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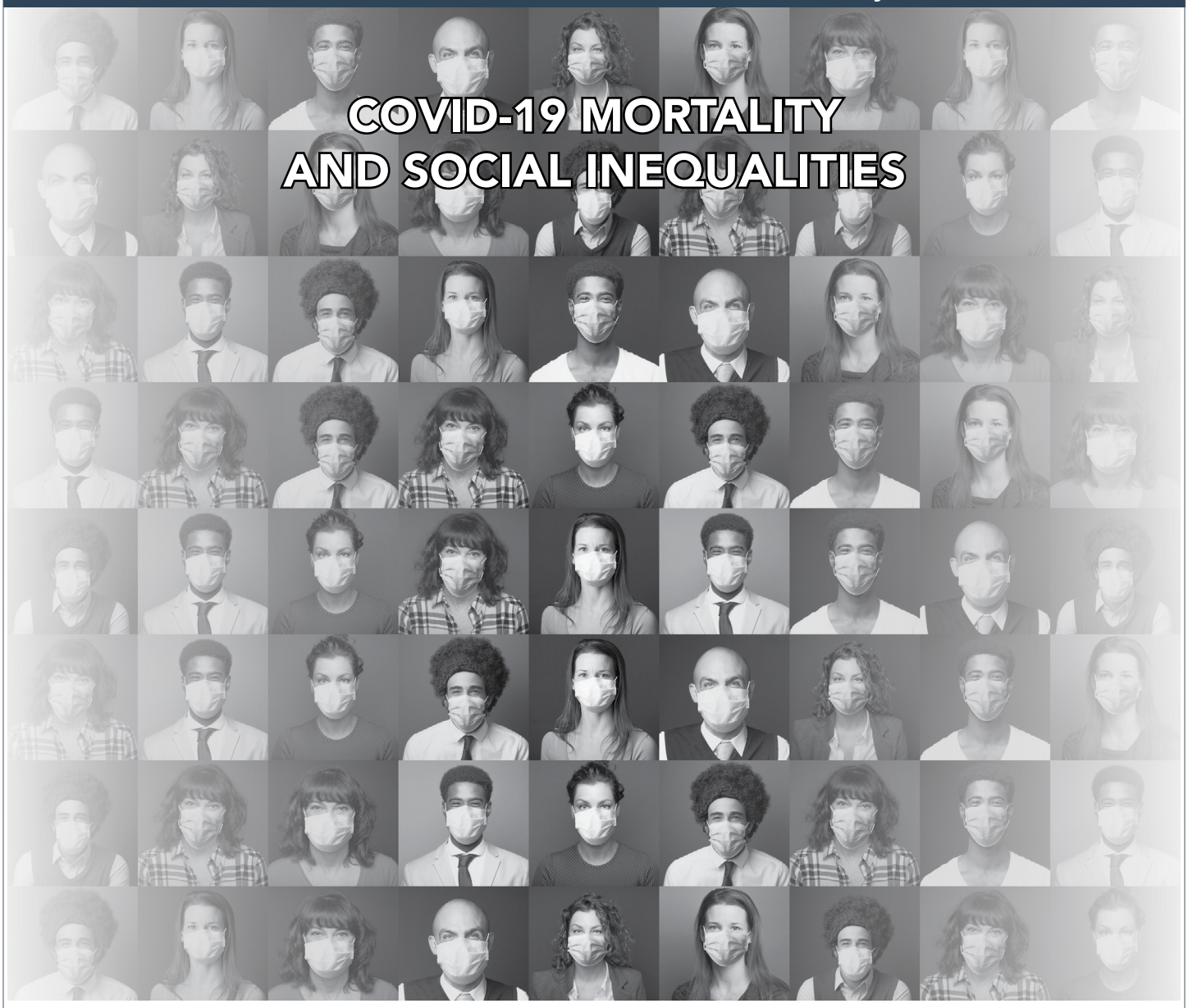
canada.ca/ccdr

January 2022 - Volume 48-1



COVID-19 MORTALITY AND SOCIAL INEQUALITIES

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CANADA COMMUNICABLE DISEASE REPORT

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ISSN SN 1481-8531 / Cat. HP3-1E-PDF / Pub. 200434

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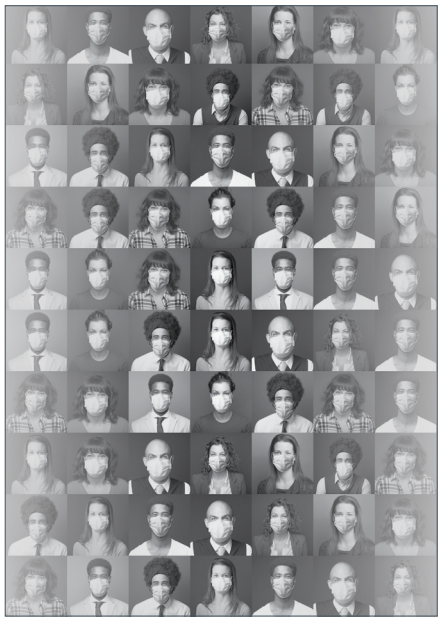

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Canadian Public Health Laboratory Network Statement on Point-of-Care Serology Testing in COVID-19

Respiratory Virus Infections Working Group[1]

Suggested citation: Respiratory Virus Infections Working Group. Canadian Public Health Laboratory Network Statement on Point-of-Care Serology Testing in COVID-19. Can Commun Dis Rep 2022;48(1):1–3. https://doi.org/10.14745/ccdr.v48i01a01

Keywords: COVID-19, serology testing, point-of-care, Canada, antibodies to SARS-CoV-2

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Introduction

Point-of-care (POC) serology tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), detect the human antibody response to infection or vaccination and not the virus itself. Most are qualitative immunochromatographic (lateral-flow)-based assays that detect IgG+/-IgM from a finger prick blood sample and can provide results in less than 30 minutes. While there is widespread interest in adopting POC serology tests for COVID-19, there are currently significant limitations to this testing modality, including the incomplete understanding of the immunological response in COVID-19, suboptimal clinical validation data, uncertain correlation (or lack thereof) with clinical laboratory-based serology tests and wide variability in performance among different POC tests. Many of the key points outlined below also apply to laboratory-based COVID-19 serology testing.

Current position for acute diagnostics

Serology POC tests for COVID-19 are not recommended for use as a diagnostic tool for acute infection and only three products are approved by Health Canada to date. In general, these tests are not able to detect antibodies until at least a week or more after symptoms have started, and therefore are not suitable for diagnosis of acute SARS-CoV-2 infection at this time. We recommend that nucleic acid detection (e.g. real-time polymerase chain reaction) remain the first line test for the diagnosis of acute SARS-CoV-2 infection, as advised by the World Health Organization (1).

Key points

- It can take at least 7–14 days, and sometimes longer, after symptom onset for antibodies to develop, therefore the use of serology POC tests in the early phase of infection can result in a false negative COVID-19 diagnosis at a time when patients are most infectious (i.e. a negative result does not rule out infection).
- False negative interpretations may occur in elderly and immunocompromised patients, who are unable to mount an adequate antibody response.
- Since serology POC tests do not detect virus, a positive or negative result does not determine whether a person is infectious.
- Positive results may be due to past or recent infection with SARS-CoV-2 or from COVID-19 vaccination.
- Most POC serology tests are unable to differentiate antibodies developed from previous infection from those generated in response to COVID-19 vaccination. Given the rapid expansion of COVID-19 vaccination, this further limits the use of serology POC tests.
- As with other COVID-19 serological platforms, false positive results may occur if these kits cross-react with antibodies from recent or past exposure to other coronaviruses, including human coronaviruses.
- Other infections, as well as non-infectious conditions (e.g. rheumatoid factor-positive diseases), may also cause false positive results.
- False positive results are more likely in areas of low prevalence and low vaccine uptake. The local epidemiology and pretest probability of the individual (i.e. clinical and epidemiological risk factors) need to be taken into consideration when interpreting POC serology results.

- Due to the visual interpretations of most POC serology tests, false positive and negative results may arise from incorrect or subjective reading.
- As per recommendations from the National Advisory Committee on Immunization, there is no indication for serology prior to or after COVID-19 vaccination.
- Any kits used need to be thoroughly evaluated for performance characteristics (sensitivity, specificity) before being used clinically, including in-field use conditions.

An evolving and exceptional use for POC serology testing may be considered when laboratory-based serology testing is not available or is unable to meet the necessary rapid turnaround times to help identify COVID-19 patients most likely to benefit from anti-SARS-CoV-2 monoclonal antibody therapy. Serology testing currently has limited clinical utility; however, some jurisdictions have recommended its use to help inform treatment decisions for COVID-19 patients, as early clinical trial data showed that some monoclonal antibody therapies (e.g. casirivimab + imdevimab) were most effective in seronegative patients. Even in this context, we recommend that serology POC tests be performed in a laboratory setting to help mitigate some of the risks outlined above and validated before use as described below. When possible, laboratory-based SARS-CoV-2 serology testing is preferred.

Current position for use as "immunity certificates or passports"

There has been ongoing discussion around the use of antibody testing as evidence of immunity to facilitate individual movement in public areas and to permit international travel. The knowledge around immunity to SARS-CoV-2 is rapidly evolving; however, at this time, the correlates of protection and duration of immunity are not well understood. As such, we do not recommend using serology, including POC tests, for determining individual immunity or for establishing exemptions from public health measures.

Key points

- Since there is currently no correlate of protection, it is unknown if the levels of antibodies detected by serology POC tests are sufficient for protection.
- Since POC tests do not provide a quantitative result, their utility may be limited even once a correlate of protection is established.
- COVID-19 antibodies may persist for at least six months; however, the rate at which antibodies decline over time varies by age, immune status of the individual and severity of disease.
- Binding antibodies detected by serology POC tests may not correlate with neutralizing (i.e. protective) antibodies.
- Since it takes at least 7–14 days (longer in some individuals) to mount an antibody response, a negative result does not exclude an active infection or rule out infectiousness; therefore, it does not confirm that an individual cannot transmit SARS-CoV-2. Serology tests should not replace molecular (or antigen) testing for travel or other screening purposes.
- Although reinfection or infection after vaccination is relatively rare, a positive serology result does not guarantee protection from infection, especially with intense exposures and the emergence of SARS-CoV-2 variants that have immune escape potential.
- Since serology POC tests do not detect T-cell mediated immunity to SARS-CoV-2, which is also important for long-term protection, a negative result is not proof that an individual is not immune.
- Modelling has shown that public health measures, such as masking and physical distancing, will be required to control the spread of SARS-CoV-2 until the time that population vaccine coverage and adequate population immunity are achieved. Thus, a positive serology result, including from POC testing, may provide a false sense of protection from SARS-CoV-2 infection at the individual level.

Important considerations is implementing point-of-care testing

The role of serology in the diagnosis of SARS-CoV-2 infection, patient management and immunity testing is of limited utility. Once the dynamics of the serological response in COVID-19 are better understood and a correlate of protection is identified, serology may play an important role in the population-based public health response. If serology POC testing is implemented for a specific purpose (e.g. testing for monoclonal antibody treatment), the following should be considered:

- Extensive validation of the test(s) against a gold standard (viral neutralization assays or another laboratory-based serological assay). Performance characteristics (sensitivity, specificity, positive and negative predictive values, cross-reaction to other coronaviruses) should be established using sera from patients infected with SARS-CoV-2 (ancestral and variants), other respiratory viruses, including seasonal coronaviruses, and healthy controls.
- Provide adequate training to healthcare/laboratory workers to perform the test and interpret the result.
- Performing a risk assessment for infection with SARS-CoV-2 and bloodborne infections for the operator. We recommend that universal protective measures to prevent bloodborne pathogen transmission (at a minimum, gloves and gowns) be used when running POC assays until the risk to the operator can be formally assessed.
- Establishing an ongoing quality control/quality assurance program prior to implementation.

- Establishing provisions to ensure the capture of testing data for individual patient records and surveillance purposes and the requirement for participation in external quality assessment to maintain high-quality testing.

Based on currently available information, the Canadian Public Health Laboratory Network recommends that COVID-19 POC serological assays not be used for routine clinical or immunity testing at this time. In line with recommendations by the National Advisory Committee on Immunization (2), serology testing should not be used to document vaccination status or to assess response to COVID-19 vaccination. As more information becomes available on immunological correlates of protection, duration of immunity, test performance and assays are validated against gold standard serological methods, clinical application of POC assays will be re-evaluated. Molecular testing, such as real-time polymerase chain reaction, remains the primary test method for laboratory confirmation of acute SARS-CoV-2 infection and diagnosis of COVID-19.

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Divergences between healthcare-associated infection administrative data and active surveillance data in Canada

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Abstract

Background: Although Canada has both a national active surveillance system and administrative data for the passive surveillance of healthcare-associated infections (HAI), both have identified strengths and weaknesses in their data collection and reporting. Active and passive surveillance work independently, resulting in results that diverge at times. To understand the divergences between administrative health data and active surveillance data, a scoping review was performed.

Method: Medline, Embase and Cumulative Index to Nursing and Allied Health Literature along with grey literature were searched for studies in English and French that evaluated the use of administrative data, alone or in comparison with traditional surveillance, in Canada between 1995 and November 2, 2020. After extracting relevant information from selected articles, a descriptive summary of findings was provided with suggestions for the improvement of surveillance systems to optimize the overall data quality.

Results: Sixteen articles met the inclusion criteria, including twelve observational studies and four systematic reviews. Studies showed that using a single source of administrative data was not accurate for HAI surveillance when compared with traditional active surveillance; however, combining different sources of data or combining administrative with active surveillance data improved accuracy. Electronic surveillance systems can also enhance surveillance by improving the ability to detect potential HAIs.

Conclusion: Although active surveillance of HAIs produced the most accurate results and remains the gold-standard, the integration between active and passive surveillance data can be optimized. Administrative data can be used to enhance traditional active surveillance. Future studies are needed to evaluate the feasibility and benefits of potential solutions presented for the use of administrative data for HAI surveillance and reporting in Canada.

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Suggested citation: Boulanger V, Poirier E, MacLaurin A, Quach C. Divergences between healthcare-associated infection administrative data and active surveillance data in Canada. Can Commun Dis Rep 2022;48(1):4–16. https://doi.org/10.14745/ccdr.v48i01a02

Keywords: surveillance, healthcare-associated infection, administrative data

Introduction

Each year, many Canadians acquire an infection during their hospital stay that increases morbidity and mortality, and that bears a financial cost to the healthcare system (1). These healthcare-associated infections (HAI) are preventable, measurable, and are the most frequently reported adverse event in healthcare worldwide. Every year, it is estimated that 220,000 Canadian patients develop a HAI (2). Many HAIs are now caused by antimicrobial resistant organisms (AROs), which make them difficult to treat. The Public Health Agency of Canada (PHAC) estimates that approximately 2% of patients admitted to large, academic Canadian hospitals will acquire an infection with an ARO during their hospital stay (3). Surveillance, including monitoring and reporting of HAI, is a critical component of infection prevention and control and needs to be strengthened at the national level. Although coronavirus disease 2019 (COVID-19) did not originate as a HAI, the current

pandemic has revealed how critical it is to have reliable and consistent data in order to formulate an effective response to infection. When asked to provide projections regarding the course of COVID-19 virus, Prime Minister Trudeau said that "….the inconsistency in the data from across Canada is part of the delay in offering a nationwide picture" (4).

In Canada, PHAC collects national data on multiple HAIs through the Canadian Nosocomial Infection Surveillance Program (CNISP); a program established in 1994 as a partnership between PHAC, the Association of Medical Microbiology and Infectious Disease Canada and sentinel hospitals from across Canada (5). The objectives of CNISP are to provide national and regional benchmarks, identify trends on selected HAIs and AROs, and provide key information to help inform the development of federal, provincial and territorial infection prevention and control programs and policies (5). At present, the CNISP network comprises 87 acute-care sentinel hospitals from ten provinces and one territory. The network's goal is to have all Canadian acute care hospitals adopt the CNISP HAI surveillance definitions and contribute data to the national surveillance system (2). Despite the desire to expand the surveillance program, CNISP is limited 1) by funding capacity, 2) by lack of human resources available to participate in national surveillance (2) and 3) because most hospitals already report to their provincial government and are unwilling to enter data twice. As a result, CNISP HAI rates may not provide a complete picture and some segments of the Canadian hospital population are underrepresented—such as smaller, community hospitals (6).

National statistics reported by PHAC relating to HAIs only include data from hospitals that participate in CNISP as they all follow standardized case definitions, methods and case reporting. Currently HAI rates reported by provinces and territories or posted by individual hospitals cannot be combined as case definitions, methods of data collections and calculation of rates vary from hospital to hospital and between provinces and territories (2). Active surveillance is done by Infection Prevention and Control (IPC) practitioners and each province, territory, administrative region or hospital can determine their own surveillance protocols based on local epidemiology and resources, making it difficult to evaluate improvement efforts and compare HAI rates in Canadian hospitals (7).

On the other hand, Canada has a wealth of administrative health data including insurance registries, inpatient hospital care, vital statistics, prescription medications and electronic health record system (8). Exploring the potential of integrating these diverse administrative health data sets could provide a more robust picture of HAIs across Canada.

The hospital discharge abstract database (DAD), housed at the Canadian Institute for Health Information (CIHI), collects demographic and clinical information from patient discharge summaries from all acute care facilities in Canada, except in Québec (Québec has its own discharge abstract database—*Maintenance et exploitation des données pour l'étude de la clientele hospitalière (MED-ÉCHO)*—that reports to CIHI's Hospital Morbidity Database) (9). Information is entered in the database by professional coders from all hospitals and is used by CIHI to produce data and analytic reports. The CIHI's Data and Information Quality Program is recognized internationally for its high standard (10). However, discharge summaries are not standardized across the country and reflect only what is entered into the summary by the attending physician. The CIHI could, however, be a potential partner to support data collection and reporting of HAIs for acute care hospital. We conducted a scoping review to identify existing gaps between administrative data and active surveillance data for healthcare-associated infection surveillance and to propose possible integration strategies to optimize data.

Methods

Research question

The main research question was "What are the discrepancies between HAI administrative data and active surveillance data in Canada?". The research sub-questions were: Are administrative data valid for HAI surveillance? For each type of HAI, what are the discrepancies between administrative data and hospital surveillance data? We performed this scoping review following the PRISMA extension for scoping review (11).

For this review, HAI included *Clostridioides difficile* (*C. difficile*; CDI), catheter-associated bloodstream infection (CLABSI) or catheter-associated urinary tract infection (CAUTI) or urinary tract infection (UTI) (CAUTI), methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant Enterococci (VRE), carbapenem-resistant Enterobacteriaceae (CPE), antimicrobial resistant organism (ARO or AMR), bloodstream infection (BSI), surgical site infections (SSI) and ventilator-associated pneumonia (VAP).

Relevant literature

We performed a search developed in collaboration with a medical research librarian. The inclusion criteria consisted of articles evaluating passive surveillance of specific or various HAIs in Canada. We included articles (qualitative, quantitative and mixed-method studies) published between 1995 and November 2, 2020 in Canada. The search strategy contained terms relative to location (Canada), surveillance, data source and HAI. In addition, we performed a second search with the same terms (except for the location) and only including systematic reviews.

A pilot selection process was carried out to identify databases with relevant studies and three electronic databases were searched: MEDLINE, EMBASE and Cumulative Index to Nursing and Allied Health Literature (CINAHL), in English and French with no date restriction. The search strategies were created on MEDLINE then adapted for the other databases

(**Supplemental Data S1**). After deduplication, two reviewers independently screened citations by title and abstract. Selected articles were evaluated for eligibility at the full-text level. The first reviewer also performed a hand search of the grey literature and reviewed the references list of all eligible and published studies to identify any articles that were not initially captured through electronic search. Conflicts were resolved through discussion until consensus was reached.

Data extraction and quality assessment

An electronic data form was developed on Distiller SR (Evidence Partners, Ottawa, Canada) for this scoping review. The following data were extracted from each article: general information; study details; types of HAI and surveillance; source of data; outcomes and results.

Both reviewers assessed each study's quality/risk of bias of each study using ROBINS-I for non-randomized studies (12) and AMSTAR-2 tool for systematic review (13). Overall, studies were ranked at low, moderate or high risk of bias. Any disagreement or inconsistency between the reviewers were resolved through discussion. The complete data collection and quality assessment items are shown in **Supplemental Data S2**.

