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TRAVEL HEALTH

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Contact the Editorial Office

ccdr-rmtc@phac-aspc.gc.ca
613.301.9930

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TRAVEL HEALTH

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EDITORIAL

A Science Strategy for the Public Health Agency of Canada

Sarah Viehbeck[1]*, Kimberly Girling[1], Erin Dunn[1]

Affiliation

[1] Chief Science Officer and Vice President of Science and Policy Integration, Public Health Agency of Canada, Ottawa, ON

***Correspondence:**
sarah.viehbeck@phac-aspc.gc.ca

A foundation of scientific excellence should be the base of a world-class public health system.

Science is at the core of the Public Health Agency of Canada's (PHAC) mission to improve the health of all the people and communities within Canada. It is enshrined in our enabling legislation, which gives Canada's Chief Public Health Officer the role of providing "the Minister and the President [of PHAC] with public health advice that is developed on a scientific basis". As the national public health institution of Canada, the science we fund, conduct and use enables effective, evidence-informed decision-making, supports strong communication to the public and empowers people in Canada to take measures to protect and promote their health.

Science and research are essential to promote preparedness and resilience of public health systems. Through rigorous scientific activities, informed and contextualized through community engagement, we can understand public health threats and how they differ across and between populations, anticipate challenges, identify opportunities for equity-based solutions and respond effectively with tailored and relevant interventions. This work is often unseen, as the PHAC puts together early signals and acts in advance of emerging health threats to avert crises or minimize their impacts on people in Canada.

Scientific capacity, including a highly skilled science workforce supported by a series of robust enabling infrastructures, underpin Canada's ability to anticipate and respond to emerging health threats and can serve as an insurance policy towards national preparedness, health security and innovation. While collaboration and coordination across the system in an emergency is imperative, it is crucial to have baseline capacity within the federal government to ensure it can rapidly respond to threats at the earliest moment of detection.

During the COVID-19 pandemic response, PHAC had to adapt our scientific activities to meet the pressing needs of a public health crisis. These adaptations included building up existing and strengthening new capacities, such as genomics, wastewater surveillance, behavioural sciences and serosurveillance, as well as fostering new approaches to link science to decision-making and public health guidance. These changes involved fostering new or existing science advisory tables and facilitating new approaches to communicate science. While Canada's response to COVID-19 was strong, there is an opportunity to apply lessons learned and best practices from an acute emergency towards resilience and science excellence in our PHAC planning towards future public health challenges. Many of these lessons learned reports emphasized the importance of institutionalizing science advice systems, strengthening coordination and collaboration across jurisdictions and internal and external expertise, and improving readiness and efficiency, to be more resilient towards future challenges (1–3).

In December 2024, PHAC released its *PHAC Science Strategy 2024–2025 to 2029–2030: Advancing health, well-being, and equity through science* (4). Informed by robust domestic and international engagement, including dedicated dialogues with Canadian Indigenous communities, the Strategy reflects a purposeful shift towards a more open and collaborative model for our scientific work. Geared to be public-facing and with a global outlook, the Science Strategy aligns with other national public health science agendas and will support PHAC in the following areas:

- Planning and prioritizing scientific activities and guiding science investments
- Communicating clearly and transparently about science and how it is used in public health decisions and guidance
- Supporting the science workforce and capacity building
- Guiding scientific collaborations in a strategic and sustainable way

The Science Strategy takes a broad and inclusive view of science, including diverse disciplines from social and equity-based science to physical sciences and diverse ways of knowing, including Indigenous and cultural knowledge. It introduces a broadened definition of science at PHAC, developed through an antiracism lens, which embraces multiple ways of knowing, values integrity and fosters inclusion and partnership. This approach acknowledges that addressing complex public health challenges requires diverse perspectives and multidisciplinary solutions.

The Science Strategy articulates a clear value proposition for our science activities, positioning PHAC in the global public health landscape: leading and enabling science that is relevant, trustworthy and timely to policy and practice in the service of equitable public health impact at the national level. The science priorities it set focus on areas where PHAC is best positioned to contribute scientifically and can add the most value for people and communities in Canada:

- Advancing data science and the science of public health surveillance by innovating in surveillance methodologies and improving access to quality public health data
- Evolving the science of public health communication to better help people in Canada make informed decisions about their health based on strong, trusted scientific evidence
- Strengthening implementation science by studying how our public health programs and policies work to increase their impact
- Integrating science in public health emergencies by making sure science is at the heart of emergency preparedness, response and recovery

A cornerstone of this work is our commitment to meaningful collaboration with Indigenous partners. Through long-term reciprocal relationships, we aim to weave Indigenous knowledge with PHAC's existing scientific practices, support the decolonization of public health science and take actionable steps to integrate anti-racism principles into our work.

This Science Strategy represents more than a set of priorities—it is a forward-looking vision of our science culture so that the science we lead and enable is transparent, collaborative and impactful. We cannot achieve this work in isolation; to advance our science priorities, we will look to create new and foster existing scientific partnerships and make our scientific activities more visible and operationally transparent. These strategic collaborations will support PHAC's scientific work so that we can remain credible, timely, relevant and trustworthy into the future.

Authors' statement

SV — Conceptualization, supervision, writing–review & editing
KG — Conceptualization, writing–original draft
ED — Conceptualization, writing–original draft

Competing interests

Dr. Viehbeck is the Chief Science Officer and Vice President of Science and Policy Integration at PHAC. She was the lead for the Science Strategy development.

ORCID numbers

Sarah Viehbeck — 0000-0002-3110-1432
Kimberly Girling — 0000-0001-9780-4731

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Assessing the impact of the COVID-19 pandemic on trends of select travel-acquired enteric illnesses in Canada

Lauren Rusk[1]*, Russell Forrest[1], Meghan Hamel[1]

Abstract

Background: Millions of Canadians contract enteric illnesses each year, many of which are acquired during, or are otherwise associated with, international travel. As the number of Canadians travelling fluctuates throughout the year, a corresponding change in the number of travel-acquired enteric illnesses was expected. A change in the number of travel-acquired enteric illnesses was also expected during the COVID-19 pandemic restrictions.

Objective: This study aims to explore trends in the number and distribution of select travel-acquired enteric infections in Canada, from May 2017 to April 2023.

Methods: To evaluate trends, Student's t-tests and negative binomial regression modelling were conducted. Percent changes and relative risks were calculated to assess the impact of the pandemic on travel-acquired enteric illnesses.

Results: Findings demonstrated a seasonal peak in the number of reported travel-acquired enteric illnesses during the winter and spring pre- and post-pandemic travel restrictions (May 2017–February 2020 and September 2021–April 2023). Additionally, there was a decrease in the number of travel-acquired enteric illnesses added to enteric illness travel clusters with cases in more than one province or territory (multi-jurisdictional) during and after the lifting of COVID-19 travel restrictions. However, cases reported post-travel restrictions had a higher risk of being added to a multi-jurisdictional enteric illness travel cluster compared to the pre-travel restriction phase.

Conclusion: Nonessential travel restrictions and changes in the healthcare-seeking behaviours due to the pandemic likely account in part for the change in the number of travel-acquired enteric illnesses observed while travel restrictions were implemented and after they were lifted. Further research is required to explain the increased risk of illnesses being added to multi-jurisdictional enteric illness travel clusters after the lifting of travel restrictions compared to pre-COVID-19.

Affiliation

[1] Centre for Food-Borne, Environmental and Zoonotic Infectious Diseases, Public Health Agency of Canada, Guelph, ON

***Correspondence:**
lauren.rusk@phac-aspc.gc.ca

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Keywords: COVID-19, enteric illness, travel-acquired illness, travel, trends

Introduction

Each year, millions of Canadians experience enteric illnesses, of which approximately 25% are acquired during international travel (1). Research suggests that the incidence of travel-acquired enteric illness correlates with the number of travellers, peaking during periods of high travel activity (2,3). In Canada, this tends to occur during the winter months and previous studies in Ontario and British Columbia have confirmed this increase at the provincial level (4–6).

In March 2020, the World Health Organization declared the SARS-CoV-2 virus outbreak a pandemic. This led to countries implementing various public health measures to try and curb

its spread (7). These measures also impacted the transmission of other infectious diseases. For example, multiple countries reported a decrease in the observed incidence of enteric infections (8–11). One explanation for this decrease may be a corresponding decline in the number of travel-acquired cases of enteric illness due to the implementation of nonessential travel restrictions (8,9,11,12). In Canada, nonessential travel restrictions were in effect from March 2020–August 2021 (13,14). During this period, a reduction in the number of reported travel-acquired enteric illness cases was observed (8). However, trends and a more detailed analysis of the changes in the risk of travel-acquired enteric infections before, during and after this period remain insufficiently studied.

After nonessential travel restrictions were lifted, the phrase "revenge travel" emerged to describe the expected surge in travel activity as people rescheduled cancelled plans (15). It was hypothesized that this might lead to an increase in travel-acquired enteric infections. Currently, little is known about the extent of the "revenge travel" phenomenon and its potential effects on the number of travel-acquired enteric illness cases in Canada.

This study aims to analyze trends in travel-acquired enteric infections in Canada at the national level and assess how travel-acquired enteric infections were influenced by the imposition and removal of nonessential travel restrictions during the COVID-19 pandemic.

Methods

Data sources

Since 2017/2018, whole-genome sequencing (WGS) has been routinely performed in Canada on various enteric pathogens, including *Salmonella*, *Listeria*, *Escherichia coli* and *Shigella*, at the National Microbiology Laboratory or by a PulseNet Canada-certified provincial laboratory. Whole-genome sequencing data is shared with PulseNet Canada and compared nationally using whole-genome multi-locus sequencing typing (wgMLST) within a central BioNumerics v7.6.3 database (Applied Maths, United States). PulseNet Canada assigns cluster codes to *Salmonella*, *Listeria*, *E. coli* and *Shigella* clusters when two or more isolates (where at least one is clinical) group together within 10 wgMLST allele differences within a specified period. The criteria for common *Salmonella* serotypes (including *S.* Enteritidis, *S.* Heidleberg and *S.* Typhimurium) is three or more isolates grouping together within 10 wgMLST allele differences with at least two isolates within five alleles within a specified period. Clusters can be either single jurisdictional, with cases occurring in only one province/territory, or multi-jurisdictional, if cases occur in multiple provinces/territories. Any case that does not group within 10 wgMLST allele differences of another case is considered sporadic. As single-jurisdictional clusters and sporadic cases are not routinely investigated at the national level, these were excluded from our analyses.

Epidemiologists at the Public Health Agency of Canada (PHAC) review all multi-jurisdictional clusters and classify them to aid with follow-up. Only clusters classified as travel-related were included in our analyses. A cluster was deemed travel-related if 1) there was strong epidemiological evidence to suggest the illnesses were acquired while outside of Canada (i.e., people acquired an enteric illness while outside Canada but were tested in Canada upon their return), 2) the cluster was genetically related (i.e., within 10 wgMLST allele differences) to another previously classified travel cluster or 3) the serotype is not endemic to Canada (i.e., *S. typhi* and *S. enterica* serovar Paratyphi A) (16). At the time of our study, no multi-jurisdictional travel-related clusters of *Listeria* had been identified in Canada at the federal level. Therefore, only *Salmonella*, *E. coli* and *Shigella* were considered.

Using these criteria, we analyzed cases added to multi-jurisdictional *Salmonella* travel clusters in Canada from May 2017 to April 2023 and *E. coli* and *Shigella* travel clusters from June 2018 to April 2023 as a representation for all travelled-acquired cases of enteric illness. The date used for cases was the earliest of the following dates: 1) the isolation date, 2) the date the isolate was received for WGS or 3) the date the case was reported to PHAC.

Data for the number of Canadians travelling internationally was retrieved from a publicly available Statistics Canada dataset (17). These data were collected by the Frontier Counts program, which counts the number of individuals entering Canada. For this study, the number of Canadian residents returning from countries other than the United States was used. Travel to the United States was excluded due to the similarities in the Canadian and American food supply and because, to date, there has not been a multi-jurisdictional enteric illness cluster solely associated with travel to the United States identified in Canada.

