)	36 (3.4%)	46 (4.7%)	90 (8.3%)
SXT	139 (7.5%)	177 (9.5%)	117 (11.0%)	105 (10.6%)	161 (14.9%)

Abbreviations: AXO, ceftriaxone using the parenteral meningitis Clinical and Laboratory Standards Institute interpretive standard; CHL, chloramphenicol; CLA, clarithromycin; CLI, clindamycin; DOX, doxycycline; ERY, erythromycin; LEV, levofloxacin; PEN, penicillin using the parenteral meningitis Clinical and Laboratory Standards Institute interpretive standard; SXT, trimethoprim/sulfamethoxazole

Table 4: Percentage of antimicrobial resistance of invasive *Streptococcus pneumoniae* serotypes collected, 2021

Serotype	Percentage of isolates with antimicrobial resistance[a]							
	PEN	AXO	ERY	CLA	CLI	CHL	DOX	SXT
3[b]	-	-	5%	8%	6%	13%	14%	-
4[b]	-	-	4%	11%	9%	10%	17%	1%
6A[b]	-	-	100%	100%	-	-	-	50%
9V[b]	26%	11%	33%	29%	-	-	23%	29%
14[b]	-	-	100%	100%	67%	-	-	67%
18C[b]	-	-	100%	25%	-	-	25%	25%
19A[b]	35%	10%	82%	74%	42%	6%	44%	32%
19F[b]	11%	7%	20%	13%	15%	-	13%	7%
22F[c]	-	-	50%	56%	2%	-	2%	-
33F[c]	-	-	67%	77%	-	-	-	-
8[d]	-	-	-	-	-	-	-	2%
10A[d]	-	-	-	-	-	-	-	8%
11A[d]	-	-	24%	23%	-	-	-	19%
12F[d]	-	-	25%	20%	-	2%	69%	69%
15B/C[d,e]	-	-	42%	35%	10%	-	3%	3%
9N[f]	2%	-	12%	13%	3%	-	8%	3%
17F[f]	-	-	-	9%	-	-	9%	-
20[f]	-	-	-	1%	1%	1%	1%	-
6C	6%	-	40%	50%	6%	-	6%	19%
7C	-	-	-	-	-	-	-	56%
10B	-	-	-	-	-	-	33%	-
13	-	-	33%	25%	25%	-	25%	-
15A	20%	-	60%	59%	55%	5%	47%	-
16F	-	-	18%	11%	11%	7%	7%	7%
22A	-	-	-	-	-	-	-	50%
23A	-	-	50%	48%	44%	-	48%	8%
23B	-	-	8%	5%	-	-	-	4%
24F	-	-	-	100%	100%	-	50%	-
28A	-	-	-	-	-	33%	33%	-
34	-	-	13%	13%	13%	-	13%	7%
35B	57%	4%	38%	52%	-	-	-	30%
35D	50%	-	-	67%	-	-	-	-
35F	-	-	-	13%	13%	-	7%	-

Abbreviations: AXO, ceftriaxone using the parenteral meningitis interpretive standard; CHL, chloramphenicol; CLA, clarithromycin; CLI, clindamycin; DOX, doxycycline; ERY, erythromycin; PEN, penicillin using the parenteral meningitis Clinical and Laboratory Standards Institute interpretive standard; SXT, trimethoprim/sulfamethoxazole

[a] "-" denotes no resistance (0%) to the antimicrobial

[b] Component of PCV13

[c] Component of PCV15

[d] Component of PCV20

[e] Serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to precisely differentiate between the two types (18,19)

[f] Component of PPV23

Table 5: Percentage of antimicrobial resistance of invasive *Streptococcus pneumoniae* serotypes collected, 2022

Serotype	Percentage of isolates with antimicrobial resistance[a]							
	PEN	AXO	ERY	CLA	CLI	CHL	DOX	SXT
1[b]	-	-	-	-	-	-	33%	33%
3[b]	-	-	4%	4%	1%	6%	6%	1%
4[b]	-	-	9%	9%	7%	3%	14%	12%
14[b]	75%	-	50%	50%	50%	-	50%	75%
7F[b]	-	-	3%	3%	-	-	-	-
9V[b]	69%	3%	72%	71%	-	-	70%	72%
18C[b]	-	-	33%	33%	17%	-	33%	17%
19A[b]	40%	2%	77%	77%	58%	2%	47%	42%
19F[b]	4%	-	4%	4%	4%	-	4%	4%
23F[b]	67%	-	67%	67%	33%	33%	33%	67%
22F[c]	-	-	50%	49%	2%	2%	3%	-
33F[c]	-	-	73%	73%	-	-	-	27%
15B/C[d,e]	3%	-	25%	27%	10%	-	18%	3%
10A[d]	-	-	29%	-	-	-	-	-
11A[d]	3%	-	33%	34%	3%	-	3%	3%
12F[d]	-	-	30%	31%	-	3%	35%	36%
8[d]	-	-	3%	3%	-	-	2%	-
9N[f]	5%	-	5%	5%	-	-	8%	3%
17F[f]	22%	-	11%	11%	-	-	-	-
20[f]	-	-	8%	9%	8%	-	11%	2%
6C	-	-	50%	50%	17%	17%	33%	17%
6D	-	-	-	-	-	100%	100%	100%
7C	-	-	-	-	-	-	8%	69%
13	-	-	40%	40%	40%	-	60%	60%
15A	15%	-	38%	38%	31%	4%	27%	4%
16F	-	-	5%	5%	5%	5%	5%	-
17A	-	-	100%	100%	100%	-	100%	-
23A	-	-	26%	29%	26%	-	29%	9%
23B	-	-	11%	8%	-	-	-	29%
24A	-	-	-	-	-	-	-	100%
24F	-	-	67%	67%	67%	-	67%	-
28A	-	-	-	-	-	50%	50%	-
35B	57%	-	36%	36%	7%	7%	7%	14%
31	-	-	17%	17%	-	-	-	-
34	8%	-	-	-	-	-	-	-
38	-	-	40%	40%	-	-	40%	20%

Abbreviations: AXO, ceftriaxone using the parenteral meningitis interpretive standard; CHL, chloramphenicol; CLA, clarithromycin; CLI, clindamycin; DOX, doxycycline; ERY, erythromycin; PEN, penicillin using the parenteral meningitis Clinical and Laboratory Standards Institute interpretive standard; SXT, trimethoprim/sulfamethoxazole

[a] "-" denotes no resistance (0%) to the antimicrobial

[b] Component of PCV13

[c] Component of PCV15

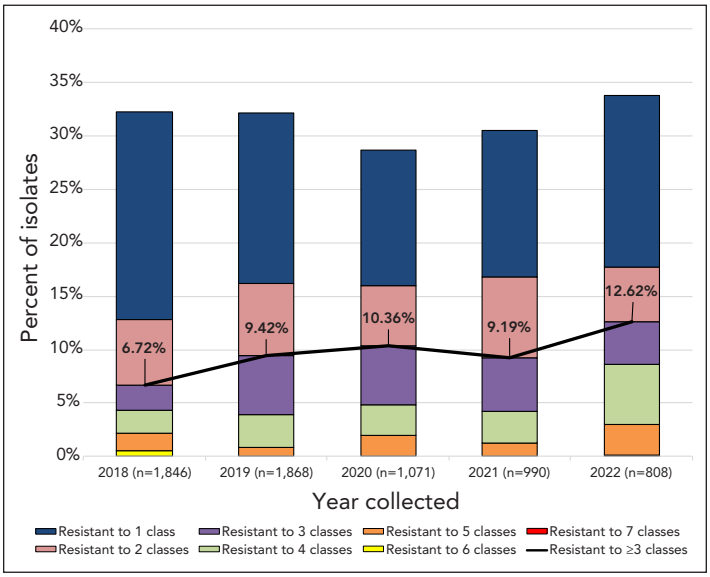
[d] Component of PCV20

[e] Serotypes 15B and 15C were grouped together as 15B/C because of reported reversible switching between them *in vivo* during infection, making it difficult to precisely differentiate between the two types (18,19)

[f] Component of PPV23

Multidrug-resistant IPD increased from 6.7% (n=124) of the isolates tested in 2018 to 12.5% (n=135) in 2022 (p<0.0001) (**Figure 4**, Appendix, **Table S9**). Of the serotypes where 10 or more isolates were collected in 2021, the highest rates of MDR were in 15A (50%, n=10), 23A (44%, n=11), 19A (38.7%, n=12) and 9V (28.6%, n=35). In 2022, the highest rates of MDR were identified in 9V (70.7%, n=41), 19A (43.5%, n=27), 15A (30.8%, n=8) and 23A (26.5% n=9) (Table 3, Appendix, **Figure S25a**). The most common MDR pattern in 2021 was macrolide-clindamycin-tetracycline (n=30), including 10 serotype 23A (Appendix, **Table S10a**). For 2022, beta-lactam-macrolide-tetracycline-trimethoprim/sulfamethoxazole was the most common MDR pattern (n=43) with 9V accounting for 41 of these. Serotypes 15A and 23A, for both 2021 and 2022, were resistant to macrolides, clindamycin and tetracycline (n=10 and n=17, respectively). Multidrug resistant serotype 9V isolates were most commonly resistant to four antimicrobial classes (beta-lactam, macrolide, tetracycline and trimethoprim/sulfamethoxazole; n=41), while the most common MDR pattern for serotype 19A was beta-lactam-macrolide-clindamycin-tetracycline-chloramphenicol (n=20) (Appendix, **Figure 25b** and **Table S10b**).

Figure 4: Annual trend of multidrug resistance of invasive *Streptococcus pneumoniae*, 2018–2022[a]



[a] Antimicrobial classes include: beta-lactams (amoxicillin/clavulanic acid, penicillin using meningitis breakpoints, ceftriaxone using meningitis breakpoints, imipenem, and meropenem); macrolides (clarithromycin); fluoroquinolones (levofloxacin); tetracyclines (doxycycline); folate pathway inhibitors (trimethoprim-sulfamethoxazole); phenicols (chloramphenicol); lincosamides (clindamycin); and oxazolidinones (linezolid)

Discussion

The national incidence rate of IPD in Canada for 2021 was 5.6 cases per 100,000 population, which was very similar to 2020 incidence levels (5.9 cases), but far below the incidence in pre-COVID years that ranged from a low of 9.0 cases in 2009 to a high of 10.9 cases in 2018 (Figure 1). The lower rate can be partially attributed to continued COVID-19 non-pharmaceutical intervention strategies (NPIs) instituted in Canada in 2020, such as masking and physical distancing, working and schooling from home, and travel restrictions (24,25). Global studies of pneumococcal disease and co-infection with viruses, such as respiratory syncytial virus (RSV), influenza and metapneumovirus, suggest that decreased incidence of IPD is not only due to NPIs but also associated with decreased circulation of these viruses during COVID-19 lockdown (26–31). A comprehensive interrupted time series study by Rybak *et al.* that included multiple surveillance systems in France concluded that as pneumococcal carriage rates did not change during periods of NPI use, decreased IPD could be linked to decreased viral infection (29). Gradual lifting of COVID-19 restrictions occurred in Canada in 2022, including a total removal of all travel restrictions in October (24,32). There is concern that a period of increased IPD may occur due to "immunity debt" (lack of stimulation to immune systems) in children, following the lifting of COVID-19-related protective measures (27,33,34). Canadian incidence rates for young children aged <1 year and 1 to 4 years jumped from 5.95 to 10.27 and 6.13 to 9.51 cases per 100,000 population, respectively, from 2020 to 2021. An increase was not seen in older age groups (Figure 1). Although incidence rates for IPD are not yet available for 2022, Canada will likely follow the same trend as other countries. The Invasive Respiratory Infection Surveillance (IRIS) Consortium analyzed surveillance data from over thirty countries, including Canada, and reported a worldwide decrease in IPD incidence during the COVID-19 lockdown followed by an increase late in 2021 (35). Increases in the number of IPD isolates received by NML coincided with the lifting of NPIs, particularly in the last quarter of 2022 (Appendix, Figure S1).

PCV13 serotypes 3 and 4 remained the most common serotypes overall for 2021 and 2022. While the prevalence of serotype 3 saw a dip during the 2021 period of NPI strategies in Canada, serotype 4 continued to rise over this same time. This trend can possibly be attributed to the population dynamics and age groups associated with these serotypes. Multiple studies in the western regions of North America show an association of serotype 4 to adults at risk due to homelessness and drug and alcohol abuse (36–38). Serotype 3 is commonly associated with multiple age groups who would have been more influenced by NPIs than the at-risk populations associated with serotype 4 (39). Poor immunogenicity of serotype 3 remains an issue; preliminary *in vitro* immunogenicity studies of the PCV15 vaccine formulation show increased immune response to serotype 3 in comparison to PCV13, but real-world evidence is needed to corroborate these studies (40–42).

Antimicrobial resistance rates for clarithromycin and erythromycin remained high (both around 24%) but did not trend upward during the study period. Of note is an increase in penicillin resistance (4.7%–8.3%), which can be attributed to an increase in penicillin-resistant serotypes 9V and 19A collected during 2021 and 2022. Over the five-year study period from 2018 to 2022, there was a significant increase in MDR among the isolates

tested (6.7%–12.5%, $p<0.0001$). Serotypes 15A and 19A, which have historically exhibited high levels of MDR in Canada, remain a concern; however, similar to the results of the SAVE study described by Adam *et al.*, increased diversity of MDR serotypes was seen (43). Seventy-one percent of all serotype 9V tested exhibited MDR in 2022 as well as 27% of serotype 23A. This will be crucial to monitor going forward, as a steady increase of common MDR serotypes could have a significant impact on patient outcomes in the future.

Limitations

Caution should be exercised when interpreting the data presented in this report. Provinces and territories may only submit a subset of their isolates to NML for testing. Numbers of isolates submitted to NML versus information submitted to CNDSS may differ due to differences in submission protocols from the provinces. Data for 2020 and 2021 may not be reflective of actual trends, as the COVID-19 pandemic impacted disease incidence in all age groups. Significant increases may have been driven by the large increase in isolates collected in 2022.

Conclusion

The incidence of IPD in Canada varied very little from 2020 and 2021 after a significant decrease from 2019 to 2020 (incidence rates for 2022 are not available at the time of printing). PCV13 vaccine serotypes 3 and 4 are a major concern in adult age groups, and 15B/C in children <5 years of age. Continued surveillance of IPD serotypes and antimicrobial resistance in Canada is important to monitor existing trends, identify new trends, and assess the effect of newly recommended PCV15 and PCV20 vaccines.