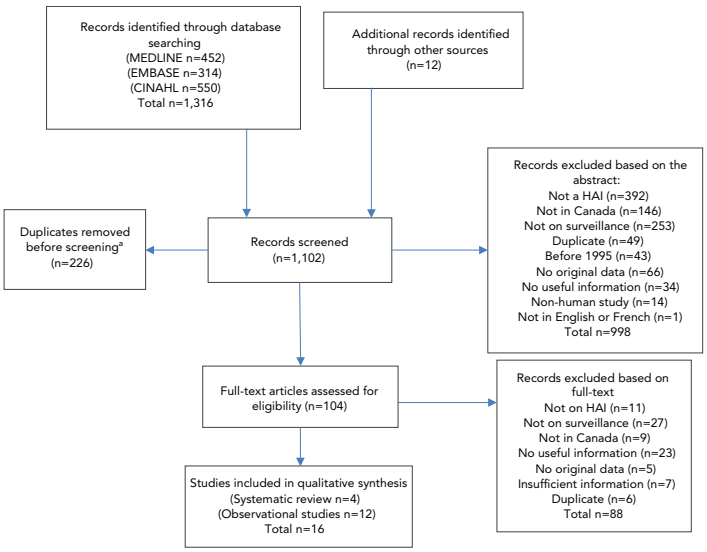
Data analysis

A qualitative descriptive approach was used to synthesize the data collected. Principal studies characteristics, summary of performance statistics and quality assessment scores were summarized into tables. We presented a summary of findings for each study grouping into categories depending on the type of administrative data used and the scope of the study. We focused on how the administrative data were used for HAI surveillance, the divergence in results with traditional surveillance and if author recommended administrative data to enhance surveillance. A synthesis of systematic reviews was also presented with studies categorized as review assessing validity of administrative data or review assessing validity of electronic surveillance system.

Results

Overall, 1,316 studies were identified through the electronic search and 12 from hand searches. After deduplication, 1,102 studies remained, of which 104 were selected for a full-text review. Finally, 16 studies were included in the scoping review from electronic search. Twelve studies were observational studies (14–25), and four were systematic reviews (26–29) (**Figure 1**).

Figure 1: Study identification flow chart



Abbreviation: HAI, healthcare-associated infection
[a] Using EndNote X9.1.1 software

Study characteristics

Of the 12 observational studies included, six focused on SSI, three on CDI, two on MRSA and one on BSI. Studies were performed from 2009 to 2020 and eight were from Alberta. Seven studies compared administrative data with hospital surveillance data and seven studies used data linkage. All studies used DAD as the source of administrative data (alone or combined with other sources). The main characteristics of all included studies are summarized in **Table 1**.

Table 1: Observational studies—Study characteristics

First author, year	Study design	Study population and sample size (n=)	Administrative data source	Condition(s)	Province(s)	Risk of bias
Crocker, 2020	Cohort study	All index laminectomy and spinal fusion procedure cases in Alberta from 2008 to 2015 (n=21,222)	DAD + NACRS[a]	Surgical site infection	Alberta	Low
Ramirez-Mendoza, 2016	Cohort study	All acute-care patients in Alberta and Ontario from April 2012 to March 2013 (n=217)[b]	DAD[a]	Methicillin resistant *Staphylococcus aureus*	Alberta and Ontario	Low
Pfister, 2020	Cohort study	All acute-care patients in Alberta from April 2015 to March 2019 (IPC n=9,557, DAD n=8,617)	DAD[a]	*Clostridioides difficile*	Alberta	Low

Table 1: Observational studies—Study characteristics (*continued*)

First author, year	Study design	Study population and sample size (n=)	Administrative data source	Condition(s)	Province(s)	Risk of bias
Rennert-May, 2018	Cohort study	All primary hip or knee arthroplasty cases in Alberta from April 2012 to March 2015 (n=24,512)	DAD[a]	Surgical site infection	Alberta	Low
Almond, 2019	Cohort study	All acute-care patients in Alberta from April 2015 to March 2017 (n=4,737)	DAD + laboratory data[a]	*Clostridioides difficile*	Alberta	Low
Rusk, 2016	Cohort study	All primary hip or knee arthroplasty cases in Alberta from April 2013 to June 2014 (n=11,774)	DAD + NACRS[a]	Surgical site infection	Alberta	Low
Daneman, 2011	Cohort study	All cesarean delivery cases at Sunnybrook Health Science Centre from January 2008 to December 2009 (n=2,532)	DAD + NACRS + physician claims[a]	Surgical site infection	Ontario	Low
Lethbridge 2019	Cohort study	All hip or knee replacement surgery cases in Nova Scotia from 2001 to 2015 (n=36,140)	DAD + NACRS + physician claims	Surgical site infection	Nova Scotia	Low
Leal, 2010	Cohort study	All adult patient in Calgary Health Region in 2005 (sample of n=2,281)	Cerner's PathNet laboratory + Oracle[c]	Bloodstream infection	Alberta	Low
Lee, 2019	Cohort study	All adult patients in four adult acute-care facilities in Calgary region from April 2011 to March 2017 (n=2,430)	DAD	Methicillin resistant *Staphylococcus aureus*	Alberta	Low
Daneman, 2009	Cohort study	All elderly patients hospitalized for elective surgery in Ontario from April 1992 to March 2006 (n=469,349)	DAD + Ontario Health Insurance Plan + Ontario Drug Benefits database	Surgical site infection	Ontario	Low
Daneman, 2012	Cohort study	All patients (older than one year old) admitted to an acute-care hospital in Ontario from April 2002 to March 2010 (n=180)[b]	DAD[a]	*Clostridioides difficile*	Ontario	Low

Abbreviations: DAD, discharge abstract database; IPC, Infection Prevention and Control; NACRS, National Ambulatory Care Reporting System
[a] Compared with active surveillance data
[b] Number of hospitals
[c] Regional warehouse's Oracle database system

Four systematic reviews were also included, three on the use of electronic surveillance system (ESS) and one on the use of administrative data for HAI surveillance. All reviews included at least one article from Canada. The study characteristics are summarized in **Table 2**.

Within-study risk of bias

Observational studies were assessed for risk of bias using the ROBIN-1 tool (Table 1). Most of these studies used similar methodology but lacked information on missing data (**Supplemental Table S3**). However, they were all assessed as low risk of bias.

Systematic reviews were assessed using the AMSTAR-2 tool (Table 2, **Supplemental Table S4**). One article was considered at moderate risk of bias as it did not report its protocol or describe included studies in adequate details. Three articles were considered at high risk of bias as some did not report their protocol or assess the risk of bias, quality or heterogeneity of included studies.

Summary of findings

Studies using one administrative database compared with active surveillance

Validation studies showed that DAD used alone for capturing HAI cases is not valid in comparison with IPC traditional active hospital surveillance. For example, Rennert-May *et al.* (17) assessed the validity of using the ICD-10 code administrative database (DAD) to identify complex SSIs within three months of hip or knee arthroplasty. The study found that the ICD codes in DAD were highly specific (99.5%) but had a sensitivity of 85.3% and a predictive positive value of only 63.6%. They concluded that DAD was not able to accurately determine if someone had an SSI according to surveillance definition (**Table 3**). Pfister *et al.* (15) came to the same conclusion with a validation study on DAD capturing CDI cases. The CDI rate was 28% higher in the DAD compared to IPC surveillance, showing that DAD seems inadequate to capture true infection incidence. Findings show that the DAD includes recurrent CDI and cannot distinguish

Table 2: Systematic Review—Study characteristics

First author, year	Number of included studies, year	Objective	Databases	Conclusion	Other information	Risk of bias
Van Mourik, 2015	57 studies from 1995 to 2013	Accuracy of administrative data used for HAI surveillance	Medline, Embase, CINAHL, Cochrane	Administrative data had limited and highly variable accuracy	n=1/3 studies included had important methodological limitation	Moderate
Leal, 2008	24 studies from 1980 to 2007	Identify and appraise published literature assessing validity of ESS compared with conventional surveillance	Medline	Electronic surveillance has good utility compared to conventional surveillance	No assessment of quality of studies included	High
Freeman, 2013	24 studies from 2000 to 2011	Assess utility of ESS for monitoring and detecting HAI	Medline, Cochrane, Ovid, Embase, Web of science, Scopus, JSTOR, Wiley Online Library, BIOSIS Preview	Hospital should develop and employ ESS for HAI	Majority of studies have emphasis on linkage of electronic database	High
Streefkerk, 2020	78 studies up to January 2018	Give insight in the current status of ESS, evaluating performance and quality	Embase, Medline, Cochrane, Web of Science, Scopus, CINAHL, Google Scholar	With a sensitivity generally high but variable specificity, ESS as yet to reach a mature stage, need further work	Authors selected 10 best studies that may constitute a reference for ESS development	High

Abbreviations: CINAHL, Cumulative Index to Nursing and Allied Health Literature; ESS, electronic surveillance system; HAI, hospital-associated infections

Table 3: Observational studies—Summary of performance statistics

First author, year	Comparator	Results						Conclusion
		Infection rate	TP, FP, FN, TN, Total	Sensitivity	Specificity	Positive predictive value	Negative predictive value	
Crocker, 2020	DAD + NACRS compared with published traditional surveillance data	2.7 per 100 procedures of laminectomy 3.2 per 100 procedures of spinal fusion	N/A	N/A	N/A	N/A	N/A	Rate reported by administrative data was similar to published rate from traditional surveillance Need validation study to verified results
Ramirez-Mendoza, 2016	DAD compared with IPC data	Alberta (cases per 10,000 patient-days) DAD: 0.43 IPC: 0.91 Ontario (cases per 10,000 patient-days) DAD: 0.25 IPC: 0.21	N/A	N/A	N/A	N/A	N/A	Using Pearson correlation there was good evidence of the comparability of administrative and IPC surveillance data
Pfister, 2020	DAD compared with IPC data	DAD: 6.49 per 1,000 admissions IPC: 5.06 per 1,000 admissions	5,477 TP 1,400 FP 968 FN 344 TN Total: 8,169	85%	N/A	80%	N/A	DAD was moderately sensitive, but likely inadequate to capture true incidence

Table 3: Observational studies—Summary of performance statistics (*continued*)

First author, year	Comparator	Results						Conclusion
		Infection rate	TP, FP, FN, TN, Total	Sensitivity	Specificity	Positive predictive value	Negative predictive value	
Rennert-May, 2018	DAD compared with IPC data	N/A	220 TP 126 FP 38 FN 24,128 TN Total: 24,512	85.3%	99.5%	63.6%	99.8%	Administrative data had reasonable testing characteristics, but IPC surveillance was superior
Almond, 2019	DAD + laboratory data compared with IPC data	DAD/lab (per 10,000 patient-days) 4.96 for HAI IPC (per 10,000 patient-days) 3.46 for HAI	1,998 TP 690 FP 71 FN 1,320 TN Total: 4,079	96.6%	65.7%	74.3%	94.9%	Laboratory surveillance method was highly sensitive, but not overly specific
Rusk, 2016	DAD + NACRS + IPC compared with IPC data alone	DAD/NACRS/IPC: 1.7 per 100 procedures IPC: 1.3 per 100 procedures	N/A	89.9%	99%	N/A	N/A	Medical chart review for cases identified through administrative data was an efficient strategy to enhance IPC surveillance
Daneman, 2011	DAD + NACRS + physician claims compared with IPC data	N/A	N/A	77.3%	87%	17.4%	99.1%	Administrative data had poor sensitivity and positive predictive value and were inadequate as a quality indicator
Lethbridge, 2019	DAD or NACRS compared with DAD + NACRS + physician claim	Difference of 0.44 between DAD or NACRS alone and all data together	N/A	N/A	N/A	N/A	N/A	Rates were underestimated using single-source administrative data

Abbreviations: DAD, discharge abstract database; FN, false negative, FP, false positive, HAI, hospital-associated infections, IPC, Infection Prevention and Control; NACRS, National Ambulatory Care Reporting System; N/A, not applicable; TN, true negative, TP, true positive

symptomatic from asymptomatic cases. In fact, DAD had only a moderate sensitivity of 85% and a positive predictive value of 80% (Table 3).

On the other hand, Daneman *et al.* evaluated if mandatory public reporting by hospital was associated with reduction in hospitals CDI rates in Ontario (23). Aside from the main analysis, they performed a cross-validation of CDI rates from administrative data against rates reported by single institutions via the mandatory public reporting system. They used Pearson correlation coefficients weighted for hospital bed-days and found an excellent concordance across the institutions (23).

The same coefficient was used in the study by Ramirez Mendoza *et al.* (18) that compared DAD with surveillance data for hospital-acquired MRSA in Alberta and Ontario. The results showed strong correlation between DAD and IPC surveillance data. The study concluded that there was good evidence of comparability between these datasets; however, rate or denominator diverged widely between administrative data and active surveillance data (Table 3). Some authors did not agree with the study conclusion or methodology, notably with the choice of Pearson correlation using hospital-level data and the difference of rates or denominators between administrative and surveillance data (30).

Studies combining multiple administrative databases

Results show that combining databases increases the accuracy, yet still not as accurate as traditional active surveillance. Lethbridge *et al.* (24) combined multiple types of administrative data and compared them with a single source administrative data to identify SSIs following hip and knee replacement in Nova Scotia. Used alone, DAD and National Ambulatory Care Reporting System (NACRS) had higher rates than physician billing but underestimated the infection rate with a percentage difference of 44% compared with the combination of the three databases. This implies that approximately 17% of infected cases would have been missed with DAD or NACRS alone. The authors concluded that combining databases enhanced SSI surveillance.

Daneman *et al*. (20) validated the accuracy of DAD, NACRS and physician claim database against traditional surveillance for the detection of cesarean delivery SSI within 30 days of surgery in Ontario. They found a sensitivity of only 16.7% for DAD used alone, 37.9% for DAD combined with NACRS and 77.3% for DAD combined with NACRS and physician claims database. All had a high specificity (87%–98.3%) but a very low predictive positive value (17.4%–27.4%) (Table 3). The authors recommended that the administrative data not be used as a quality indicator for interhospital comparison.

In contrast, Crocker *et al*. (14) compared infection rates calculated using a combination of DAD and NACRS to identify spinal procedure and SSIs. They showed that these rates were comparable with postoperative SSI rate published using traditional surveillance (Table 3). However, the validity of the results was not verified in this study.

Studies combining administrative database with laboratory database

Studies showed that laboratory records could be used to enhance administrative data. For example, Almond *et al.* (25) assessed the validity of a laboratory-based surveillance method to identify hospital-acquired CDI (HA-CDI). Laboratory data alone can result in overestimation of CDI rates, with positive laboratory result not meeting the case definitions for HA-CDI (e.g. asymptomatic colonization, recurrent CDI). However, this study assessed the alternative of linking positive CDI laboratory records to DAD. The study demonstrated a very high sensitivity but a specificity of 65.7% and a positive predictive value of 74.3% (Table 3). These results indicated that 26% of cases classified as HAI were not true HAI cases, resulting in a higher rate observed with this method. In addition, authors completed a receiver operator characteristic (ROC) analysis to see if using a time from admission (collection date−admission date) of ≥4 days was the appropriate algorithm to use for classifying hospital-acquired cases in the laboratory dataset. The ROC analysis indicated that more cases were classified correctly five days after admission. Thus, a simple change in the laboratory detection using longer time from admission to classify cases as healthcare-associated may increase the specificity with a small cost to sensitivity.

Another study from Leal *et al*. pushed one step further by developing an electronic surveillance system (ESS) for monitoring BSI by linking laboratory and administrative databases (21). The ESS included definitions for classifying BSI and their location; nosocomial, healthcare-associated-community onset or community-acquired infection. The system was compared with chart review done by a research assistant and an infectious diseases physician. Chart review and ESS identified 329 and 327 BSI episodes respectively. The authors found high concordance regarding acquisition location of infection (Kappa=0.78) and they were able to improve definitions after *post hoc* revision. Surveillance data obtained through ESS identified and classified BSI with a high degree of agreement with manual chart review.

Studies using administrative data to enhance active surveillance

Studies showed that administrative data can be used to enhance IPC surveillance. Lee *et al.* (16) assessed the benefits of linking population-based IPC surveillance with DAD for hospital-acquired (HA) and community-acquired (CA) MRSA cases in Alberta. This enabled IPC surveillance to have more relevant information available in a timely manner. The authors were able to successfully link 94.6% of the total surveillance records and identify key differences between patients with HA and CA-MRSA, showing that administrative data could be used to enhance hospital surveillance.

Through a retrospective cohort study, Rusk *et al*. (19) evaluated a new strategy to improve traditional IPC surveillance by using administrative data to trigger medical chart review. Eligible patients followed by the IPC team were linked to DAD and NACRS and these administrative databases provided diagnosis and procedure codes for each visit and/or readmission. The strategy using administrative data captured 87% of cases identified by IPC surveillance, with a sensitivity of 90% and specificity of 99%. This confirmed that the administrative data-triggered medical chart review is an efficient strategy to improve SSI surveillance.

Study to improve hospital comparison using administrative data

Daneman *et al*. (22) demonstrated that administrative data (DAD + physician claims) can be used to create a modified Nosocomial Infections Surveillance surgical risk stratification index comparable with the one used for clinical surveillance. This index allowed for the adjustment of infection rate when comparing with other facilities. The study concluded that both administrative and clinical sources can contribute to infection surveillance, with administrative data used to identify patients with possible infections or improving detection of post-discharge diagnoses.

Systematic review and administrative data

Only one study (26) assessed the accuracy of administrative data for surveillance of HAI. Others reviewed articles on ESS using electronic medical records for HAI surveillance compared to traditional surveillance, but included many articles that used a combination of administrative data and ESS (27–29). Administrative data was found to have very heterogeneous sensitivity and positive predictive value, generally low to modest with a particularly poor accuracy for the identification of device-associated HAI (e.g. CLABSI, CAUTI) (**Table 4**) (26,28).

Table 4: Systematic review—Summary of performance statistics by type of hospital-associated infection

First author, year	Number of articles included	Sensitivity (SE), Specificity (SP), Positive Predictive Value (PPV), Negative Predictive value (NPV)					Other information
		SSI	BSI/CLABSI	CDI	Pneumonia/VAP	UTI/CAUTI	
Freeman, 2013	n=44 (SSI=6 BSI=11 UTI=4 Pneumonia=4 Other=8 Multiple HAI=12)	SE=60%–98% SP=91%–99%	SE=72%–100% SP=37%–100%	SE=80%–83% SP=99.9%	SE=71%–99% SP=61%–100%	SE=86%–100% SP=59%–100%	Three studies used single-source data, 37 used multi-source data including laboratory, four used multi-source data excluding laboratory
Van Mourik, 2015	n=57 (SSI=34 BSI=24 Pneumonia=14 UTI=15 Other=7)	SE=10%–100% PPV=11%–95%	**CLABSI** - Sensitivity below 40% for all but one study - SE higher for BSI/sepsis	-	**Pneumonia** SE and PPV around 40% **VAP** SE=37%–72% PPV=12%–57%	SE below 60% PPV below 25% SE higher in UTI than CLAUTI	Gain in sensitivity of almost 10% when combining database Studies with higher risk of bias were more optimistic
Streefkerk, 2020	n=78 (SSI=29 BSI=33 Pneumonia=16 UTI=18)	SE=0.02–1.0 SP=0.59–1.0	SE=0.32–1.0 SP=0.37–1.0	-	SE=0.33–1.0 SP=0.58–1.0	SE=0.02–1.0 SP=0.59–1.0	Sensitivity was generally high, but specificity very variable

Abbreviations: BSI, bloodstream infection; CAUTI, catheter-associated urinary tract infection; CDI, *C. difficile* infection; CLASBI, catheter-associated bloodstream infection; SSI, surgical site infection; UTI, urinary tract infection; VAP, ventilator-associated pneumonia; -, no result presented in this study

In general, the highly variable accuracy for administrative data was mainly due to the amount of different diagnostic codes used between studies (26). Van Mourik *et al.* assessed the accuracy of administrative data. One-third of included study had important methodological limitations and ones with higher risk of bias were associated with a more optimistic picture than those employing robust methodologies (26). On the other hand, Leal *et al.* found a good sensitivity and excellent specificity for administrative data (**Table 5**) (29). However, populations and methodologies were very heterogeneous, and the quality of the studies included in the review was not assessed. All four reviews found that combining administrative data sources with other sources for surveillance, in particular with microbiology data, improved the accuracy. Studies also found that microbiology data had a good sensitivity (28,29); however, Freeman *et al.* concluded that ESS using microbiology data alone tended to overestimate HAI (27). Streefkerk *et al.* (28) also found that microbiology data combined with antibiotic prescription and laboratory (biochemistry, hematology, etc.) data were more accurate than microbiology alone (Table 5). Finally, most studies concluded that administrative data were advantageous to track HAI requiring post-discharge surveillance (e.g. SSI).

Systematic review and electronic surveillance system

Results showed that electronic surveillance using algorithms for HAI detection from electronic medical records had not yet reached a mature stage but presented good opportunities and potential. Most concluded that ESS should be developed and used in hospitals, recognizing that these methods can reduce burden associated with traditional manual surveillance (27–29). In fact, sensitivity was generally high and specificity variable for most ESS compared with traditional active surveillance (Tables 4 and 5). Freeman *et al.* found that a lot of computer algorithms for electronic surveillance outperformed manual chart review method (27). A majority of studies in this review emphasized the linkage of electronic databases with "in-house" surveillance system rather than commercial software (27). Streefkerk *et al.* demonstrated that the best ESS used a two-step procedure with cases selection using ESS was followed by confirmatory assessment of selected cases by the IPC team (28). In the same review, seven studies tried to develop an ESS that could find all HAIs, with a sensitivity ranging from 0.78 to 0.99. Leal *et al.* demonstrated that ESS were potentially inexpensive, efficient and could reach a sensitivity of 100% when the infection of interest is defined by the presence of a positive culture (29).