Statistical analyses

Three time periods were analyzed: pre-COVID-19 pandemic travel restrictions (before travel restrictions related to the COVID-19 pandemic were issued; May 2017–February 2020), COVID-19 pandemic travel restrictions (March 2020–August 2021) and post-COVID-19 pandemic travel restrictions (after the travel restrictions were revoked; September 2021–April 2023). Cases were assigned to these phases based on the earliest available date described above.

Trends in the number of cases of enteric illness added to multi-jurisdictional enteric illness travel clusters were assessed using two-sided Student's t-tests to compare the mean monthly number of cases between phases. A negative binomial regression model was also employed. Negative binomial regression is suitable for modelling discrete count data that is left-censored

at zero, which is common in epidemiological studies (18). Variables included in model building were time (in one-month increments), meteorological season (winter=December–February, spring=March–May, summer=June–August, fall=September–November), the monthly number of Canadians travelling internationally and the presence of travel restrictions. Two-way interactions between independent variables were also assessed. Model selection was preformed using stepwise selection along with the Akaike Information Criterion (AIC) and likelihood-ratio test.

Percent changes in the number of travellers and cases between phases were evaluated. Relative risks (RR) were calculated to assess changes in the risk of cases being added to multi-jurisdictional enteric illness travel clusters, comparing the COVID-19 travel restrictions and post-travel restrictions phases to a pre-COVID-19 reference period of equal length.

All statistical analyses were conducted in Stata/MP 15 (Stata Corporation, United States) and utilized an alpha value of 0.05.

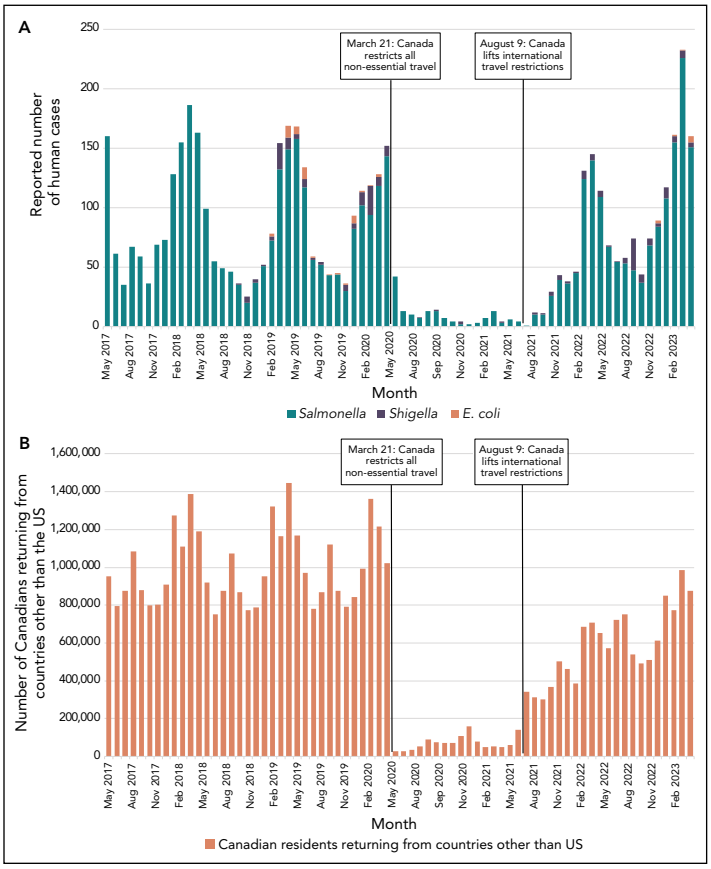
Results

Trends in travel-acquired enteric infections

From May 2017 to February 2020, the number of travel-acquired *Salmonella* infections added to multi-jurisdictional enteric illness travel clusters in Canada was significantly higher in February and March (p=0.0436 and p=0.0312, respectively; **Figure 1**) compared to other months. Travel-acquired cases of *Shigella* and *E. coli* did not exhibit any significant seasonal trends between June 2018 and February 2020. No seasonal trends were observed from March 2020 to August 2021 for all three pathogens while nonessential travel restrictions were in effect. From September 2021 to April 2023, the total number of monthly travel-acquired enteric infections added to multi-jurisdictional enteric illness travel clusters in Canada was significantly higher in March and April (p=0.0053 and p=0.0017, respectively). These increases correspond with increased international travel by Canadians during the winter and spring (Figure 1).

The negative binomial regression model that best fit the data (AIC=619.62) included all independent variables and the interaction term between time and nonessential travel restrictions (**Table 1**). The RR for a reported case of enteric illness being added to a multi-jurisdictional enteric illness travel cluster was higher during the winter (RR 1.32; 95% CI: 1.03–1.7) and spring (RR 2.26; 95% CI: 1.77–2.9) compared to the summer, with no significant difference in RR between the summer and fall.

Figure 1: Trends in A) Canadian travel-acquired enteric infections added to multi-jurisdictional clusters and B) Canadians returning from international travel[a], May 2017–April 2023



Abbreviations: *E. coli*, *Escherichia coli*; US, United States
[a] Data were collected by the Frontier Counts program, which counts the number of individuals entering Canada. Data from countries other than the United States were used

Impact of COVID-19 pandemic travel restrictions

Between June 2020 and August 2021, the number of Canadians returning from countries other than the United States decreased by 90.3% compared to the same period in 2018–2019 (1,447,595 travellers vs. 14,924,122 travellers). This decline in travellers corresponded with a 91.4% decrease in the number of reported cases of enteric illness added to multi-jurisdictional travel clusters (100 cases vs. 1,163 cases), which was observed across all three pathogens (**Figure 2**). Despite the overall decrease, the RR of reported cases of enteric illness being added to multi-jurisdictional travel clusters during the COVID-19 travel restriction phase did not change compared to the pre-COVID-19 travel restrictions phase (**Table 2**).

Table 1: Model coefficients from the negative binomial regression model

Variable	β	Standard error	95% CI		Z value	*p*-value
			LL	UL		
Intercept	−192	57.87	−300.88	−86.64	−3.32	<0.001
Meteorological season						
Summer	Referent	-	-	-	-	-
Fall	−0.041	0.13	−0.29	0.2	−0.33	0.74
Spring	0.82	0.13	0.57	1.06	6.52	<0.001
Winter	0.28	0.13	0.031	0.53	2.25	0.025
Number of travellers (centred at 668,199.4)	1.36e-6	2.10e-7	9.31e-7	1.8e-6	6.49	<0.001
Time (measured in one-month intervals)	0.097	0.029	0.043	0.15	3.38	<0.001
Restrictions on nonessential travel						
No	Referent	-	-	-	-	-
Yes	3,273	529.7	2,261.5	4,327.81	6.18	<0.001
Interaction term between time and travel restrictions	−1.62	0.26	−2.14	−1.12	−6.18	<0.001

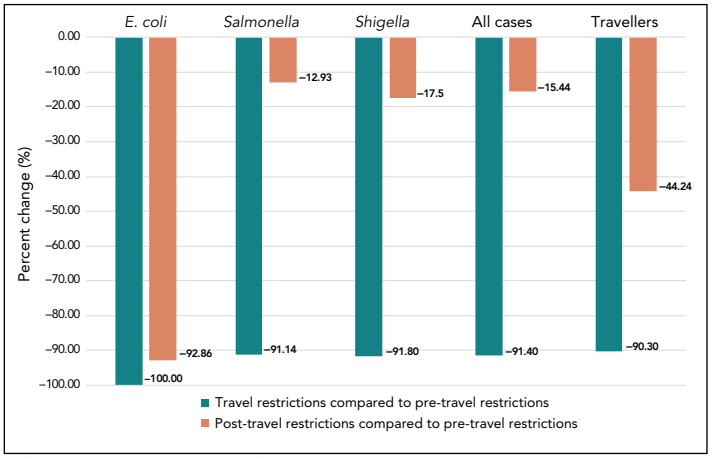
Abbreviations: CI, confidence interval; LL, lower limit; UL, upper limit; -, not applicable

Table 2: Relative risks by pathogen, between phases of COVID-19 pandemic travel restrictions[a]

Comparison	Pathogen							
	Salmonella		*Shigella*		*Escherichia coli*		Overall	
	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value	RR (95% CI)	*p*-value
COVID-19 travel restrictions to pre-COVID-19 travel restrictions	0.91 (0.74–1.13)	0.44	0.85 (0.34–2.10)	1	0 (0.0–0.0)	0.11	0.89 (0.72–1.09)	0.26
Post-COVID-19 travel restrictions to pre-COVID-19 travel restrictions	1.57 (1.45–1.70)	<0.001	1.46 (1.11–1.92)	0.007	0.34 (0.16–0.73)	0.003	1.53 (1.42–1.64)	<0.001

Abbreviations: CI, confidence interval; RR, relative risk
[a] Reference period: pre-COVID-19 travel restriction period

Figure 2: Percent change in the number of Canadians returning from international travel and the number of travel-acquired enteric infections added to multi-jurisdictional enteric illness clusters by pathogen between phases of COVID-19 travel restrictions



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

Post-COVID-19 pandemic nonessential travel restrictions

Following the lifting of international travel restrictions in August 2021, both international travel by Canadians and the reported number of enteric infections added to multi-jurisdictional travel clusters increased, but overall neither had returned to pre-pandemic levels (Figure 1). From September 2021 to February 2023, international travel was 44.2% lower compared to the 2018–2020 reference period (10,206,099 travellers vs. 18,304,311 travellers). Similarly, the number of reported enteric infections added to multi-jurisdictional travel clusters decreased by 15.4% (1,309 cases vs. 1,548 cases). Despite this, the RR of enteric illnesses added to multi-jurisdictional travel clusters was higher during the post-COVID-19 travel restriction phase compared to the pre-COVID-19 travel restriction phase, primarily due to an increased risk of travel acquired salmonellosis (Table 2).

Discussion

Anecdotal evidence suggested that travel-acquired enteric illnesses in Canada peak during the winter months; however, this had not yet been confirmed nationally. This study finds that indeed international travel by Canadians is highest from January to April, corresponding with a peak in the reported number of travel-acquired enteric illnesses added to multi-jurisdictional travel clusters. This seasonal pattern aligns with trends observed in other countries, where travel-acquired enteric infections peak with increased travel activity (2,3). In Canada, this peak is primarily driven by an increase in the reported number of *Salmonella* infections, consistent with provincial-level trends observed in Ontario (4,5).

The COVID-19 pandemic prompted the Canadian government to introduce public health measures aimed at reducing the spread of the SARS-CoV-2 virus. These measures helped to reduce the incidence of not only COVID-19 but many other infectious diseases, including enteric diseases (8–11). Several hypotheses have been proposed for the reduction in enteric illness incidence rates during the pandemic including changes in exposure-causing behaviours, changes in healthcare-seeking behaviours and a decrease in international travel. In March 2020, Canada imposed restrictions on nonessential international travel, which remained in effect until August 2021 (13,14). These restrictions reduced international travel by Canadians by 90.3% compared to the pre-pandemic reference period. As approximately 25% of enteric infections in Canada are travel-related (1), a reduction in enteric infections was anticipated and confirmed, with a 91.41% decrease in reported travel-acquired enteric infections. However, the absence of a significant change in RR suggests that this decrease was likely due to less international travel rather than changes in the risk of contracting an enteric illness abroad.

As the COVID-19 travel restrictions ended, many expected a spike in travel activity as individuals capitalized on the re-established ability to travel. We hypothesized that there would be an increase in international travel by Canadians and a corresponding increase in the number of travel-acquired enteric infections. Contrary to this, travel by Canadians was slow to rebound completely, with a 44.24% reduction in the number of Canadian travellers compared to pre-COVID-19 levels. Moreover, the number of reported travel-acquired enteric infections added to multi-jurisdictional travel clusters decreased by 14.76%. Despite this decline, the RR of 1.53 (95% CI: 1.42–1.64) suggests a higher risk of travel-acquired cases of enteric illness being added to multi-jurisdictional clusters during this period. It is possible that, due to the COVID-19 pandemic, Canadians are now more health-conscious and aware of the health risks associated with international travel. Furthermore, given that many symptoms of enteric infections mirror those of COVID-19, more ill Canadians may have sought a medical diagnosis upon returning to Canada during this period out of fear that they had contracted COVID-19. This would result in cases of enteric illness being reported that historically may have gone undetected. Another possible explanation is that there were changes in the travel destinations of Canadians after the pandemic. As different countries have differing rates of enteric disease, this also could have contributed to the increased risk observed.