Authors' statement

AG — Formal analysis, data curation, visualization, writing–original draft, writing–review & editing of final version
ARG — Formal analysis, validation, investigation, data curation, visualization, writing–review & editing
BL — Resources, methodology, writing–review & editing
AM — Resources, methodology, writing–review & editing
GJT — Resources, methodology, writing–review & editing
GGZ — Resources, methodology, writing–review & editing
JVK — Resources, methodology, writing–review & editing
LH — Resources, methodology, writing–review & editing
JMinion — Resources, methodology, writing–review & editing
PVC — Resources, methodology, writing–review & editing
HS — Resources, methodology, writing–review & editing
DH — Resources, methodology, writing–review & editing
YY — Resources, methodology, writing–review & editing
XD — Resources, methodology, writing–review & editing
LS — Resources, methodology, writing–review & editing
JMcFadzen — Resources, methodology, writing–review & editing
KF — Writing–review & editing
IM — Conceptualization, validation, methodology, supervision, project administration, writing–review & editing

Competing interests

None.

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Appendix

Supplemental figures and tables are available upon request to the author.

Table S10a: Multidrug resistance profiles of invasive *Streptococcus pneumoniae* serotypes, 2021
Table S10b: Multidrug resistance profiles of invasive *Streptococcus pneumoniae* serotypes, 2022

Table S11a: Number of invasive *Streptococcus pneumoniae* isolates serotyped by the National Microbiology Laboratory (NML) in comparison to the total number of cases reported to Canadian Notifiable Diseases Surveillance System (CNDSS), 2021

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Invasive group A streptococcal disease surveillance in Canada, 2021–2022

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Abstract

Background: Invasive group A streptococcal (iGAS, *Streptococcus pyogenes*) disease has been a nationally notifiable disease in Canada since 2000. This report summarizes the demographics, *emm* types, and antimicrobial resistance of iGAS isolates collected in Canada in 2021 and 2022.

Methods: The Public Health Agency of Canada's National Microbiology Laboratory collaborates with provincial and territorial public health laboratories to conduct national surveillance of invasive *S. pyogenes*. *Emm* typing was performed using the Centers for Disease Control and Prevention *emm* sequencing protocol or extracted from whole-genome sequencing data. Antimicrobial susceptibilities were determined using Kirby-Bauer disk diffusion according to Clinical and Laboratory Standards Institute guidelines or predicted from whole-genome sequencing data based on the presence of resistance determinants.

Results: Overall, the incidence of iGAS disease in Canada was 5.56 cases per 100,000 population in 2021, decreasing from the peak of 8.6 cases per 100,000 population in 2018. A total of 2,630 iGAS isolates were collected during 2022, representing an increase from 2021 (n=2,179). In particular, there was a large increase in isolates collected from October to December 2022. The most predominant *emm* type overall in 2021 and 2022 was *emm*49, at 21.5% (n=468) and 16.9% (n=444), respectively, representing a significant increase in prevalence since 2018 ($p<0.0001$). The former most prevalent type, *emm*1, increased from 0.5% (n=10) in 2021 to 4.8% (n=125) in 2022; similarly, *emm*12 increased from 1.0% (n=22) in 2021 to 5.8% (n=151) in 2022. These two types together accounted for almost 25% of isolates collected in late 2022 (October to December). Antimicrobial resistance rates in 2021 and 2022 included: 14.9%/14.1% erythromycin resistance, 4.8%/3.0% clindamycin resistance, and <1% chloramphenicol resistance.

Conclusion: The increase of iGAS isolates collected in Canada is an important public health concern. Continued surveillance of iGAS is critical to monitor expanding *emm* types and antimicrobial resistance patterns.

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Keywords: iGAS, *Streptococcus pyogenes*, Canada, *emm*, surveillance, antimicrobial resistance, group A *Streptococcus*

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Introduction

Invasive group A *Streptococcus* (iGAS, *Streptococcus pyogenes*) is responsible for a wide range of human diseases, the most serious of which include bacteraemia, streptococcal toxic shock syndrome, necrotizing fasciitis, and endocarditis (1). In Canada, the overall incidence of iGAS infections has steadily increased since becoming a notifiable disease in 2000, peaking at a rate of 8.61 cases per 100,000 population in 2018 (2). In 2020, Canada reported decreased submissions of iGAS isolates, attributed to the containment measures put in place to control the SARS-CoV-2 pandemic (COVID-19) (2). There was also a significant shift in the *emm* types most commonly associated with disease in Canada, shifting from the formerly prevalent *emm*1 toward *emm*49 and *emm*76 (2).

In late 2022, the World Health Organization (WHO) reported that several countries in Europe had been observing increased cases of iGAS and scarlet fever, predominantly in children (3), starting off a season of increased focus on iGAS in many countries. As COVID-19 pandemic restrictions have loosened and person-to-person disease transmission has intensified, it is increasingly important to monitor the prevalence of both iGAS disease and associated *emm* types and antimicrobial resistance. This report provides a summary of iGAS isolates collected in Canada in 2021 and 2022.

Methods

Surveillance program

As previously described, surveillance of iGAS in Canada consists of a passive, laboratory-based system where invasive *S. pyogenes* isolates from all provincial and territorial public health laboratories (except Alberta) are forwarded to the National Microbiology Laboratory (NML) in Winnipeg for further testing (2). In 2021, a total of 2,179 iGAS isolates were reported, including 1,787 submitted directly to NML by provincial and territorial public health laboratories, as well as data for a further 392 isolates collected and tested by the Provincial Laboratory for Public Health in Edmonton, Alberta (ProvLab Alberta); in 2022, a total of 2,630 iGAS isolates were reported, including 2,108 submitted directly and data for 522 tested by ProvLab Alberta (**Table 1**). Sterile clinical isolation sites include blood, cerebrospinal fluid, deep tissue, biopsy and surgical samples, bone, and any clinical sources associated with necrotizing fasciitis or toxic shock syndrome.

Population-based incidences of iGAS disease up to 2021 were obtained through the Canadian Notifiable Disease Surveillance System (CNDSS). Population data for incidence rates were obtained from Statistics Canada's July 1st, 2021, annual population estimates.

Table 1: Number of invasive *Streptococcus pyogenes* isolates collected by each Canadian province/region, 2021–2022

Province	Age group (years)						Not given	Total
	<2	2–4	5–14	15–49	50–64	≥65		
2021								
British Columbia	2	1	2	153	125	76	0	359
Alberta	7	5	8	199	123	47	3	392
Saskatchewan	4	2	2	83	33	13	1	138
Manitoba	5	7	2	91	49	35	0	189
Ontario	9	1	8	352	227	176	7	780
Québec	7	5	3	90	73	57	2	237
Atlantic[a]	0	1	0	32	20	8	1	62
Northern[b]	2	1	1	4	11	3	0	22
Canada	**36**	**23**	**26**	**1,004**	**661**	**415**	**14**	**2,179**
2022								
British Columbia	6	4	7	151	147	109	1	425
Alberta	13	6	21	276	126	80	0	522
Saskatchewan	6	2	3	63	30	17	0	121
Manitoba	7	0	11	85	52	46	0	201
Ontario	8	13	23	315	258	282	6	905
Québec	15	12	27	134	87	90	0	365
Atlantic[a]	2	2	2	44	11	15	4	80
Northern[b]	0	0	0	7	2	2	0	11
Canada	**57**	**39**	**94**	**1,075**	**713**	**641**	**11**	**2,630**

[a] Includes isolates from New Brunswick, Prince Edward Island, Nova Scotia, and Newfoundland and Labrador
[b] Includes isolates from Yukon, Northwest Territories, and Nunavut

Isolate testing

Streptococcus pyogenes isolates were confirmed by a positive pyrrolidonyl-β-naphthylamide (PYR) reaction and susceptibility to bacitracin (4). From January 2021 to October 2022, *emm* typing was performed on all iGAS isolates submitted to NML and ProvLab Alberta using the Centers for Disease Control and Prevention (CDC)'s *emm* sequencing protocol available online. The sequences obtained were compared with the CDC *emm* database and results reported to the type level. Antimicrobial susceptibilities for iGAS during this time were determined using Kirby-Bauer disk diffusion for chloramphenicol (30 µg), erythromycin (15 µg), clindamycin (2 µg), penicillin (10 µg), and vancomycin (30 µg) according to Clinical and Laboratory Standards Institute (CLSI) guidelines (5). From November 2022 to December 2022, all iGAS isolates submitted to NML were whole-genome sequenced using the Illumina platform, with *emm* type identified directly using the WGS Analysis and Detection of Molecular Markers (WADE) pipeline. Antimicrobial resistance interpretation (susceptible, resistant) was also predicted using WADE, based on the presence/absence of resistance markers for: chloramphenicol (*cat*), macrolides/lincosamides (*ermA*, *ermB*, *ermT*, *mefA/E*) and β-lactams (*pbp2x*).

Supplementary testing was performed on all *emm*1 isolates submitted to NML in 2021–2022 to determine the prevalence of the novel $M1_{UK}$ lineage. The $M1_{UK}$ genotypes were determined by mapping whole-genome sequencing reads against reference strain MGAS5005 and identifying 27 characteristic genomic single nucleotide variants (SNVs), as previously described (6,7).

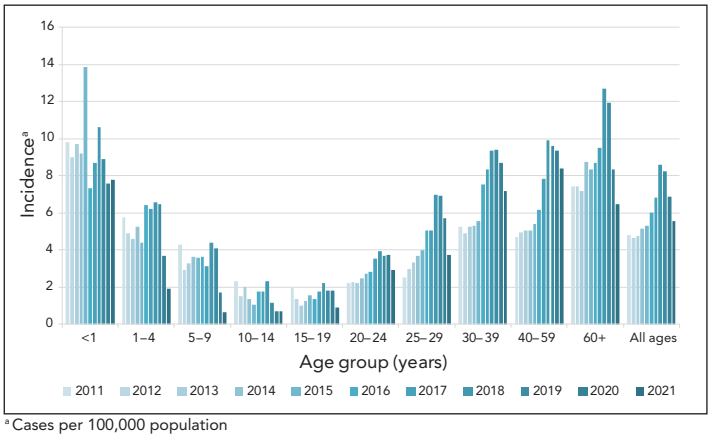
Data analysis

Demographic data submitted with bacterial isolates included patient age, sex, clinical source, province, and date of collection. Multiple isolates with the same *emm* type and collected from the same patient within 14 days were counted once with the most invasive isolation site assigned. Meningitis-related isolates were regarded as most invasive, followed by blood, then other sterile sites. The laboratory data were aggregated by age into <2, 2–4, 5–14, 15–49, 50–64 and ≥65-year-old age groups, and regionally into Western (British Columbia, Alberta, Saskatchewan, Manitoba), Central (Ontario, Québec), Eastern (New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador), and Northern (Yukon, Northwest Territories, Nunavut) regions of Canada. Statistical significance of trends was assessed using the Cochran-Armitage test of trend, with a *p*-value of <0.05 considered to be statistically significant.

Results

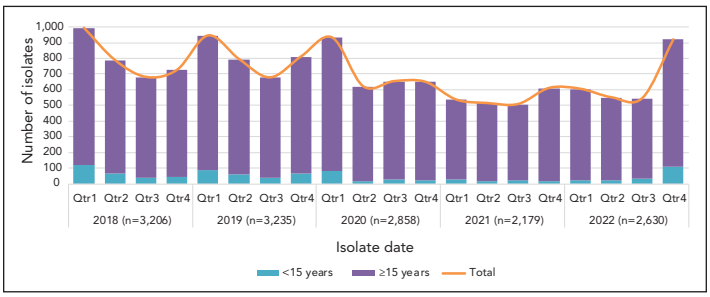
After peaking at 8.61 cases per 100,000 population in 2018, the overall incidence of iGAS disease in Canada decreased in 2020 and 2021. The overall incidence rate in 2021 was 5.56 cases per 100,000 population, which is the lowest overall incidence in Canada since 2015 (**Figure 1**, **Appendix, Supplemental Table S1**). There was an increase in the number of iGAS isolates submitted in 2022 (n=2,630) in comparison to 2021 (n=2,179). In particular, there was a large increase in isolates collected in the final quarter (Q4; October to December) of 2022 (**Figure 2**), the total of which was considerably higher than Q4 in 2018 and 2019 (pre-pandemic years). Of note during 2022-Q4 it was an increased number of isolates collected from children younger than 15 years of age, in comparison to previous quarters.

Figure 1: Annual incidence rates of invasive *Streptococcus pyogenes* cases in Canada, 2011–2021[a]



[a] Cases per 100,000 population

Figure 2: Number of invasive *Streptococcus pyogenes* isolates collected each quarter[a] for children younger than 15 years and patients 15 years of age and older[b], 2018–2022



Abbreviation: Qtr, quater
[a] Qtr1, January to March; Qtr 2, April to June; Qtr 3, July to September; Qtr 4, October to December; all month ranges are inclusive
[b] Yearly isolate counts include those where no age was given

The overall proportion of iGAS isolates collected from pediatric age groups remained stable over the two years, with infants <2 years of age accounting for 1%–2% of isolates, toddlers aged 2–4 years for 1%–1.5%, and children aged 5–14 years for 1%–3%. Proportions for other age groups had more fluctuation. Patients aged 15–49 years represented 46.1% of isolates collected in 2021 and 40.9% of those collected in 2022; adults aged 50–64 years 30.3% and 27.1%; and seniors aged 65 years and older for 19.0% and 24.4%. Of the isolates for which sex information was available, isolates from male patients represented 61.8% and 61.7% of isolates in 2021 and 2022, respectively. Blood was the predominant clinical isolation site, accounting for 69.3% of isolates collected in 2021 and 70.5% in 2022. Additional information on specimen source by age and *emm* type can be found in Appendix, **Figures S1–S5**.