Table 5: Systematic review—Summary of performance statistics by type of surveillance

First author, year	Number of articles included	Sensitivity (SE), Specificity (SP) (range or average)						Other information
		Administrative data	Laboratory data			Administrative data + laboratory data	Other	
			Microbiology	Microbiology + antibiotic prescription	Microbiology + antibiotic prescription + chemistry			
Streefkerk, 2020	n=78 (AD=7, L=61, O=10)	SE=30%[a] SP=94.5%[a]	SE=77% SP=92%	SE=92% SP=86%	SE=93% SP=94%	-	SE=86% SP=90%	In general, good sensitivity for studies using microbiology data
Leal, 2008	n=24 (AD=7, L=6, AD + L=6, O=5)	SE=59%–96%[b] SP=95%–99%[b]	SE=63%–91% SP=87%–99%			SE=71%–95% SP=47%–99%	-	AD + L combined had higher SE but lower SP than for either alone

Abbreviations: AD, administrative data study; L, laboratory data study; O, other; -, no result presented in this study
[a] International Classification of Diseases (ICD) coding only
[b] International Classification of Diseases (ICD) coding + pharmacy + claims databases

However, ESS were less efficient when the infection is diagnosed based on clinical evaluation of symptoms or tests other than a positive microbiology culture. Moreover, the quality of data and linkage may influence the quality of the ESS (29). Freeman *et al.* also concluded that in some studies, the lack of clinical data in an electronic format reduced the ability of ESS to detect HAI (27).

Discussion

Canada has a great wealth of administrative health data collected at the provincial/territorial level from diverse parts of the healthcare system. However, these data are not used to their full potential and their increased use could enhance HAI surveillance efforts and decrease the workload associated with traditional active surveillance. This scoping review explored the use and validity of administrative data used alone or combined with other data sources for HAI surveillance in Canada. Overall, studies showed that using one source of administrative data alone for surveillance of HAI is not sufficiently accurate in comparison with traditional active surveillance. However, combining different sources of data improved accuracy. Moreover, combining administrative data with active surveillance was shown to be an effective strategy to enhance active surveillance and decrease work burden for IPC teams.

Advantage and inconvenience of administrative data

Administrative data are not collected for surveillance purposes. However, they have a lot of attractive characteristics that make them interesting for the enhancement of HAI surveillance. They are inexpensive, available from nearly all healthcare facilities, collected in a consistent manner, subjected to quality check and do not add an administrative burden to clinicians or patients (31). Deterministic linkages can also be performed between databases that collect healthcare number, as each Canadian has a unique identifying health number.

Furthermore, many studies demonstrated that administrative data are advantageous for tracking HAIs requiring post-discharge surveillance (19,20,22,26). This is very important for infections like SSIs, where the majority are developed after discharge (19,32–34). For example, in the study by Rusk *et al.*, 96% of SSI cases were identified after discharge and 43% of confirmed SSI cases were identified at a facility other than where the procedure was performed (19). These results show that conducting active SSI surveillance only at the operative hospital limits SSI detection. The best practices for surveillance of healthcare-associated infection published by Public Health Ontario state that "to date there is no generally accepted method for conducting post-discharge surveillance for SSIs outside the hospital setting… Infection Prevention and Control Professional are encouraged to develop innovative approaches for the detection of post-discharge SSIs that do not interfere with the time spent on other components of their surveillance system" (35). Examples of solutions proposed included the use of administrative databases and electronic screening of patients' records post-discharge for symptoms and signs of infection (35).

Barriers in accurate administrative data for hospital-acquired infection surveillance in Canada

In Canada, CIHI collects clinical data through the Clinical Administrative Databases that consists of two separate databases: The Discharge Abstract Database–Hospital Morbidity Database; and NACRS (36). At this time, CIHI publicly reports on some HAIs such as in-hospital sepsis, UTIs and ARO, most at the national level only, using data collected from DAD. The

CIHI has a comprehensive data quality program and any known quality issues are addressed by the data provider or documented in data limitations documentation available to all users (36). However, there are still many barriers to be overcome before accurate administrative data for HAI surveillance could be produced. Studies show that the lack of accuracy is an important limitation in using administrative data as a quality indicator for hospital comparison. For instance, the variability of medical practice, the documentation and discharge coding amongst facilities, the interpretation of medical coders, the fact that data collection relies on primary care provider and that information is based on their capacity to detect and report a HAI (possible misclassification errors, human errors) (15,19,37,38). Essentially, information is limited by what is reported in the medical chart and depends mainly on adequate clinician documentation.

For example, reporting to the DAD database requires the physician to adequately fill the discharge summary, including HAIs if known. HAIs are usually not detected in real time and may likely be assessed differently by a clinician and the infection prevention and control team, the latter following standardized definitions. The health records department's professional coding specialist then translates charts and discharge summaries into standard codes. A study conducted in 2015–2016 in Alberta interviewed coders on physician-related barriers to producing high-quality administrative data (39). These barriers included incomplete and nonspecific documentation by physicians, physicians and coders using different terminology (e.g. physician diagnostic not in ICD-10 list), lack of communication between coders and physicians (mainly in urban settings) and the fact that coders are limited in their ability to add, modify or interpret physician documentation. Finally, coders are not allowed to use supporting documentation that could increase specificity of diagnostic codes (e.g. laboratory reports) (39). In fact, an important limitation for CIHI is that in general, the physician documentation takes priority over all other documentation, even if laboratory reports or other documentation indicate a different diagnosis. Yet there are multiple studies demonstrating that laboratory data could be used to enhance administrative data (13,21,29,37). Hence, allowing coders to use laboratory data could be a feasible solution to improve coding accuracy.

Integration of administrative data in infection prevention and control surveillance

Studies also demonstrated that the use of administrative data by IPC team can enhance HAI surveillance and reduce the workload for IPC professionals. Lee *et al*. demonstrated that linking surveillance data with administrative data allows to have detailed information in a timely manner and they urged jurisdictions and healthcare systems to consider adopting this type of data linkage for surveillance practices (16). Rusk *et al*. demonstrated an efficient strategy to identify potential SSI cases for further IPC review using administrative data codes, improving case-finding consistency and reducing time and resources needed (19). All these studies showed that administrative data can be used to enhance traditional surveillance by IPC team. The reverse could also be true. As noted previously, coders can only use physician documentations to report diagnoses. On the other hand, traditional surveillance by IPC professional is considered the gold-standard of surveillance and results in accurate data. If coders could access IPC surveillance outcome, this may enhance the validity of physician documentation and interpretation by coders.

Integration of administrative data in electronic surveillance systems

Another potential approach to make surveillance less labor-intensive is to use electronic surveillance systems. In the current review, seven observational studies used data linkage of electronic databases and three systematic reviews assessed electronic surveillance systems. Leal *et al*. developed a complete ESS to identify and classify BSI with a high degree of agreement with manual chart review (21). Results from the systematic review by Freeman *et al*. suggested that ESS implementation is feasible in many settings and should be developed by hospitals (27). The ESS can also be developed to detect more than one HAI. Moreover, the systematic review by Steefkerk *et al*. on ESS presented the 10 best studies selected based on the overall quality and performance score, and the majority used a two-step procedure using administrative, electronic medical records or microbiology data followed by a confirmatory assessment by the IPC professional (28). In this case, ESS could be designed to favor sensitivity over specificity, knowing that manual review will exclude false positives (31). Streefkerk *et al*. presented seven studies with ESS that could detect all HAIs (28). Their review even included one study describing an excellent performing algorithm to detect HAI in real time with a sensitivity of 0.99 and a specificity of 0.93; HAIs included UTI, BSI, respiratory tract infection, gastrointestinal tract infection, skin and soft tissue infection and other infections (parotitis, chickenpox, neurological infections, etc.) (40). However, these seven studies were not performed in Canada. In fact, other countries already have electronic data in place in their facilities and implementation of ESS for HAI surveillance is thus feasible. In Canada, not all hospitals have access to a good electronic health record system.

Some provinces are good models for surveillance using electronic data. For example, most studies included in this scoping review were from provinces that have electronic systems (e.g. Alberta, Ontario). Alberta is a good example for HAI surveillance as all acute-care sites conduct traditional surveillance using a single surveillance protocol and a centralized online data entry system (41). This system allows administrative information to be shared between all its facilities. Québec also has a centralized electronic system created for the *Surveillance Provinciale des Infections Nosocomiales* program using uniform definitions to detect HAI (42); however, no study from Québec met our inclusion criteria. One study by Gilca *et al*. is worth considering:

this study included 83 acute-care hospitals participating in CDI surveillance in the province of Québec (43). Authors compared administrative and surveillance data and found an excellent agreement between rates obtained from MED-ÉCHO (hospital discharge database) and CDI incidence according to provincial surveillance. However, the origin of acquisition for CDI cases was not indicated in the administrative database. Thus, it was not possible to separate nosocomial from community-acquired cases with only the use of administrative data.

A study conducted in three states in the United States and in the province of Ontario, Canada assessed the information technology challenges and strategies of developing and implementing a multihospital electronic system to prevent MRSA (44). They included 11 hospitals, all with an understaffed information technology group, and with seven different systems having unique information technology structure and unique data system. They found innovative strategies to enable automated collection, sharing, analysis and reporting of data in a compatible format for all hospitals. The study was published in 2013, and authors are currently applying the same strategies to develop ESS for other HAIs. This study is a good example of the feasibility of implementing ESS using different hospital systems.

Strengths and limitations

We used standardized and robust methods to identify, review and assess quality of the published literature with all steps performed by two independent reviewers. Two different search strategies were used to ensure that all Canadian studies were included as well as systematic reviews that included at least one study in Canada. Our review included a small number of studies; however, we are confident that our search strategies combined with hand-search captured all relevant available articles. This is the first review to report on divergences between administrative data and surveillance data for HAI surveillance in Canada.

This review has several limitations. We included only studies that were published in French or English; however, as French and English are the two official languages in Canada, we do not expect to have missed important studies. Observational studies identified represent only three Canadian provinces, with two-thirds of the studies from Alberta. Alberta has a province-wide integrated healthcare system that is easily queried, which is not the case with the systems in the remaining provinces. While our review included both articles published in English or French, our search was conducted using only English terms. We searched only three databases and we may have missed relevant articles included in other databases. This study was conducted on Canadian data only and may not be generalizable to other countries.

Conclusion

This scoping review identified numerous divergences between administrative data and active surveillance data for HAI surveillance in Canadian hospitals. However, it also identified possible solutions, depending on the HAI under surveillance, and demonstrated that administrative data can be used to enhance HAI surveillance. Electronic surveillance systems have the potential to save time and human resources and combining multiple administrative datasets may also improve data accuracy. The IPC team who used administrative data or electronic surveillance systems were able to reduce their workload in active surveillance. Although active surveillance of HAIs produced the more accurate results and remains the gold-standard, further studies on HAI surveillance in Canada should focus on the feasibility of data sharing between provinces through electronic systems, the feasibility for medical coders to have access to documentation other than physician documentation, and the feasibility of using administrative data to help reduce the burden of active surveillance.

Authors' statement

VB — Conceptualization, methodology, investigation, validation, formal analysis, writing–original draft
EP — Investigation, validation, writing–review
AM — Conceptualization, resources, writing–review and editing, funding acquisition
CQ — Conceptualization, writing–review & editing, supervision, funding acquisition

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

Competing interests

None of the authors had any conflicts of interest to disclose.

Acknowledgements

V Boulanger and E Poirier are supported through a MITACS Accelerate/ Healthcare Excellence Canada internship. We thank M Clar for her assistance in the literature search strategy. L Prelude and A Chapman for their support and D Diallo for her assistance with English translation. C Quach is the Tier-1 Canada Research Chair in Infection Prevention: from hospital to the community.

Funding

This work was funding by Healthcare Excellence Canada and MITACS Accelerate and Healthcare Excellence Canada.

Supplemental material

These documents can be accessed on the Supplemental data file.

Supplemental Data S1
Supplemental Data S2
Supplemental Table S3
Supplemental Table S4

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COMMENTARY

The Yukon's experience with COVID-19: Travel restrictions, variants and spread among the unvaccinated

Sara McPhee-Knowles[1]*, Bryn Hoffman[2], Lisa Kanary[1]

Abstract

The Yukon's experience with coronavirus disease 2019 (COVID-19) has been an interesting one; the territory successfully implemented travel restrictions to limit importing the virus and rolled out vaccines quickly compared to most Canadian jurisdictions. However, the Yukon's first wave of COVID-19 in June and July 2021 overwhelmed the healthcare system due to widespread transmission in unvaccinated children, youth and adults, despite high vaccination uptake overall and mandatory masking. This experience highlights the importance of continued support for public vaccination programs, widespread vaccine uptake in paediatric populations, and the judicious relaxation of non-pharmaceutical interventions in all Canadian jurisdictions as they reopen while more contagious variants emerge.

Suggested citation: McPhee-Knowles S, Hoffman B, Kanary L. The Yukon's experience with COVID-19: Travel restrictions, variants and spread among the unvaccinated. Can Commun Dis Rep 2022;48(1):17–21. https://doi.org/10.14745/ccdr.v48i01a03

Keywords: COVID-19, Yukon Territory, pandemic response, travel restrictions, vaccination, outbreak, northern Canada

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Introduction

The coronavirus disease 2019 (COVID-19) trajectory across Canada has been an uneven one, and the Yukon Territory, Canada is an interesting case. From March 22, 2020, to June 1, 2021, there were 62 cases and two deaths due to COVID-19 in the Yukon (1). An important feature of the Yukon's public health strategy was implementing travel restrictions, where, similar to the Atlantic provinces, travellers entering the territory had to self-isolate for 14 days. The Yukon has a small, sparse population and, thanks to few access points, was able to enforce travel restrictions to limit imported cases. However, in June and July 2021, shortly after lifting some restrictions, the Yukon experienced its first wave of COVID-19 with community transmission, despite having the highest vaccination rate in Canada by the end of May (2). From June 1 to August 2, 2021, Yukon reported 541 new cases of COVID-19 as part of three distinct outbreaks and six deaths in a population of about 42,000 (3). Most people who became ill were unvaccinated (4), with only 14% of cases fully vaccinated, and none of the COVID-19 patients who died were fully vaccinated (1). On July 28, 2020, the government reported that a total of 52 people were hospitalized during this wave; of that group, 43 were unvaccinated or only partially vaccinated. Fourteen cases, 11 of whom were unvaccinated, were in critical condition and were medically evacuated to larger centers (5). In this commentary, we present the Yukon's experience with the COVID-19 pandemic and highlight lessons learned from its late wave of COVID-19 in June and July 2021.

Background

The Yukon is Canada's second smallest jurisdiction by population. About 75% of the population lives in Whitehorse, the territory's capital, and the remainder in 15 smaller communities (3). There are three hospitals. Whitehorse General, the largest, has 56 beds, a range of services including a four-bed intensive care unit, and accommodates 32,000 emergency visits and 3,703 admissions per year. Two community hospitals in Watson Lake and Dawson City have emergency services and six bed inpatient units each, with 112 and 80 admissions per year and 2,627 and 2,812 emergency visits annually, respectively (6). This overall hospital capacity is historically adequate for the population; however, medical evacuation or medical travel is often required for high acuity cases or those requiring specialist care (7). This leaves the Yukon at higher risk during the COVID-19 pandemic, as a significant outbreak could overwhelm healthcare capacity. If cases are also surging in other jurisdictions, medical evacuation to larger centres, such as Vancouver or Edmonton (8), may not be possible.

Following devolution in 2003, the Yukon territorial government assumed responsibility for public health, along with other provincial powers, from the Canadian federal government. Eleven of the 14 Yukon First Nations are self-governing and able to draw responsibilities from the territorial government, including some related to health, after they pass their own legislation (9). In the 2016 census, approximately 23% of the population identified as having Indigenous ancestry (10). The Yukon's economy is largely based on government; Yukon depends heavily on federal transfers (11). Mining, services and tourism are also important drivers. Because of self-isolation requirements following travel, tourism decreased by 25% in the first quarter of 2020 compared to 2019 (12). The unique demographic, economic and institutional context of the Yukon influenced the pandemic response.

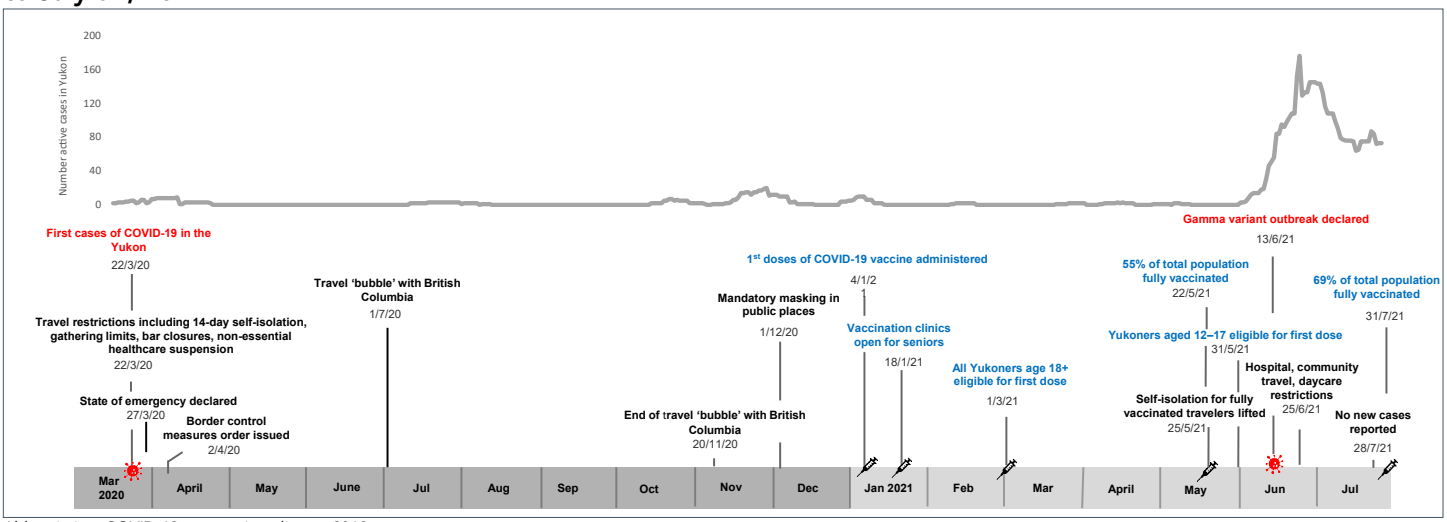
Pandemic response

The Government of Yukon, enabled by its status as a "proto-province" (13), lead the pandemic response; the Council of Yukon First Nations, representing Yukon First Nations governments, also played a role in coordination and communication. Early on, the Yukon government enacted typical public health restrictions such as restricting gatherings, closing bars and personal care services, and suspending healthcare services. The first cases of COVID-19 in Yukon were announced on March 22, 2020 (**Figure 1**), after restrictions were in place. Restricting out-of-territory travel as of March 22, 2020, limited importing cases into the Yukon: a 14-day self-isolation was required for all travellers entering the territory. Yukoners were requested to limit their rural community travel, and some First Nations governments set up check points into their traditional territories. A border control measures order was issued on April 2, 2020, to enforce self-isolation requirements at border entry points (14). A travel "bubble" with British Columbia was established on July 1, 2020, allowing travel between the two jurisdictions without self-isolation; however, the bubble ended on November 20, 2020, after cases began increasing in the Yukon (15). These travel restrictions effectively prevented a major COVID-19 outbreak in the Yukon for the first year of the pandemic. Mandatory masks for Yukoners over the age of five years in public places were instituted on December 1, 2020—one of the last Canadian jurisdictions to mandate mask-wearing (16) since there had been such limited COVID-19 cases present in the Yukon (Figure 1).

The first doses of the Moderna COVID-19 vaccine were administered in Yukon on January 4, 2021, earlier than Canadian provinces because of the territory's limited hospital capacity. Mobile vaccination teams were deployed to communities outside of Whitehorse (17). As of May 22, 2021, 55.22% of the total population was fully vaccinated (2). Self-isolation requirements were lifted on May 25, 2021 for fully vaccinated domestic travellers, or for fully vaccinated Yukoners returning after domestic travel (Figure 1) (18). This announcement created an additional incentive for vaccination.

Shortly after self-isolation requirements for travellers were lifted, an outbreak of the Gamma variant was declared on June 13, 2021 (Figure 1) (19). Transmission occurred at secondary school graduation parties, bars (20), daycares and the Whitehorse Emergency Shelter; transmission was mostly in unvaccinated adults, youth and children (4). Graduation season facilitated disease transmission because graduates and family members travelled between communities, and attended both informal, unmasked, celebrations and larger, organized gatherings with COVID-19 measures in place. In fact, the outbreak can be linked back to a single infected individual who attended a large party (20). On July 14, 2021, 240 of 414 cases had been confirmed as the Gamma variant (21).