Limitations

There are some limitations to this study that must be taken into consideration. First, the reported number of travel-acquired enteric infections used underestimates the true burden of travel-associated enteric illness in Canada. Our sampling frame consisted of cases of enteric illness for which a specimen was submitted for testing and WGS, and subsequently assigned to a multi-jurisdictional cluster. Cases of enteric illness often go unreported as many individuals never submit a specimen for testing and are therefore not captured by public health surveillance systems. Additionally, during the pandemic, laboratory testing for COVID-19 was prioritized, which may have reduced testing for enteric pathogens and resulted in further underreporting during this period. Furthermore, cases that were not part of a multi-jurisdictional enteric illness cluster were excluded as they are not routinely investigated at the federal level in Canada.

Additionally, when providing potential explanations for the increased risk since the lifting of travel restrictions, we could not assess whether the travel destinations of Canadians had changed. Therefore, it is not possible to conclude whether changes in travel behaviours amongst Canadians may have contributed to the increased RR.

Finally, misclassification is a concern. At the national level, epidemiologists review exposure details for cases, including whether cases travelled outside of Canada during their exposure period. If a number of cases in a multi-jurisdictional enteric illness cluster report international travel to the same destination, the cluster is classified as travel-associated. Subsequent cases added to the cluster are assumed to be travel-acquired based on their genetic relatedness, but this is generally not confirmed via exposure data. Similarly, clusters identified within 10 wgMLST allele differences to a cluster that was previously classified as a travel cluster are classified as travel-acquired without confirmation via exposure data. Therefore, it is possible that some cases included in this study may not be travel-acquired even though they are in a cluster that is classified as travel-associated. Additionally, due to the limited nature of the exposure information available at a national level, the immigration status of cases is often unknown, which may result in some cases of enteric illness being misclassified. Finally, cases were aggregated by month and categorized into phases based on the earliest date available for each case. All the dates used occurred after the cases' symptom onset date, which may have caused the case to be misclassified into the wrong month. Future studies should apply quantitative methods to evaluate the impact of potential misclassification and other systemic errors.

Conclusion

Identifying peak periods for travel-acquired enteric illnesses in Canada allows for timely deployment of public health resources and targeted messaging to increase awareness and reduce travel-related risks. The findings of this study highlighted seasonal increases in the number of travel-acquired enteric infections added to multi-jurisdictional enteric illness travel clusters during the winter and spring months. The reduction in cases during the pandemic is likely due to fewer people travelling during this time. While this helps clarify the impact of COVID-19 on these infections, further research is needed to understand the heightened risk during the post-pandemic travel restriction phase.

Authors' statement

LR — Methodology, formal analysis, writing–original draft, writing–review & editing
RF — Conceptualization, methodology, formal analysis, writing–review & editing
MH — Conceptualization, methodology, writing–review & editing

Competing interests

None.

ORCID numbers

Lauren Rusk — 0009-0004-8042-8118
Russell Forrest — 0000-0003-1875-388X
Meghan Hamel — 0009-0006-4058-0726

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Enhanced screening for tuberculosis infection among immigrants in southern New Brunswick: A cross-sectional pilot study

Isdore Chola Shamputa[1]*, Duyen Thi Kim Nguyen[2,3], Hope Mackenzie[4], Derek J Gaudet[5], Alicia Harquail[2], Kim Barker[2], Duncan Webster[6,7,8]

Abstract

Background: In 2021, approximately 77% of active tuberculosis (TB) disease (TBD) cases in Canada were among foreign-born individuals. Less than 3% of TBD cases in Canada are detected through pre-arrival Canadian immigration medical examinations (i.e., chest X-rays), and the remaining 97% are likely due to reactivation of undiagnosed latent TB infection (TBI) post-arrival. In New Brunswick, the proportion of TBD cases among foreign-born individuals gradually increased from about 33% (1/3 individuals) in 2013 to 100% (14/14 individuals) in 2023. The objective of this study was to estimate the prevalence of TBI among immigrants in southern New Brunswick, identify potential predictors for positive TBI screening and assess participant experiences with the pilot TBI screening procedure.

Methods: A cross-sectional study was conducted from November 2021 to November 2023 among immigrants ≥19 years old who had no history of TBD and were born in a country with a TB incidence rate of ≥40/100,000 population or were referred by healthcare professionals. Participants were recruited through various channels and underwent TBI screening using the interferon-gamma release assay, followed by a survey on their screening experience.

Results: Of the 264 participants, 49 (18.6%) screened positive for TBI. Factors associated with higher odds of screening TBI-positive included birthplace in a "highly to severely endemic" (≥300/100,000 population) TB-incidence country (OR=3.24; 95% CI: 1.07–9.81) and increased age (OR=1.05; 95% CI: 1.01–1.08). Participants rated the pilot TBI screening procedure positively (mean scores ranged from 4.03–4.55 on a five-point Likert scale).

Conclusion: Results suggest that immigrants born in countries with TB incidences of ≥300/100,000 population should be considered for screening and treatment of TBI. The pilot TBI screening procedure yielded positive feedback. Further research with a larger sample is recommended.

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Affiliations

[1] Department of Nursing and Health Sciences, University of New Brunswick, Saint John, NB

[2] Department of Health, Government of New Brunswick, Saint John, NB

[3] Faculty of Business, University of New Brunswick, Saint John, NB

[4] Microbiology Laboratory, Saint John Regional Hospital, Saint John, NB

[5] Department of Psychology, University of New Brunswick, Saint John, NB

[6] Dalhousie Medicine New Brunswick, Dalhousie University, Saint John, NB

[7] Division of Medical Microbiology, Department of Laboratory Medicine, Saint John Regional Hospital, Saint John, NB

[8] Division of Infectious Diseases, Department of Medicine, Saint John Regional Hospital, Saint John, NB

***Correspondence:**
chola.shamputa@unb.ca

Introduction

Approximately 25% of the global population has latent tuberculosis (TB) infection (TBI) (1,2), of which 5%–10% go on to develop active TB disease (TBD) (3–5). In 2023, there were 10.8 million TBD cases and 1.25 million TBD-related deaths worldwide (5). While more than 80% of the TBD cases and deaths occur in low- and middle-income countries (5), high-income countries also report TBD cases, in part due to immigration and international travel (6–9).

In 2021, Canada had a TBD incidence rate of 4.8 cases per 100,000 population and 76.7% of the cases were among individuals born outside Canada (10). The Atlantic Canadian

province of New Brunswick (NB) has experienced a notable rise in immigration in the last decade (11,12). Coinciding with this immigration growth is the increase in the proportion of TBD cases among foreign-born individuals. For example, the proportion of foreign-born TBD cases has gradually risen from 33% (n=1) in 2013 to 100% of cases in 2022 (n=17) and 2023 (n=14) (*personal communication, Public Health Agency of Canada TB Task Force Meeting, November 26–27, 2024*). The rise of TBD in NB provides an opportunity for the provincial healthcare system to explore additional preventative strategies to curb the increase of TBD and protect and promote the health of its population, while continuing to welcome new immigrants to the province.

Current pre-arrival Canadian immigration medical examinations focus on detecting TBD through screening with chest X-ray (13). The current screening system does not assess for TBI, thus creating a gap where individuals with TBI are at-risk of TB reactivation post-arrival. Research has shown that <3% of TBD cases diagnosed among immigrants to Canada are detected through the immigration post-landing surveillance program (14). In 2019, Immigration, Refugees and Citizenship Canada (IRCC) broadened screening requirements to include pre-arrival TBI screening for certain high-risk immigration applicants (**Box 1**) (13). To our knowledge, this program has not been evaluated and the number of TBD cases averted is unknown. While the TB incidence rate of a person's country of birth has been shown to be a risk factor for TBI (15–18), it is noticeably absent from the recent IRCC recommendations (13). Interestingly, there are currently no widely established avenues for routine TBI screening for immigrants in Canada, despite its potential to curb increasing prevalence of TBD, and the call from experts for enhanced screening efforts (19).

Box 1: Immigration, Refugees and Citizenship Canada screening criteria for tuberculosis infection[a]

Screening criteria for tuberculosis infection

1. Individuals seropositive for human immunodeficiency syndrome
2. Individuals who have been in close contact with TB disease in the last five years
3. Individuals with a history of certain head and neck cancers within the previous five years
4. Individuals undergoing dialysis or suffering from advanced chronic kidney disease
5. Individuals who have had solid organ or bone marrow transplants and are receiving immunosuppressive therapy

[a] Adapted from Immigration, Refugees and Citizenship Canada. Canadian panel member guide to immigration medical examinations 2020. Ottawa, ON: IRCC. https://www.canada.ca/en/immigration-refugees-citizenship/corporate/publications-manuals/panel-members-guide.html

The purpose of this study was to enhance current TBI screening in southern NB, which presently follows the IRCC TB screening protocol, by investigating the potential value of a targeted TBI pilot screening program among immigrants in southern NB. This study seeks to address the gap from IRCC's current TB screening system, by estimating the TBI prevalence among immigrants in southern NB, identifying potential predictors of screening positive for TBI and evaluating the experience of immigrants taking part in the pilot TBI screening procedure. To our knowledge, this is the first Canadian study to offer routine TBI screening to all immigrant streams (e.g., temporary foreign workers, family reunion, permanent residents, international students, refugees), whereas in previous Canadian TBI studies, the primary focus was on the refugee populations (20–23).

The interferon-gamma release assay (IGRA) was used for TBI screening in this study instead of the traditional tuberculin skin test (TST). The IGRA offers several advantages, including the use of antigens more specific to *Mycobacterium tuberculosis*, a single visit for blood draw, screening not influenced by the Bacille Calmette–Guérin (BCG) vaccination or previous exposure to certain non-tuberculous mycobacteria and improved consistency in results with fewer concerns regarding inter-rater reliability (24,25).

Methods

Study design

A cross-sectional study was conducted among immigrants to Canada, from November 4, 2021, to November 21, 2023. Participants were eligible if they were ≥19 years old and resided in southern NB, and were either: a) born in a high-TB-incidence country, defined as ≥40 cases per 100,000 population) (7), b) were referred to Public Health NB by IRCC or c) were at high risk of TBI due to having a TBD-positive partner or having lived in a high-TB-incidence country, or were considered to be at high-risk of TBI following the post-arrival health assessments (PAHAs) of government-assisted refugees (GARs) by NB Primary Health Care. Participants with a history of TBD or TBD treatment were excluded from this study.

Participant recruitment

Participants were recruited using posters, social media channels, snowball sampling, public health channels or PAHAs of GARs. Prospective participants contacted the research team using the phone number or email provided on recruitment materials or met with a research team member in-person after their PAHAs. To help minimize potential recruitment bias, this study included all eligible immigrants at risk of TBI, irrespective of the language they spoke, when they arrived in Canada, or their immigration stream.

Sample size was estimated *a priori* as previously described (26,27). Based on an estimated prevalence of TBI of 25% (2), our calculation yielded an estimated minimum sample size of 160 individuals. The published study protocol describes a minimum sample size estimate of 240 individuals, but this discrepancy is due to removing two predictors (i.e., comorbidities and immigration stream) (28). Co-morbidities were

removed because they were not feasible to collect due to lack of access to personal medical records, and immigration stream was omitted because it resulted in too many dummy variables, which would have reduced the power of the analysis. Due to the aforementioned reasons, only four of the six original variables were included in the study's regression analyses (i.e., age, sex, gender and incidence rate classification).

Procedure

Potential participants were asked to provide demographic information, including sex, gender, date of birth, country of birth, date of arrival in Canada and type of Canadian entry visa to assist with screening for eligibility.

Pilot tuberculosis infection screening process

Those that met the study's eligibility criteria were provided a consent form to review. Consent forms were translated into the seven most spoken languages among immigrants in southern NB (29). Following written consent, a research member organized phlebotomy appointments at one of two local hospitals, chosen by the participant. During phlebotomy, hospital staff guided participants through established protocols. For participants recruited at PAHAs, the study was explained by a research team member in their chosen language with the help of a virtual translation service. The YMCA of Greater Saint John staff, which is the local immigrant-serving organization responsible for GAR settlement, arranged phlebotomy appointments and accompanied participants. Other community partners, such as the Saint John Newcomers Centre and PRUDE Inc., also offered close collaboration to support study participants.