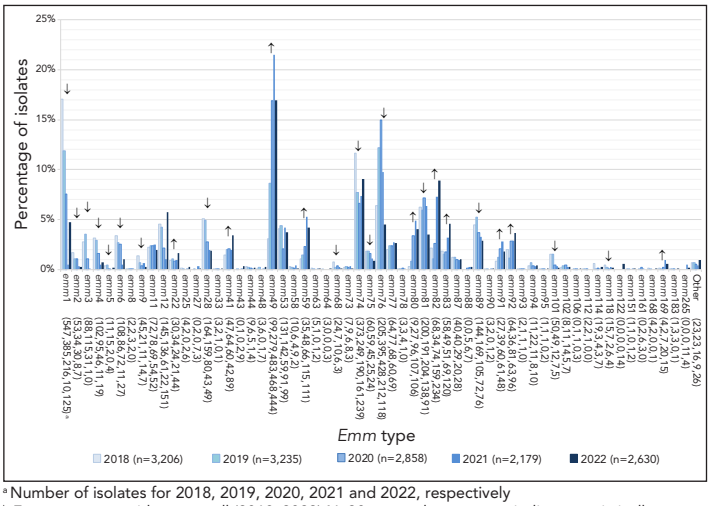
The most predominant *emm* type overall in 2021 and 2022 was *emm*49, at 21.5% (n=468) and 16.9% (n=444), respectively, representing a significant increase in prevalence since 2018 (from 3.1%, n=99; $p<0.0001$) (**Figure 3**). Other *emm* types that demonstrated significantly increasing trends from 2018 to 2022 include *emm*22 (0.9%–1.7%; $p=0.025$), *emm*41 (1.5%–3.4%; $p<0.0001$), *emm*59 (1.1%–4.2%; $p<0.0001$) *emm*80 (0.3%–4.0%; $p<0.0001$), *emm*82 (2.1%–8.9%; $p<0.0001$), *emm*83 (1.8%–4.6%; $p<0.0001$), *emm*91 (0.8%–1.8%; $p<0.0001$), and *emm*92 (2.0%–3.7%; $p<0.0001$). Other *emm* types demonstrated significantly decreasing trends (see Figure 3), such as *emm*1 from 17.1% (n=547) of all iGAS isolates collected in 2018 to 4.8% (n=125) in 2022 ($p<0.0001$). A percent prevalence of 4.8% in 2022 is a sharp increase from 2021, where *emm*1 only accounted for 0.5% (n=10) of isolates collected; this recent increase is statistically significant ($p<0.0001$). Of note, 49.0% (n=47) of *emm*1 isolates sequenced in 2022 were the novel $M1_{UK}$ lineage; in comparison, in 2015 (the year the first $M1_{UK}$ isolate was identified in Canada), only 2.6% (n=3) of sequenced *emm*1 isolates were $M1_{UK}$. Another type of interest is *emm*12, which did not demonstrate a significant trend from 2018 to 2022; however, *emm*12 decreased significantly from 4.5% (n=145) in 2018 to 1.0% (n=22) in 2021 ($p<0.0001$), before significantly rising back up to 5.8% (n=151) in 2022 ($p<0.0001$). Counts of *emm*1 and *emm*12 saw a particular re-emergence in late 2022, together accounting for almost 25% of isolates collected in Q4 (**Figure 4**).

In 2021, the most common *emm* type from children <15 years of age was *emm*49 (28.2%, n=24). *Emm*49 dropped to the third most common type in this age group in 2022, instead replaced by *emm*12 (25.8%, n=49) and *emm*1 (24.2%, n=46) (Appendix, **Figure S6**). In patients aged 15 years and older, *emm*49 (21.3%, n=442) and *emm*76 (10.0%, n=207) were most common in 2021. In 2022, *emm*49 (17.0%, n=412) was also the most common type in the age group, followed by *emm*74 (9.7%, n=236) and *emm*82 (9.5%, n=230) (Appendix, **Figure S7**).

Emm types associated with Western Canada (**Figure 5**) included *emm*49 (25.1%, n=271 in 2021; 15.3%, n=194 in 2022) and *emm*74 (13.5%, n=145 in 2021; 16.9%, n=214 in 2022). In Central Canada, *emm*49 (14.9%, n=152 in 2021; 17.2%, n=219 in 2022) and *emm*82 (13.4%, n=136 in 2021; 12.8%, n=162 in 2022) were predominant in both 2021 and 2022. *Emm*49 was the most common type isolated in Eastern Canada in both 2021 (56.5%, n=35) and 2022 (35.0%, n=28). Isolates from Northern Canada were highly represented by *emm*49 in 2021 at 45.5% (n=10), though only 22 isolates were submitted from this region. In 2022, only 11 isolates were submitted and there was no one common type (Appendix, **Figures S8–S11**).

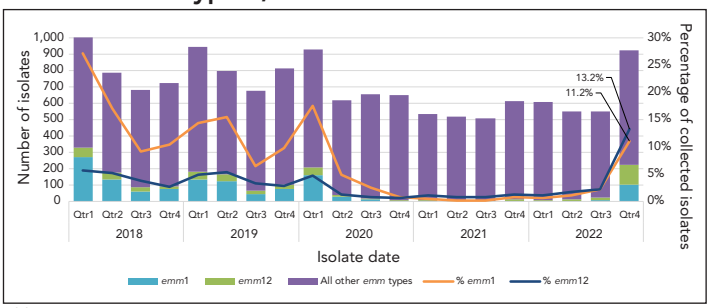
Upon request, NML provides assistance to provincial and territorial public health laboratories for iGAS outbreak/case cluster investigations (including non-invasive isolates from screening) and jurisdictional *emm* increases. During 2021, NML assisted in four outbreak investigations from various jurisdictions,

Figure 3: Prevalence of invasive *Streptococcus pyogenes emm* types in Canada, 2018–2022[a,b]



[a] Number of isolates for 2018, 2019, 2020, 2021 and 2022, respectively
[b] For *emm* types with an overall (2018–2022) N≥30: up or down arrows indicate statistically significant trends toward increasing or decreasing prevalence for the 2018–2022 timespan, using the chi-squared test for trend. *Emm* types with no arrow either did not demonstrate a statistically significant trend, or did not have an overall N≥30

Figure 4: Number of invasive *Streptococcus pyogenes* isolates collected each quarter[a] for *emm*1, *emm*12 and all other *emm* types[b], 2018–2022

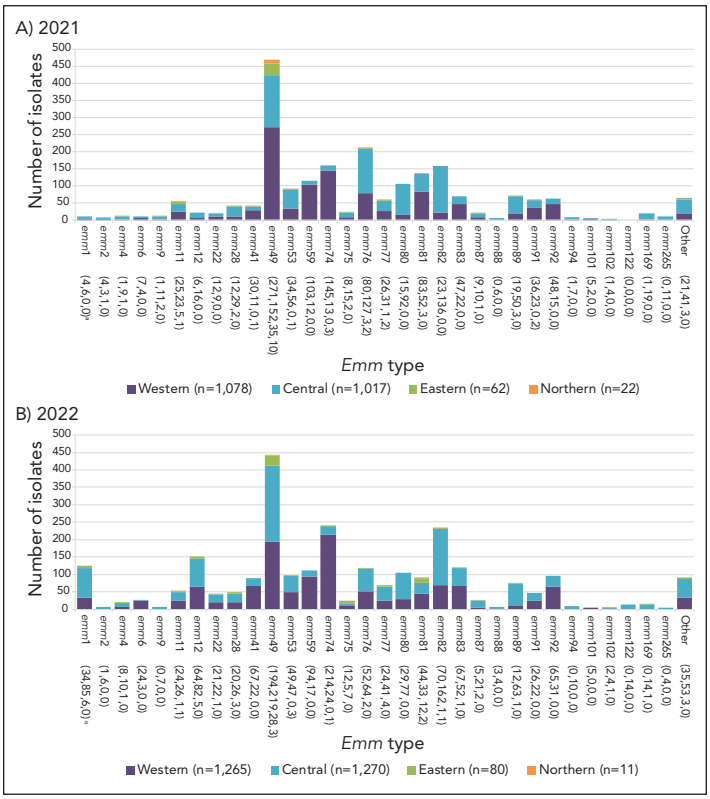


Abbreviation: Qtr, quater
[a] Qtr1, January to March; Qtr 2, April to June; Qtr 3, July to September; Qtr 4, October to December; all month ranges are inclusive
[b] Yearly isolate counts include those where no age was given

including *emm*53 (n=3 cases), *emm*76 (n=45), *emm*77 (n=2) and one multi-*emm* type outbreak (*emm*49 and *emm*53, n=8). An increased number of requests were received in 2022, where NML assisted with a jurisdictional increase (*emm*49) and seven outbreak investigations, including *emm*1.3 (n=3), *emm*41.11 (n=7 and n=9), *emm*49 (n=4), *emm*89 (n=23 and n=4) and two multi-*emm* type outbreaks (*emm*49, *emm*53, *emm*76, *emm*77, *emm*83.1, *emm*91 and *emm*169.3, n=20; *emm*6.4, *emm*41.11, *emm*49, *emm*59, *emm*74, *emm*75 and *emm*83.1, n=26).

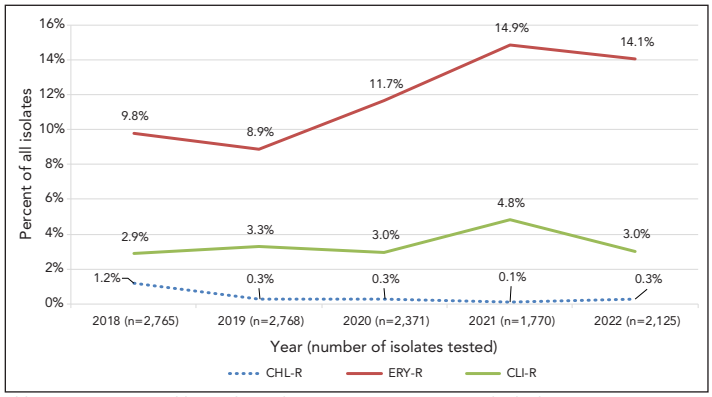
Antimicrobial resistance among iGAS isolates remained low in 2021–2022 (**Figure 6**, Appendix, **Table S2**). Erythromycin resistance increased significantly from 9.8% in 2018 to 14.1% in 2022 ($p<0.0001$), while chloramphenicol resistance decreased significantly from 1.2% to 0.3% ($p<0.0001$). Clindamycin resistance remained relatively stable over the study period (2.9%–4.8%). There was no resistance observed to penicillin or

Figure 5: Regional distribution of invasive *Streptococcus pyogenes* isolates[a] collected in A) 2021, and B) 2022, by *emm* type



[a] Number of isolates in the Western, Central, Eastern, and Northern regions of Canada, respectively

Figure 6: Antimicrobial resistance of invasive *Streptococcus pyogenes* in Canada, 2018–2022



Abbreviations: CHL-R, chloramphenicol-resistant; CLI-R, constitutively clindamycin-resistant; ERY-R, erythromycin-resistant

vancomycin. *Emm* types associated with erythromycin resistance and constitutive and inducible clindamycin resistance were similar in 2021 and 2022, including *emm*11 (88.9%/93.5% erythromycin resistance; 27.8%/22.6% constitutive clindamycin resistance; 66.7%/71.0% inducible clindamycin resistance); *emm*77 (92.3%/82.0%; 0%/0%; 92.3%/82.0%); *emm*83 (29.5%/42.7%; 4.9%/1.8%; 29.5%/42.7%) and *emm*92 (100%/95.5%; 0%/4.5%; 96.7%/69.3%) (Appendix, **Figures S12–S13**, **Tables S3–S4**).

Discussion

In 2021, 2,127 cases of iGAS were reported to CNDSS, with a national incidence rate of 5.56 cases per 100,000 population, a considerably lower rate than the peak seen in 2018 (8.61 cases per 100,000 population). This low incidence in 2021 is consistent with the lower rate seen in 2020 (6.85 cases per 100,000 population) and can likely be attributed to indirect effects of the containment measures put in place in 2020 to prevent the spread of the SARS-CoV-2 pandemic virus (COVID-19). Numerous studies have observed that invasive bacterial disease activity due to pathogens transmitted by respiratory droplets (including *S. pyogenes*) decreased during this time (2,8–10).

Beginning in 2022, many countries began to see levels of iGAS disease increase once again. In December 2022, the WHO reported that five European countries had been observing increased cases of iGAS and scarlet fever, predominantly in children (3). Subsequently, the United States' CDC advised of increased paediatric iGAS disease in several states, including Colorado, Minnesota, and Texas (11–13), and the Pan American Health Organization (PAHO) published an informative note urging member countries to remain watchful for iGAS cases after several were identified in Uruguay (14). In Canada, there was an increase in the number of iGAS isolates submitted to NML in 2022 in comparison to 2021. Though the total yearly count did not exceed the highest totals collected pre-pandemic (years 2018 and 2019), there was a large increase in isolates collected in 2022-Q4, including in children. The WHO indicated that the increase in iGAS infections may be due to increased population mixing following a period of reduced circulation of GAS during the COVID-19 pandemic, and increased circulation of respiratory viruses (3); respiratory viruses and viral co-infections are associated with GAS infections and may increase the risk of invasive disease (3,15). Though our current study is unable to provide any Canadian data on viral co-infections with iGAS, several studies, including those in France, the United Kingdom, and the United States, reported increased rates of viral infection prior to or concurrent with iGAS infections (12,16,17). Associated viruses included influenza, respiratory syncytial virus, SARS-CoV-2 pandemic virus, human metapneumovirus, and rhinovirus (12,16,17).

Of note, countries reporting an increase in paediatric iGAS disease in late 2022 universally identified *emm* types 1 and 12 as the predominant cause of cases (12,13,18–21). In Canada, prevalence of *emm*1 was decreasing considerably going into the COVID-19 pandemic and was virtually non-existent in 2021 (0.5% of collected isolates). Though *emm*1 counts remained relatively low at the beginning of 2022, the prevalence did increase in Canada in Q4, as was seen in other countries. Almost half of *emm*1 isolates tested in 2022 were the $M1_{UK}$ lineage originally described by Lynskey *et al.*, as associated with hyperproduction of the SpeA exotoxin (7). Belgium, Netherlands, and the

United Kingdom have also noted high rates (~75%) of the $M1_{UK}$ lineage in 2022 (22–24). *Emm*12 has similarly been associated with toxigenic lineages; this type has previously been linked with outbreaks of scarlet fever, with associated lineages possessing exotoxin SpeC and superantigen SSA, as well as antimicrobial resistance (25). Prior to 2022, prevalence of *emm*12 was decreasing significantly in Canada. A large increase in prevalence in 2022-Q4 (just over 13% of all isolates collected), resulted in an increase to ~6% overall in 2022. Little antimicrobial resistance was seen in *emm*12 during that time. Studies in the United States (Colorado, Minnesota, Texas) also did not identify any resistance during their late 2022 increases of *emm*12 (12,13). In Portugal, the 2022 iGAS increase was characterized by *emm*12 isolates with high genomic diversity, with no expansion of a particular lineage (20). Further genomic characterization of *emm*12 isolates in Canada would be useful to identify toxin profiles and potential outbreak lineages.