Figure 1: Timeline of key events related to the COVID-19 pandemic in Yukon Territory, Canada from March 1, 2020 to July 31, 2021



Abbreviation: COVID-19, coronavirus disease 2019

Yukon's Chief Medical Officer of Health encouraged those not yet vaccinated to book appointments and for all Yukoners to "stick to six" people for gatherings, but lowered formal gathering limits to 10 indoors with masks and 20 outdoors (22). Other public health measures included cancelling some graduation events (23), urging parents to keep children home from daycare (22) and increased restrictions by the Yukon Hospital Corporation (4). Cases were present in most Yukon communities. Many Yukon First Nations requested that travellers refrain from visiting. Contact tracing, testing and vaccination teams were at capacity; the Premier requested additional support from the federal government (22). On July 28, 2021, no new cases were reported for the first time since June 5, 2021; as of July 31, 2021, 68.63% of the total population was fully vaccinated (Figure 1) (2). All remaining public health restrictions were lifted on August 4, 2021, including the requirement for travellers who were not vaccinated to self-isolate and mandatory indoor masking (24); this decision received some public criticism, including from the Kwanlin Dün First Nation's chief (25).

Insights

Some insights can be gleaned from Yukon's experience with COVID-19. The first is the importance of mitigating case importations through self-isolation requirements for travellers entering a region. To illustrate, modeling studies for Newfoundland demonstrated that without introducing a self-isolation requirement for travellers, there would have been 12.4 times more COVID-19 cases in the early weeks of the pandemic (26). Managing case importations is critical in small jurisdictions with limited hospital capacity, such as the Yukon, Northwest Territories and Nunavut. Remote regions may also be able to monitor entry points more easily than larger, better-connected centers. This policy choice meant that the tourism industry was disproportionately affected compared with many other Yukon businesses, and it will not be sustainable in the long-term under these conditions.

A further consideration for the Yukon, and other jurisdictions that did not experience high COVID-19 case counts earlier in the pandemic, was that moving forward with reopening plans meant increasing cases and therefore risk, compared with areas that reopened due to decreasing case counts. There was also a question of timing; reopening shortly before graduation, when there was increased travel between Yukon communities, likely contributed to the rapid outbreak spread.

A central insight, of importance in late 2021 as other Canadian jurisdictions reopened, is that high vaccination rates and mandatory masking were not enough to prevent outbreaks in unvaccinated populations, which put a strain on the local healthcare system. Secondary school students, as part of the 12–17 year age group, were not eligible for vaccination prior to reopening (27), whereas children in daycare were too young to be vaccinated, and some communities had lower vaccination rates than others (28). Policy decisions based on an overall percentage of vaccinated people ignore that unvaccinated groups, because of age or lifestyle, tend to interact, which facilitates disease spread.

Although children do not typically suffer severe illness from COVID-19 (29), daycares were hotspots in Yukon's summer outbreak (22). To manage the outbreak, the Chief Medical Officer of Health recommended that parents who are not essential workers keep their children home if possible. As parents are limited in their ability to work without access to reliable childcare and typically women bear more of the burden for childcare responsibilities, which has been exacerbated by the pandemic (30), this recommendation came with economic consequences that disproportionately impacted women. Currently, children younger than five years of age are ineligible for vaccination and are therefore vulnerable to the more contagious variants of COVID-19.

Conclusion

A lesson can be taken from the Yukon's experience: travel restrictions in the remote region were effective at mitigating disease importation early during the pandemic, but once these restrictions were removed, the highly contagious Gamma variant circulated in unvaccinated populations. Even with high vaccine uptake and masking, outbreaks occurred that strained public health and healthcare capacity. This is a cautionary tale for other jurisdictions as public health measures are being removed and vaccine uptake has plateaued. Extended COVID-19 disease burden in the Yukon could include unintended consequences, such as more paediatric cases, daycare and school closures and their associated economic and mental health impacts, more difficulties for businesses, and an overburdened healthcare system. These impacts are also being seen elsewhere in Canada during the fourth wave. Widespread vaccination across age groups and communities is needed to reduce the severity of future COVID-19 waves.

Authors' statement

All authors contributed to conceptualization, writing, as well as review and editing, of this commentary.

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

Competing interests

None.

Acknowledgements

The authors would like to thank R Hulstein for his thoughtful comments on an earlier draft.

Funding

Financial support for this study was provided by the Yukon University Scholarly Activity Grant.

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Epidemiological analysis of the emergence and disappearance of the SARS-CoV-2 Kappa variant within a region of British Columbia, Canada

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Abstract

Background: The Kappa variant is designated as a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant of interest (VOI). We identified 195 Kappa variant cases in a region of British Columbia, Canada—the largest published cluster in North America.

Objectives: To describe the epidemiology of the Kappa variant in relation to other circulating SARS-CoV-2 variants of concern (VOC) in the region to determine if the epidemiology of the Kappa variant supports a VOI or VOC status.

Methods: Clinical specimens testing positive for SARS-CoV-2 collected between March 10 and May 2, 2021, were screened for the detection of known circulating VOCs; approximately 50% of specimens were subsequently selected for whole genome sequencing (WGS). Epidemiological analysis was performed comparing the characteristics of Kappa cases to the main circulating variants in the region (Alpha and Gamma) and to non-VOC/VOI cases.

Results: A total of 2,079 coronavirus disease 2019 (COVID-19) cases were reported in the region during the study period, of which 54% were selected for WGS. The 1,131 sequenced cases were categorized into Kappa, Alpha, Gamma and non-VOC/VOI. While Alpha and Gamma cases were found to have a significantly higher attack rate among household contacts compared to non-VOI/VOC cases, Kappa was not.

Conclusion: Epidemiological analysis supports the designation of Kappa as a VOI and not a VOC. The Alpha and Gamma variants were found to be more transmissible, explaining their subsequent dominance in the region and the rapid disappearance of the Kappa variant. Variant surveillance strategies should focus on both detection of established VOCs and detection of potential new VOCs.

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Suggested citation: Ghafari C, Benusic M, Prystajecky N, Sbihi H, Kamelian K, Hoang L. Epidemiological analysis of the emergence and disappearance of the SARS-CoV-2 Kappa variant within a region of British Columbia, Canada. Can Commun Dis Rep 2022;48(1):22–6. https://doi.org/10.14745/ccdr.v48i01a04

Keywords: SARS-CoV-2, COVID-19, Kappa variant, variant of concern, variant of interest, variant surveillance

Introduction

The B.1.617 severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant was designated as the fourth variant of concern (VOC) by the World Health Organization (WHO) in May 2021 due to concerns of higher transmissibility and potential decreased effectiveness of treatment and vaccines (1). Since then, B.1.617 has been further delineated to B.1.617.2 (Delta), which remains a VOC, and B.1.617.1 (Kappa), now a variant of interest (VOI) (2). Concern remains with Kappa as a spike in cases in late May 2021 prompted control measures in Australia (3). In this article, the epidemiology of Kappa within a region of British Columbia, Canada, from March 10 to May 2, 2021 is reported in relation to other circulating variants. The objective of this analysis is to determine if the epidemiology of Kappa supports this downgrading to a VOI status, or if Kappa is epidemiologically similar to concurrently circulating VOCs.

Methods

Between March 10 and May 2, 2021, clinical specimens testing positive for SARS-CoV-2 were screened for VOC detection by a quantitative polymerase chain reaction assay targeting the N501Y and E484K mutations in the spike gene, allowing for detection of Alpha, Beta and Gamma variants (4). If positive for N501Y, samples were presumptive positive for Alpha; if positive for N501Y and E484K, samples were presumptive positive for Beta and Gamma; if negative for N501Y and E484K, samples were not a VOC; and if negative for N501Y and positive for E484K, samples were not a VOC. Approximately 30% of VOC-positive and 20% of VOC-negative specimens were selected for whole genome sequencing (WGS).

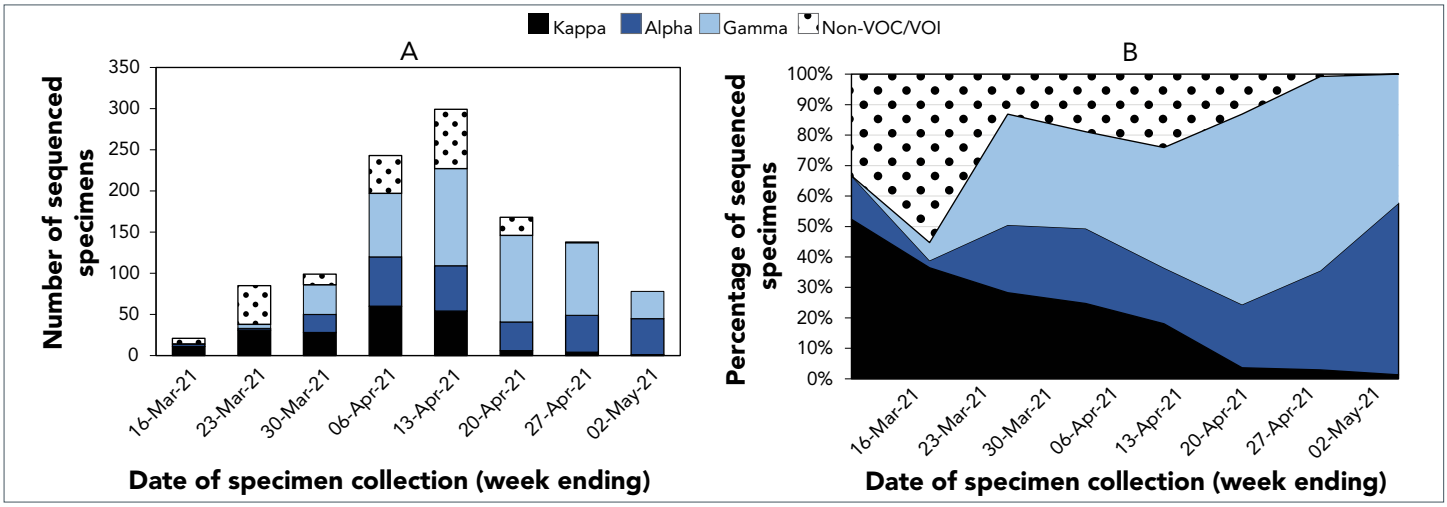
Once Kappa was detected in the region, sequencing of select additional VOC-negative specimens was carried out based on geography and contact tracing interviews (n=162). Specimens were sequenced using a 1,200 bp amplicon-based sequencing approach (5) on an Illumina MiSeq or NextSeq. The SARS-CoV-2 consensus sequences were generated using a modified Nextflow pipeline for the ARTIC network's field bioinformatics tools (6). Lineages were assigned using Pangolin (version 2.4.2, pangoLEARN (7)) and sequencing quality control (QC) metrics were assessed using nCoV-tools (version 1.5.1). Specimens with more than 85% genome coverage and no QC flags (i.e. excess ambiguity) were used in subsequent analyses. Phylogenetic analysis occurred using the Nextstrain project, an open-source platform for analyzing and visualizing genomic data. Augur version 10.2.0 and Auspice version 2.21.0 were used for bioinformatic analysis and visualization of data, respectively. Consensus sequences have been deposited to GISAID (Global Initiative on Sharing Avian Influenza Data).

Kappa was compared with non-VOCs or VOIs according to WHO criteria (8), and to the main circulating VOCs in the region, Alpha and Gamma. Epidemiological indicators included pertained to demographics and criteria used to establish VOCs: transmissibility; virulence; and vaccine effectiveness. Transmissibility assessment was limited to household contacts to control for variable intensity and duration of contact that occurs in the community. Virulence was assessed by hospitalization within 14 days of specimen collection and death attributed to coronavirus disease 2019 (COVID-19) by June 1, 2021. Cases were categorized into vaccine status of either no recorded dose, partially vaccinated (at least 14 days after 1st dose) and fully vaccinated (at least 14 days after 2nd dose). Statistical analysis was performed comparing Kappa to Alpha and Gamma cases, Kappa to non-VOC/VOI cases, and Alpha and Gamma to non-VOC/VOI cases. Chi-square or Kruskal Wallis tests were performed using STATA (Release 16; StataCorp LLC), with statistical significance set at alpha=0.05.

Results

Between March 10, 2021, and May 2, 2021, 2,079 COVID-19 cases were reported in the Island Health region; 54% of specimens were selected for WGS. The proportion of specimens sent for WGS remained relatively stable throughout the study period. An epidemic curve of 1,131 sequenced cases categorized into Kappa, Alpha, Gamma and non-VOC/VOI is shown in **Figure 1**. The first Kappa specimen was collected on 10 March 2021 and initially detected in approximately half of sequenced cases in the Island Health region. While the number of Kappa cases per week increased and peaked at over 50 per week in the first two weeks of April 2021, the relative proportion of Kappa cases decreased due to the large relative increase of Alpha and Gamma cases. As of 14 July 2021, the last Kappa case was reported on May 2, 2021. Nineteen Delta and four Beta cases were detected and excluded from this analysis as they were relatively rare VOC/VOIs in the region during this period.

Figure 1: Number (A) and percentage (B) of COVID-19 cases sequenced specimens[a] confirmed within the Island Health region of British Columbia, Canada, March 10–May 2, 2021



Abbreviations: COVID-19, coronavirus disease 2019; VOC, variant of concern; VOI, variant of interest
[a] As Kappa, Gamma or non-variant of concern/variant of interest

Table 1 compares the characteristics of Kappa, Alpha and Gamma and non-VOC/VOI cases. Age distribution was similar between Kappa and non-VOC/VOI cases, but significantly different compared with Alpha and Gamma cases ($p<0.01$). Just over half of Kappa cases were female (52.8%), while the majority of Alpha and Gamma and non-VOC/VOI cases were male (53.9% and 58.2%, respectively). The suspected source was similar for the three variant categories, with approximately three quarters of the cases (73.0%–77.3%) linked to a confirmed case or cluster and the rest unknown. One Kappa case was linked to international travel and was not epidemiologically responsible for the primary introduction of Kappa into the region. No significant difference was detected in the attack rate among household contacts between Kappa and Alpha and Gamma (33.7% vs. 37.7%) or non-VOC/VOI (33.7% vs. 27.7%). However, Alpha and Gamma had a statistically higher attack rate compared with non-VOC/VOI (37.7% vs. 27.7%, $p=0.01$). Similar proportions of symptomatic cases were seen across the categories. Hospitalization rates were not significantly lower for Kappa cases compared with Alpha and Gamma cases (1.5% vs. 4.5%, $p=0.06$). Case fatality rates were low (0.5%–0.6%) and statistically similar across all groups. The majority of cases were unvaccinated (95.7%–97.6%) and no statistical differences were seen in vaccine breakthrough cases.

Table 1: Comparison of characteristics of Kappa, Alpha and Gamma and non-variant of concern/variant of interest cases within the Island Health region of British Columbia, Canada, March 10–May 2, 2021

Characteristics of cases	SARS-CoV-2 variant						*p*-value		
	Kappa		Alpha and Gamma		Non-VOC/VOI		Kappa vs. Alpha and Gamma	Kappa vs. non-VOC/VOI	Alpha and Gamma vs. non-VOC/VOI
	n	%	n	%	n	%			
Demographics									
Number of cases (total=1,131)	195	17.2	728	64.4	208	18.4	N/A	N/A	N/A
Median age in years (IQR)	34	21–54	33	23–50	36	25–56	0.63	0.46	0.10
Age group (years)									
0–17	31	15.9	110	15.1	29	13.9	<0.01	0.96	<0.01
18–44	88	45.1	382	52.5	99	47.6			
45–64	46	23.6	178	24.5	51	24.5			
65–74	16	8.2	46	6.3	16	7.7			
75+	14	7.2	12	1.7	13	6.3			
Sex									
Female	103	52.8	336	46.2	87	41.8	0.10	0.03	0.27
Male	92	47.2	392	53.9	121	58.2			
Suspected source[a]									
International travel	1	0.6	1	0.2	0	0.0	0.34	0.58	0.39
Linked to confirmed case or cluster	131	73.2	525	77.3	138	73.0			
Unknown	47	26.3	153	22.5	51	27.0			
Transmissibility									
Attack rate among household contacts	67/199	33.7	217/576	37.7	52/188	27.7	0.20	0.31	0.01
Virulence									
Symptomatic	171	87.7	629	86.4	183	88.0	0.64	0.83	0.45
Hospitalized within 14 days of specimen collection	3	1.5	33	4.5	8	3.9	0.06	0.16	0.67
Deaths attributed to COVID-19	1	0.5	5	0.6	1	0.5	0.79	0.96	0.64
Vaccine effectiveness									
No recorded dose	188	96.4	697	95.7	203	97.6	0.83	0.48	0.45
Partially vaccinated	7	3.6	30	4.1	5	2.4			
Fully vaccinated	0	0	1	0.1	0	0			

Abbreviations: COVID-19, coronavirus disease 2019; IQR, interquartile range; N/A, not applicable; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VOC, variant of concern; VOI, variant of interest

[a] 84 cases were excluded where no exposure category was recorded, representing 7%–9% of each of the variant categories

Figure 2 provides a phylogenetic tree of Kappa cases in this study. Amongst the 195 cases, seven distinct genomic clusters were identified. The genomic clusters mirrored geographic distribution of cases and were consistent with transmission patterns identified through contact tracing interviews. The genomic clusters did not include any cases from other regions of British Columbia. None of the cases in the seven genomics clusters had documented travel histories.

Discussion

While responsible for more than one in six cases over the study period, approximately one third of cases for the first three weeks of the study, and seven distinct genomic and epidemiological clusters, Kappa has disappeared from the region with the last case detected on May 2, 2021. During the same period, Alpha and Gamma became the dominant strains in the region. The finding that Alpha and Gamma had a statistically higher attack rate among household contacts than non-VOC/VOI suggests that collectively these variants are more transmissible, supported by their designation as VOCs. This higher transmissibility may explain why Alpha and Gamma seemed to have outcompeted Kappa, which had a household attack rate statistically similar to non-VOC/VOIs. A similar trend was observed in the United Kingdom where, despite an initial rapid increase in the proportion of Kappa cases, Kappa is now responsible for fewer than 0.1% of recent VOC/VOI cases (8). In India, the proportion of sequenced cases were over 40% Kappa variant in March 2021, but has now fallen to less than 20% as Delta variant has dominated (9).

The lower case hospitalization rate for Kappa compared with Alpha and Gamma seen in this study is consistent with United Kingdom findings where 1.0% of Kappa cases have been hospitalized, compared with 2.8% of Alpha cases, and none of the over 400 cases of Kappa have died (10). While no difference in vaccine breakthrough cases were seen between Kappa and non-VOC/VOI cases in this study, a study using serum from vaccinated individuals showed 2.7-fold reduction in geometric mean neutralization titers against the Kappa variant compared with a non-VOC/VOI strain (11).

Given that Kappa was not circulating in Canada prior to its detection in this region of British Columbia, it is assumed to have been introduced via international travel. The genomic cluster data suggest a single introduction of Kappa into the region, though none of the cases had travel histories. The collection date for the earliest sample (March 10, 2021) is after the Canadian government introduced mandatory testing and quarantine for returning travellers (February 22, 2021). It is possible that the initial introduction preceded the introduction of this program and was not captured through routine testing.

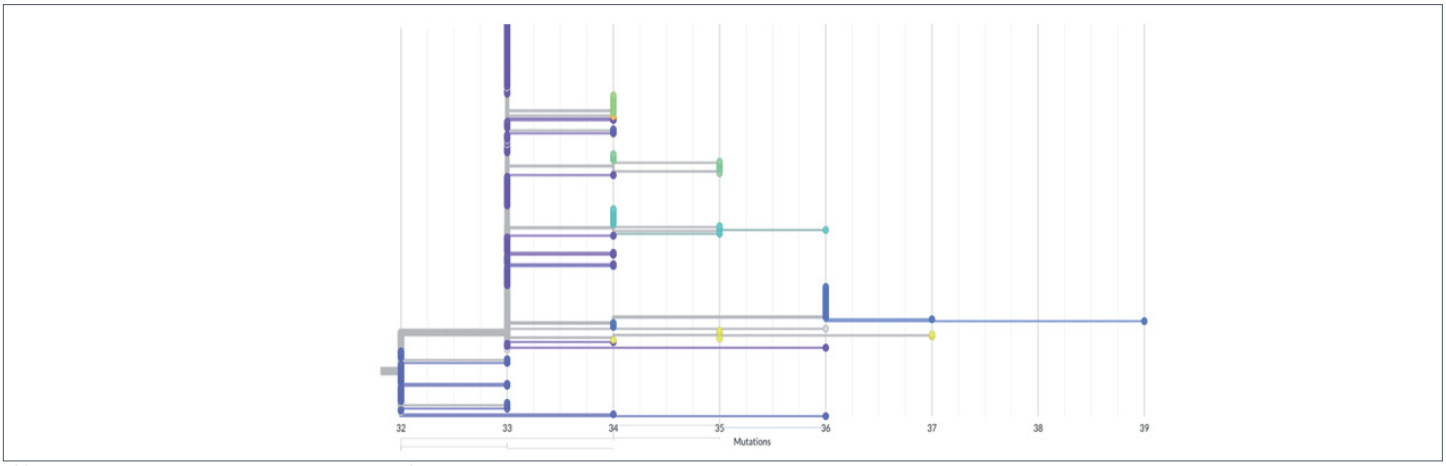
Limitations

This study is likely underpowered, which poses a challenge to determine small differences between Kappa, Alpha and Gamma, and non-VOC/VOI cases. During the study period, there was also high coverage of first dose mRNA vaccine among the most vulnerable (particularly those over 70 years old), and an overall first dose vaccine coverage that rose from ~10% to 25% for adults in the region, which likely reduced the relative risk of infection and severity among vulnerable people, reducing the power of this study to provide distinctions among variant categories.