Materials

All blood samples were transported to the Saint John Regional Hospital Microbiology Laboratory for TBI screening. Screening was performed using the IGRA (QuantiFERON-TB Gold Plus; QIAGEN, Germantown, Maryland, United States [US]) as per the manufacturer's recommendations. The IGRA results were categorized as either positive (≥0.35 IU/mL), negative (<0.35 IU/mL) or indeterminate (29). An IGRA was repeated if samples yielded an indeterminate result. If the result remained indeterminate, next steps were determined through review and clinical assessment by an infectious disease specialist. The IGRA results and relevant diagnostic data were accessed and communicated to participants by a healthcare provider. Participants positive for TBI were offered clinical assessment. In cases, where the IGRA was positive, TBD was ruled out and participants were offered TB preventive treatment (TPT). The TPT results will be provided in a follow-up paper.

Following the screening procedure, participants were asked to complete a TBI pilot screening process experience survey using Qualtrics, an online survey platform. The survey was intended to gather information regarding their experience of participating in this study, and included 11 questions on five-point Likert scales, along with open-ended questions. Participants completed the survey virtually through an email containing an attachment or a link to the survey, provided by a research team member. The survey questions focused on 1) equity, diversity, and inclusion; 2) barriers and facilitators to TBI screening, such as language, cultural factors, accessibility of the blood collection facility, interactions with healthcare professionals; and 3) the overall ease or difficulty of participating in the study (see **Appendix 1**) (28).

Data analysis and management

The TB incidence rate of a participant's country of birth was obtained through World Health Organization (WHO) data (30) to create incidence rate categories. Participants were classified as being born in countries with incidence rates considered to be low (<10/100,000 population), lower-moderate (10–49/100,000 population), upper moderate (50–99/100,000 population), endemic (100–299/100,000 population), highly endemic (300–499/100,000 population) or severely endemic (≥500/100,000 population), as per the WHO classification (31). Due to low counts in certain categories, and to maintain adequate statistical power, incidence categories were combined into three new categories for the analyses: "sub-endemic" (0–99/100,000 population), comprising low, lower-moderate and upper moderate, and "highly to severely endemic" (≥300/100,000 population), comprising highly endemic and severely endemic. The "endemic" category (100–299/100,000 population) remained unchanged (31).

In terms of data management and analysis, survey data was completed in Qualtrics, exported to Excel and merged with participants' demographic data; thereafter, the data was de-identified and stored on an encrypted OneDrive account. The quantitative de-identified data was imported into IBM SPSS Statistics (version 29; Armonk, New York, US) for analysis. Categorical measures were presented as frequencies and percentages, and continuous measures were presented using means and standard deviations (SD). Associations between predictors and TBI were presented as odds ratios (ORs) with 95% confidence intervals (CIs).

For the sensitivity analysis, literature suggests that recent immigrants are at a higher risk of developing TBD from TBI within the first two to five years of their arrival (32); thus, binary logistic regression analysis was repeated using data from those that had arrived in the last five years, as this cohort would benefit most from being screened and treated.

Ethical approval

This study was approved by the Horizon Health Network (file #: RS 2021–3046) and University of New Brunswick (file #: 033-2021) Research Ethics Boards.

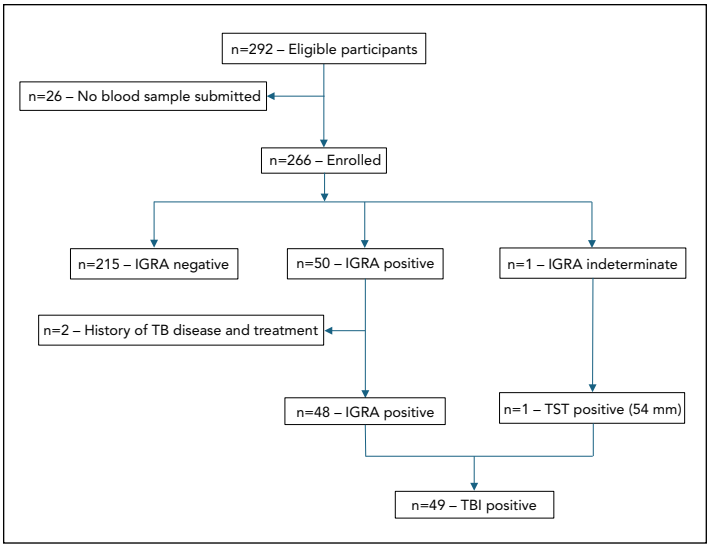
Results

Participants

Of 292 participants who consented to this study, a total of 28 participants were excluded as they had not submitted blood specimens for TBI screening (n=26) or had a previously undisclosed history of TBD and treatment (n=2). Among 26 participants who did not provide blood samples for TBI screening, 17 were born in "endemic" to "highly to severely endemic" TB incidence countries, of whom 16 (94.1%) relocated to other provinces. After excluding the aforementioned participants, the total sample size was 264 (**Figure 1**).

The average age of the 264 participants was 36.8 years (SD=10.27), ranging from 19 to 67 years. More than half (53.8%) identified as female. Self-reported biological sex and gender identity was consistent across participants, except for one participant who identified their biological sex as male and identified their gender as a trans-female. Given the near-identical count for biological sex and gender identity, sex was retained in the regression analyses, while gender was dropped. Additional descriptive characteristics are presented in **Table 1**.

Figure 1: Participant flowchart



Abbreviations: IGRA, interferon-gamma release assay; TB, tuberculosis; TBI, tuberculosis infection; TST, tuberculin skin test

Table 1: Descriptive statistics of participants (n=264)

Characteristic	Variables	TBI		n
		Positive[a] (%)	Negative (%)	
Sex	Male	21 (17.2%)	101 (82.8%)	122
	Female	28 (19.7%)	114 (80.3%)	142
	Total	49 (18.6%)	215 (81.4%)	264
Age group (years)	19–24	3 (8.6%)	32 (91.4%)	35
	25–34	11 (14.1%)	67 (85.9%)	78
	35–44	22 (22.0%)	78 (78.0%)	100
	45–54	8 (21.1%)	30 (78.9%)	38
	55–64	4 (36.4%)	7 (63.6%)	11
	65 and older	1 (50.0%)	1 (50.0%)	2
	Total	19 (7.2%)	215 (81.4%)	264
Year of arrival in Canada	2000	0 (0.0%)	1 (100%)	1
	2001	1 (100%)	0 (0.0%)	1
	2002	0 (0.0%)	1 (100%)	1
	2007	0 (0.0%)	3 (100%)	3
	2010	0 (0.0%)	4 (100%)	4
	2012	0 (0.0%)	2 (100%)	2
	2013	0 (0.0%)	2 (100%)	2
	2014	1 (100%)	0 (0.0%)	1
	2015	0 (0.0%)	1 (100%)	1
	2016	1 (33.3%)	2 (66.7%)	3
	2017	0 (0.0%)	7 (100%)	7

Table 1: Descriptive statistics of participants (n=264) (*continued*)

Characteristic	Variables	TBI		n
		Positive[a] (%)	Negative (%)	
Year of arrival in Canada (*continued*)	2018	1 (10.0%)	9 (90.0%)	10
	2019	3 (16.7%)	15 (83.3%)	18
	2020	0 (0.0%)	6 (100%)	6
	2021	5 (16.1%)	26 (83.8%)	31
	2022	18 (19.4%)	75 (80.6%)	93
	2023	19 (23.8%)	61 (76.2%)	80
	Total	49 (18.6%)	215 (81.4%)	264
Country of birth by World Health region	Western Pacific	7 (20.6%)	27 (79.4%)	34
	Americas	4 (16.7%)	20 (83.3%)	24
	Africa	11 (24.4%)	34 (75.6%)	45
	South-East Asia	2 (6.7%)	28 (93.3%)	30
	Europe	0 (0.0%)	8 (100%)	8
	Eastern Mediterranean	25 (20.3%)	98 (79.7%)	123
	Total	49 (18.6%)	215 (81.4%)	264
TBI screening results by recruitment category	Born in high TB incidence country[b]	44 (20.4%)	172 (79.6%)	216
	Referred by Public Health[b]	1 (50.0%)	1 (50.0%)	2
	Recruited via PAHAs[b]	4 (10.3%)	35 (89.7%)	39
	At-risk of TBI[c]	0 (0.0%)	7 (100%)	7
	Total	49 (18.6%)	215 (81.4%)	264
TB incidence by country of birth (per 100,000 population)	Sub-endemic (0–99)	15 (13.8%)	94 (86.2%)	109
	Endemic (100–299)	25 (20.0%)	100 (80.0%)	125
	Highly to severely endemic (≥300)	9 (30.0%)	21 (70.0%)	30
	Total	49 (18.6%)	215 (81.4%)	264
Primary healthcare provider (doctor/nurse practitioner) in Canada	No	49 (21.7%)	177 (78.3%)	226
	Yes	0 (0.0%)	38 (100%)	38
	Total	49 (18.6%)	215 (81.4%)	264

Abbreviation: PAHA, post-arrival health assessment; TB, tuberculosis; TBI, tuberculosis infection
[a] Includes one individual with an indeterminate IGRA and positive tuberculin skin test
[b] ≥40/100,000 population
[c] Due to TBD-positive partner or having lived in a high-TB-incidence country (born in a low-TB-incidence country, i.e. <40/100,000 population)

Tuberculosis infection screen outcome

Of 264 participants, 18.6% (n=49) had a positive TBI screening. One participant had an indeterminate IGRA result on two separate screens due to a reactive negative control. Subsequent TST in the indeterminate case revealed an induration of 54 mm. Based on the participant's demographics, clinical evaluation and radiological studies, this participant was categorized as TBI-positive (Figure 1). Table 1 includes TBI screening results by sex, age range, year of arrival in Canada, country of birth by WHO region, recruitment category, TB incidence of country of birth and primary healthcare provider.

When comparing IGRA screening results by recruitment categories, most of the positive results were found among immigrants born in high-TB-incidence countries. Similarly, when analyzed based on TB incidence rate classifications, a higher proportion of participants born in "highly to severely endemic" TB countries screened positive for TBI (30%), compared to those born in TB-"endemic" (20%) and "sub-endemic" (14%) countries (Table 1).

Binary logistic regression

Binary logistic regression was used to predict TBI screen outcome using age, sex and TB incidence category by country of birth as predictors. Odds ratios were examined to determine the impact of each variable. The binary logistic regression model was statistically significant, χ^2 (4)=13.42, p=0.009, with a Nagelkerke R^2 value of 0.08. The odds of a positive screen were approximately 3.5 times higher for individuals born in a "highly to severely endemic" country compared to those born in countries classified as "sub-endemic" (OR=3.45; 95% CI: 1.28–9.27). Also, age was found to increase the odds of a positive TBI screen (OR=1.05; 95% CI: 1.02–1.08). Neither sex, nor birth in a TB "endemic" country, was found to be statistically significant (**Table 2**). Sensitivity analyses results were consistent with the main results (**Appendix 2**, **Table A1**).

Participant experience of the tuberculosis infection screen process

To assess the participants' experience in the TBI pilot screening procedure, means and SDs were calculated to assess each survey item response and interpreted with guidance described previously (33). Surveys regarding the pilot TBI screening procedure were completed by 176 participants (66.7 overall response rate), with more than half (54.1%) being self-reported female respondents. The mean age was 36.78 years (SD=9.75). Participant responses are presented in **Table 3**. Participants rated the ease of locating the phlebotomy site most favourably (M=4.55, SD=0.68) and wait times for phlebotomy least favourably (M=4.03, SD=1.03). Participants reported positive attitudes towards TB and expressed willingness to recommend TBI screening to others.

Discussion

This pilot study was the first to offer routine TBI screening among immigrants in Atlantic Canada. It differs from previous studies in Canada in several key ways: a) TBI screening was offered to all immigrant groups, rather than focusing on refugee populations; b) it employed the IGRA, in contrast to the traditional TST; and c) the research team collaborated closely with immigrant-serving community partners, which was deemed important for raising awareness and the successful completion of TBI screening and treatment programs in this setting. With respect to the current TB screening practices in NB, our study identified nearly 50 TBI-positive individuals of which only one was referred by IRCC to Public Health NB. These results highlight potential opportunities for increased screening for TBI amongst immigrants in NB.