The most common *emm* type collected in Canada since 2020 has been *emm*49. At the time of writing our previous annual report in 2020 (2), *emm*49 was not common in the literature as a frequent or emerging type. However, more recently, a study from the United States identified *emm*49 as increasingly associated with antimicrobial resistance. Li *et al*. have identified a macrolide and lincosamide-resistant sublineage of *emm*49 that has rapidly expanded in the state of Maryland to become the dominant lineage (26). A Spanish study also noted the emergence of *emm*49 in late 2022 after previously being rarely detected in the country. These isolates differed from the American lineage in that they demonstrated resistance to only tetracycline (21). Though antimicrobial resistance in *emm*49 was rarely detected in Canada in 2021 and 2022 (<2% erythromycin resistance), it will be important to monitor for the emergence of drug-resistant clones.

Streptococcus pyogenes remains susceptible to penicillin, the first-line antimicrobial treatment for iGAS infections, however, resistance to erythromycin (a second-line therapy) continues to increase in Canada. In 2021 and 2022, commonly collected *emm* types in Canada with high levels (>40%) of erythromycin resistance were similar to those reported in 2020, including *emm*11, *emm*77, *emm*83, and *emm*92 (2). Of these, *emm*83 and *emm*92 demonstrated significant increases over the 2018 to 2022 time period. Similar studies from other countries confirm that these *emm* types demonstrate resistance elsewhere, such as Spain (*emm*11, *emm*77) and the United States (*emm*11, *emm*83, *emm*92) (26,27). Of note is *emm*92, which was identified in West Virginia, United States, as an *emm* type with uniform resistance to macrolides/lincosamides that is disproportionately affecting patients with a history of intravenous drug use (28). In Canada, iGAS disease outbreaks often occur in at-risk groups, such as persons experiencing homelessness or those who abuse substances, closed populations such as long-term care facilities, and Indigenous communities (29,30); it will be of significant concern if drug-resistant *emm*92 continues to expand in Canada into vulnerable populations.

Limitations

Caution should be exercised when interpreting the data presented in this report, as the overall interpretation of the results is limited to only isolates available for testing. Only a subset of the laboratory isolates from each province may have been submitted for testing, therefore, this report does not reflect the true incidence or rates of disease in Canada. The representativeness of the proportions of isolates submitted to NML for testing as compared to the CNDSS are presented in Appendix, **Table S5**. Not all provinces and territories report line list data to CNDSS, which means that only aggregated data are available at the national level. Therefore, CNDSS data and NML laboratory data are presented differently in terms of age grouping.

Conclusion

Though the number of isolates collected was low in 2021, iGAS counts increased in 2022, particularly in the latter part of the year. *Emm*49 remained the most common type collected in Canada for 2021 and 2022; however, *emm*1 and *emm*12 began to rapidly increase in prevalence in the final quarter of 2022. As iGAS counts continue to rise following the COVID-19 pandemic, continued surveillance is imperative to monitor *emm* types and antimicrobial resistance in Canada. Enhancing surveillance to include linked epidemiological and laboratory data would improve our knowledge and interpretation of how iGAS *emm* types and antimicrobial resistance patterns affect at-risk groups in Canada.

Authors' statement

ARG — Formal analysis, data curation, visualization, writing–original draft, review & editing of final version
AG — Formal analysis, validation, investigation, data curation, visualization, writing–review & editing
GJT — Resources, methodology, writing–review & editing
JVK — Resources, methodology, writing–review & editing
AM — Resources, methodology, writing–review & editing
MCD — Resources, methodology, writing–review & editing
LH — Resources, methodology, writing–review & editing
JMinion — Resources, methodology, writing–review & editing
PVC — Resources, methodology, writing–review & editing
HS — Resources, methodology, writing–review & editing
DH — Resources, methodology, writing–review & editing
YY — Resources, methodology, writing–review & editing
XD — Resources, methodology, writing–review & editing
LS — Resources, methodology, writing–review & editing
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Competing interests

None.

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Appendix

Supplemental figures and tables are available upon request to the author.

Table S1: Annual incidence rates of invasive *Streptococcus pyogenes* in Canada by age group, 2011–2021
Figure S1: Clinical isolation sites of *Streptococcus pyogenes* from children younger than 15 years of age in A) 2021 (n=85) and B) 2022 (n=190)
Figure S2: Clinical isolation sites of *Streptococcus pyogenes* from patients 15 years of age or older in A) 2021 (n=2,094) and B) 2022 (n=2,436)
Figure S3: Percentage of invasive *Streptococcus pyogenes* isolates from blood in 2021 (n=1,509) and 2022 (n=1,853), by *emm* type
Figure S4: Percentage of invasive *Streptococcus pyogenes* isolates from other sterile sites in 2021 (n=664) and 2022 (n=769), by *emm* type
Figure S5: Percentage of invasive *Streptococcus pyogenes* isolates from cerebrospinal fluid in 2021 (n=6) and 2022 (n=8), by *emm* type
Figure S6: Prevalence of invasive *Streptococcus pyogenes emm* types isolated from patients less than 15 years old in 2021 (n=85) and 2022 (n=190)
Figure S7: Prevalence of invasive *Streptococcus pyogenes emm* types isolated from patients 15 years and older in 2021 (n=2,080) and 2022 (n=2,425)
Figure S8: Prevalence of the ten most common invasive *Streptococcus pyogenes emm* types collected from Western Canada in A) 2021 and B) 2022
Figure S9: Prevalence of the ten most common invasive *Streptococcus pyogenes emm* types collected from Central Canada in A) 2021 and B) 2022
Figure S10: Prevalence of the ten most common invasive *Streptococcus pyogenes emm* types collected from Eastern Canada in A) 2021 and B) 2022
Figure S11: Prevalence of the ten most common invasive *Streptococcus pyogenes emm* types collected from Northern Canada in A) 2021 and B) 2022
Table S2: Antimicrobial-resistant invasive *Streptococcus pyogenes* isolates by year, 2018–2022
Figure S12: Percentage of macrolide and lincosamide resistant *Streptococcus pyogenes* isolates collected in 2021, by *emm* type
Figure S13: Percentage of macrolide and lincosamide resistant *Streptococcus pyogenes* isolates collected in 2022, by *emm* type
Table S3: Percentage of macrolide and lincosamide resistant *Streptococcus pyogenes* isolates collected in 2021, by *emm* type
Table S4: Percentage of macrolide and lincosamide resistant *Streptococcus pyogenes* isolates collected in 2021, by *emm* type
Table S5: Number of invasive *Streptococcus pyogenes* isolates types by the National Microbiology Laboratory (NML) in comparison to the total number of cases reported to the Canadian Notifiable Diseases Surveillance System (CNDSS) in 2021, by patient age group

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Canadian laboratory incidents with human pathogens and toxins: An overview of reports, 2016–2022

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Abstract

Background: When the Public Health Agency of Canada's *Human Pathogens and Toxins Act* and *Human Pathogens and Toxins Regulations* came into force, the reporting of laboratory incidents to the Laboratory Incident Notification Canada (LINC) surveillance system became mandatory. This report summarizes the laboratory exposure and non-exposure data reported from 2016 to 2022, with a particular focus on factors that are not typically presented in LINC's annual report.

Methods: Reported laboratory incidents from 2016 to 2022 were analyzed. Exposures were analyzed by severity, occurrence and root cause, and affected individuals were analyzed by disease outcome, role and applied interventions. Non-exposures were analyzed by incident type. Exposure and non-exposure incident rates were calculated.

Results: Events reported to LINC totalled 928. Of those, 355 were confirmed non-exposures, 361 were confirmed exposures, and 111 were other events. Both exposure and non-exposure incident rates per 100 active licences peaked in 2018 (9.44 and 7.11, respectively). Most exposures were rated as minor or negligible severity. The most cited exposure occurrence types were sharps-related and procedure-related (23% each), and standard operating procedure-related root causes were most cited (24%). While 781 individuals were affected in the exposure incidents, most did not develop a laboratory-acquired infection (n=753; 96%) and received at least one form of treatment post-exposure (n=717; 92%). Inadvertent possession/production cases were the most common non-exposure incidents reported.

Conclusion: Exposure and non-exposure incident rates have decreased since 2018. Among exposure incidents, sharps-related and procedure-related occurrences were the most common, and the root cause was usually a standard operating procedure. Non-exposure incidents were mostly inadvertent possession/production cases. Exposure and illness outcome severity was mostly minor.

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Keywords: human pathogens and toxins, laboratory incidents, laboratory exposures, exposure severity, Laboratory Incident Notification Canada

Introduction

Human pathogens and toxins (HPTs) are routinely handled in laboratories for research purposes, as well as to detect and diagnose illnesses. Occasionally, individuals who work in laboratories are exposed to and infected by the HPTs they handle. These cases have been recorded worldwide and have highlighted the importance of biosafety and biosecurity measures (1,2).

The Public Health Agency of Canada (PHAC) promotes the safe handling of HPTs through the *Human Pathogens and Toxins Act* (HPTA) and the *Human Pathogens and Toxins Regulations* (HPTR). Under the HPTA and HPTR, any laboratory conducting activities within the scope of the HPTA must be licensed to do so, and licence holders are required to report laboratory incidents to PHAC (3,4).

Laboratory Incident Notification Canada (LINC) was launched in December 2015 as a comprehensive surveillance system that would receive incident reports required by the HPTA and the HPTR. Situations reported to LINC can generally be grouped into three categories: exposure incidents, non-exposure incidents, and other events requiring notification. Exposure incidents are incidents where one or more individuals have "contact with, or close proximity to, infectious material or toxins that may result in infection or intoxication, respectively" (5). This includes cases where exposure leads to a laboratory-acquired infection (LAI). Non-exposure incidents include the inadvertent possession, production, or release of an HPT that one is not licensed to work with. Instances where HPTs are missing, lost or stolen are also categorized as non-exposure incidents (5). Finally, as an example of an "other event requiring notification," licensed parties must report upcoming changes to the laboratory that could affect biocontainment (5).

Laboratory Incident Notification Canada publishes annual reports that describe the laboratory incidents that occurred each year (6–12) to raise awareness about laboratory safety and highlight important information on laboratory exposures in Canada. These reports focus on exposure incidents and present incidents by main activity being performed at the time of the exposure incident and by sector (e.g., academia, government, industry). Information regarding the biological agent(s) involved, root cause(s) of the exposures and affected individuals (main role, years of experience, route of exposure) is also provided, along with reporting delay times and exposure incident rates.

The objective of this article is to analyze all relevant laboratory incidents reported to LINC between 2016 and 2022, examine factors not typically presented in the annual reports (e.g., the severity of incidents and interventions for exposed individuals), and discuss year-to-year trends.

Methods

Exposure incidents, non-exposure incidents, and other events requiring notification are reported through PHAC's Biosecurity Portal using standardized forms. The choice of form depends on the type of event being reported, with distinct forms available for each category. Each form includes a set list of questions for the reporter to answer; most questions are mandatory and closed-ended. Entered data is captured via the Microsoft Customer Relationship Management system and reviewed for consistency and completeness by LINC employees.

The LINC surveillance data was extracted to Microsoft Excel on August 8, 2023, and then processed and analyzed using R 4.2.1. Given that, more than one report can be submitted for a single incident if the reporter has information to add or correct. When multiple records for the same incident were submitted, only the most recent data was retained.

Reports about incidents that are outside the scope of the HPTA are sometimes submitted to LINC. For example, the HPTA does not regulate activities that involve Risk Group 1 (RG1) agents, nor does it require incidents with RG1 agents to be reported. These types of reports are stored by LINC but are often incomplete because they are not mandatory. Consequently, these reports have been excluded from analysis and are referred to as "ruled out." Affected individuals were ruled out if the event itself was ruled out or if the individual was otherwise determined not to be exposed. This study focuses on incidents that involved Risk Group 2, 3 and 4 (RG2, RG3 and RG4, respectively) agents, which must be reported to LINC under the scope of HPTA.

Data from incidents that occurred between January 1, 2016, and December 31, 2022, was used in this analysis. Reports with an unknown incident date that were reported during this period were included. The severity, occurrence types, and root causes of exposure incidents were examined. Data on affected individuals, such as illness presentation, roles and treatments received, was also examined.

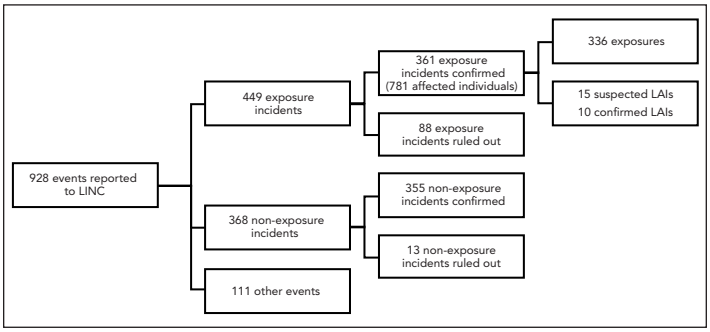
Data is continuously updated as LINC receives more information on incidents. Therefore, there may be minor discrepancies between the values published in LINC's annual reports and those in this report (e.g., the total number of exposure incidents in a given year).

Results

Between January 1, 2016, and December 31, 2022, 928 events were reported to LINC. After investigation, 88 exposure incidents and 13 non-exposure incidents were ruled out. The following were retained: 361 exposure incidents,

355 non-exposure incidents, and 111 other events requiring notification (**Figure 1**). Among the 361 confirmed exposure incidents, 15 were suspected LAIs and 10 were confirmed LAIs. These LAIs are described in detail in another publication (13). While 819 persons were initially reported as being exposed in the 361 laboratory exposure incidents, 38 persons were ruled out, bringing the total to 781 exposed people between 2016 and 2022.

Figure 1: Types of events reported to Laboratory Incident Notification Canada, Canada, 2016–2022

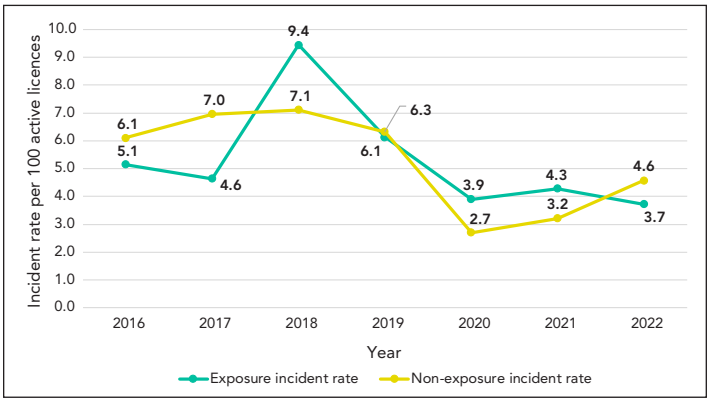


Abbreviations: LAIs, laboratory-acquired infections; LINC, Laboratory Incident Notification Canada

Table 1 provides a comprehensive overview of how many laboratory incidents were reported from 2016 to 2022. For context, the number of active licences steadily increased over these seven years, rising from 835 in 2016 to 1,048 in 2022. Conversely, the number of exposure incidents demonstrated some fluctuations, with the highest count recorded in 2018 (93 incidents) and the lowest in 2020 and 2022 (both 39 incidents). The number of non-exposure incidents showed some variation as well, with the highest count in 2018 (70 incidents) and the lowest in 2020 (27 incidents). Year-over-year trends show that 2018 experienced a notable increase in both exposure and non-exposure incidents, while 2020 marked a significant decrease in these incidents.