Conclusion

Conclusions regarding virulence and vaccine effectiveness are difficult to make due to hospitalizations, deaths and vaccine breakthrough cases being relatively rare events; however, the epidemiology of Kappa within the Island Health region of British

Figure 2: SARS-CoV-2 genetic diversity for Kappa cases within the Island Health region of British Columbia, Canada, March 10–May 2, 2021[a]



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

[a] This tree is rooted to the original Wuhan reference strain (MN908947.3) and displays sequences based on the number of mutations that differ from this reference strain (x-axis). Branch colour is based on genetic relatedness, as determined using the Cluster Picker algorithm

Columbia, Canada, supports the assertion by WHO that Kappa does not meet the VOC criteria.

Lastly, the variant surveillance described here emphasizes the importance of performing WGS on at least a portion of cases that are categorized as non-VOC based on polymerase chain reaction of N501Y and E484K mutations. Without WGS of these samples, it is unlikely that Kappa or Delta would have been identified within the region, which guided targeted WGS based on epidemiological links to monitor spread. A similar variant surveillance strategy could be utilized with the intention of maintaining detection of variants which may not share the common mutations found in Alpha, Beta and Gamma variants.

Authors' statement

CG and MB — Analyzed the epidemiological data
NP, HS, KK, LH — Analyzed the genomic data

All authors contributed to the conceptualization, methodology and writing of the manuscript.

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

Competing interests

None.

Acknowledgements

The Island Health Case and Contact Management Surveillance team and Dr. S Allison were involved in management of the cases referred to in this study. Staff at the British Columbia Centre for Disease Control Public Health Laboratory performed variant of concern (VOC) qPCR and sequencing of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) clinical specimens.
Dr. A Jassem and Dr. J Tyson contributed to VOC screening and whole genome sequencing testing.

Funding

None.

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Social inequalities in COVID-19 mortality by area and individual-level characteristics in Canada, January to July/August 2020: Results from two national data integrations

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Abstract

Background: Despite early reports of social determinants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and coronavirus disease 2019 (COVID-19) burden, national Canadian reporting on COVID-19 inequalities has been limited. The objective of this study is to describe inequalities in COVID-19 mortality in Canada using preliminary data, as part of the Pan-Canadian Health Inequalities Reporting Initiative.

Methods: Two provisional Canadian Vital Statistics Death Database integrations were used. Data concerning deaths between January 1 and July 4, 2020, among private-dwelling residents were linked to individual-level data from the 2016 short-form Census, and disaggregated by sex and low-income status, dwelling type, household type and size. Data concerning deaths between January 1 and August 31, 2020 linked to 2016 Census area data were disaggregated by sex and neighbourhood ethno-cultural composition quintiles (based on the proportion of residents who are recent immigrants, visible minorities, born outside of Canada, with no knowledge of English or French), income quintiles and urban residence. The COVID-19 age-standardized mortality rate (per 100,000 population) differences and ratios between groups were estimated.

Results: As of July/August 2020, apartment dwellers, residents of urban centres, neighbourhoods with the highest ethno-cultural composition or lowest income experienced 14 to 30 more COVID-19-related deaths/100,000 compared with reference groups (residents of single-detached homes, outside of urban centres, with lowest ethno-cultural concentration or highest income, respectively). Per 100,000 population, sex/gender inequalities were also larger in these four groups (11 to 18 more male than female deaths) than in the reference groups (two to four more male than female deaths).

Conclusion: These findings highlight how populations facing socioeconomic disadvantage have experienced a higher overall burden of deaths. Areas for future research are discussed to guide health equity-informed pandemic response.

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Suggested citation: Blair A, Pan SY, Subedi R, Yang F-J, Aitken N, Steensma C. Social inequalities in COVID-19 mortality by area and individual-level characteristics in Canada, January to July/August 2020: Results from two national data integrations. Can Commun Dis Rep 2022;48(1):27–38. https://doi.org/10.14745/ccdr.v48i01a05
Keywords: SARS-CoV-2, COVID-19, mortality, social determinants of health, health equity, Canada

Introduction

Early regional (1–3), provincial (4,5) and national (6,7) reporting in Canada has indicated that the burden of coronavirus disease 2019 (COVID-19) has not been experienced equally across all populations. Bivariate analyses suggest that racialized and lower-income populations have experienced higher rates of COVID-19 infection and mortality than white or higher-income groups, across several Canadian jurisdictions (1,2,7). These studies highlight the importance of social and economic

conditions known collectively as social determinants of health (8) in shaping the distribution of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections and COVID-19 morbidity and mortality (9,10).

Several hypotheses have been proposed to explain inequalities in COVID-19 mortality, each tied to underlying social determinants of health (9). First, they may be due to inequalities in SARS-CoV-2 infections due to systemic social and economic inequalities in living or working conditions (9,11,12) in which prevention strategies, such as physical distancing or improved ventilation, are more difficult to apply or have not been implemented (13–15). Second, they may be attributable to long-standing (11) socioeconomic inequalities in the prevalence of underlying conditions and behaviours, such as smoking, obesity or diabetes, that place socioeconomically disadvantaged populations at higher risk of COVID-19 morbidity (16). Third, they may be attributable to underlying socioeconomic inequalities in healthcare access, use and quality (9,11,17).

National-level reporting of COVID-19 mortality across socioeconomic groups in Canada remains limited (18) despite an expressed need from researchers and communities (19–21) to inform equitable pandemic preparedness and response. To fill this gap in national COVID-19 data reporting, this analysis sought to summarize individual and area-level absolute and relative inequalities in COVID-19 mortality that occurred between January and August 2020. This analysis is part of an ongoing effort of the Pan-Canadian Health Inequalities Reporting (HIR) Initiative (11).

Methods

Data sources

Data for this report come from two data integrations performed by Statistics Canada (for which the data integration team included co-authors RS, FJY, NA). Statistics Canada's data integration process refers to the combining two or more datasets. The data integrations described here were performed in the context of the COVID-19 pandemic to inform several studies, including the present one. One of the integrations performed was between the provisional Canadian Vital Statistics Death Database (CVSD) and the 2016 short-form Canadian Census of population (22). This individual-level record linkage was probabilistically linked to the Derived Record Depository in the Social Data Linkage Environment at Statistics Canada (23). The Social Data Linkage Environment is described as a "highly secure environment that facilitates the creation of linked population data files for social analysis. It is not a large integrated data base" (23). Among the provisional death records reported between January 1 and July 4, 2020, 96.4% were probabilistically linked in the Derived Record Depository of the Social Data Linkage Environment. The linkage rate for the short-form census respondents to the Derived Record Depository was 96.8%. This CSVD-Census linked data source includes COVID-19 deaths) that occurred between January 1 and July 4, 2020, for residents of private dwellings which represents 98% of the Canadian population (N=4,430 deaths; 1,990 females, 2,440 males; all counts are rounded in accordance with Statistics Canada's disclosure rules (6,22,24). Deaths that occurred in collective dwellings, including long-term care, were excluded.

The other data integration was between the provisional Canadian Vital Statistics Death Database and the area-level measures via the supplementary geographic information provided on the 2016 Census Postal Code Conversion File plus (PCCF+) (25). This CVSD-PCCF+ linked data source includes COVID-19 deaths that occurred between January 1 and August 31, 2020, regardless of dwelling status (rounded total of 9,265 COVID-19 deaths; 4,990 females, 4,275 males). Among the COVID-19 death records reported between January 1 and August 31, 2020, 99.7% had postal codes found in the PCCF+.

The Canadian Vital Statistics Death Database data are provisional and incomplete for several reasons. Namely, the dataset is sensitive to provincial and territorial reporting delays and it excludes deaths that occurred in the Yukon. However, COVID-19 mortality rates estimated using provisional Vital Statistics data are relatively similar (within 5%) to those obtained using COVID-19 surveillance data (22). In addition, individuals' characteristics recorded in the 2016 Census may have changed by the time deaths were recorded in 2020. Nonetheless, these integrations are the best available sources of national Canadian data regarding the socioeconomic characteristics of COVID-19 deaths. They can provide early evidence about emerging public health issues to guide future research. They also provide baseline information upon which to base future monitoring.

Measures

The outcome studied was COVID-19 mortality, operationalized as cumulative age-standardized mortality rates per 100,000 population (hereafter referred to as "mortality rates per 100,000"; details on standardization are provided below). The Canadian Vital Statistics Death Database identifies COVID-19 deaths based on death certificates where COVID-19 is listed as the underlying cause of death. The ICD-10 codes U071 and U072 were used to identify, respectively, deaths among individuals who had received a positive SARS-CoV-2 test result (regardless of laboratory test used) and individuals identified as "possible" or "probable" cases, or who were "pending a (positive) test result."

Seven stratification measures were used to capture known social determinants of health, as identified in the Social Determinants of Health framework (8). From the integration of provisional Vital Statistics and short form 2016 Census data, four individual-level measures were used (i.e. based on the deceased's personal characteristics, recorded in the Census) to estimate disaggregated rates and inequalities. These measures were as follows: Statistics Canada's household after-tax low-income measure (26) (low-income versus not low-income

[reference group]); dwelling type (i.e. apartment building fewer than five storeys, apartment building with five or more storeys, apartment in a duplex, row house, semi-detached house, versus single-detached house [reference group]) (6); household type (i.e. one-person, couple with children, couple without children, multigenerational household, two-or-more person non-census family household excluding multigenerational households, "other" census family household, versus lone-parent household [reference group]) (6); and household size (i.e. two, three, four, five-or-more person, versus one-person household [reference group]) (6).

From the integration of provisional Vital Statistics and PCCF+ data, three area level (27) measures were used (i.e. measures of the deceased's neighbourhood characteristics at the time of death, based on residential postal code information) to estimate disaggregated rates and inequalities. These measures were as follows: residence inside versus outside (reference group) of a Census Metropolitan Area (CMA) (i.e. large urban centre of 100,000 or more residents (28); after-tax national income per-person-equivalent quintiles (reference group: quintile 5, highest income); and quintiles of the national ethno-cultural composition dimension of the Canadian Index of Multiple Deprivation (reference group: quintile 1, lowest concentration). The latter is a composite indicator that captures the concentration of individuals who are recent immigrants (in the previous five years), designated as a visible minority, born outside of Canada or have no knowledge of either English or French. This type of measure can help capture populations that may be more vulnerable to systemic discrimination and disadvantage. For example, those who immigrate to Canada, particularly individuals identified as visible minorities, can experience structural or institutional forms of discrimination, particularly racial discrimination (i.e. "systemic" racism (29)), in areas such as labour and housing (11,12).

Data were also disaggregated by sex. Though only data on sex (presumed at birth; "female" or "male") was available, this study hereafter refers to "sex/gender inequalities". As done in previous reporting (11), this usage is based on the assumption that the inequalities in COVID-19 mortality between males and females, like with other health conditions, are driven by determinants tied to both constructs of biological sex and gender (11).

Analyses

Rates overall and by sex were age-standardized using the direct method, based on the 2011 standard Canadian population, using age intervals of five years (30). Details on age groups, formulas and weights have been described previously (30). Rates were age-standardized to allow for comparison between groups that may have differences in age structure (30,31). Confidence intervals for these rates were set at 95% and were calculated using the standard error of the standardized rate (details and formulas are provided in **Supplemental Table S1**) (32).

Age-standardized rates and confidence interval estimations were conducted using SAS 9.4 (33) and SAS Enterprise Guide 7.1 (34) software.

To assess relative and absolute inequalities in COVID-19 mortality, rate differences and ratios were estimated between subgroups, overall and by sex (according to principles of Sex and Gender Based Analysis Plus; SGBA+) by subtracting and dividing rates between subgroups, with 95% confidence intervals estimated using the standard error of the rates for each group in the comparison (formulas are provided in Supplement Table S1) (35,36). Figures were created using R software (version 4.0.2) (37). Since the inequality estimates were based on bivariate analyses, e-values (38) were estimated to assess the potential sensitivity of findings to unmeasured confounding. E-values capture the minimum size of an association between an unmeasured confounder and both the social stratification measures and the outcome of COVID-19 mortality risk to explain away an observed risk ratio. The e-value was estimated as follows: $RR_{observed} + \sqrt{\{RR_{observed} * (RR_{observed} - 1)\}}$ (38). Higher e-values indicate that relatively strong confounding associations would be needed to completely explain away the observed exposure–outcome association (38).

Results

Distribution of COVID-19 mortality across sub-populations

At the start of the pandemic, between January 1 and July 4, 2020, COVID-19 mortality rates varied across the individual-level subgroups (**Table 1**). The lowest and the highest rates observed across the subgroups measured were among those living in two types of dwellings, respectively: rates ranged from nine deaths (for residents of single-detached homes) to 23 and 26 deaths (for residents of apartments) per 100,000. Rates were higher among males than females.

Between January 1 and August 31, 2020, COVID-19 mortality rates also varied according to area-level subgroups (**Table 2**). Per 100,000, rates ranged from four deaths (for residents outside of large urban centres) to 33 to 37 deaths (for residents of large urban centres, areas with lowest income and highest ethno-cultural concentration). Rates in these populations were again higher among males than females.

Absolute and relative inequalities in COVID-19 mortality across subgroups

Between January 1 and July 4, 2020, among the subgroups measured, the largest absolute inequalities in COVID-19 mortality among residents of private dwellings were observed between residents of apartments (in duplexes or multi-story

Table 1: Age-standardized mortality rate per 100,000 population among residents of private dwellings, between January 1 and July 4, 2020, across individual-level stratifiers from the 2016 Census, overall and by sex

Stratifiers	Age-standardized mortality rate per 100,000 population					
	Overall		Females		Males	
	Rate per 100,000	95% CI	Rate per 100,000	95% CI	Rate per 100,000	95% CI
Low-income measure status (after tax)						
Not low-income	14	13, 14	11	10, 11	18	17, 19
Low-income	19	18, 20	15	14, 17	27	25, 30
Private dwelling type						
Single-detached house	9	9, 10	7	7, 8	11	11, 12
Row house	13	11, 15	9	7, 11	19	15, 22
Semi-detached house	16	13, 18	12	9, 15	20	16, 24
Apartment in a building with five or more storeys	23	21, 24	18	16, 19	33	30, 35
Apartment in a building with fewer than five storeys	24	23, 26	18	16, 20	36	33, 39
Flat or apartment in a duplex	26	23, 29	19	16, 21	37	32, 42
Household type						
Lone-parent family	13	12, 15	12	10, 13	19	14, 23
Multigenerational household	14	13, 16	13	11, 15	17	14, 20
One person household	15	14, 15	11	11, 12	22	21, 24
Other census family household[a]	15	13, 17	13	11, 16	16	13, 20
Couple without children	16	16, 17	14	12, 15	18	17, 19
Couple with children	19	17, 22	10	7, 14	24	20, 27
Two or more person non-census family (excluding multigenerational)	23	20, 27	19	15, 23	32	25, 39
Household size						
1 person	15	14, 15	11	11, 12	22	21, 24
2 persons	15	15, 16	12	11, 13	18	17, 19
3 persons	15	14, 17	11	9, 12	21	18, 24
4 persons	14	11, 16	11	9, 14	16	12, 19
5 persons or more	17	15, 19	15	12, 17	20	16, 23

[a] This represents all households that are not multigenerational where there is one census family with additional persons or more than one census family

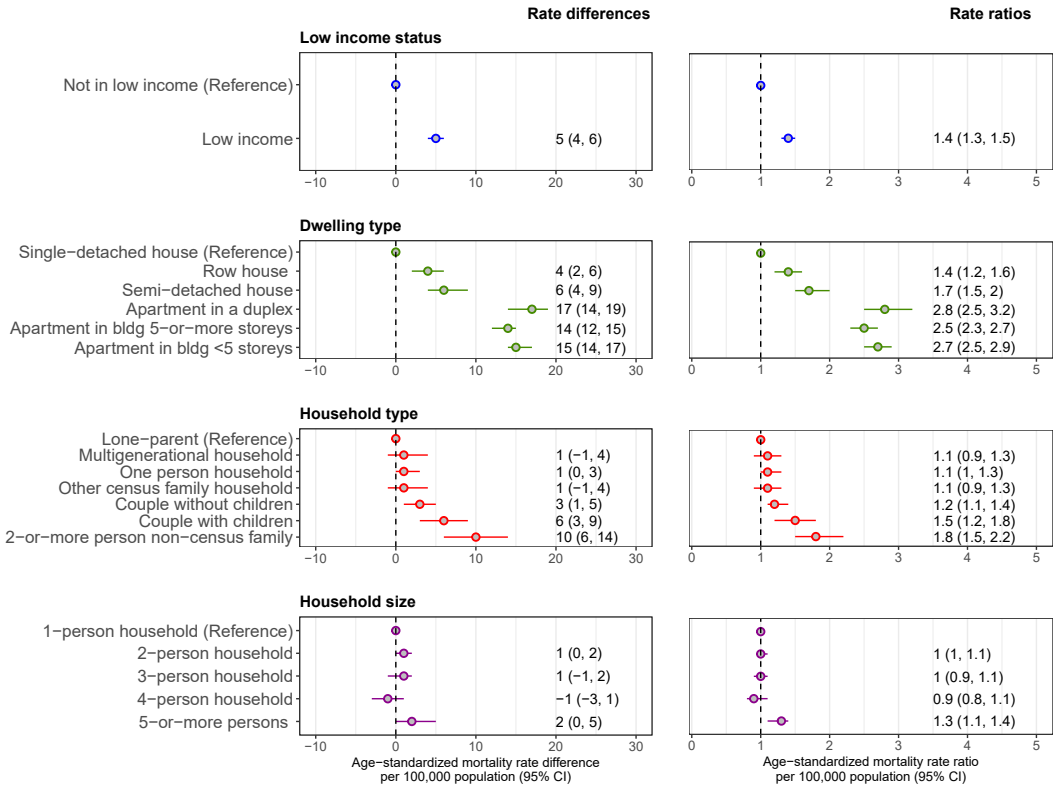
buildings) and those of detached homes. There were 14 to 17 more deaths per 100,000 (between 2.5 and 2.8 times higher rates) among apartment residents compared with single-detached home residents (**Figure 1**) (data presented in Figures 1 to 4 are available in **Supplemental Tables S2** to **S5**, respectively). Smaller inequalities were observed between those living in other dwelling types (row and semi-detached houses) and those living in single-detached homes (observed rate ratios ranged from 1.4 to 1.7, rate differences of 4 to 6 more deaths per 100,000). Similarly, smaller inequalities were also observed across household type and low-income status subgroups; observed rate ratios ranged from 1.1 to 1.8, and rate differences of one to 10 more deaths per 100,000 in these subgroups (Figure 1). There were small to no differences in rates across household sizes (as indicated by 95% confidence intervals that crossed the null) (Figure 1). Sensitivity e-value analyses were conducted to assess the potential risk of confounding bias on these bivariate inequality estimates. Findings suggest that the observed inequalities in COVID-19 mortality risk according to low-income status, household type and dwelling type could be fully explained away by an unmeasured confounder with an association of RR=2.1 to 5.0 (depending on the social strata), with both the latter exposure measures and the outcome of COVID-19 mortality, respectively (**Supplemental Table S6**). That is, the unmeasured confounder would have to have a stronger association than those observed for the factors measured in this study (Figure 1).