This study had three key findings. First, a TBI prevalence of 18.6% was found among immigrants in southern NB. Second, increased age and birth in a country with a "highly to severely endemic" TB incidence were identified as factors associated with greater odds of screening positive for TBI. Third, the IGRA worked well in this setting and study participants reported

Table 2: Logistic regression analysis of positive tuberculosis infection screen results

Predictor variable	ß	SE	*p*-value	Odds	95% CI for odds ratio	
					Lower	Upper
Age	0.048	0.016	**0.003**	1.049	1.016	1.083
Sex	−0.106	0.329	0.747	0.899	0.472	1.713
Endemic	0.516	0.364	0.156	1.675	0.821	3.421
Highly to severely endemic	1.237	0.505	**0.014**	3.446	1.280	9.272

Abbreviations: CI, confidence interval; SE, standard error
Note: Model χ^2=13.42, p=0.009, Nagelkerke R^2=0.08, N=264. The dependent variable in the analysis was coded as 0=negative result and 1=positive result. Bolded p-values are statistically significant

Table 3: Survey ratings regarding the pilot tuberculosis infection testing procedure

Item	N	Mean	SD
I received information on why the latent tuberculosis test was being done.	153	4.52	0.61
The blood collection office was easy to find.	172	4.55	0.68
The blood collection office was easy to travel to.	171	4.53	0.61
The blood collection process was simple (e.g., registration, blood collection).	172	4.49	0.64
The waiting time for blood collection was reasonable.	166	4.03	1.03
The healthcare provider (i.e., doctor, nurse) answered all my questions.	168	4.35	0.81
I was satisfied with the overall experience with the latent tuberculosis screening process and/or care I received.	172	4.46	0.77
I would recommend other people to do a latent tuberculosis screening test.	169	4.52	0.65
My knowledge regarding tuberculosis improved by participating in the study.	169	4.12	0.96
My attitudes regarding tuberculosis improved by participating in the study.	167	4.25	0.79

Abbreviation: SD, standard deviation

that the pilot TBI screening procedure used in this study was satisfactory.

The prevalence of TBI in this study is comparable to earlier reports of immigrants in other low TB incidence countries (34,35), but lower than global and Canadian estimates of 25% (36,37). We suspect this difference may be attributed to the local pattern of immigration during the study period and/or the smaller study sample size.

Results regarding the association between birth in a "highly to severely endemic" TB incidence country and TBI are akin to previous research (35,37,38). These findings indicate that TBI screening for immigrants born in "endemic" and "sub-endemic" countries may be of less value than screening immigrants from countries with "highly to severely endemic" TB incidence. Likewise, our results associating older age with positive TBI screening are congruent with earlier reports (39–42). One plausible explanation for these associations is that older age and high TB incidence in the immigrant's country of birth increases the participants' vulnerability for TBI due to greater time to the potential exposure to TBD, emphasizing the need to institute mitigating factors, such as TB awareness campaigns, early detection and TPT to protect and enhance overall health.

It is noteworthy that most participants who relocated to other provinces before providing blood samples for TBI screening were born in "endemic" and "highly to severely endemic" countries. This is concerning, as TBI is not reportable in most public health jurisdictions and cases may go unidentified with the potential for development of TBD. Study participants expressed general satisfaction with the TBI screening process, and the use of the IGRA as the screening tool was a novel component of this study. However, participants desired shorter wait times for sample collection. Additionally, there was a recognized need for increased awareness campaigns aimed at improving understanding and attitudes toward TB.

Regarding the year of arrival and TBI screening, it is important to recognize that immigrants to Canada who have lived in the country for an extended time may travel back to their home country. Although they may have tested negative for TBD during their initial immigration screening, these subsequent visits could be associated with new exposures and the potential for subsequent development of TBD (43). However, this would have had minimal impact on our sample, as over three-quarters of study participants arrived within the previous three years.

Use of the IGRA allowed for several distinct advantages in this pilot screening study. Many study participants had a prior history of BCG, which lowers the specificity of the TST (25,44). In addition, many participants were recent immigrants with multiple competing obligations and new to a local health system with many barriers. As such, minimizing the complexity and the number of clinic visits was desirable. Many immigrants were undergoing phlebotomy for other PAHA-associated testing and thus the IGRA could be easily incorporated into this process. No additional follow-up reading was required, as would have been the case with the use of the TST (25). In a setting of low TB incidence, where proficiency with TST administration and reading may be inadequate, the IGRA provided objective results, avoiding issues of inter-observer variability (44). Furthermore, in a post-pandemic setting with strained healthcare resources, a shortage of clinical staff, and a lack of quality assessment with TST, the IGRA can promote efficiency in the use of local resources. The cost effectiveness of the IGRA over the TST in this setting continues to be assessed and will benefit from further study.

In March 2024, the Public Health Agency of Canada established a one-year time-limited TB task group, whose membership includes representatives from each province, territory and national Indigenous organizations. The timeliness of these findings is relevant to the anticipated recommendations to be shared with the Communicable and Infectious Disease Subcommittee of the Public Health Agency of Canada in March of 2025.

Limitations

Results from this study should be interpreted with caution. First, the study participation acceptance rate was not calculated, due to various recruitment methods, which made it difficult to track those who declined to participate. Thus, feedback regarding participants' experiences of the pilot TBI screening procedure may be biased towards those who are concerned about TB. Second, this study had a relatively small sample size, and the fluctuating immigration patterns during the study period may limit the generalization and application of the study's results to inform policy. Also, the study produced fewer positive screening results than the expected number that was based on the global TBI incidence estimate. Although statistical power was maintained, this came at the cost of excluding predictors such as immigration stream. Further, while we intended to include all six WHO TB recommended incidence categories into the model, sample size necessitated the collapse of some categories, resulting in the use of only three broader categories. Future research should aim to include all six recommended categories to establish a more granular understanding of the risk associated with WHO-designated incidence rate categories. Third, data on comorbidities were not gathered, due to challenges in obtaining accurate information. Such data could have offered insights into the risk of early progression from TBI to TBD. More stringent inclusion criteria, refining recruitment methods, and expanding the sample size could help address these limitations. Fourth, the nature of the study limited the ability to account for potential confounding factors, as it was not an experimental study with random sampling or stringent controls. While all immigrants were eligible to participate, only those who volunteered during the recruitment period were included, which may introduce self-selection bias. We recognize the potential for other confounding

variables, but addressing them was beyond the scope of this study. Although the regression analysis accounts for age and sex, no additional data were collected to control for other potential confounders.

Conclusion

This study provides initial insights into the prevalence and contributing factors associated with screening positive for TBI among immigrants in southern NB. Study results highlight the role for screening immigrants from countries with a TB incidence of ≥300/100,000 population using the IGRA. With further refinement, the TBI screening procedure used in this study could be valuable for broader program application.

Authors' statement

ICS — Conceptualization, methodology, acquired the financial support, investigation, data curation, software, validation, formal analysis, writing–original draft, writing–review and editing
DTKN — Conceptualization, methodology, validation, acquired the financial support, writing–original draft, writing–review and editing
HM — Writing–review and editing, supervision
DJG — Validation, data curation, software, formal analysis, writing–original draft, writing–review and editing
AH — Investigation, writing–review and editing
KB — Conceptualization, supervision, acquired the financial support, writing–review and editing
DW — Conceptualization, investigation, validation, acquired the financial support, supervision, data development, writing–review and editing

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

Competing interests

ICS, KB and DW report receiving in-kind donation of QuantiFERON®-TB Gold Plus test kits used in the study from QIAGEN Inc. QIAGEN Inc. also covered a portion of the article processing charges for the published protocol of this study.

ORCID numbers

Isdore Chola Shamputa — 0000-0003-1888-8936
Kim Barker — 0000-0001-5391-8999
Duncan Webster — 0000-0001-7692-7150

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Appendix 1: Participant Survey

Instructions: Please circle the response that best describes your agreement with the statement.

1. I received information on why the latent tuberculosis test was being done.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5

2. The blood collection office was easy to find.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5

3. The blood collection office was easy to travel to.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5

4. The blood collection process was simple (e.g., registration, blood collection).

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5

5. The waiting time for blood collection was reasonable.

Too long	Somewhat long	Neutral	Somewhat short	Very short
1	2	3	4	5

6. The healthcare provider (i.e., doctor, nurse) answered all my questions well.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5

7. I was satisfied with the overall experience with the latent tuberculosis screening process and/or care I received.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5
If you were not satisfied, why?				

8. I would recommend other people to do a latent tuberculosis screening test.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5
If you not, please explain:				

9. My knowledge regarding tuberculosis improved by participating in the study.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5
Please explain:				

10. My attitudes regarding tuberculosis improved by participating in the study.

Strongly disagree	Disagree	Neutral	Agree	Strongly agree
1	2	3	4	5
Please explain:				

11. Do you have any suggestions on how the latent tuberculosis testing process can be improved?

Yes	No
1	2

If yes, please provide your suggestions below:

Appendix 2: Sensitivity analysis

Analyses were conducted using one additional strategy. As research has shown that recent immigrants are more at risk of developing tuberculosis (TB) disease (TBD) from remotely acquired TB infection (TBI), we decided to run the binary logistic regression using data from immigrants who had arrived in the last five years (i.e., since 2019). There was no significant change in the pattern of results. Two hundred and twenty-eight individuals were included in this alternative analysis, with 183 testing negative and 45 testing positive for TBI. Binary logistic regression was used to predict TBI test outcome using age, sex and TB incidence category of the participants' country of birth as predictors. Odds ratios were examined to determine the impact of each variable. The binary logistic regression model was statistically significant, χ^2 (4)=13.98, p=0.007, with a Nagelkerke R^2 value of 0.09. The odds of a positive test were approximately 3.6 times higher for individuals born in a country classified as highly to severely endemic as compared to those born in countries classified as sub-endemic (OR=3.64; 95% CI: 1.26–10.55). Age was found to increase the odds of a positive TBI screen (OR=1.05; 95% CI: 1.02–1.09); that is, every additional year of age increased the odds of a positive screen by 1.05 times. In other words, the odds of obtaining a positive screen increased by 5% for every additional year a participant was aged. Neither participant sex, nor being born in a TB endemic country, was found to be statistically significant (Table A1).

Table A1: Logistic regression analysis data of participants arriving between 2019–2023

Predictor variable	ß	SE	*p*-value	Odds	95% CI for odds ratio	
					Lower	Upper
Age	0.051	0.018	**0.004**	1.053	1.017	1.090
Sex	−0.258	0.347	0.458	0.773	0.391	1.526
Endemic	0.592	0.386	0.126	1.807	0.847	3.854
Highly to severely endemic	1.292	0.543	**0.017**	3.641	1.256	10.550

Abbreviations: CI, confidence interval; SE, standard error
Note: Model χ^2=13.98, p=0.007, Nagelkerke R^2=0.09, N=264. The dependent variable in the analysis was coded as 0=negative result and 1=positive result. Bolded *p*-values are statistically significant

Cutaneous larva migrans in Canadian travellers returning from the Caribbean: A 10-year surveillance analysis from CanTravNet

Andrea Boggild[1,2], Rachel Bierbrier[3,4], Michael Libman[4], Cedric Yansouni[4], Anne McCarthy[5], Jan Hajek[6], Wayne Ghesquiere[7], Yazdan Mirzanejad[6,8], Katherine Plewes[6], Jean Vincelette[9], Susan Kuhn[10], Pierre Plourde[11], Christina Greenaway[4,12], Kevin Kain[1,13], Shaun Morris[14,15], Sapha Barkati[4]*

Abstract

Background: Cutaneous larva migrans (CLM) is one of the most common dermatoses affecting travellers to the tropics.

Objective: To describe demographic and travel correlates of travellers returning to Canada from the Caribbean with CLM over a 10-year pre-pandemic period.

Methods: Demographic and travel-related data on ill travellers encountered either during or after completion of their travel/migration and seen in any of eight CanTravNet sites from January 1, 2009, to December 31, 2018, with a final diagnosis of CLM were extracted and analyzed. During this time, access to first-line therapy, ivermectin, was available via Health Canada's Special Access Programme.