When examining the proportion of exposure incidents per 100 active licences, 2018 stood out as the year with the highest rate (9.44), while 2022 had the lowest (3.72), as shown in **Figure 2**. The proportion of non-exposure incidents per 100 active licences also peaked in 2018 (7.11) and reached its lowest point in 2020 (2.72).

Figure 2: Exposure and non-exposure incident rates, Canada, 2016–2022



Severity of exposure incidents

As part of the investigation process for exposure incidents, reporters are asked to assess the severity of incidents. Reporters must provide a subjective rating that is based on the incident's impact on individuals, other staff, and public health. Definitions for each level of severity are provided in **Appendix, Table A1**. Among the 361 exposure incidents reported between 2016 and 2022, 84% were either negligible or minor in severity (**Figure 3**). Exposure incidents of minor severity accounted for 48% (n=172) of incidents, while incidents of negligible severity accounted for 37% (n=132) of incidents. Only two incidents (0.01%) were classified as majorly severe; both involved a suspected LAI. No exposure incident was classified as catastrophic, which is the highest level of severity.

The two major incidents occurred in 2017 and 2019. The first incident was an exposure by inhalation of *Mycobacterium* spp. in a histology laboratory. The affected individual received the appropriate post-exposure treatment. The source of the second incident was not confirmed; it could not be determined whether the infection was acquired in the laboratory or through a community outbreak in the worker's region. For both incidents, measures were taken to mitigate the risk of reoccurrence, including additional training and decontamination of laboratory areas.

Table 1: Number of confirmed exposure and non-exposure incidents and respective incident rates, Canada, 2016–2022

Year	Number of active licences	Number of exposure incidents	Number of non-exposure incidents	Exposure incidents per 100 active licences	Non-exposure incidents per 100 active licences
2016	835	43	51	5.15	6.11
2017	905	42	63	4.64	6.96
2018	985	93	70	9.44	7.11
2019	996	61	63	6.12	6.33
2020	999	39	27	3.90	2.70
2021	1,027	44	33	4.28	3.21
2022	1,048	39	48	3.72	4.58

Figure 3: Total reported severity of exposure incidents, Canada, 2016–2022

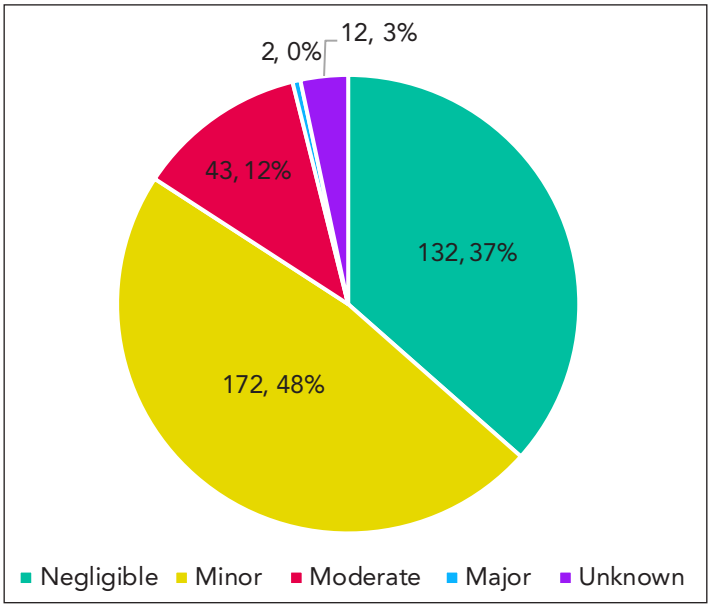
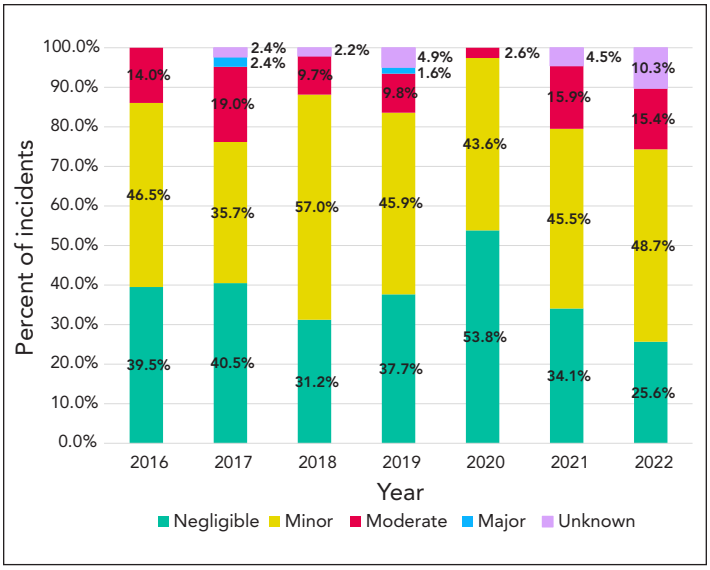


Figure 4: Reported severity of exposure incidents each year, Canada, 2016–2022



While similarities in the proportions of severity of incidents were observed every year from 2016 to 2022 (**Figure 4**), there were some differences. Most notably, there was a higher proportion of minor incidents in 2018 (57%), and 2020 marked the highest proportion of negligible incidents (54%) and the lowest proportion of moderate incidents (3%).

Occurrence types for exposure incidents

When submitting an exposure report, reporters must select one or more occurrence types that best characterize the incident. **Table 2** presents the percentage of citations for each occurrence type out of the total number of occurrence types cited in all exposure events. Sharps-related and procedure-related issues were the most cited occurrence types overall. Definitions for occurrence types are found in Appendix, **Table A2**.

Root causes of exposure incidents

When carrying out an investigation following an exposure incident, one or more root causes can be cited in the exposure follow-up report. **Table 3** shows the percentage of root causes for each year. From 2016 to 2022, 863 root causes were cited in the 361 exposure incidents. Overall, the most cited root causes were related to standard operating procedures (n=211, 24%), human factors (n=183, 21%) and equipment (n=114, 13%). Through the years, human factors were increasingly cited as a root cause (+1.46 citations per year) while there was a decrease in citations related to standard operating procedures (−3.29 citations per year) and other root causes (−2.36 citations per year). Examples of each type of root cause can be found in Appendix, **Table A3**.

Table 2: Reported occurrence types of exposure incidents, Canada, 2016–2022

Occurrence type	Percentage of total occurrence types each year															
	2016		2017		2018		2019		2020		2021		2022		2016–2022	
	(N=62)		(N=56)		(N=118)		(N=79)		(N=55)		(N=56)		(N=60)		(N=486)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Animal-related	7	11	1	2	8	7	1	1	0	0	8	14	5	8	30	6
Equipment-related	1	2	1	2	8	7	6	8	6	11	3	5	1	2	26	5
Loss of containment	2	3	4	7	8	7	3	4	1	2	2	4	2	3	22	5
Other	7	11	9	16	11	9	12	15	5	9	6	11	6	10	56	12
PPE-related	10	16	6	11	12	10	8	10	8	15	10	18	8	13	62	13
Procedure-related	13	21	12	21	27	23	18	23	16	29	10	18	15	25	111	23
Sharps-related	14	23	13	23	28	24	16	20	13	24	12	21	15	25	111	23
Spill	5	8	8	14	14	12	11	14	6	11	2	4	5	8	51	10
Unknown	3	5	2	4	2	2	4	5	0	0	3	5	3	5	17	4

Abbreviation: PPE, personal protective equipment
Note: The total percentage for each column does not necessarily add up to 100% due to the rounding of numbers in the table

Affected individuals

Between 2016 and 2022, 781 individuals were exposed to an HPT, which is an average of 2.16 affected individuals per exposure incident. Most exposed individuals (n=753, 96%) did not go on to develop a LAI. For exposed individuals, 2% (n=17) were suspected of having a LAI, while 1% (n=8) had a confirmed LAI. Less than 1% (n=3) were reported as having seroconversion.

Of those that experienced acute illness (n=23, 3%), six individuals recovered within a week, 11 recovered within one to two weeks, and three individuals recovered after the two-week mark. Recovery time remains unknown for three individuals. No report of chronic illness resulting from a laboratory exposure was received between 2016 and 2022.

Among all years, the most common role of exposed individuals was that of a technician/technologist (**Figure 5**). They represented 74% of all exposed individuals between 2016 and 2022 (n=581). Students represented the second-largest group of exposed individuals (10% of all exposed individuals).

Multiple choices of interventions can be selected for each affected individual. Of the 781 individuals who were exposed, 8% (n=64) did not receive any treatment or participate in a health consultation. For the remaining 92% (n=717), at least one form of intervention was employed. The average number of interventions employed per exposed individual was 2.2 interventions. As shown in **Table 4**, the most common intervention was an occupational health consultation within seven days of exposure. For affected individuals, 31% (n=245) not only received an intervention within seven days of exposure, but also received an intervention beyond seven days of exposure (data not shown on the table).

Table 3: Reported root causes of exposure incidents, Canada, 2016–2022

Root cause	Citations as a percentage of total root causes each year															
	2016 (N=92)		2017 (N=97)		2018 (N=237)		2019 (N=145)		2020 (N=99)		2021 (N=109)		2022 (N=84)		2016–2022 (N=863)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Communication	10	11	10	10	25	11	17	12	9	9	11	10	7	8	89	10
Equipment	7	8	11	11	32	14	20	14	13	13	17	16	14	17	114	13
Human factors	8	9	13	13	53	22	35	24	24	24	30	28	20	24	183	21
Management and oversight	11	12	7	7	25	11	21	14	11	11	11	10	10	12	96	11
SOP	31	34	35	36	53	22	27	19	25	25	21	19	19	23	211	24
Training	7	8	8	8	27	11	17	12	10	10	15	14	7	8	91	11
Other	18	20	13	13	22	9	8	6	7	7	4	4	7	8	79	9

Abbreviation: SOP, standard operating procedure
Note: The total percentage of root causes for each year does not necessarily add up to 100% due to the rounding of numbers in the table

Figure 5: Role of affected individuals in exposure incidents each year, Canada, 2016–2022

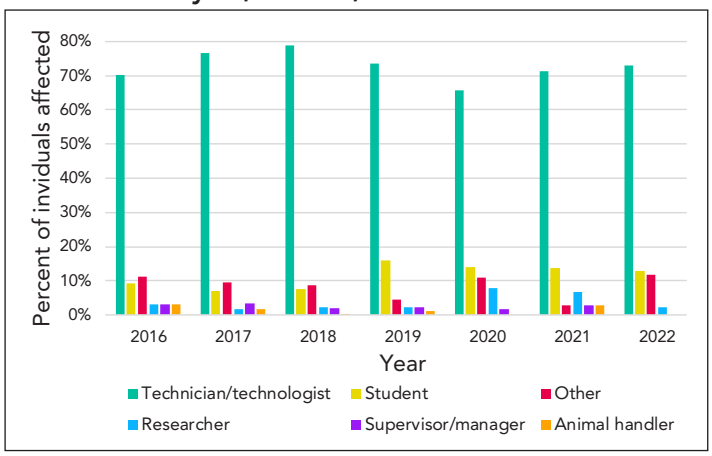


Table 4: Interventions for exposed individuals, Canada, 2016–2022

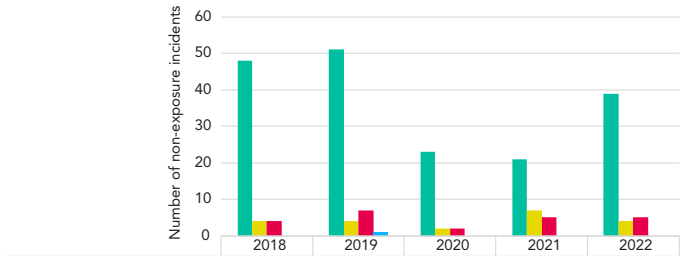
Interventions employed	n[a]	%
Within 7 days of exposure	**644**	**82%**
OH consultation	513	66%
Medical consultation	389	50%
PEP	215	28%
First-aid	138	18%
Beyond 7 days of exposure	**318**	**41%**
OH consultation	200	26%
Medical consultation	159	20%
Drug treatment	53	7%
PEP	46	6%

Abbreviations: OH, occupational health; PEP, post-exposure prophylaxis
[a] Multiple options can be selected for one exposed individual
Note: The denominator of the percentage calculation for each intervention employed is the total number of affected individuals (781 individuals)

Non-exposure incidents

Since March 2018, reporters have been able to specify what type of non-exposure incident they are reporting (**Figure 6**). Between 2018 and 2022, most non-exposure incidents involved the inadvertent possession/production of an HPT (ranging from 64% to 86%). In 2021, the proportion of reports involving inadvertent release (21%) and missing or lost biological agents (15%) peaked. LINC received only one report of a stolen biological agent in 2019. The report was filed by the institution following a student's threat to steal a biological agent. When PHAC followed up with the reporter for more details, it was determined that no theft had occurred, and the incident was subsequently ruled out.

Figure 6: Types of non-exposure incidents, Canada, 2018–2022



	2018	2019	2020	2021	2022
Inadvertent possession/production	48 (86%)	51 (81%)	23 (85%)	21 (64%)	39 (81%)
Inadvertent release	4 (7%)	4 (6%)	2 (7%)	7 (21%)	4 (8%)
Missing or lost biological agent	4 (7%)	7 (11%)	2 (7%)	5 (15%)	5 (10%)
Stolen biological agent	0 (0%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)

Discussion

Over the past seven years of operation, LINC has received 361 confirmed exposure incidents and 355 non-exposure incidents (6–12). During that time, 781 individuals were exposed to an HPT, and 25 of those individuals developed, or were suspected to have developed, an LAI. According to reporters, most exposure incidents posed a low individual and public health risk. This is supported by the fact that most individuals did not experience any illness following exposure to an HPT. Individuals who did experience illness recovered within a couple of weeks.