Between January 1 and August 31, 2020, among the subgroups measured, the largest absolute inequalities in COVID-19 mortality overall were observed between residents living within versus outside large urban centres. There were 30

Table 2: Age-standardized mortality rate per 100,000 population among all residents, January 1 and August 31, 2020, across area-level stratifiers from the 2016 Census, overall and by sex

Stratifiers	Age-standardized mortality rate per 100,000 population					
	Overall		Females		Males	
	Rate per 100,000	95% CI	Rate per 100,000	95% CI	Rate per 100,000	95% CI
Census metropolitan area (CMA)						
Living in large urban centers (Census Metropolitan Area, CMA)	33	32, 34	29	28, 29	39	38, 41
Living outside large urban centers (non-CMA)	4	3, 4	3	2, 3	5	4, 5
Ethno-cultural composition						
Quintile 1 (lowest concentration)	16	15, 17	14	13, 15	18	17, 20
Quintile 2	13	12, 14	12	11, 13	14	13, 16
Quintile 3	19	18, 20	16	15, 17	22	20, 24
Quintile 4	30	29, 31	25	24, 27	37	35, 39
Quintile 5	37	35, 38	31	30, 33	44	42, 47
After-tax neighbourhood income						
Quintile 1 (lowest income)	37	36, 39	30	29, 32	48	46, 50
Quintile 2	20	19, 20	16	15, 17	24	22, 25
Quintile 3	20	19, 21	18	17, 20	22	20, 24
Quintile 4	18	17, 19	16	15, 17	21	20, 23
Quintile 5	17	16, 18	16	15, 18	18	17, 20

Figure 1: Rate differences and ratios in age-standardized mortality rates (per 100,000) by individual-level characteristics, January 1 to July 4, 2020



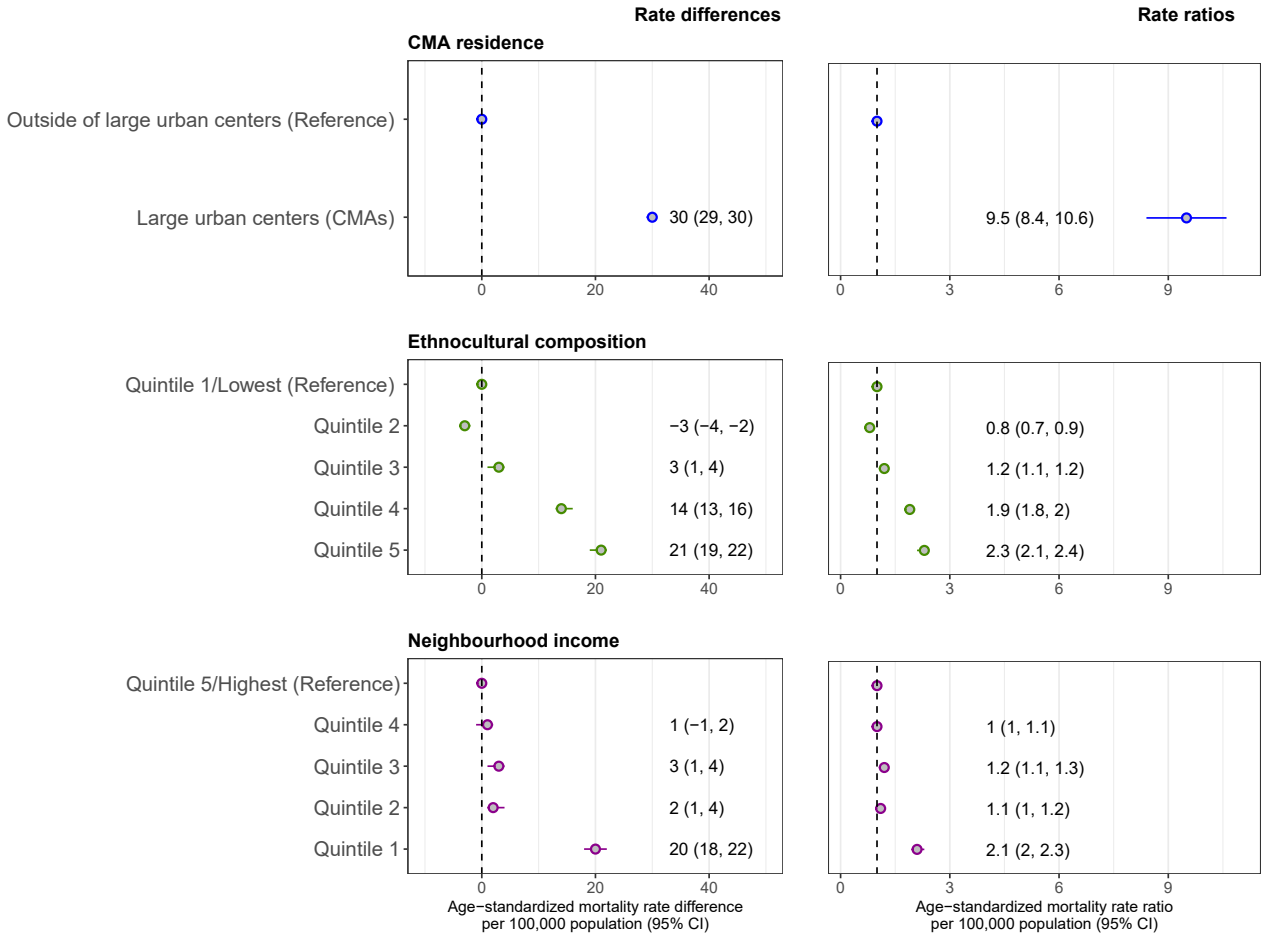
more deaths per 100,000 (9.5 times higher rates) within urban centres (**Figure 2**). Large inequalities were also observed across ethno-cultural and income quintiles. Per 100,000, there were 14 to 21 more deaths (1.9 to 2.3 times higher rates) in the highest ethno-cultural composition concentration areas (quintiles 4 and 5 versus quintile 1) and 20 more deaths (2.1 times higher rates) in lowest income areas (quintile 1 versus quintile 5) (Figure 2). Sensitivity analyses suggested that the latter observed associations could only be fully explained away by an unmeasured confounder with an association of RR=3.2 to 18.5, depending on the social strata, with both the latter exposures and the outcome, respectively (**Supplemental Table S7**). Rate differences for the other neighbourhood income quintile groups (quintiles 2 to 4) and ethno-cultural quintile groups (quintiles 2 to 3), ranged from one to three deaths per 100,000 (ratios of 0.8 to 1.2), with many of the 95% confidence intervals crossing the null (Figure 2).

Sex/gender inequalities in COVID-19 mortality across sub-populations

Between January 1 and July 4, 2020, among residents of private dwellings, the largest inequalities in mortality between males and females were among apartment dwellers (difference of 15 to 18 more deaths per 100,000, male-to-female ratios of 1.8 to 2) (**Figure 3**). Within other dwelling type subgroups, rate differences ranged from four to 10 deaths per 100,000 (male-to-female ratios of 1.6 to 2.1) (Figure 3).

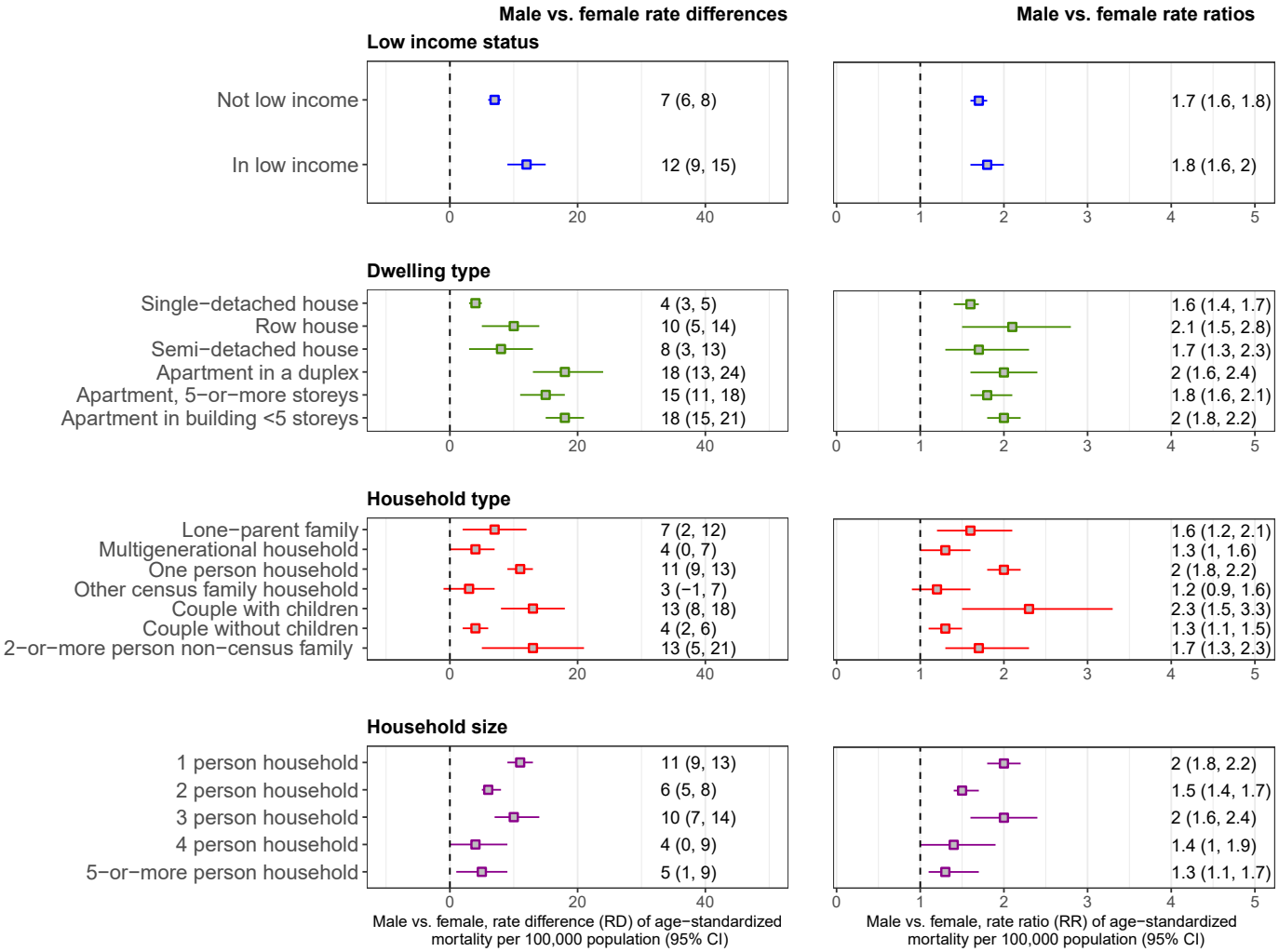
Among household types, the largest sex/gender inequalities were within one-person households, two-or-more non-census family households and couples with children (rate differences of 11 to 13 per 100,000, male-to-female ratios of 1.7 to 2.3) (Figure 3). In the other household types, differences ranged from three to seven per 100,000 (male-to-female ratios of 1.2 to 1.6), with several 95% confidence intervals crossing the null (Figure 3).

Figure 2: Rate differences and ratios in age-standardized mortality rates (per 100,000) by area-level characteristics, January 1 to August 31, 2020



Abbreviation: CMA, Census Metropolitan Area

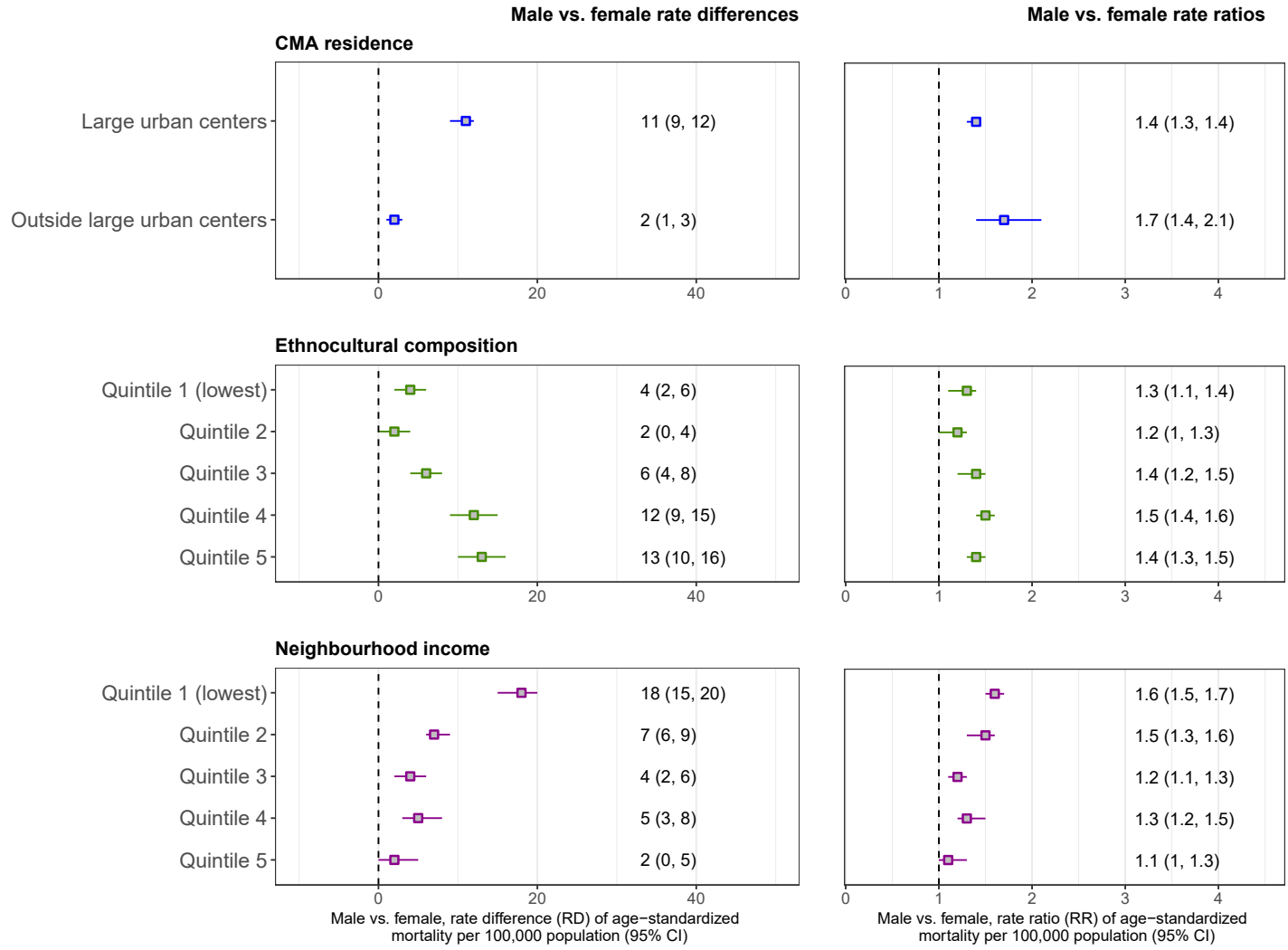
Figure 3: Age-standardized mortality rate differences and ratios between males and females (reference group) by individual-level subgroups, January 1 to July 4, 2020



Males experienced 12 more deaths per 100,000 (male-to-female ratio of 1.8) in low-income groups, compared with seven more deaths per 100,000 (male-to-female ratio of 1.7) in groups not in low-income (Figure 3). Lastly, compared with females, males experienced between six and 11 more deaths in one to three-person households (1.5 to 2 times higher rates) (Figure 3). In the other household size subgroups, the 95% confidence intervals for the rate differences and ratios were close to the null (Figure 3).

Similarly, between January 1 and August 31, 2020, sex/gender inequalities varied across area-level disaggregates. There were 11 more male than female deaths per 100,000 in CMAs compared with two more male deaths per 100,000 outside of urban centres (**Figure 4**). The difference in mortality rates between males and females was highest in areas with lowest income or highest ethno-cultural composition concentration: per 100,000, there were 18 more male deaths in income quintile 1 (1.6 times higher rates) and 13 more male deaths in ethno-cultural composition quintile 5 (1.4 times higher rates) (Figure 4).

Figure 4: Age-standardized mortality rate differences and ratios between males and females (reference group) by area-level subgroups, January 1 to August 31, 2020



Abbreviation: CMA, Census Metropolitan Area

Discussion

This study aimed to provide a snapshot of the individual and area-level inequalities in COVID-19 mortality in Canada at the start of the pandemic. At an individual-level, the largest inequalities in mortality were observed between apartment residents and single-detached house residents. At an area-level, large inequalities were observed between those living in large urban centres, in lowest income and highest ethno-cultural composition concentration areas, compared with respective reference groups. Inequalities in male versus female mortality rates were also higher in each of the above subgroups. These findings highlight how populations facing socioeconomic disadvantage have experienced a higher overall burden of deaths.

The observed inequalities, particularly in relation to income and ethno-cultural composition, are consistent with previous Canadian findings at regional (1–3), provincial (4,5) and national (6,7,39) levels. Further, inequalities by sex/gender and area-level income are also aligned with what has been observed for other infectious and chronic disease outcomes and overall mortality in Canada (11,40,41).

Previous reporting has highlighted that inequalities in COVID-19 mortality are likely attributable to social and economic differences in SARS-CoV-2 infection (13–15), and distributions of underlying mortality risk factors, including chronic condition prevalence and access to and use of health services (9). For example, systemic inequities in working and living conditions can shape inequitable distributions of infections and morbidity risk (8). The larger sex/gender inequalities in COVID-19 mortality observed in some subgroups are likely an indication of the

interplay between sex-based immunological factors (42) and gendered domestic and occupational experiences that shape infection and morbidity risk, including risk behaviours (e.g. smoking, lower use of health care services (11)) and chronic disease prevalence (42).

Further, included in hypothesized social determinants of COVID-19 outcomes are public health measures, which can have differential impacts across populations, especially with regards to SARS-CoV-2 transmission. For example, a Toronto Foundation report indicated how closures of nonessential workplaces were associated with lower SARS-CoV-2 transmission rates in higher-income neighbourhoods, where more residents could work from home (43). This policy appeared to be less effective in areas with lower income and higher concentration of visible minority populations (43). It is common for universal public health strategies to have differential impacts if certain socioeconomic groups face structural barriers in experiencing the benefits of interventions (44,45), such as inability to work from home (46), absence of discretionary time or linguistic differences (11). Strategies that combine universal and targeted approaches, based on the proportionate needs of populations, are believed to be able to overcome these limitations (47).

Perhaps most importantly, the burden of COVID-19 observed in some groups but not others highlights how inequalities in COVID-19 mortality could plausibly be avoided and therefore considered inequitable (48). In light of these findings, it is evident that work needs to be done in Canada to advance health equity during this pandemic and into the future so that these inequities can be prevented, as proposed in the Key Health Inequalities in Canada report (11).

Limitations

This study has several limitations. First, this analysis is intended to better understand differences in mortality between populations, using the best available sources of data. However, as noted, the provisional data used herein likely underestimated COVID-19 mortality rates. The rates reported do not capture all COVID-19 deaths that occurred in Canada in the study period. It is unclear how under-reporting may have influenced the magnitude of inequalities observed. It is also not yet known how differences in under-reporting across groups, or spatial-temporal changes in under-reporting or transmission rates, may have influenced the size of inequalities across time. Second, due to limitations in data access, this study did not explore interactions between measures, nor was a multivariate analysis performed to identify the precise pathways through which these inequalities manifest. Although sensitivity analyses performed suggested moderate to minimal vulnerability to confounding bias for observed associations, future multivariate analyses are needed to address these data gaps. Third, individuals' personal or area-level characteristics may have changed between the time of the 2016 Census collection and when the deaths occurred. It is unclear how this may have influenced inequality estimates. It was not possible in this study to distinguish which of the deaths integrated with area-level data, or inequalities therein, occurred among residents of long-term care institutions and which occurred in private dwellings. These remain important areas of future study. Lastly, this study did not explore several other social determinants, including gender, Indigeneity or race/ethnicity, as these data were not available. An exploration of these social determinants, and of inequalities by province and territory, at later time points during the pandemic, including following the advent of variants of concern (49) and immunization campaigns, remain other important areas of future investigation.

Conclusion

The burden of COVID-19 mortality between January and July/August 2020 was not experienced equally across all populations and communities in Canada. This study highlights the role of social determinants of health and socioeconomic inequalities in shaping inequitable distributions of COVID-19 burden, and the need to consider these factors in future analyses, to prepare a health equity-informed pandemic response.

Authors' statement

AB — Conceptualized the study, performed analyses of absolute and relative inequalities, interpreted the data, drafted the manuscript, and revised the manuscript
SYP — Conceptualized the study, performed analyses of absolute and relative inequalities, drafted and provided feedback on the manuscript
NA — Estimated disaggregated rates and provided feedback on the manuscript
FJY — Estimated disaggregated rates and provided feedback on the manuscript
RS — Estimated disaggregated rates and provided feedback on the manuscript
CS — Conceptualized the study and provided feedback on the manuscript

Competing interests

None.

Acknowledgements

This analysis is a product of the Pan-Canadian Health Inequalities Reporting (HIR) Initiative. Established in 2012 and led by the Public Health Agency of Canada (PHAC), the HIR Initiative involves a collaboration between PHAC, Statistics Canada, the Pan-Canadian Public Health Network, the Canadian Institute for Health Information and the First Nations Information Governance Centre. Past HIR Initiative reporting has included an online health inequality data visualization tool (the Health Inequalities Data

Tool) and the 2018 *Key Health Inequalities in Canada: A National Portrait*. We would like to acknowledge the contributions of Scott Van Millingen and Hongbo Liang on the development of the HIR Initiative COVID-19 Data Tool and the Health Inequalities Data Tool.

Funding

This work was supported by the Public Health Agency of Canada.

Supplemental material

These documents can be accessed on the Supplemental tables file.

Supplemental Table S1
Supplemental Table S2
Supplemental Table S3
Supplemental Table S4
Supplemental Table S5
Supplemental Table S6
Supplemental Table S7

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National FluWatch mid-season report, 2021–2022: Sporadic influenza activity returns

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Abstract

Surveillance for Canada's 2021–2022 seasonal influenza epidemic began in epidemiological week 35 (the week starting August 29, 2021) during the ongoing coronavirus disease 2019 (COVID-19) global public health emergency.

In the 2021–2022 surveillance season to date, there has been a return of persistent sporadic influenza activity, and the first influenza-associated hospitalizations since mid-2020 have been reported. However, as of week 52 (week ending 01/01/2022) activity has remained sporadic, and no influenza-confirmed outbreaks or epidemic activity have been detected. There has been a delay or absence in several traditional seasonal influenza milestones, including the declared start of the influenza season, marked by a threshold of 5% positivity, which historically has occurred on average in week 47. The 429 sporadic detections reported in Canada to date have occurred in 31 regions across seven provinces/territories. Nearly half (n=155/335, 46.3%) of reported cases have been in the paediatric (younger than 19 years) population. Three-quarters of the cases were influenza A detections (n=323/429, 75.3%). Of the subtyped influenza A detections, A(H3N2) predominated (n=83/86, 96.5%). Of the 12 viruses characterized by the National Microbiology Laboratory, 11 were seasonal strains. Among the seasonal strains characterized, only one was antigenically similar to the strains recommended for the 2021–2022 Northern Hemisphere vaccine, though all were sensitive to the antivirals, oseltamivir and zanamivir.