Results: Of 17,644 travellers presenting to CanTravNet over the enrolment period, 328 (1.9%) returned from the Caribbean with CLM. The median age of travellers with CLM was 34 years (interquartile range: 25–50 years), with females accounting for 58% of cases. Ninety-five percent (n=313) travelled for tourism. Jamaica was the most common source country, with 216 cases (67%), followed by Barbados (n=27, 8%) and the Dominican Republic (n=23, 7%). Cases in 2018 were imported predominantly from Jamaica (n=58, 73%) and the Dominican Republic (n=12, 15%). Age, sex and purpose of travel were similar across years. The percentage of all imported cases of CLM that originated from the Caribbean increased from 9% in 2016 to 24.5% in 2018.

Conclusion: Proportions and absolute numbers of CLM in travellers returning to Canada from the Caribbean are increasing. Improved awareness of this common dermatosis among physicians and travellers, as well as improved access to effective therapies, will reduce associated morbidity.

Affiliations

See Appendix

***Correspondence:**
sapha.barkati2@mcgill.ca

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Keywords: ivermectin, dermatosis, zoonosis, helminthic infection, tropical, GeoSentinel, tourism

Introduction

Cutaneous larva migrans (CLM) is a zoonotic helminthic infection caused most often by *Ancylostoma caninum, Ancylostoma braziliense* and *Uncinaria stenocephala* (1). Animal hookworms live in the intestines of dogs and cats, and their eggs are released in the feces, hatching within a day in soil or sand. Within a week, the eggs develop into larvae capable of infecting humans through direct skin contact. Cutaneous larva migrans is acquired via transcutaneous penetration of the larval helminths into intact skin. Humans are accidental hosts and organisms responsible for CLM lack digestive enzymes enabling penetration of human basement membrane (1). Humans cannot transmit the infection to other humans or animals. Although not endemic to Canada, the infection is imported by travellers who typically consult primary care, emergency departments, dermatology, infectious disease and tropical medicine experts for management.

Cutaneous larva migrans is a clinical diagnosis characterized by the classic presentation of a pruritic serpiginous tract that advances on average of 2–3 mm per day (2). The typical distribution involves areas exposed to contaminated soil or sand, usually the foot or buttocks, but can be extensive (3,4). Patients often report intense pruritus that is disruptive to sleep, concentration and quality of life, and can persist for the duration of the helminth lifespan, on average five to six weeks, but upwards of a year or more in some patients (5,6).

The GeoSentinel Surveillance Network is a multinational provider-based surveillance system of international travellers and migrants presenting to travel/tropical medicine clinics (7). There are eight Canadian sites of participation in GeoSentinel spread across major urban centers within the country. The Canadian sites constitute CanTravNet, a national surveillance network with a catchment area of approximately 45% of the Canadian population. The Network serves as a resource to identify emerging pathogens, monitor disease activity and analyze population-based data.

Cutaneous larva migrans is the most commonly reported cutaneous disorder in returned travellers captured by the GeoSentinel Network (8). Notably, CLM can be acquired through travel to almost every continent, including sub-tropical areas of North America (9,10). From 2009 through 2011, 7% of travel-related diagnoses in Canada were for CLM in travellers returning from the Caribbean (11). Since the last study, no additional research has described the epidemiology of CLM in Canadian travellers returning from abroad.

The objective of this surveillance report is to describe demographic and travel correlates of travellers returning to Canada from the Caribbean with CLM over a 10-year pre-pandemic period during which time access to the first-line treatment in Canada, ivermectin, was uniformly available via the Special Access Programme of Health Canada. Better characterization of this disease in Canadian travellers may prompt expansion of resources available through Health Canada to treat this common travel-related dermatosis and increase awareness of its diagnosis among healthcare providers.

Methods

Data source

Eight Canadian sites in large urban centres from five provinces (British Columbia, Alberta, Manitoba, Ontario and Québec), also belonging to the GeoSentinel Global Surveillance Network, constitute CanTravNet (11). CanTravNet sites are staffed by licensed infectious disease physicians with expertise in travel-acquired illnesses and tropical medicine. Demographic and travel-related data were collected using the data platform of the GeoSentinel Surveillance Network (for additional details, see https://geosentinel.org) (7,12,13). The diagnosis of CLM is made clinically and the site director can choose this diagnosis from the 475 options classified as either etiologic or syndromic. The GeoSentinel data collection protocol is reviewed by the institutional review board officer at the National Center for Emerging and Zoonotic Infectious Diseases at the US Centers for Disease Control and Prevention and has been classified as public health surveillance, not human subject research requiring approval from institutional review boards. Local site institutional review board approval was obtained where required. Final diagnoses include specific etiologies (e.g., CLM) and syndromes (e.g., rash).

Definitions and classifications

Seven travel purpose designations were used, including tourism, business, missionary/volunteer research/aid work, visiting friends and relatives, education and planned medical care; or "migrants", which captured those travelling for immigration, refugee settlement or asylum-seeking. Visiting friends and relatives travel is as defined by Leder *et al.*, though classification of the purpose of travel is based on the clinician's best judgment when there was more than a single possible location of exposure (12).

Inclusion criteria

Demographic, clinical and travel-related data on ill Canadians and migrants encountered either during or after completion of their travel/migration and seen in any of the eight CanTravNet sites from January 1, 2009, to December 31, 2018, with a final diagnosis of CLM were extracted and analyzed. The decade for inclusion was selected as a representative pre-pandemic decade, during which time access to the drug of choice, ivermectin, was uniformly available via the Special Access Programme of Health Canada.

Analysis

Extracted data were managed in a Microsoft Access database and travellers were described by purpose of travel, demographics and itinerary. Data on sex and travel region were available for all travellers, and all were included in the analyses even if travellers' age or their specific country of travel were missing. Descriptive analyses including medians with interquartile ranges [IQR] and proportions were calculated for continuous and categorical variables, respectively. The significance of the trend in case distribution over the year was assessed using a Poisson regression model. All statistical computations were performed using Stata/BE 17.0 (StataCorp, College Station, Texas, United States).

Results

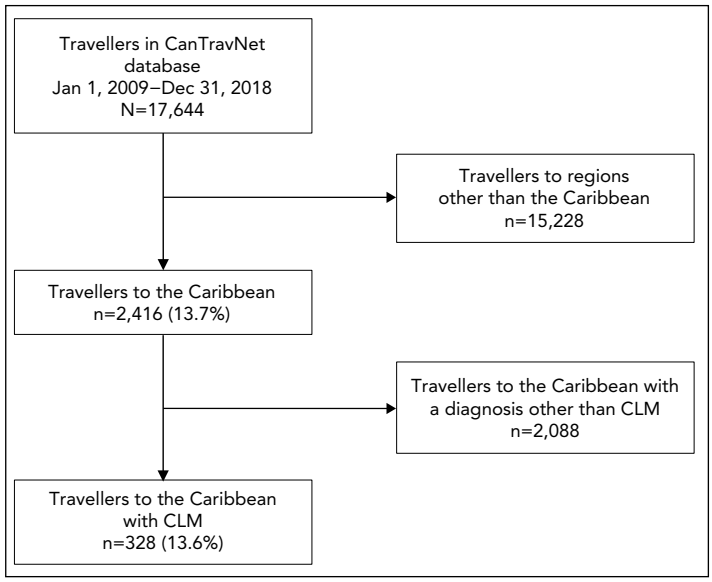
A total of 17,644 travellers presented to a CanTravNet site between January 1, 2009, and December 31, 2018. Of all recorded travellers, 2,416 (13.7%) returned from travel to the Caribbean. Of travellers to the Caribbean seeking post-travel medical care, 328/2,416 (13.6%) were diagnosed with CLM (**Figure 1**) Median age of the returned travellers with CLM was 34 years (IQR: 25–50 years), with males accounting for 42% (n=139) and females for 58% (n=189) of cases (**Table 1**). Cases were more common in the 18–34 years and 35–65 years age groups, which together accounted for 80% of the total cases. While cases were reported throughout the year, there were consistently a higher number of cases between December and March, coinciding with the Canadian winter season.

Table 1: Cases of cutaneous larva migrans among Canadian travellers returning from the Caribbean by year

Year of import	Number of cases (%)[a]	Age, years, median (IQR)	Sex, M/F n (%)	Travelling for tourism, n (%)	Top three source countries (n; %)		
					First place	Second place	Third place[b]
2018	81 (24.5%)	32.0 (19–50)	39/42 (48%/52%)	80 (99%)	Jamaica (58; 73%)	Dominican Republic (12; 15%)	Antigua and Barbuda (2; 3%) Barbados (2; 3%) Saint Lucia (2; 3%)
2017	63 (25.7%)	39.0 (27–53)	24/39 (38%/62%)	58 (92%)	Jamaica (45; 71%)	Dominican Republic (8; 13%)	Barbados (3; 5%) Martinique (3; 5%)
2016	27 (9.0%)	33.0 (12–53)	7/20 (26%/74%)	26 (96%)	Jamaica (15; 58%)	Cuba (3; 12%)	Saint Lucia (2; 8%) Saint-Martin (2; 8%)
2015	23 (9.2%)	38.0 (27–52)	9/14 (39%/61%)	23 (100%)	Jamaica (15; 65%)	Barbados (2; 9%) Cuba (2; 9%) Grenada (2; 9%)	Antigua and Barbuda (1; 8%) Saint Vincent and the Grenadines (1; 8%)
2014	32 (11.9%)	38.0 (20–50)	13/19 (41%/59%)	31 (97%)	Jamaica (20; 65%)	Cuba (7; 23%)	Barbados (1; 3%) Bahamas (1; 3%) Martinique (1; 3%) Saint-Martin (1; 3%)
2013	36 (13.4%)	37.5 (25–49)	17/19 (47%/53%)	32 (89%)	Jamaica (23; 64%)	Barbados (6; 17%)	Saint Lucia (5; 14%)
2012	23 (11.0%)	32.0 (25–44)	10/13 (43%/57%)	23 (100%)	Jamaica (20; 87%)	Barbados (1; 4%) Cuba (1; 4%) Guadeloupe (1; 4%)	-
2011	17 (9.1%)	37.0 (29–48)	8/9 (47%/53%)	15 (88%)	Barbados (7; 41%)	Jamaica (6; 35%)	Cuba (4; 18%)
2010	11 (6.5%)	36.0 (26–50)	6/5 (55%/45%)	11 (100%)	Jamaica (8; 72%)	Saint Lucia (2; 18%)	Aruba (1; 9%)
2009	15 (7.9%)	28.0 (15–36)	6/9 (40%/60%)	14 (93%)	Jamaica (6; 40%)	Barbados (4; 27%)	Cuba (2; 13%) Guadeloupe (2; 13%)
Total[c]	328 (13.6%)	34.0 (25–50)	139/189 (42%/58%)	313 (95%)	Jamaica (216; 67%)	Barbados (27; 8%)	Dominican Republic (23; 7%)

Abbreviations: F, female; IQR, interquartile range; M, male; -, not applicable
[a] Percentage derived from the denominator of total travellers to the Caribbean each year presenting to a CanTravNet site
[b] All countries noted were tied for third place
[c] Total cases of cutaneous larva migrans seen at CanTravNet sites between January 1, 2009, and December 31, 2018=570; thus, cases from the Caribbean represent 57.5% of total cases

Figure 1: Flow diagram of cutaneous larva migrans in Canadian travellers returning from the Caribbean, 2009–2018



Abbreviation: CLM, cutaneous larva migrans

The purpose of travel was tourism in 95% (n=313) of the travellers with CLM. Jamaica was the most well-represented source country, accounting for 216 cases (66.7%), followed by Barbados (n=27, 8.3%) and the Dominican Republic (n=23, 7.1%) (**Table 2**).