Changes in root causes of exposure incidents

In the investigatory process after an exposure incident occurs, reporters are asked for the plausible root cause(s) of the incident. One or more root causes can be selected. The number of citations reporting standard operating procedures as a root cause as a proportion of all cited root causes of exposure incidents decreased from 2016 to 2022. This decline may be a result of LINC's investigatory process. When an exposure report is submitted to LINC, root causes and corrective actions are established to prevent similar incidents from reoccurring. This process may have prompted licensed facilities to refine their standard operating procedures, thus reducing the number of incidents caused by poor or missing documentation.

A root cause of incidents that increased in the number of citations every year relative to 2016 involved human factors. According to the exposure reporting form, human factors include decisions made by individuals working directly with HPTs (e.g., deviating from a standard operating procedure) and decisions made by other individuals who influence the work environment (e.g., managers who provide insufficient time to do a job safely). From 2016 to 2022, the proportion of all root causes that cited human factors increased from around 10% of citations at the beginning of the program, to around 25% in later years. This increase may be explained by changes in the exposure reporting form. In March 2018, several multiple-selection questions were added to the form and these questions provided specific examples of human factors. The clarification of human factors as a root cause may have helped reporters recognize their role in the incidents they were reporting. In fact, the greatest year-to-year increase in reports citing human factors was observed in 2018, which was the year the form was amended.

Interventions for individuals exposed to human pathogens and toxins

Exposure to HPTs when conducting controlled experiments poses the risk of acquiring an infection. Appropriate post-exposure follow-up on the exposed individual can prevent or mitigate the severity of disease. While the mandated reporting of LAIs is unique to Canada, the outcomes of affected individuals in other countries has been captured through case studies. Case studies have suggested that timely administration of post-exposure prophylaxis can minimize or prevent infections. When administered early, post-exposure prophylaxis has been shown to be effective in preventing the acquisition of disease in high-risk individuals (14).

When conducting controlled activities, the correct implementation of nationally and internationally certified protocols with proper microbiological practices, containment devices, satisfactory facilities, protective barriers and specialized education and training may decrease the risk of exposure of laboratory staff to acquiring a laboratory infection (15). Details on post-exposure interventions for the affected individuals are collected by LINC. Of the reported exposure incidents in Canada, 82% of the affected individuals received a medical intervention within seven days of exposure, meaning that actions were taken to assess the health of the individual, and that appropriate health measures were taken for the majority of affected individuals.

Exposure incidents of negligible to minor severity

Results showed that most exposure incidents (n=304, 84%) for the period of interest had a negligible to minor level of severity, which represents a low to minimal risk for disease in the individual and other staff members, as well as low or no risk to

public health. A moderate level of severity was reported for 12% (n=43) of all exposure incidents, representing a moderate risk for the individual, the employee and public health. Only 1% (n=2) of all the exposure incidents were reported at a major severity level, representing a high risk of disease in the individual or employee and a significant risk to public health. The trend in severity of exposure incidents every year was similar from 2016 to 2022. It should be noted that the severity level is self-assessed by the reporter on site.

The fact that the majority of incidents had a negligible to minor level of severity suggests that laboratory procedures and safety measures seem highly effective in preventing major and catastrophic laboratory incidents. Several factors can contribute to the biosafety of staff members in licensed laboratories in Canada, such as preventive strategies that help mitigate the risk associated with working with human pathogens and toxins in laboratory settings. All biosafety measures in place in the laboratory, including proper training, use of personal protective equipment, and standard operating procedures play an important role in protecting laboratory staff members and reducing the risk of exposure incidents. The ongoing training of laboratory employees is also essential to gain the necessary awareness of safety in handling biohazardous materials (15). PHAC also plays a key role in the response, support, and information sharing needed to improve biosafety standards through its laboratory incident surveillance program.

Awareness of general biosafety measures has also increased during the SARS-CoV-2 pandemic (16). The Government of Canada's *Canadian Biosafety Standard, Third Edition* is the national standard for facilities conducting activities with human pathogens and toxins. This document outlines the minimum physical containment, operational practice, and performance and verification testing requirements for facilities where RG2, RG3 and RG4 human or terrestrial animal pathogens or toxins are handled and stored (17).

Limitations

The main strength of this study is that it is based on the mandatory and standardized reporting of laboratory incidents across Canada. All reports are reviewed by LINC employees and data can be updated if needed. Furthermore, LINC has been continuously collecting data since its inception in December 2015, which allows for an understanding of how Canada's laboratory biosecurity landscape has changed over time.

A limitation of this study is that potential under-reporting of exposure and non-exposure incidents can make the data incomplete. To date, LINC has not been able to establish the extent of under-reporting. However, PHAC carries out regular inspections of licensed facilities to verify compliance with *Canadian Biosafety Standards* (17). One requirement of this standard is to keep an internal record of all biosafety and biosecurity incidents. During a laboratory inspection, a cross-reference check is carried out to ensure that internally recorded incidents were reported to PHAC. It is also important to consider that the data is self-reported and that measures like incident severity are based on the judgment of the reporter. The reporter may not be directly involved in the incident and must rely on another individual's account of what occurred. Additionally, there are limitations to the calculations that involve the number of active licences. These calculations are done with the final number of licences active at the end of the given year. This does not give an accurate picture of active licence number fluctuations, as licence additions and revocations occur throughout the year.

No explicit explanation exists for the increase in the number of exposure incidents in 2018. It remains unknown whether the increase was due to an actual increase in incidents or in incident reporting. It is possible that as the surveillance program became more established, there was increased awareness of the need to report and the importance of doing so, which may have resulted in increased reporting.

Though data on international instances of LAIs have been captured through surveys (2), PHAC's surveillance system provides a comprehensive mandated reporting system that operates at the national level to collect and analyze data on all laboratory incidents that involve HPTs. However, due to the lack of systematic worldwide reporting, it is difficult to compare Canadian laboratory incident data with that of other countries.

It should also be noted that although the percentage of citations for each occurrence type out of the total number of occurrence types cited for all exposure events was presented, certain occurrences, such as those involving animals, can only happen in facilities that work with animals, while other occurrences (i.e., procedure-related) have the potential to occur in all facilities.

Finally, the full impact of the coronavirus disease 2019 (COVID-19) pandemic on laboratory incident reporting and trends is not yet known. While many laboratories were actively involved in COVID-19 testing and research, laboratories also faced closures and reduced on-site staffing to mitigate virus transmission among employees. These changes in laboratory activity may have influenced the exposure and non-exposure incident rates from 2020 to 2022.

Conclusion

Between 2016 and 2022, the exposure incident rate decreased over time, reaching its lowest point of 3.7 exposure incidents per 100 active licences in 2022. Year after year, the number of non-exposure reports followed a similar trend, with the majority of report types being inadvertent possession or production. The severity of the laboratory exposure incidents was mostly reported as negligible and minor. The most cited occurrence types were sharps-related, spills, and procedure-related. An overall increase in human factors and a decrease in standard

operating procedures as a cited root cause was observed. Affected individuals, mostly technicians or technologists, rarely developed an illness.

The increased awareness of safe laboratory practices is integral to reducing biohazardous risk in these settings. The LINC surveillance system program will continue to provide oversight and disseminate laboratory incident information to the public and to licensed laboratories to increase awareness of risks when working with HPTs.

Authors' statement

NB — Conceptualization, methodology, data analysis, writing–original draft, writing–review & editing
AG — Incident monitoring, methodology, data analysis, writing–original draft, writing–review & editing
CA — Incident monitoring, methodology, data analysis, writing–original draft, writing–review & editing
AND — Writing–original draft, writing–review & editing, supervision
ML — Writing–review & editing

Competing interests

There are no competing interests to declare.

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Appendix

Table A1: Levels of severity for exposure incidents

Level of severity	Definition
Negligible	Minimal risk for disease in the individual/other staff AND no risk to public health
Minor	Low risk for disease in the individual/other staff and/or low risk to public health
Moderate	Moderate risk for disease in the individual/other staff and/or moderate risk to public health (limited spread among close contacts, no deaths)
Major	High risk of severe disease/death in the individual/other staff and/or significant public health impact (community spread/outbreak/fatalities)
Catastrophic	High risk of severe disease in the individual/other staff AND severe public health impact (severe epidemic/high mortality, etc.)

Table A2: Definitions of occurrence types

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

Abbreviation: PPE, personal protective equipment

Table A3: Root causes and examples

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

Outbreak of Human Trichinellosis — Arizona, Minnesota, and South Dakota, 2022

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Abstract

Trichinellosis is a parasitic zoonotic disease transmitted through the consumption of meat from animals infected with *Trichinella* spp. nematodes. In North America, human trichinellosis is rare and is most commonly acquired through consumption of wild game meat. In July 2022, a hospitalized patient with suspected trichinellosis was reported to the Minnesota Department of Health. One week before symptom onset, the patient and eight other persons shared a meal that included bear meat that had been frozen for 45 days before being grilled and served rare with vegetables that had been cooked with the meat. Investigation identified six trichinellosis cases, including two in persons who consumed only the vegetables. Motile *Trichinella* larvae were found in remaining bear meat that had been frozen for >15 weeks. Molecular testing identified larvae from the bear meat as *Trichinella nativa*, a freeze-resistant species. Persons who consume meat from wild game animals should be aware that that adequate cooking is the only reliable way to kill *Trichinella* parasites and that infected meat can cross-contaminate other foods.

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Investigation and Results

Index Patient Notification

In July 2022, the Minnesota Department of Health was notified of a man aged 29 years who was hospitalized with fever, severe myalgias, periorbital edema, eosinophilia, and other laboratory abnormalities (**Table 1**); health care providers suspected trichinellosis. The patient had sought care for his symptoms, which commenced in early July, four times and had been hospitalized twice over a 17-day period. During his second hospitalization, providers obtained a history of bear meat consumption, and empiric albendazole treatment for probable trichinellosis was initiated. An investigation was launched to confirm the diagnosis, identify additional cases, and ascertain the source of infection to prevent future cases. The index patient's diagnosis was confirmed by a positive *Trichinella* immunoglobulin (Ig) G antibody test result.

Potential Exposure Source Identification

Six days before symptom onset in the index patient, he and eight extended family members from three states (Arizona, Minnesota, and South Dakota) had gathered for several days in South Dakota and shared a meal that included kabobs made from the meat of a black bear (*Ursus americanus*), which had been harvested by one of the family members in northern Saskatchewan, Canada in May 2022. The hunting outfitter had recommended freezing the meat to kill parasites. The meat was frozen in a household freezer* for 45 days until being thawed and grilled with vegetables. The

Table 1: Demographic characteristics, clinical data, and laboratory test results from persons who consumed a meal that included bear meat infected with *Trichinella nativa* — Arizona, Minnesota, and South Dakota, 2022

Case status	Age, yrs, sex	Consumed bear meat	Signs and symptoms	Hospitalized	Received trichinellosis-directed treatment	WBC count, (x 1,000)/mL, (% eos)[a]	Creatine kinase[a], units/L	*Trichinella* antibody test results	Metagenomic sequencing test results
Confirmed	12, F	Yes	Abdominal pain, myalgias, fever, and periorbital edema	Yes	Yes, albendazole	8 (37%)	2,495[b]	Positive	Positive, *Trichinella* species
Confirmed	29, M	Yes	Abdominal pain, diarrhea, myalgias, fever, and periorbital edema	Yes	Yes, albendazole	27 (22%)	1,040[c]	Positive	Positive, *Trichinella* species
Probable	29, F	No[d]	Myalgias and fever	No	No	ND	ND	ND	ND
Probable	54, F	No[d]	Headache and myalgias	No	No	ND	ND	Negative	ND
Probable	57, M	Yes	Diarrhea, myalgias, fever, and periorbital edema	Yes	Yes, albendazole	13 (9%)	323[e]	Negative	ND
Probable	62, M	Yes	Diarrhea and headache	No	No	ND	ND	Negative	ND
Negative	14, M	Yes	None	NA	No	ND	ND	ND	ND
Negative	61, F	Yes	None	NA	No	ND	ND	Negative	ND

Abbreviations: eos, eosinophils; F, female; M, male; NA, not applicable; ND, not done; WBC, white blood cell
[a] Initial results are from hospitalization during which trichinellosis was suspected. Reference ranges varied among different laboratories that conducted testing
[b] Reference range=4–88
[c] Reference range=39–208
[d] Consumed vegetables that were cooked and served with the bear meat
[e] Reference range=39–308

meat was initially inadvertently served rare, reportedly because the meat was dark in color, and it was difficult for the family members to visually ascertain the level of doneness. After some of the family members began eating the meat and noticed that it was undercooked, the meat was recooked before being served again. The family reunion concluded before onset of illness in the index patient.

Laboratory Investigation and Case Definition

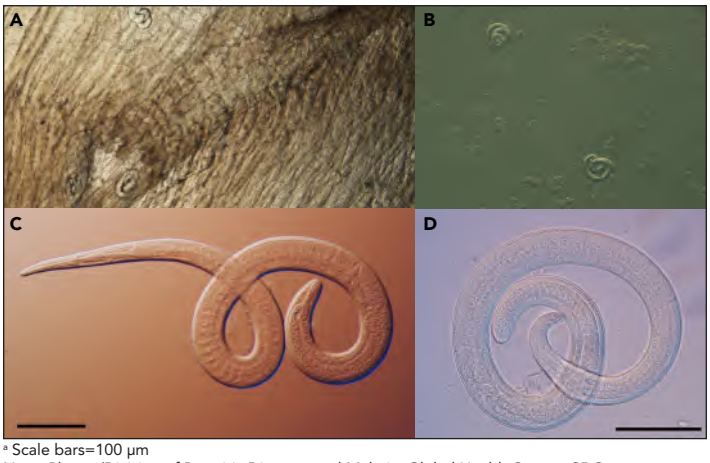
Public health authorities in Arizona, Minnesota, and South Dakota interviewed eight of the nine persons who had attended the implicated meal. The ninth attendee was a person aged <18 years whose exposure status could not be confirmed; however, that person reportedly remained healthy. Testing of paired acute and convalescent sera for *Trichinella* IgG antibodies was recommended for the eight exposed persons and was completed for six. Pathogen-agnostic microbial cell-free metagenomic DNA sequencing (1) was performed on plasma samples from the index patient and one other person who had sought care twice before being hospitalized with fever, myalgias, abdominal pain, periorbital edema, and laboratory abnormalities. Trichinellosis cases were classified according to the 2014 case definition from the Council for State and Territorial Epidemiologists (CSTE),† (i.e., the presence of clinically compatible symptoms in a person who had consumed an epidemiologically implicated meal or meat in which the parasite was demonstrated [probable] or had a positive serologic test result for *Trichinella* antibodies [confirmed]). Samples of frozen bear meat were obtained from the household freezer and sent to CDC for artificial tissue digestion and microscopic examination for larvae and molecular testing for *Trichinella* spp.