Until very recently, seasonal influenza epidemics had not been reported since March 2020. Evidence on the re-emergence of seasonal influenza strains in Canada following the A(H1N1) pdm09 pandemic shows that influenza A(H3N2) and B epidemics ceased through the 2009–2010 season and second wave of A(H1N1)pdm09, but then re-emerged in subsequent seasons to predominate causing epidemics of higher intensity than in the pre-pandemic seasons. When and where seasonal influenza epidemic activity resumes cannot be predicted, but model-based estimates and historical post-pandemic patterns of intensified epidemics warrant continued vigilance through the usual season and for out-of-season re-emergence. In addition, ongoing population preparedness measures, such as annual influenza vaccination to mitigate the intensity and burden of future seasonal influenza epidemic waves, should continue.

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Suggested citation: Bancej C, Rahal A, Lee L, Buckrell S, Schmidt K, Bastien N. National FluWatch mid-season report, 2021–2022: Sporadic influenza activity returns. Can Commun Dis Rep 2022;48(1):39–45. https://doi.org/10.14745/ccdr.v48i01a06

Keywords: influenza, surveillance, Canada, human/epidemiology, human/virology, seasons, influenza A virus, influenza B virus, non-pharmaceutical interventions

Introduction

The global public health response to the coronavirus disease 2019 (COVID-19) pandemic has suppressed seasonal influenza epidemic activity since March 2020 and now continues to contain seasonal influenza epidemics into the period of the usual 2021–2022 Northern Hemisphere season (1–6).

Canada's 2019–2020 influenza season was truncated by public health measures aimed at reducing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission, and has remained at interseasonal levels since (1,7–9). Throughout the usual Northern Hemisphere 2020–2021 season, and despite increased influenza testing, a mere 69 laboratory-confirmed

influenza detections, and no laboratory-confirmed influenza outbreaks or hospitalizations, were recorded in Canada by participating provinces and territories (P/T) (10).

Globally, reports of localized influenza outbreaks have been scarce throughout the pandemic period, with regional outbreaks of A(H3N2) limited to South and Southeast Asia, B/Victoria epidemics in China, and A(H1N1) in West Africa (11–13). However, with increased easing of COVID-19 public health measures, there appears to have been a rise in both verified and unverified reports of localized influenza outbreaks during the 2021–2022 Northern Hemisphere surveillance period (14,15).

Surveillance in Canada for the 2021–2022 influenza season began August 29, 2021 (epidemiological week 35-2021) (6). This report describes FluWatch surveillance for the re-emergence of sporadic, localized and epidemic seasonal activity in Canada, in the context of easing global and domestic public health measures during the first 18 weeks of the 2021–2022 national influenza season (August 29, 2021 to January 1, 2022 [epidemiological weeks 35 to 52]).

Methods

Design

The FluWatch program is a national composite surveillance system consisting of virological surveillance, influenza and influenza-like illnesses (ILI) activity level surveillance, syndromic surveillance, outbreak surveillance, severe outcome surveillance and vaccine monitoring in Canada. Annually, ongoing influenza surveillance occurs from epidemiological week 35 to 34 of the following year. With the exception of vaccine coverage and effectiveness, which are assessed at mid-season and season end, the FluWatch network of labs, hospitals, doctor's offices, P/T ministries of health and individual Canadians reports data into FluWatch weekly for cases and events occurring during the preceding epidemiological week.

Definitions and data sources

Aggregate laboratory detections are reported to FluWatch by P/T public health laboratories and hospitals that comprise the Respiratory Virus Detections Surveillance System. Number of tests, number of positive tests and the percentage of tests positive for influenza and other respiratory viruses are calculated. Depending on the province, reverse transcription polymerase chain reaction (RT-PCR) tests were conducted on patient specimens from outpatient ILI cases (most reporting P/Ts restricted outpatient testing to groups at increased risk of influenza complications), emergency department acute respiratory infection cases and/or hospitalized severe acute respiratory illness cases, as well as from outbreaks.

Case-level data on laboratory-confirmed influenza detections were supplied on a sub-set of influenza positive cases from aggregate laboratory detections.

For historical time-series of influenza seasons from 2007–2008 onwards, the dominant influenza A strain was assigned as the influenza A subtype(s) comprising 40% or more of the subtyped influenza A. Prior to 2009–2010 sub-typing data were available only for the sample of surveillance specimens characterized antigenically or genetically by the National Microbiology Laboratory (NML).

Influenza/ILI activity levels were reported to FluWatch based on assessments by P/T epidemiologists. Activity levels are classified as follows: 1) no activity (no laboratory-confirmed influenza detections in the reporting week; however, sporadically occurring ILI may be reported); 2) sporadic (sporadically occurring ILI and laboratory-confirmed influenza detection(s) with no outbreaks detected within the influenza surveillance region); 3) localized (increased ILI and laboratory-confirmed influenza detection(s) and outbreaks in schools, hospitals, residential institutions and/or other types of facilities occurring in less than 50% of the influenza surveillance region); and 4) widespread (evidence of increased ILI and laboratory-confirmed influenza detection(s) and outbreaks in schools, hospitals, residential institutions and/or other types of facilities occurring in greater than or equal to 50% of the influenza surveillance region).

Laboratory-confirmed influenza outbreaks were reported to FluWatch by P/T. All P/Ts reported laboratory-confirmed influenza outbreaks that occurred in hospitals and long-term care facilities. Laboratory-confirmed influenza outbreaks in other settings, including remote/isolated communities, workplaces, schools/universities or correctional facilities, were reported by some P/Ts. An outbreak was considered influenza-confirmed if two or more cases of ILI are reported in the setting during a seven-day period with at least one case laboratory-confirmed as influenza.

For severe outcomes surveillance, P/T Ministries of Health from Alberta (AB), Saskatchewan (SK), Manitoba (MB), Prince Edward Island (PE), Newfoundland and Labrador (NL), Nova Scotia (NS), New Brunswick (NB), Yukon Territories (YT) and Northwest Territories (NT) reported hospitalizations, intensive care unit admissions and deaths associated with laboratory-confirmed influenza to FluWatch. Two sentinel networks, the Canadian Immunization Monitoring Program ACTive (paediatric) and the Canadian Immunization Research Network – Serious Outcomes Surveillance Network (adult), reported influenza-associated laboratory-confirmed paediatric and adult hospitalizations, intensive care unit admissions and deaths, as well as additional case-level enhanced surveillance data, from sentinel sites in various P/Ts to FluWatch.

For virus characterization, NML received influenza isolates from P/Ts, sampled at various points in the season, for strain characterization, antiviral resistance testing. The NML also conducted partial genome sequencing of the hemagglutinin gene of some of the isolates.

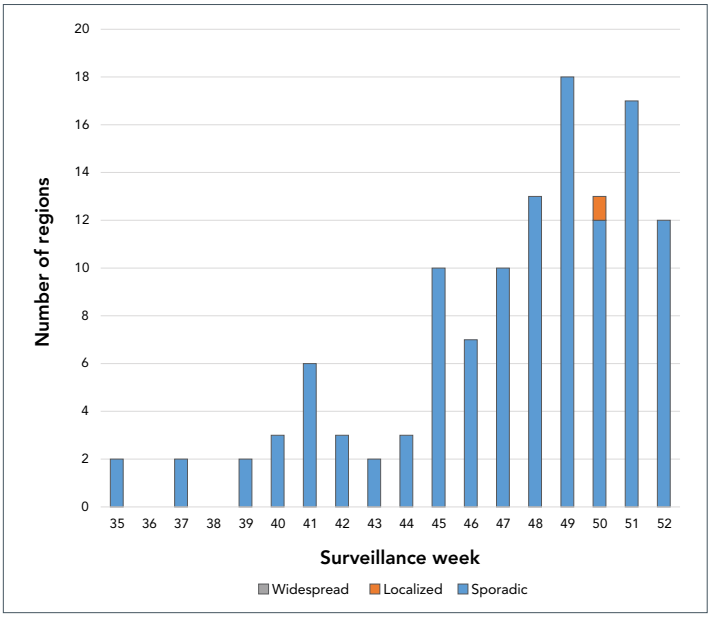
Statistical methods

Weekly data were input via a portal on the Canadian Network for Public Health Intelligence or directly integrated in SAS V9.4. Data cleaning, aggregation and estimation of rates and proportions were conducted in SAS V9.4. Data visualization for spatial/geographic analysis was conducted using ArcGIS and descriptive statistics and temporal trends were estimated in SAS V9.4 and visualized in Excel.

Results

From August 29, 2021 to January 1, 2022 (weeks 35 to 52), there were persistent and increasing reports of sporadic influenza activity. This sporadic activity occurred in 31 regions across seven P/Ts (British Columbia [BC], AB, MB, Ontario [ON], Québec [QC], NB, NS) (**Figure 1**).

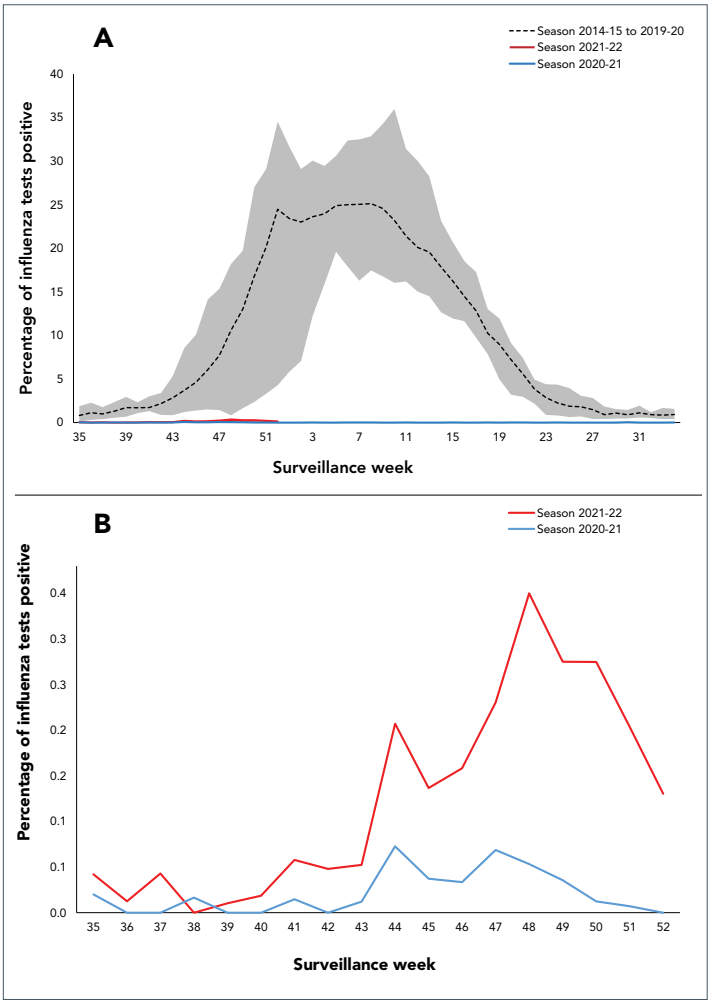
Figure 1: Number of regions reporting sporadic, localized or widespread influenza activity, by epidemiological week, Canada, weeks 35-2021 to 52-2021[a]



[a] Total number of regions reporting: 52

The first influenza cases for the 2021–2022 season were detected at the start of the surveillance period in week 35 and sporadic influenza detections have persisted and slowly increased in number through to week 49. However, the percent positivity had not reached the threshold of 5% necessary to declare the start of the seasonal influenza epidemic, remaining below 0.5% this season to date (**Figure 2**). A sharp drop in influenza cases began and persisted through weeks 50 to 52, concurrent with the rise of the SARS-CoV-2 Omicron variant and re-institution of intensified public health measures.

Figure 2: Percentage of influenza tests positive, by report week, Canada, 2021–2022 influenza season to date (weeks 35 to 52) compared with historical average and minimum-maximum (seasons 2014–2015 to 2019–2020)



A majority of the 429 sporadic influenza detections to date have been reported by BC, followed by QC and ON. Two provinces (NL PE) and two territories (NT, Nunavut) have yet to report any influenza detections this season and one province (SK) detected only travel-related cases. Influenza A comprised three-quarters of detections, with influenza A detected in higher numbers in all P/Ts (with A(H3N2) the predominant subtype detected) (**Figure 3**).

In the 2021–2022 season to date, influenza remained at interseasonal levels in Canada (Figure 2A and 2B); however, activity is currently increasing, with n=96/429 (22.4%) of the detections being recorded in the two most recent epidemiological week(s). The first influenza hospitalizations and intensive care unit admissions reported since mid-2020 have occurred, with the first reports beginning in week 43; however, activity remains sporadic and no influenza-associated outbreaks or epidemic activity have been detected.

Figure 3: Spatial distribution of (sporadic) influenza detections (n=429) by influenza type/subtype, Canada, weeks 35-2021 to 52-2021

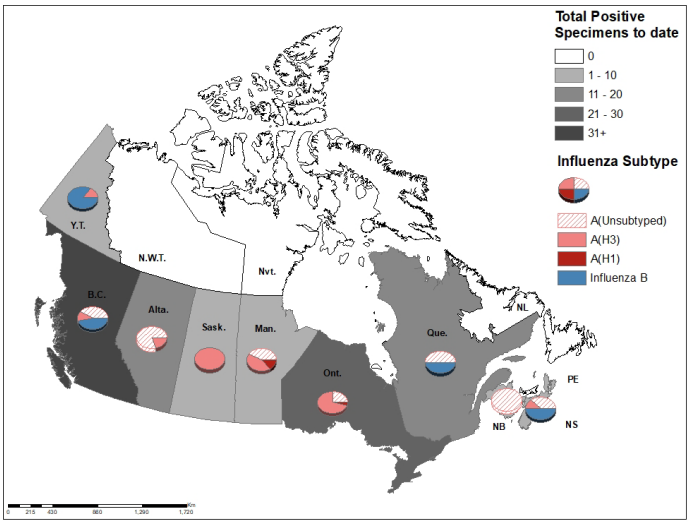
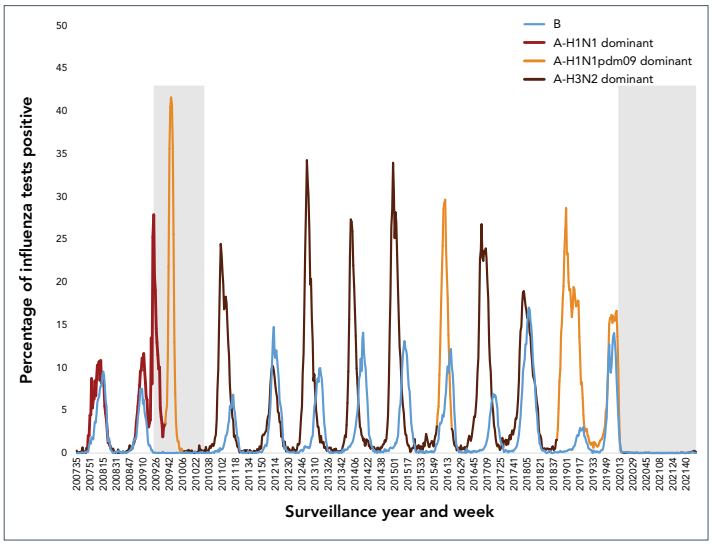


Figure 4: Seasonal epidemics of influenza by type or subtype before, during and following the 2009 H1N1 pandemic, Canada, weeks 35-2007 to 52-2021



Note: Grey area denotes the period of the 2009 H1N1 pandemic (June 11, 2009 to August 11, 2010), and of the COVID-19 pandemic (March 11, 2020 and ongoing as of time of publication), as declared by the World Health Organization (16,17)

Reported cases have been predominately (n=155/335, 46.3%) in the paediatric (younger than 19 years) population.

The majority of detections thus far have been influenza A detections (n=323/429, 75.3%). Of the subtyped influenza A detections, A(H3N2) has predominated (n=83/86, 96.5%). Among the 11 seasonal viruses characterized by the NML (two A(H1N1)pdm09, nine A(H3N2)), only one was antigenically similar to the vaccine strains, and all were sensitive to the antivirals, oseltamivir and zanamivir. One sporadic detection, subsequently identified as a swine influenza variant A(H1N2)v, was reported in week 41-2021 but could not be further characterized.

During the influenza A(H1N1)pdm09 pandemic in Canada, detections of non-pandemic influenza strains (influenza A(H3N2), influenza A(H1N1) [the pre-pandemic circulating influenza] and influenza B) were all suppressed through the 2009–2010 season and second wave of A(H1N1)pdm09. Influenza B percent positivity ranged from 0.0% to 0.21% and non-pandemic influenza A strains were virtually absent during the period of the 2009 H1N1 pandemic. Influenza A(H3N2) re-emerged during the 2010–2011 and 2011–2012 seasons, with more severe epidemics than pre-pandemic. It also caused notably severe epidemics in the 2012–2013 and the two seasons that followed with the 2014–2015 (increased average activity peaking at 34% positive) and 2016–2017 (increased average activity peaking at 26.8% positive) seasons being particularly intense A(H3N2) seasons. Influenza B also re-emerged in 2010–2011, but with a less severe epidemic, followed by a more severe one in 2011–2012 when it co-circulated and co-dominated with A(H3N2) (**Figure 4**).

Discussion

Canada saw a return and continuation of sporadic activity through most weeks of the 2021–2022 season to date (weeks 35-2021 to 52-2021). Activity remained sporadic throughout this period with only one region reporting localized activity in week 50 and no laboratory-confirmed influenza outbreaks reported. As of week 52-2021, activity remained below the epidemic threshold. The sporadic detections were a mix of influenza A and B, with influenza A(H3N2) predominating.

Similarly, in the global context, most countries continued to report lower than typical influenza activity with fewer than normal detections and very few localized outbreaks (11–13), through the typical early part of the Northern Hemisphere influenza season. Until December 2021, no epidemic activity had been reported anywhere since April 2020 (5,6). Recent surveillance reports from December 2021 from the European Centre for Disease Prevention and Control and United States Centers for Disease Control and Prevention indicated the start and intensification of seasonal epidemic activity in several parts of the Northern Hemisphere (18,19). Detections reported to the Global Influenza Surveillance and Response System (GISRS) and isolates reported to the Global Initiative on Sharing All Influenza Data (GISAID) remain a fraction of what they were pre-pandemic. Decreased genetic diversity in circulating influenza viruses has been reported with a virtual absence of influenza B/Yamagata (11). A high proportion of sporadic detections globally, which have been characterized, showed antigenic differences from the recommended vaccine strains (20,21).

Case level information on the sporadic detections to date in Canada showed some differences in pattern as compared with those observed during recent seasonal influenza epidemics that occurred prior to the COVID-19 pandemic. Burden is typically highest in seniors, but sporadic detections to date have been largely in the paediatric and younger adult population. Influenza A(H1N1)pdm09 and B detections tend to occur disproportionately in children, while A(H3N2) are disproportionate in seniors, but to date, A(H3N2) infections predominated and were disproportionately seen in children and younger adults. However, it is too soon to discern any emerging patterns or possible reasons for these findings given the lack of community transmission.

A key question concerns when activity will increase beyond sporadic detections and seasonal influenza epidemics re-emerge in Canada. As long as public health measures reduce influenza transmission by 30% or more, community circulation of influenza is likely to remain suppressed (22). Reduced international travel reduces the risk of re-introduction of seasonal strains from pockets where they are circulating and domestic policy measures aimed at reducing transmission of SARS-CoV-2 and its emerging variants, including those recently implemented against the SARS-CoV-2 Omicron variant, are likely to maintain or re-establish reductions in influenza transmission as well (11,23).

Another key question concerns the likely impact or severity of seasonal influenza epidemics when they re-emerge. Modelling published ahead of the 2020–2021 Northern Hemisphere influenza season demonstrated that while timing of re-emergence is unpredictable, more intense and severe epidemics of influenza and other seasonal respiratory viruses such as respiratory syncytial virus (RSV) are likely to occur when circulation and transmission resumes owing to lower population immunity against the non-pandemic pathogens and strains, especially in the young (24). The surveillance findings presented here, as well as modelling studies found more severe influenza A(H3N2) and B epidemics, occurred in the years following the 2009 H1N1 pandemic (25,26). Though the pandemic pathogens differ and the stringency and duration of public health measures greater with the COVID-19 pandemic, the experience following the emergence of influenza A(H1N1)pdm09 may give some insight into the behavior of endemic viruses after a period of suppression as well as into the performance of medical countermeasures. Vaccine strain selection against influenza has been challenging during the COVID-19 pandemic due in part to the low global influenza circulation and the resultant limited availability of candidate vaccine viruses (27). National influenza centres, in Canada as well as globally, have reported a relatively high proportion of isolates detected that are antigenically different from the vaccine strains and vaccine effectiveness has not been assessed since the 2019–2020 Northern Hemisphere season (28).