Table 2: Source Caribbean countries for cases of cutaneous larva migrans evaluated at CanTravNet sites, January 2009–December 2018

Country	Number	Percentage
Jamaica	216	66.7
Barbados	27	8.3
Dominican Republic	23	7.1
Cuba	21	6.5
Saint Lucia	11	3.4
Guadeloupe	4	1.2
Martinique	4	1.2
Saint-Martin	3	0.9
Antigua and Barbuda	3	0.9
Bahamas	2	0.6
Grenada	2	0.6
Turks and Caicos	2	0.6
Cayman Islands	1	0.3
Aruba	1	0.3
Haiti	1	0.3
Puerto Rico	1	0.3
Saint Vincent and the Grenadines	1	0.3
Trinidad and Tobago	1	0.3

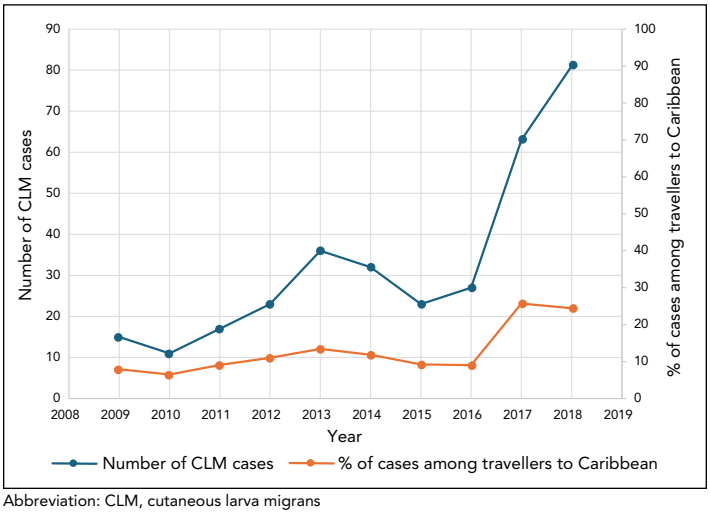
The majority of reported CLM cases presented to CanTravNet sites were from Toronto (n=191, 58.2%), followed by Montréal (n=92, 28.1%), Ottawa (n=22, 6.7%) and Calgary (n=13, 4.0%) (**Table 3**).

Table 3: Site distribution for cases of cutaneous larva migrans evaluated at CanTravNet sites, January 2009–December 2018

Site	Number	Percentage
Toronto	191	58.2
Montréal	92	28.1
Ottawa	22	6.7
Calgary	13	4.0
Vancouver	9	2.7
Winnipeg	1	0.3

The average number of CLM cases among travellers to the Caribbean increased to 81 in 2018, three times what was reported in 2016 (Table 1). Compared to 2009, there was a fivefold increase in CLM cases in 2018 (Poisson regression coefficient 0.197; 95% CI: 0.156–0.239) (**Figure 2**). Before 2017, the annual proportion of ill returned travellers presenting to a CanTravNet site with CLM from the Caribbean was approximately 6.5%–13.4% (Table 1). In the years 2017 and 2018, however, that proportion increased to 25.7% and 24.5%, respectively (Table 1).

Figure 2: Number and percentage of cases of cutaneous larva migrans among travellers returning from the Caribbean, 2009–2018



Abbreviation: CLM, cutaneous larva migrans

Discussion

Our surveillance report describes the landscape of CLM in ill Canadian travellers returning from the Caribbean over the course of a decade. Jamaica, Barbados and the Dominican Republic were the most common Caribbean source countries for this helminthic infection. Overall, our data demonstrate an increase in the number of yearly CLM cases, peaking from 2016 through 2018, where recorded CLM cases increased threefold. As noted by Lederman *et al.* and confirmed in our analysis, CLM was most prevalent in the 18–65 years age group; however, our analysis revealed a higher proportion of females with CLM compared to their study. Additionally, both studies identified Barbados and Jamaica as the leading countries (8).

Cutaneous disorders (e.g., CLM, arthropod bite reactions, abscesses and allergic reactions) in returning travellers are frequent causes for medical consultation, accounting for up to 18% of visits to specialized travel clinics (8). Specifically, CLM accounted for 9.8% of dermatoses in returned travellers who visited the GeoSentinel Surveillance Network clinics from January 1997–February 2006 (8). At 25%, it was the most common dermatosis reported in a French cohort of returning travellers from 1991 to 1993 (14) and represented 13% of 1,076 dermatological diagnoses in a Canadian cohort from September 2009–September 2012 (15). In a previous GeoSentinel study (June 1996–August 2004), CLM was most commonly associated with travel to the Caribbean (16). Given that the International Organization of Tourism reported an almost twofold increase in international travel to the Caribbean from 1995 to 2017, clinicians providing care to ill returned travellers may expect to encounter an increasing number of cases of CLM if this travel trend continues (17).

Cutaneous larva migrans remains an important travel-related dermatosis. Although usually self-limited, the disease is associated with significant and prolonged morbidity, often over months, related to pruritus, sleep disturbance and secondary bacterial infection, prompting consultation in specialized travel medicine clinics. As reported in prior cohorts of CLM cases in Canada, median duration of symptoms is typically over a month, and can range from less than a week to close to a year before care-seeking and/or effective treatment occurs. Prior to presenting to specialized clinics, many patients receive ineffective (e.g., mebendazole, topical antimicrobials) and potentially harmful (e.g., corticosteroids, oral antimicrobials) therapeutic interventions by other providers (18,19).

Treatment of CLM is indicated for those who are symptomatic. Albendazole and ivermectin are the two most recognized treatments for CLM. Topical thiabendazole may also be used (19). Although readily available in many regions internationally, access to treatment for CLM in Canada is more limited. In Canada, CLM is considered of little public health significance given the lack of propensity to propagate outside of the accidental host; however, significant morbidity may be associated with those affected by the disease, warranting prompt and effective treatment. Prior to late 2018, physicians were required to apply to Health Canada's Special Access Programme in order to obtain access to ivermectin, which remains the process for access to albendazole. The application process through the Special Access Programme did not guarantee access to ivermectin and led to delays in treatment initiation (20,21). With recent Health Canada approval of ivermectin for strongyloidiasis, off-label access in Canada for CLM has become easier (22,23).

The approval of ivermectin by Health Canada was a significant step in improving access to effective medications for travel acquired diseases. Although Canada lacks access to many drugs on the World Health Organization's essential medication list, specifically those related to management of imported infectious diseases, the approval of ivermectin has enabled more timely access to effective therapy for a variety of helminthiases (24). Lack of access to effective therapies for imported infectious diseases is a significant issue given that there were approximately 12 million Canadians returning from international travel and 21.1 million international tourists to Canada in 2018 (25,26). Further, Canada is home to many refugees and migrants, who originate from countries endemic to many tropical and travel-related diseases (27). Therefore, ongoing advocacy to obtain essential medications is critical to provide first-line patient care in the context of evolving trends in travel and migration among the Canadian population.

Counselling on preventive strategies in travellers is a fundamental component of a pre-departure visit. All physicians offering pre-travel consultations should reiterate the importance of closed-toed shoes and sitting on towels or blankets when contacting sand or soil in areas endemic for CLM. Additionally, those travelling home to visit friends and relatives should be cautioned about the risk of acquiring CLM of the hands and knees via gardening, an activity that also portends risk of strongyloidiasis acquisition. In an outbreak of CLM amongst Canadian travellers in 2000, use of sandals was associated with lower risk of acquiring infection (28). Avoidance of excoriation of pruritic areas can reduce the risk of secondary bacterial infection (29). For early management to decrease disease morbidity, travellers should be encouraged to visit a medical provider should any skin lesions appear upon return from travel (29).

Limitations

There are several limitations to our study. First, the report is a surveillance analysis of prospectively entered data that are analyzed in a retrospective manner; as such, we are limited to analyzing the data fields present in the surveillance instrument and are unable to obtain more granular exposure details, such as high-risk activities or contact with specific types of animals. The use of surveillance data limits our ability to report full details on clinical presentation, evolution, disease morbidity, treatment

selection and response to therapy, as this is not recorded by GeoSentinel's surveillance instrument. As GeoSentinel only captures data from travel health clinics, our review does not represent all cases of CLM across Canada within our defined period, nor may our findings extend to travellers returning to other home countries. Furthermore, individuals who present to travel health clinics may differ behaviourally, demographically, or socioeconomically from the general population of travellers, thereby potentially introducing selection bias. Additionally, since the drug of choice for treatment of CLM, ivermectin, was approved by Health Canada in late 2018, which coincides with our end date of enrolment, it is uncertain how formulary access to ivermectin by non-specialists may have influenced representation of CLM as a diagnosis in the CanTravNet database. Moreover, given that the database does not contain information on all returning travellers, only those who presented to post-travel clinics for illness, no denominator exists for statistical calculation of incidence rates or absolute risk. Finally, the data presented herein captured a representative decade of cases presenting for care at our centres pre-pandemic and, as such, our ability to comment on the impact of pandemic-related travel cessation and then subsequent partial recovery on the epidemiology of CLM in Canada is limited. Despite limitations, GeoSentinel and CanTravNet remain important surveillance systems that provide valuable data on the epidemiology of travel- and migration-associated infectious diseases.

Conclusion

Cutaneous larva migrans is a common travel-related dermatosis in Canadians returning from the Caribbean. Cutaneous larva migrans was predominantly observed in the 18–65 years age group, with a greater proportion of females compared to males. Barbados and Jamaica were identified as the most affected countries. With rising frequency of CLM in our clinics, increased awareness among healthcare providers and appropriate counselling of travellers, combined with improved access to effective therapy, can reduce disease morbidity. Overall, CLM is a common, typically self-limited travel-related dermatosis that can cause significant morbidity related to sleep and functional disturbance. Cutaneous larva migrans may continue to emerge in travellers once air travel has recovered to pre-pandemic levels. Moreover, CLM is a zoonotic disease for which large-scale surveillance data on source animals in high-risk areas are lacking. Results from our analysis suggest that CLM may be increasing in frequency in Canadian travellers returning from the Caribbean. Awareness of this common dermatosis in the returning traveller is important for Canadian physicians, so that timely and appropriate therapy can be initiated.

Authors' statement

AKB — Conceptualization, methodology, investigation, formal analysis, data interpretation, writing–original draft, writing–review & editing
RB — Investigation, formal analysis, data interpretation, writing–original draft, writing–review & editing
ML — Investigation, data interpretation, writing–review & editing
CY — Investigation, data interpretation, writing–review & editing
AM — Investigation, data interpretation, writing–review & editing
JH — Investigation, data interpretation, writing–review & editing
WG — Investigation, data interpretation, writing–review & editing
YM — Investigation, data interpretation, writing–review & editing
KP — Investigation, data interpretation, writing–review & editing
JV — Investigation, data interpretation, writing–review & editing
SK — Investigation, data interpretation, writing–review & editing
PP — Investigation, data interpretation, writing–review & editing
CG — Investigation, data interpretation, writing–review & editing
KK — Investigation, data interpretation, writing–review & editing
SM — Investigation, data interpretation, writing–review & editing
SB — Conceptualization, methodology, investigation, formal analysis, data interpretation, writing–original draft, writing–review & editing

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

Competing interests

Dr. Boggild oversees the Tropical Disease Fund for Excellence of the University Health Network Foundation, which has received an unrestricted educational grant from Seegene Canada.
Dr. Yansouni reports the following relationships in the last three years, all of which are outside the scope of the submitted work: Independent Data Monitoring Committees (IDMC) for Medicago Inc. and InventVacc Biologicals Inc.; the World Health Organization Antimicrobial Resistance Diagnostic Initiative, Technical Working Group; and the World Health Organization Typhoid Diagnostic Reference Panel (TyDReP) to Assess *In Vitro* Diagnostics for Typhoid, Expert Group.