Additional Case Detection and Exposure Source Confirmation

Among the eight interviewed persons, five consumed the bear meat, and eight consumed the vegetables that had been cooked with it. Six of the eight persons who attended the meal, including four who consumed the bear meat and the vegetables, and two who consumed only the vegetables (but no meat), had symptoms

consistent with trichinellosis, and met case criteria (two confirmed and four probable). Patients with trichinellosis ranged in age from 12 to 62 years and lived in three states: Arizona (one), Minnesota (four), and South Dakota (one). All cases were diagnosed in the patients' state of residence. Three of the six symptomatic persons, two of whom sought care at least twice before being offered treatment, were hospitalized. The three hospitalized persons received trichinellosis-directed treatment with albendazole§. All six symptomatic persons recovered; the nonhospitalized patients did not receive trichinellosis-directed treatment because their symptoms had resolved with supportive care only, and the benefit of treatment after larval invasion of muscle is unclear (2). Six persons submitted a serum sample, each collected within 4 weeks of symptom onset; two specimens tested positive for *Trichinella* IgG antibodies by enzyme-linked immunosorbent assay. Two persons submitted a plasma sample for microbial cell-free DNA sequencing during hospitalization for trichinellosis-compatible symptoms, and both plasma samples tested positive for *Trichinella* spp. DNA. Microscopy identified motile *Trichinella* larvae (>800 larvae/g) in samples of bear meat that had been frozen for 110 days in a household freezer (**Figure 1**). Real-time multiplex polymerase chain reaction testing (3) of the bear meat was positive for *T. nativa* and whole genome sequencing identified mitochondrial sequences 100% identical to *T. nativa*.

Figure 1: Microscopic examination of encapsulated larvae in a direct black bear meat muscle squash prep (A), larvae liberated from artificially digested bear meat (B), motile larvae viewed with differential interference contrast microscopy (C and D)[a] from black bear meat suspected as the source of an outbreak of human *Trichinella nativa* infections — Arizona, Minnesota, and South Dakota, 2022



[a] Scale bars=100 µm
Note: Photos/Division of Parasitic Diseases and Malaria, Global Health Center, CDC

Public Health Response

The family member who harvested the bear and provided meat samples for testing was advised to discard any remaining meat. All identified trichinellosis cases were reported to appropriate state health departments and to CDC. CDC notified the Public Health Agency of Canada of the outbreak and the confirmed source of infection. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy±.

Discussion

Trichinellosis is rarely reported in the United States. As a result of changes in pork production practices from historical norms that fostered transmission, most cases reported in recent years are attributed to consumption of meat from wild game (4). During January 2016–December 2022, seven U.S. trichinellosis outbreaks, including 35 probable and confirmed cases, were reported to CDC; bear meat was the suspected or confirmed source of infection in the majority of those outbreaks (CDC, unpublished data, 2022). Estimates of *Trichinella* infection prevalence among wild animal host species vary widely. A *Trichinella* infection prevalence range of at least 1% to 24% among black bears in Canada and Alaska has been reported, and even higher prevalences of *Trichinella* infection are reported among species of predators that are strict carnivores (e.g., polar bear, wolverine, and cougar) (5). The frequency with which black bear meat is the implicated source of human infection might be driven by hunting practices, ecological factors, and the relatively high parasite density observed in the muscle of infected black bears compared with that of other species (6,7).

Because symptoms of trichinellosis are typically nonspecific, diagnosis of infection requires a high index of suspicion; however, periorbital edema and certain laboratory abnormalities (e.g., eosinophilia and elevated creatine kinase levels) can provide etiologic clues. In this outbreak, two of the hospitalized patients sought care multiple times before receiving a diagnosis. Four of the six patients met clinical and epidemiologic criteria and thus were considered probable cases. Laboratory confirmation can be challenging because of the limited sensitivity of antibody testing early in illness (8); in this investigation, acute *Trichinella* IgG test results were positive in only two of six tested patient specimens. The clinical utility of trichinellosis test results obtained after acute illness is limited, and historically, public health investigators have had difficulty obtaining convalescent serum samples from persons who have recovered. Laboratory criteria in the current CSTE trichinellosis case definition do not include nucleic acid testing of human specimens. The sensitivity of such assays to detect *Trichinella* DNA in blood is uncharacterized; however, plasma samples from both patients tested by metagenomic sequencing (1) yielded positive results for *Trichinella* DNA. As demonstrated in this outbreak, pathogen-agnostic molecular assays can be useful for detection of rare diseases when standard workup is unrevealing and if other diagnostic tests lack sensitivity.

Implications for Public Health Practice

Although freezing kills *Trichinella* species commonly implicated in pork-associated outbreaks, freeze-resistant *Trichinella* species, including *T. nativa* and the T6 genotype (9), predominate in Arctic and sub-Arctic regions (6). Larval motility was observed in bear meat that had been frozen for nearly 4 months (110 days). Persons who consume game meat, especially that harvested in northern latitudes, should be informed that adequate cooking is the only reliable way to kill *Trichinella* parasites. Cooking wild game meat to an internal temperature of ≥165°F (≥74°C) is recommended by public health authorities**; temperatures should be verified with a meat thermometer. As demonstrated in this outbreak, the color of meat is not a good indicator of cooking adequacy. Safe handling of raw meat (i.e., separating raw or undercooked meat and its juices from other foods) is recommended to prevent trichinellosis; this investigation and previous investigations suggest that *Trichinella*-infected meat can cross-contaminate other foods (10). Government and private entities that oversee and organize hunting should educate hunters about these risks and effective preventative measures.

Competing interest

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. David M. Berman reports that he is a paid laboratory medical consultant for Precision Health Solutions and reports ownership of company shares in Karius, Inc. No other potential conflicts of interest were disclosed.

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Footnotes

* The temperature of the freezer is not known.
† https://ndc.services.cdc.gov/case-definitions/trichinellosis-2014/
§ https://www.cdc.gov/trichinellosis/hcp/clinical-care/index.html
± 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.
** https://www.cdc.gov/trichinellosis/prevention/index.html

Summary

What is already known about this topic?
Human trichinellosis cases in the United States are rare and are usually acquired through consumption of wild game.

What is added by this report?
Among eight persons who shared a meal that included the meat of a black bear harvested in Canada and frozen for 45 days, six trichinellosis cases were identified. The meat was grilled with vegetables and served rare; two cases occurred in persons who ate only the vegetables. Motile freeze-resistant *Trichinella nativa* larvae were identified in remaining meat frozen for >15 weeks.

What are the implications for public health practice?
Cooking meat to an internal temperature of ≥165°F (≥74°C) is necessary to kill *Trichinella* spp. parasites. *Trichinella*-infected meat can cross-contaminate other foods, and raw meat should be kept and prepared separate from other foods to prevent cross-contamination.

An outbreak of *Salmonella* Infantis linked to shredded pork products from an unlicensed source in multiple health districts, Ontario, Canada, 2021

Victoria Osasah[1], Yvonne Whitfield[1], Affan Danish[1]*, Allana Murphy[2], Richard Mather[1], Janica Adams[1], Anna Majury[2], Mehdi Aloosh[1,3]

Abstract

Background: An outbreak of *Salmonella* Infantis was associated with the consumption of shredded pork products at multiple restaurants in Ontario between July 2021 and October 2021. The outbreak involved 36 case-patients from six public health units. The implicated shredded pork products were obtained from an unlicensed source. This is the largest reported outbreak of *Salmonella* Infantis linked to restaurant food exposures in Ontario, with complexities related to the investigation of unlicensed foods. This article aims to describe the epidemiological, food safety and laboratory investigations that led to the identification and removal of the source of the outbreak from implicated restaurants, including the challenges encountered while investigating an outbreak related to an unlicensed source of food.

Methods: Epidemiological and laboratory analyses were conducted to identify the source of the outbreak. Food safety investigations were conducted to ascertain the origin and distribution of the implicated food.

Results: Whole-genome sequencing identified the outbreak strain from the isolates of 36 case-patients across six public health units in Ontario. Seven case-patients (19%) were hospitalized. No deaths were reported. The outbreak was linked to shredded pork products (i.e., rinds or skins) that were distributed by an unlicensed meat processor and consumed at various restaurants that served Southeast Asian fusion cuisine concentrated in the Greater Toronto Area. The product was removed from implicated restaurants.

Conclusion: Historically, foods from unlicensed sources have been implicated in multiple large outbreaks and continue to be of significant public health risk. The outbreak investigation emphasized the threat of food from unlicensed sources to the public's health and the importance of additional public health interventions to prevent outbreaks linked to unlicensed sources.

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Keywords: *Salmonella*, Infantis, epidemiologic studies, outbreak, foodborne, unlicensed source, restaurant

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Introduction

Identification

In August 2021, Public Health Ontario (PHO) identified, via routine surveillance, nine cases of *Salmonella* Infantis infection within 0–7 allele differences by whole-genome multi-locus sequence typing (wgMLST). Further follow up with local public health units identified a cluster of five case-patients who dined at a common restaurant serving Southeast Asian fusion cuisine. Four additional cases reporting similar exposures were identified in three additional jurisdictions within Ontario. A total of 17 Southeast Asian fusion restaurants were implicated. This led to the activation of the Ontario Outbreak Investigation Coordinating Committee on September 10, 2021. This committee is composed of local, provincial and federal partners who jointly convened and undertook the outbreak investigation.

Background

In Ontario, salmonellosis is the second most common cause (1) of notifiable gastrointestinal infection (2). Over the past five years, approximately two per 1,000 persons per year in Ontario have experienced an illness from salmonellosis. An average of three per 100 persons are hospitalized annually in Ontario (2). Among the ten most reported serovars in the province, *Salmonella* Infantis is the fourth leading serovar (3).

The most notable outbreak of *Salmonella* Infantis in Ontario was reported in 1999 and linked to pig ear treats for pets (4). Nationally and internationally, outbreaks of *Salmonella* Infantis have been linked to poultry products as the vehicle of infection (5,6). An international outbreak of *Salmonella* Infantis linked to pork products was reported in Germany (7). Overall, the contamination of pork with *Salmonella* Infantis has been well described in the literature (6,8). According to FoodNet Canada, data have frequently identified *Salmonella* Infantis within poultry and pork products (9).

In the past decade, multiple outbreaks of salmonellosis have been associated with the distribution of food from unlicensed sources across Canada and the United States (US). Two of the larger outbreaks were linked to the distribution of food from commercial vendors (e.g., mobile food trucks and a catering company) using food from unlicensed sources (10–12). These outbreaks caused by foods from unlicensed sources have historically contributed to delays in the identification of the source of the infection, partly due to the distributor's deviations from the standard regulatory practices necessary to track and stop the distribution and use of the implicated food products. These delays have significantly impeded timely public health investigations to identify the source and prevent further distribution. A secondary consequence is the sustained availability of the implicated food for consumption while investigators are conducting investigations to identify the source, potentially contributing to an increased incidence of cases with the disease-causing organism.

Objective

Given the magnitude of this outbreak as observed with the large number of reported illnesses and its occurrence in restaurants across a wide geographical area, it was imperative to understand the epidemiology of the outbreak and the implications of distributing unlicensed food sources on the food investigation into the source of the outbreak. This article describes the epidemiological, laboratory and food safety investigations and the food safety challenges encountered and actions taken during the outbreak while investigating food from an unlicensed source.

Methods

Overview

Following an increase above the average count of case-patients that were linked by whole-genome sequencing (WGS), an outbreak was declared on September 10, 2021. By late October 2021, no additional cases were reported. The outbreak was declared over on November 11, 2021, following the identification and the removal of the source of the outbreak and a return below the average count of cases.

Case finding and data collection

The Ontario Outbreak Investigation Coordinating Committee defined an outbreak confirmed case as an infection with *Salmonella* Infantis occurring among residents or visitors in Ontario, with a genomic sequence pattern (0–7 wgMLST allele differences) consistent with the outbreak strain, and an illness onset on or after July 12, 2021. Routine data for *Salmonella* are provided by PHO's laboratory. On average, PHO's laboratory reports two *Salmonella* Infantis cases per week in Ontario.

We conducted a descriptive study using standardized hypothesis-generating questionnaires in conjunction with laboratory data on clinical and food isolates. Ethics approval was not required as this study fell within the purview of PHO's legislated mandate (13).

Case-patients with laboratory-confirmed *Salmonella* infections related to the outbreak strain were interviewed by local public health investigators, using a standardized hypothesis-generating questionnaire to obtain food, animal, water and occupational exposures during the seven-day period prior to the onset of the illness. Re-interviews of case-patients were also conducted by provincial investigators who collected additional exposure information to identify the source of the outbreak. Based on the information from the initial interviews, investigators inquired about exposure to pork and pork products, and obtained information on the location of the food purchase and consumption, including the name of the dish consumed. On September 13, 2021, a public health alert was issued on the Canadian Network for Public Health Intelligence to communicate the situation to public health partners.

Investigations

Laboratory investigations

In response to the outbreak investigation, clinical specimens obtained from case-patients who were part of the outbreak, and food specimens, including intact and opened specimens, obtained from locations where case-patients reported consuming food prior to illness, were analyzed at PHO's laboratory and the Public Health Agency of Canada's National Microbiology Laboratory. Public Health Ontario's laboratory carried out real time polymerase chain reaction (PCR) analysis using the AOAC Research Institute 031001 method for food samples submitted by public health units for *Salmonella* detection (14). All positive and indeterminate real-time PCR analysis samples were transitioned to the Health Canada reference selective method (MFHPB-20) (15) for culture-based identification, and with serotyping confirmation via traditional phenotypic agglutination (16). Cluster analysis was routinely performed on all positive samples using the PulseNet Canada wgMLST approach, which defines screening for genomic relatedness as ≤10 wgMLST allele differences between samples (17). Presumptive isolates from the reference culture method were confirmed by the enteric laboratory at PHO. Specimens with culture-positive isolates were sent for confirmatory WGS to the National Microbiology Laboratory. Isolates within 0–7 wgMLST were identified as closely related to each other.

Epidemiologic investigation

A binomial probability test was applied for the comparison of the proportions of the food exposures reported by the case-patients and the reference values from Foodbook survey respondents. The Foodbook Report is a population-based telephone survey conducted in all Canadian provinces within a one-year study period between 2014 and 2015 on food and animal exposure within a seven-day recall period (18). Microsoft Excel was used to conduct data analysis and to create epidemiological graphs. A significance level of p=0.05 was used.