There remains the possibility that when seasonal influenza epidemics resume, they will occur during a period of endemic co-circulation with SARS-CoV-2. Co-circulation and co-infection with influenza and SARS-CoV-2 have been documented, and evidence points to more severe synergistic effects in patients infected with both viruses than among those with single infections with either virus (29,30). The challenges of co-circulation of influenza and SARS-CoV-2, two high burden pathogens, in the context of a strained healthcare system and new and more stringent infection prevention and control measures for management of respiratory infectious disease cases requires integrated planning approaches.

Canada may not experience a typical influenza season yet again in 2021–2022 due to more limited opportunities for introduction and local transmission/circulation. Another season of suppressed seasonal influenza activity keeps open the possibility of out-of-season circulation and continues to increase the population at risk, especially new cohorts of children younger than five years old as well as seniors who are at a disproportionate risk of influenza A(H3N2) infection, hospitalization and death. The threat of influenza remains persistent, and it is essential for countries to be vigilant for the emergence of non-seasonal influenza viruses of pandemic potential and re-emergence of seasonal influenza for the 2021–2022 Northern Hemisphere influenza season and beyond (31,32).

Authors' statement

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

Competing interests

None.

Acknowledgements

Many thanks to all those across Canada who contribute to influenza surveillance.

Funding

FluWatch surveillance is funded by the Public Health Agency of Canada.

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Escherichia coli O103 outbreak associated with minced celery among hospitalized individuals in Victoria, British Columbia, 2021

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Abstract

Background: In April 2021, a Shiga toxin-producing *Escherichia coli* (*E. coli*) (STEC) O103 outbreak was identified among patients at two hospitals in Victoria, British Columbia (BC). The objective of this study is to describe this outbreak investigation and identify issues of food safety for high-risk products prepared for vulnerable populations.

Methods: Confirmed cases of *E. coli* O103 were reported to the Island Health communicable disease unit. The provincial public health laboratory conducted whole genome sequencing on confirmed case isolates, as per routine practice for STEC in BC. Exposure information was obtained through case interviews and review of hospital menus. Federal and local public health authorities conducted an inspection of the processing plant for the suspect source.

Results: Six confirmed cases of *E. coli* O103 were identified, all related by whole genome sequencing. The majority of cases were female (67%) and the median age was 61 years (range 24–87 years). All confirmed cases were inpatients or outpatients at two hospitals and were exposed to raw minced celery within prepared sandwiches provided by hospital food services. A local processor supplied the minced celery exclusively to the two hospitals. Testing of product at the processor was infrequent, and chlorine rinse occurred before mincing. The spread of residual *E. coli* contamination through the mincing process, in addition to temperature abuse at the hospitals, are thought to have contributed to this outbreak.

Conclusion: Raw vegetables, such as celery, are a potential source of STEC and present a risk to vulnerable populations. Recommendations from this outbreak include more frequent testing at the processor, a review of the chlorination and mincing process and a review of hospital food services practices to mitigate temperature abuse.

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Suggested citation: Smith CR, Griffiths A, Allison S, Hoyano D, Hoang L. *Escherichia coli* O103 outbreak associated with minced celery among hospitalized individuals in Victoria, British Columbia, 2021. Can Commun Dis Rep 2022;48(1):47–50. https://doi.org/10.14745/ccdr.v48i01a07

Keywords: *E. coli* infection, foodborne, disease outbreak, celery

Introduction

Foodborne illness caused by *Escherichia coli* (*E. coli*) often occurs through the consumption of contaminated food items such as fresh produce, meat and cheese products, and may result in symptoms including watery diarrhea, hemorrhagic colitis and hemolytic uremic syndrome (1,2). Pathogenic Shiga toxin-producing *E. coli* (STEC) are amongst the top 10 most common causes of foodborne illness in Canada (3). Although *E. coli* O157 remains the more common STEC, incidence rates of non-O157 STEC infections, including *E. coli* O103, have increased over time. The main factor contributing to this increase is an advancement in diagnostic testing (4).

E. coli O103 outbreaks have previously been linked to clover sprouts, bison meat, ground beef, cured mutton sausages, raw cow milk and fermented sausages (5–8). Although celery has been reported as a vehicle for *Listeria monocytogenes*, norovirus and *E. coli* O157:H7 (9–11), there have been no outbreaks of non-O157 *E. coli* associated with celery reported in the literature to date.

In April 2021 a Shiga toxin-producing *E. coli* O103 outbreak was identified among inpatients and outpatients at two hospitals in Victoria, British Columbia (BC), after an unusual increase in *E. coli*

activity triggered an investigation by local public health officials. The objective of this article is to describe the first outbreak of non-O157 *E. coli* associated with celery in Canada and to identify issues of food safety for high-risk products prepared for vulnerable populations, in order to reduce the likelihood of these outbreaks in the future.

Methods

All STEC cases are reportable to public health within BC. Local hospital and community laboratories in Victoria screen enteric samples for Stx genes (12). If positive, the local regional laboratory in Victoria tests samples for STEC isolation in culture, and these isolates are forwarded to BC Centre for Disease Control Public Health Laboratory for serotyping and whole genome sequencing (WGS). All STEC received at, or recovered by, the Public Health Laboratory are routinely serotyped using a multiplex polymerase chain reaction targeting the most common serotypes in BC: O26; O45; O111; O103; O121; and O145. All STEC isolates routinely undergo whole genome multi-locus sequence typing (wgMLST). The wgMLST schema for *E. coli* compared 17,380 loci in the *E. coli* genome according to standardized procedures used by PulseNet Canada. As per PulseNet Canada, *E. coli* isolates were considered genetically related if they are within 10 allele differences.

An unusual increase in *E. coli* O103 cases was detected in April 2021 in the Victoria area, which triggered an investigation to identify the source of the illness. The outbreak investigation took place between April 16, 2021, and May 10, 2021. A confirmed case was defined as a resident of or visitor to the Island Health region with laboratory confirmation of *E. coli* O103 and symptom onset or collection date on or after March 15, 2021. Cases were interviewed by a single interviewer with BC's routine *E. coli* questionnaire. The interviews collected information on travel, animal exposures and select high-risk foods associated with previous *E. coli* outbreaks, including beef, leafy greens and unpasteurized dairy. Exposure information was collected for the 10-day period prior to the episode date (earliest of symptom onset or specimen collection date), reflecting the incubation period of *E. coli*. For those admitted to hospital during their incubation period, hospital menus were also reviewed for the 10-day period prior to their episode date.

Local investigators inspected the kitchen of Hospital A, where the majority of cases were inpatients or outpatients. The inspectors examined cooler temperatures and logs, dishwasher temperatures, sanitizing processes, dating of product and food handling practices for any deficiencies or potential for cross contamination. Inspectors also inquired about ill food handlers. Records were reviewed to determine the suppliers of various products.

Local and federal investigators inspected the processing facility of the suspect source of the outbreak—Processor A. Inspectors collected supply records and investigated processes to determine potential sources of contamination and potential deficiencies in food safety.

The outbreak was declared over when the maximum incubation period (10 days) plus 90th percentile reporting delay had passed since the most recent episode date of a confirmed case.

Results

Six confirmed cases were identified throughout the course of the investigation. Episode dates ranged from March 20 to April 9, 2021 (**Figure 1**). The majority of cases were female (n=4/6; 67%) and the median age was 61 years (age range 24–87 years). One death was reported (n=1/6; 17%), although *E. coli* infection was not the cause of death. All cases had been admitted to, or visited, two Victoria-area hospitals during their exposure period. Of the six confirmed cases, four were admitted to Hospital A, one was admitted to Hospital B, and one case was not admitted to hospital, but visited the emergency room of Hospital A during the exposure period (**Figure 2**). For those cases with onset dates available, the median reporting delay was 19 days (range 18–23 days).

Figure 1: Confirmed cases of *Escherichia coli* O103 infection by episode date (earliest of symptom onset or specimen collection date), March–April 2021

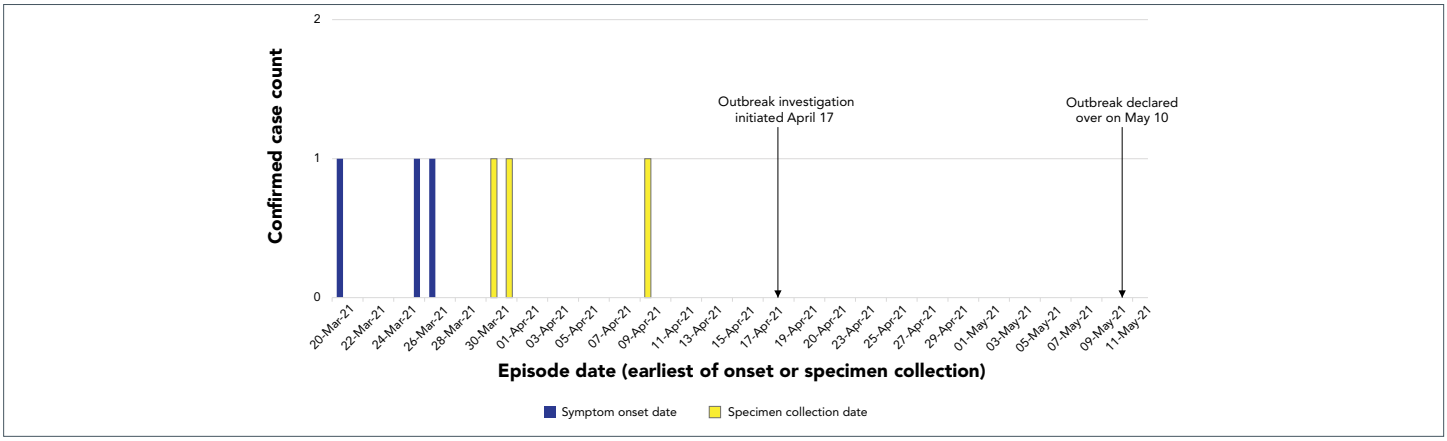
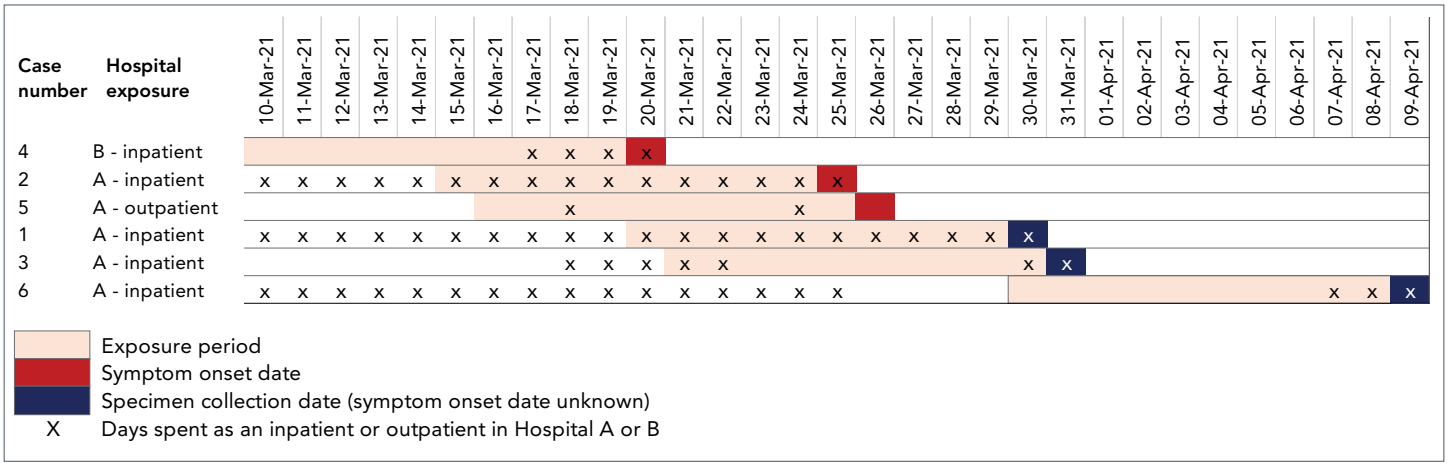
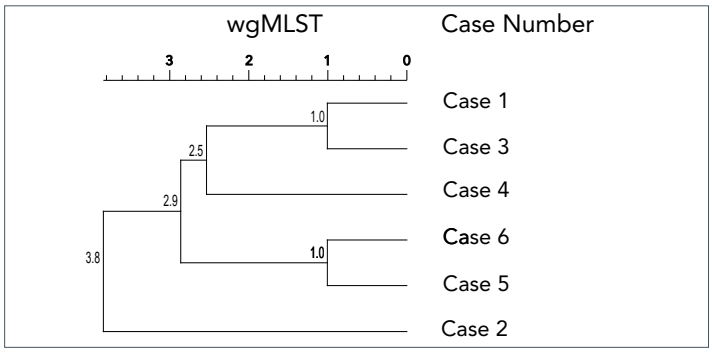


Figure 2: Gantt chart of confirmed cases indicating exposure period, episode date (earliest of symptom onset or specimen collection date), and dates in hospital



All confirmed cases from both Hospital A and Hospital B were considered highly related to each other by wgMLST within zero to four allele differences (**Figure 3**), and distinct from historic cases of *E. coli* O103. There were no related cases identified within the same timeframe of this outbreak nationally, or within the United States.

Figure 3: Phylogenic tree of *Escherichia coli* O103 outbreak cases[a]



Abbreviation: wgMLST, whole genome multi-locus sequence typing
[a] Comparisons were generated using Bionumerics v 7.6.2. The wgMLST allele differences indicated at the nodes were calculated using unweighted pair group method with arithmetic mean (UPGMA) and therefore, are not whole numbers. To determine the nearest whole number value, round up if the digit following the decimal is five or greater; round down if the digit following the decimal is less than five

Three cases were interviewed, while the remaining three could not be interviewed as they were either deceased (n=1) or medically impaired (n=2). From the interview data, the only exposures reported by at least two of three confirmed cases were ground beef (n=2/3), cheese (n=3/3), cold cuts (n=2/3), lettuce (n=2/3) and tuna sandwiches (n=3/3). No commonalities in restaurants or grocery stores were identified. The case that visited the emergency room of Hospital A reported eating only a tuna sandwich during their visit, given to them by a healthcare worker. The tuna sandwich was prepared by Hospital A food services and came from the same source as the inpatient food.

Hospital menus were reviewed for the five cases that were admitted to hospital. All five cases had exposure to prepared sandwiches during their hospital stay including tuna (n=4/5), egg (n=2/5), chicken salad (n=4/5), turkey (n=1/5) and roast beef (n=4/5) sandwiches. The only common ingredient across all sandwiches was minced celery, and minced celery within sandwiches was the only exposure reported by n=6/6 cases. Inspection of the kitchen of Hospital A, where the majority of cases were exposed to minced celery as either inpatients or outpatients, revealed no food safety or cross-contamination concerns. There were no reported illnesses among food handling staff. The inspection did reveal concerns regarding temperature abuse, with sandwiches often left out of the fridge for extended periods on trays or in patient rooms before being consumed.

Trace back investigation revealed that the minced celery used in sandwiches at both Hospital A and Hospital B was purchased from the same batch from the same local supplier—Processor A, and sourced from the Guadalupe region of California. Trace forward investigation revealed that this minced celery product was exclusively supplied to Hospital A and Hospital B, and no other facilities, distributors or stores. Chopped celery from the same batch of product was supplied to a large distribution network exclusive of Hospital A and Hospital B. Inspection of Processor A revealed two concerns. First, pathogen testing was infrequent, with the previous *E. coli* test occurring in January 2020; over a year prior to the present outbreak. Second, while the chlorination step met required standards, it occurred before mincing.

The hypothesized source of this outbreak was minced celery from Processor A. The root cause is hypothesized to be *E. coli* that persisted after chlorination and was subsequently mixed throughout the product during the mincing process. Temperature

abuse at Hospital A and Hospital B may have further contributed to propagation of *E. coli* in this product. The outbreak was declared over on May 10, 2021.

As there was no product left when the investigation had reached its conclusion, no product action was taken. Local and federal food safety authorities performed a second, joint inspection of Processor A to make recommendations for more frequent testing for *E. coli* and to conduct a review of the chlorination process. Follow-up was also conducted at Hospital A and Hospital B to propose methods to reduce the likelihood of temperature abuse by using time stamps to record when sandwiches are removed from the fridge.

Discussion

An outbreak investigation of six cases of *E. coli* O103 was conducted in April 2021. The outbreak was associated with consumption of minced celery from a local processor and sourced from California. While this is not the first *E. coli* outbreak reported in celery (11), this is the first to be caused by *E. coli* O103 and the first to exclusively impact a vulnerable, hospitalized population. This investigation resulted in several recommendations to improve food safety of this food item within the Island Health region.

Evidence from the epidemiological and food safety investigations support minced celery as the source of this outbreak. All six confirmed cases were exposed to the suspect source, and no other product was reported across all six confirmed cases, despite detailed menus for all inpatients. The outlier case, an outpatient who ate a tuna and celery sandwich only during their emergency room visit to Hospital A, added further support to celery as the suspect source. This investigation also revealed strong trace back evidence—the minced celery served in Hospital A and Hospital B was provided by the same supplier; the investigation also revealed strong trace forward evidence—the supplier provided the minced celery product only to the two hospitals, and nowhere else. Because the contaminated product was no longer available by the time of the investigation, and due to the cleaning procedures at Processor A, neither product samples nor environmental samples were available for testing. Despite the lack of laboratory evidence, the authors believe the strong epidemiological, trace back and trace forward evidence is sufficient to implicate minced celery in this outbreak.

The outbreak highlights the risk of raw vegetables provided to vulnerable populations and draws particular attention to the risk of mincing during processing. While previous work has documented the potential food safety hazards of fresh-cut produce (13), this outbreak serves to document the potential risks posed by mincing, which provides the opportunity for small amounts of bacteria remaining on the surface of a product, even after chlorination, to be spread throughout an entire batch.

Attribution of the mincing step as problematic in this outbreak scenario is further supported as trace forward investigation revealed that more coarsely chopped celery from the same batch was supplied to a wide distribution network, exclusive of Hospital A and Hospital B, with no cases of the outbreak strain of *E. coli* O103 associated with this product.

Despite providing food to a population of approximately 800 inpatients each day, identification of only six cases across Hospital A and Hospital B could potentially be explained by a low level of contamination, which may have caused illness only amongst those whose sandwiches were subjected to temperature abuse. Temperature abuse is a known vehicle for pathogen propagation (14–16), and was reported by the hospitals during the investigation follow-up. It is hypothesized that any contamination present after the mincing step in Processor A was further propagated by these reports of temperature abuse, resulting in the illnesses reported. A recommendation was made at the two implicated hospitals to add a time stamp to all sandwiches to mark the time the product was taken out of the fridge, to reduce the risk of temperature abuse moving forward.

There are several limitations to consider in the interpretation of these outbreak data. First, exposure data for celery was not available for the healthy population controls to directly compare with outbreak cases. However, given that 100% of confirmed cases had exposure to the suspect source, and this was the only common exposure across all six cases, the authors feel confident in the epidemiological evidence for this product. Second, the reporting delay for this outbreak was long, which in turn delayed the outbreak identification and investigation. Reporting delays are influenced by a multitude of factors, but comorbidities among the inpatient and outpatient cases in this outbreak may have delayed consideration of an enteric illness diagnosis and thus the requisition of a stool sample for testing. Third, several cases were missing onset dates as they could not be interviewed. For these individuals, their onset date likely predated their specimen collection date, which would also impact their exposure period. This was taken into account when interpreting the exposure data and analyzing hospital menus. Fourth, there were no food samples available to test for presence of *E. coli* O103; therefore, there was no laboratory data to definitively confirm the source of this outbreak. However, despite the lack of laboratory confirmation, the authors believe the epidemiological evidence, the trace back data and the trace forward data provided strong support of the suspect source. Lastly, it could not be determined where or how *E. coli* was introduced, as a further follow-up at the grower in the United States was outside the investigative jurisdiction of this outbreak.

Conclusion

Raw vegetables, such as celery, are a known source of *E. coli* contamination and present a risk to vulnerable populations. Mincing during the processing of raw vegetables, and

temperature abuse prior to consumption, may provide additional layers of risk. This outbreak resulted in several recommendations to reduce the risk of minced celery served in hospitals, including more frequent testing at the processor, a review of the chlorination and mincing process and a review of hospital food services practices to mitigate temperature abuse.

Authors' statement

CS — Analyzed and interpreted the data and drafted the article
AG — Analyzed and interpreted the data and drafted the article
SA — Conceptualized the work, interpreted the data and revised the article
DH — Conceptualized the work, interpreted the data and revised the article
LH — Analyzed and interpreted the data and revised the article

Competing interests

None.

Acknowledgements

None.

Funding

This work was supported by Island Health.

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Thank you to the CCDR peer reviewers of 2021

Many thanks to the following people for the time and expertise they have given to the *Canada Communicable Disease Report* (CCDR) as peer reviewers in 2021. These individuals have worked anonymously, in their spare time, with no remuneration. Their comments and insights have been vital to enhancing the quality of articles published in CCDR. CCDR aims to provide practical and authoritative information for clinicians and public health professionals in Canada and internationally.

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