Food reported by case-patients with higher than expected proportions to the reference values and with statistical significance (p<0.05) were further explored to identify similarities by purchase location, type of food and food ingredients. Information on restaurant exposures from the standardized hypothesis-generating questionnaires reported by case-patients was further analyzed to identify case-patients that dined at the same Southeast Asian fusion restaurants. A sub-analysis of the food exposures from case-patients that dined at the same restaurants was conducted and compared with other case-patients involved in the outbreak to identify a common source. In addition, household clustering was explored to identify case-patients who may have been exposed via non-primary transmission.

Food safety investigation

Local, provincial and federal food safety investigators conducted site visits at the restaurants where case-patients reported dining and investigated the implicated food product. Food items that case-patients reported consuming and were suspected as the source of illness based on epidemiological data were obtained from the restaurants, including specimens from an affiliated restaurant serving similar meals without any reported illnesses.

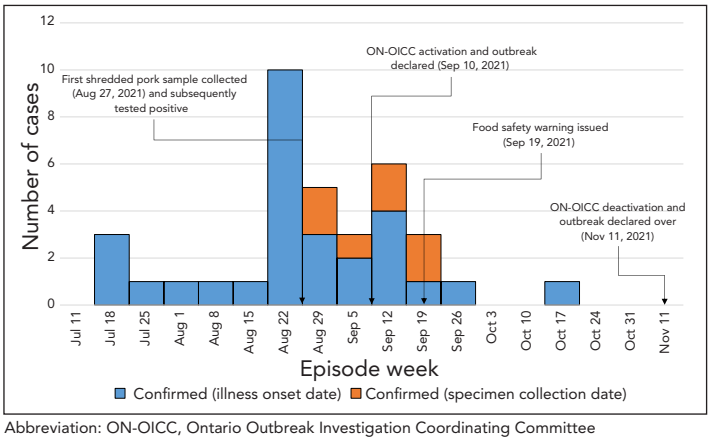
Results

Epidemiologic findings

Thirty-six case patients that met the confirmed case definition were reported across six public health units. Majority of case patients (97%) were reported across five public health units within the Greater Toronto Area (GTA) between July and October 2021. No cases were identified outside of Ontario. The median age was 26 years (range: 0–94 years). Among all case patients, clustering was observed by gender as twenty-four (67%) case patients were male. Fourteen case patients (39%) were between 10 and 29 years. Seven case patients (19%) were hospitalized during the outbreak. No deaths were reported.

Illness onset dates ranged from July 19, 2021, to October 17, 2021, with multiple temporal clusters, within the three-month span, more than one incubation period apart, and with several peaks and valleys throughout the outbreak. These clusters reflect the dining pattern of the case patients and the fact that the outbreak was restaurant-based and involved a frozen contaminated food item with a long shelf life (**Figure 1**, **Table 1**).

Figure 1: An epidemic curve of case-patients with *Salmonella* Infantis infections reported by week of illness onset or specimen collection date Ontario, July 18, 2021–October 17, 2021, (n=36)



Abbreviation: ON-OICC, Ontario Outbreak Investigation Coordinating Committee

Table 1: A distribution of the outbreak confirmed cases involved in the outbreak by illness onset date and specimen collection date, Ontario, July–October 2021

Episode week (2021)	Confirmed (illness onset date)	Confirmed (specimen collection date)
Jul 11	0	0
Jul 18	3	0
Jul 25	1	0
Aug 1	1	0
Aug 8	1	0
Aug 15	1	0
Aug 22	10	0
Aug 29	3	2
Sep 5	2	1
Sep 12	4	2
Sep 19	1	2
Sep 26	1	0
Oct 3	0	0
Oct 10	0	0
Oct 17	1	0
Oct 24	0	0
Oct 31	0	0
Nov 11	0	0

Exposure information was collected from a total of 30 case-patients (response rate: 83%) as five case-patients were lost to follow-up and one case-patient was unwilling to be interviewed. Among the 24 case-patients that provided a response for "consumption of pork", 23 case-patients (96%) responded that they either consumed or probably consumed pork, representing a higher than expected proportion than the average proportion of the general population surveyed in the Foodbook Report (61%, $p<0.005$). Among the 23 case-patients that reported consuming or probably consuming pork, 19 (83%) case-patients reported consuming shredded pork rind, pork skin or a combination with pork chops at 17 restaurants serving Southeast Asian fusion cuisine in the GTA.

Additional food exposures were explored to determine if other food exposures could have been the source of the outbreak; however, the food items reported were identified as part of the dish served with shredded pork products and lacked differences among case-patients. Additionally, laboratory evidence strengthened the hypothesis that these food items were not the source of the outbreak. Of the 23 case-patients reporting consumption of pork, a total of 20 case-patients (87%) reported dining at restaurants and consuming pork. Of the 17 restaurant locations, there were three chains involved with clustering of three or more case-patients per restaurant chain. These accounted for 12 case-patients. The remaining eight cases dined at eight different individual locations.

Food safety investigations

Investigations to trace the distribution of the implicated product included the collection of shredded pork products from the restaurants. It was determined that the shredded pork products were sold frozen in transparent plastic bags, with no labels, no lot codes, no identifiers and no cooking instructions. Pictures obtained of the unlabelled products (**Figure 2**) aided investigators in identifying and removing similar products from use from all restaurants serving Southeast Asian fusion cuisines across the GTA. The pictures also aided in identifying additional shredded pork samples for testing.

Figure 2: A picture of the implicated shredded pork product taken by investigators and issued in a Food Safety Warning[a]

[a] Information can be found on the Canadian Food Inspection Agency's Food Safety Warning page

There were no cooking instructions on the package to determine if it was a ready-to-eat product or if additional cooking was required. Some restaurant operators reported that they served the shredded pork products without additional heat treatment.

Further investigations revealed that all the restaurants shared a common meat processor of the specific shredded pork products. At the time of the outbreak investigation, the meat processor operated without a license. One of the challenges during the trace back investigation involved obtaining contact information of the meat processor from the restaurant operators. Some restaurant operators could only provide the name and telephone number of the meat processor. The contact information provided by restaurants were the same; however, investigators were unable to establish contact with the meat processor. Therefore, further information could not be obtained.

Another challenge that occurred at the restaurant-level was obtaining accurate information about the source of the shredded pork products that were purchased. Upon re-inspection, some restaurant operators provided conflicting information about the

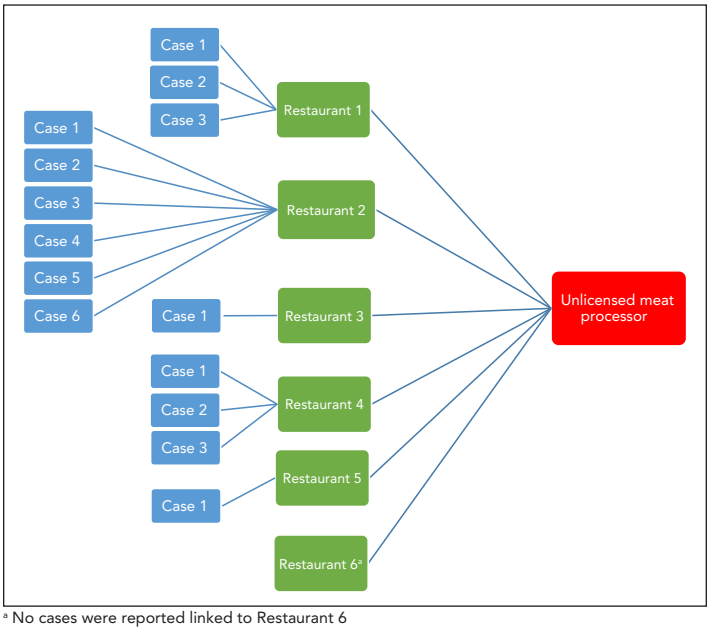
purchase source of the shredded pork products. The operators implicated a licensed supplier after initially identifying the unlicensed supplier as the purchase source. The licensed supplier was inspected and food specimens were collected. *Salmonella* was not detected in any of the food specimens that were obtained from the licensed supplier.

Laboratory findings

An initial laboratory analysis identified that a *Salmonella* Infantis isolate from an intact shredded pork product sample, obtained from one of the implicated restaurants was related by WGS to the outbreak strain. In total, 75 food samples, including 37 samples of shredded pork rind, shredded pork skin and mixed pork chops, were obtained from 17 implicated restaurants, one restaurant with no known case-patients reported, all 18 restaurants serving Southeast Asian fusion cuisine, and one private residence during the investigation. The other 38 food samples tested included rice (n=5), chicken (n=5), vegetables (n=4), beef (n=4), egg (n=3), sausage (n=2), spring rolls (n=2), tofu (n=2), vermicelli (n=2), salsa (n=2) and one sample each of sour cream, tortilla, peppers, cheese, duck, teriyaki sandwich and rice powder.

Fourteen positive food isolates from the shredded pork products obtained from seven restaurants (39%) (**Figure 3**) shared similar genetic patterns with the outbreak strain by WGS. The isolates were within seven allele differences by wgMLST from each other. Isolates from clinical specimens obtained from the case-patients were also within seven allele range by wgMLST.

Figure 3: A trace back diagram of the restaurants and number of case-patients linked to each restaurant from which the 14 positive shredded pork product isolates were obtained, Ontario, July–October 2021[a]



[a] No cases were reported linked to Restaurant 6

Public health interventions

Provincial and federal investigators issued a food safety warning (19) (Figure 2) to the public as well as to hotels, restaurants and institutions against the use of this shredded pork product. In addition, once the implicated product was identified, local investigators conducted inspections of all Southeast Asian fusion style restaurants within their jurisdictions. Investigators provided education to restaurant operators and removed the implicated shredded pork products wherever found. No additional restaurants were identified.

Discussion

Key results

Shredded pork products were identified as the source of the outbreak that led to 36 instances of illness among 17 restaurants across five health districts in the GTA and one health district outside the GTA. It was hypothesized that contamination at various stages of the food processing continuum could have occurred in the supply chain, providing multiple opportunities for the contamination and transmission of *Salmonella* Infantis in the pork products. Furthermore, undercooking and inadequate processing of the shredded pork products at either the processor or restaurant level may have occurred. The shredded pork products were unlabelled without any cooking instructions and were not further cooked at the restaurant level. The large-scale distribution of these unlicensed pork products to numerous restaurants was an unusual occurrence in Ontario.

Comparison to other *Salmonella* Infantis outbreaks and outbreaks from unlicensed sources

Although *Salmonella* Infantis is a common serovar in Ontario and has been associated with multiple outbreaks (8,20), this outbreak presented some unusual investigation patterns that were different from previous outbreak events of *Salmonella* Infantis in Ontario, mainly due to widespread distribution of unlicensed pork products to restaurants. Previous foodborne outbreaks of *Salmonella* Infantis in Canada have been associated with food sold at retail stores and consumed at home (4,20,21). This was the largest reported restaurant associated outbreak of *Salmonella* Infantis in Ontario, resulting from the consumption of food from an unlicensed food processor. However, the magnitude of the outbreak, tight clustering of cases both spatially and temporally, and distribution to large-scale gatherings (such as restaurants) was consistent with previous outbreaks associated with food from unlicensed sources (10–12). Previous outbreaks involving unlicensed sources have exemplified the impact of food from unlicensed sources on investigations into the identification of the source of an outbreak. This outbreak faced additional challenges not reported in the existing literature, which included limited available information on the distributor and manufacturer of the product and often

conflicting information from restaurant operators who provided inconsistent information about the vendor's name and location. This posed a challenge for investigators in identifying the source of the outbreak in a timely manner. Some operators were fined for obtaining food from unlicensed sources.

Limitations

There were several limitations involved with obtaining information from case-patients. Since information was obtained from case-patients following the outbreak, we cannot rule out the possibility of recall bias. However, some case-patients reviewed their credit card records for specific purchases. In addition, some case-patients required language translation. However this was not available for all case-patients, and some were hesitant to share information with investigators.

Additional limitations occurred during the food safety investigation in the identification of the unlicensed meat processor. While the meat processor was identified, the lack of contact with the meat processor severely impacted the progress of the investigation into identifying distribution channels of the implicated products. The limitations also included the lack of identification of the point in the supply chain where the contamination may have occurred.

The location and identity of the unlicensed meat processor of the shredded pork products are unknown. However, due to the higher proportion of shredded pork products in dishes served to the case-patients involved in the outbreak, local public health authorities were able to confirm the source of the outbreak through food sampling of the meals consumed by the cases. This action helped to ensure timely identification and removal of the implicated shredded pork product. Particularly in the absence of appropriate labels, photos of the unlabelled shredded pork products were pivotal in identifying the implicated products in the outbreak and for communicating information about affected food items to public health partners as well as to the hotels, restaurants and institutions.

Conclusion

Outbreaks linked to food from unlicensed sources highlight the significant public health risk that arises from the use of these sources, such as the introduction of pathogens into the food supply chain and the propagation of disease (22,23).

These food products can be illegally distributed across a wide network, particularly at the restaurant level, thereby resulting in a greater risk for illnesses. The economic impact of rising food costs could influence the purchase choices of food safety operators in attempts to lower their operating costs, where affordable alternatives could be supplied from unregulated sources (24). Restaurant operators are also less likely to cooperate with investigators in providing information about products that they knowingly obtain from unlicensed sources. Given that a single type of cuisine was involved, this may also suggest a familiar network.

Prevention requires a multi-pronged approach, involving regulations that require food sources to be licensed and effective record-keeping. The Ontario Food Premises regulations were amended in 2019 to include these requirements. In addition, education of food safety operators on the risks to the public's health of the use of foods from unlicensed sources, as well as the penalty that they would incur if they do so, may help reduce the risk. Furthermore, enforcement is an important approach to prevent such instances.

This outbreak highlighted the importance of collaboration among local, provincial and federal regulatory authorities (Ontario Outbreak Investigation Coordinating Committee). The use of additional risk-mitigating strategies, such as the inspection of all restaurants serving Southeast Asian food; the Ministry of Health issuing a notice to hotels, restaurants and institutions; and the Canadian Food Inspection Agency issuing a food advisory on the unlicensed shredded pork products, aided in identifying the product and removing it from the marketplace and increasing awareness of the implicated food product.

Authors' statement

VO — Conceptualization, methodology, writing–original draft, writing–review & editing
YW — Conceptualization, methodology, writing–original draft, writing–review & editing, supervision
AD — Writing–original draft, writing–review & editing, project administration
AMurphy — Investigation, resources, writing–review & editing, validation
RM — Conceptualization, writing–review & editing
JA — Writing–review & editing
AMajury — Validation, investigation, resources, writing–review & editing
MA — Conceptualization, writing–review & editing, supervision

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Competing interests

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