ORCID numbers

Andrea Boggild — 0000-0002-2720-6944
Rachel Bierbrier — 0000-0003-1919-9083
Michael Libman — 0000-0003-3416-6482
Cedric Yansouni — 0000-0002-4765-3469
Anne McCarthy — 0000-0001-7195-6366
Wayne Ghesquiere — 0000-0002-6998-8219
Katherine Plewes — 0000-0002-3596-3267
Pierre Plourde — 0000-0003-3089-4335
Christina Greenaway — 0000-0002-9737-3326
Kevin Kain — 0000-0001-6068-1272
Shaun Morris — 0000-0001-9809-0822
Sapha Barkati — 0000-0002-9388-855X

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Appendix

[1] Division of Infectious Diseases, Department of Medicine, University Health Network and the University of Toronto, Toronto, ON

[2] Institute of Medical Science, University of Toronto, Toronto, ON

[3] Division of Dermatology, McGill University, Montréal, QC

[4] J. D. MacLean Centre for Tropical & Geographic Medicine, McGill University, Montréal, QC

[5] Division of Infectious Diseases, Ottawa Hospital and the University of Ottawa, Ottawa, ON

[6] Division of Infectious Diseases, University of British Columbia, Vancouver, BC

[7] Infectious Diseases, Vancouver Island Health Authority, Department of Medicine, University of British Columbia, Victoria, BC

[8] Fraser Health, Surrey, BC

[9] Centre hospitalier de l'Université de Montréal, Université de Montréal, Montréal, QC

[10] Section of Pediatric Infectious Diseases, Department of Pediatrics, Alberta Children's Hospital and the University of Calgary, Calgary, AB

[11] Travel Health & Tropical Medicine Services, Population and Public Health Program, Winnipeg Regional Health Authority, Winnipeg, MB

[12] Division of Infectious Diseases, Jewish General Hospital, McGill University, Montréal, QC

[13] SAR Laboratories, Sandra Rotman Centre for Global Health, Toronto, ON

[14] Department of Pediatrics, Faculty of Medicine, University of Toronto, Toronto, ON

[15] Division of Infectious Diseases, Hospital for Sick Children, Toronto, ON

CASE SERIES

Acute histoplasmosis in four immunocompetent Canadian travellers to a cenote in Yucatán, Mexico

Elspeth MacBain[1]*, Michael Hawkes[1], David Goldfarb[2], Jan Hajek[3]

Abstract

A group of four healthy Canadian travellers visited a cenote in the Yucatán peninsula in April 2024 and subsequently developed symptomatic histoplasmosis. Diagnosis was made in the acute period with a positive urine *Histoplasma* antigen test in three of the cases. Two developed severe presentations and were treated with itraconazole, including a three-year-old child with disseminated disease. The sensitivity of different modalities for diagnostics depends on the timing and severity of illness, with *Histoplasma* urine antigen being most sensitive in early infection, serology converting 4–8 weeks following exposure and cultures generally of low sensitivity. Treatment depends on the disease manifestations and host immunologic status. Many patients have relatively mild, self-limited, influenza-like illness and the diagnosis may be overlooked. Given the number of Canadian tourists travelling to the Yucatán peninsula and the popularity of visiting cenotes, awareness of the risk of histoplasmosis associated with this exposure should be promoted.

Affiliations

[1] Department of Pediatrics, University of British Columbia, Vancouver, BC

[2] Department of Pathology and Laboratory Medicine, University of British Columbia, Vancouver, BC

[3] Department of Infectious Diseases, University of British Columbia, Vancouver, BC

***Correspondence:**
ellie.macbain@phsa.ca

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Keywords: histoplasmosis, travel medicine, fever in returned traveler, endemic fungi

Introduction

Histoplasmosis is a fungal infection caused by inhalation of the microconidia of *Histoplasma capsulatum*. It is endemic in various regions across the world and is classically associated with exposure to bat and bird excrement. In Canada, *Histoplasma* is endemic along the St. Lawrence Seaway in Ontario and Québec and recent case reports have described local acquisition in Alberta and Saskatchewan (1). *Histoplasma* is well known to be regionally endemic in the Ohio and Mississippi River Valleys of central and eastern United States and common in Mexico, Central and South America, several regions in Africa and South East Asia (1).

Infection is often asymptomatic, with population seroprevalence in some endemic areas as high as 80% (2); however, histoplasmosis can have a spectrum of clinical manifestations ranging from mild self-limited influenza-like-illness, to severe pneumonia and disseminated disease (3). Symptoms typically begin 1–3 weeks following exposure (4). Young children, immune-compromised hosts and the elderly are at higher risk of severe disease. A number of cases of histoplasmosis have been described in immunocompetent travellers to endemic areas, often in association with exposure to bat-caves (5). Histoplasmosis is not a nationally notifiable disease in Canada, so the true incidence of infection nationally is unknown and it is possible that many cases go and/or unreported.

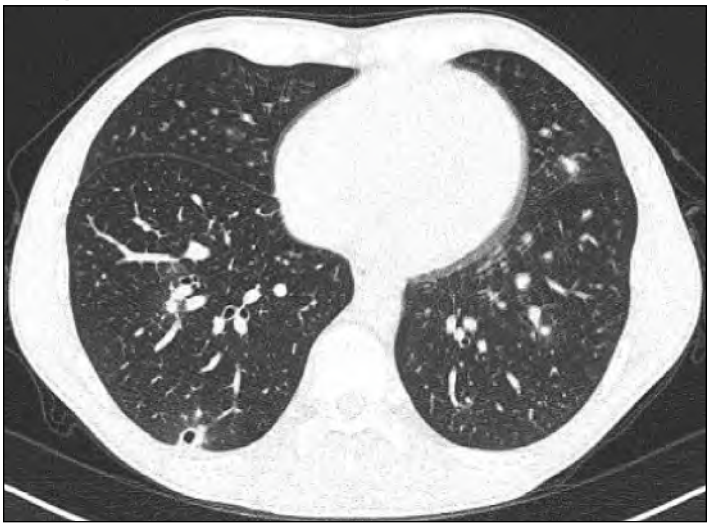
Case series

In April 2024, four (three confirmed, one suspected) Canadian travellers, two 37-year-old males, a 36-year-old female and a three-year-old male, developed symptomatic histoplasmosis after swimming in Cenote Aktunzots near Tres Reyes in the Yucatán peninsula of Mexico. They recalled seeing bats inside the cenote. Two other members of their party, a 33-year-old woman and a two-year-old male, stayed at the resort rather than attending the cenote and remained asymptomatic. Patient consent was obtained to share the following information.

Case 1

Approximately 18 days after visiting the cenote, the 37-year-old male developed fevers, myalgia, fatigue and then cough. He was found to have bilateral pulmonary nodules with cavitation and ground-glass opacities on computed tomography scan (**Figure 1**) and underwent bronchoalveolar lavage on day 14 of illness. Bacterial, fungal and mycobacterial bronchoalveolar lavage

Figure 1: Computed tomography of chest of Case 1, histoplasmosis in Canadian traveller, 2025



cultures were negative. Leptospirosis, dengue, syphilis and HIV serologies were negative. At day 11 of illness *H. capsulatum* serology was negative, but urine *Histoplasma* antigen was positive (MiraVista Diagnostics, Indianapolis, Indiana).

Because of ongoing flu-like symptoms significantly impairing his daily function, itraconazole was started on day 14 of the illness. He received a total of six weeks of itraconazole. Following treatment, his fevers abated and symptoms improved. He did not receive antibiotics. A repeat computed tomography scan six weeks after treatment discontinuation showed resolution of the cavitating nodule and reduction of bilateral nodules and ground-glass opacities. *Histoplasma capsulatum* serology repeated 10 weeks after the initial diagnosis was positive.

Case 2

Two days after Case 1 developed symptoms, his son, a previously healthy three-year-old male developed daily high-grade fevers (39°C), myalgias, abdominal pain and headaches. At time of initial assessment, he had been symptomatic for 10 days. On examination, he was noted to have an oral aphthous ulcer, several small erythematous papules on his trunk, cervical and inguinal lymphadenopathy and hepatomegaly. Alanine aminotransferase was mildly elevated at 58 U/L (normal 10–29 U/L) and lactate dehydrogenase was elevated at 585 U/L (normal 207–383 U/L). Chest X-ray revealed bilateral hilar lymphadenopathy, fine nodularity and trace pleural effusions in the bases. Abdominal ultrasound showed mild hepatomegaly with relatively increased periportal echoes ("starry sky appearance"), a bulky spleen and intra-abdominal adenopathy. *Histoplasma capsulatum* serology was initially negative and urine was positive for *Histoplasma* antigen. Human immunodeficiency virus serology was negative.

Itraconazole, dosed at 10 mg/kg/day divided BID, was initiated on day 17 of illness. His fevers resolved within 48 hours of treatment initiation and his energy quickly improved. He received three months total duration of itraconazole. Therapeutic drug monitoring was done two weeks after itraconazole initiation and monthly afterward, targeting levels between 1,420 nmol/L and 4,840 nmol/L. The patient's itraconazole level was initially in target range, then the dose was decreased to 7.5 mg/kg/day approximately six weeks into therapy, after the repeat level was elevated. He did not experience any adverse medication effects. Repeat *H. capsulatum* serology drawn approximately eight weeks after the initial diagnosis was positive. Prior to discontinuing treatment at three months, a repeat abdominal ultrasound demonstrated resolution of previous findings and reported as a normal study. Repeat chest X-rays showed interval resolution of the perihilar thickening, decreased fine nodularity bilaterally, with residual perihilar adenopathy. A chest X-ray three months post treatment discontinuation was normal.

Case 3

Several days following symptom onset of Case 1, approximately three weeks following the visit to the cenote, the other 37-year-old male developed a self-limited febrile illness with myalgia and fatigue but without respiratory symptoms. His symptoms lasted approximately 12 days. Urine *Histoplasma* antigen was positive and initial *H. capsulatum* serology was negative. Human immunodeficiency virus serology was negative. Due to absence of respiratory symptoms, no chest imaging was done. No antifungal therapy was prescribed and he made a full recovery.

Case 4

The 36-year-old female also developed cough and flu-like illness upon return to Canada, just over two weeks from exposure to the cenote. She did not have chest imaging, but was diagnosed clinically with probable community-acquired pneumonia by her family physician and was prescribed amoxicillin. Her symptoms were relatively mild and gradually resolved over the next 1–2 weeks. She did not receive antifungal therapy. Urine *Histoplasma* antigen and histoplasma serology performed approximately three weeks after her symptom onset were negative. Repeat convalescent serology was not available.

Discussion

Cenotes (sinkholes) of the Yucatán Peninsula are flooded caves that are a popular tourist attraction, drawing crowds of local and international visitors (6); however, these cenotes have previously been implicated in exposure to *H. capsulatum*. The federal Ministry of Health of Mexico declared an outbreak between July and August 2022 after five tourists were diagnosed with histoplasmosis at a local hospital after visiting a cenote located in the municipality of Homún (7). Another cenote in same region has been closed since 2019 due to association with cases of histoplasmosis among tourists (8).

The high attack rate observed in this group of exposed travellers, with two developing more severe disease, suggests they likely encountered high concentrations of *H. capsulatum* spores at the cenote. On the other hand, the relatively long period of time between exposure to symptom onset (approximately three weeks, on the upper end of the typical 1–3 week incubation period), may be suggestive of a lower inoculum.

The symptoms of histoplasmosis can be non-specific and may lead to delayed diagnosis and unnecessary invasive diagnostic procedures (9). The sensitivity and specificity of testing modalities depends on the patient's clinical syndrome, host-immune factors, timing and type of specimen collection. In general, *Histoplasma* antigen testing (e.g., MiraVista Diagnostics, Indianapolis, Indiana) is considered the most sensitive test in acute illness, but may miss milder infections with lower fungal burden in immunocompetent hosts (10).

Of our group, three individuals tested positive for urine *Histoplasma* antigen. Both of our cases who presented with more severe illness were initiated on empiric treatment while waiting for these test results. Our fourth case presented with symptoms of a non-specific influenza-like illness, suggestive of acute pulmonary histoplasmosis because of the epidemiologic context. The diagnosis was not confirmed by available laboratory testing; urine antigen testing was negative. The sensitivity of urine antigen testing is estimated to be 80% in acute pulmonary histoplasmosis, 30% in subacute pulmonary and 90% in progressive disseminated histoplasmosis (10).

All four cases had negative initial *H. capsulatum* serologies drawn approximately 2–4 weeks after exposure. In Cases 1 and 2, serologies that were repeated after 8–10 weeks turned positive. Unfortunately, repeat serologies in Cases 3 and 4 were not obtained. Histoplasma antibody testing was performed via immunodiffusion by the Alberta Provincial Laboratory for Public Health and included detection of both H and M antibodies (11). *Histoplasma capsulatum* antibodies typically take 4–8 weeks to become detectable in peripheral blood. Serology is estimated to have a sensitivity of approximately 65% in acute pulmonary histoplasmosis, 95% in subacute pulmonary, 83% in chronic pulmonary and 75% in progressive disseminated histoplasmosis. Antibody testing is most useful in subacute and chronic forms of histoplasmosis where sensitivity of urine antigen is decreased (10). Fungal cultures of the one patient who underwent bronchoalveolar lavage were ultimately negative. Culture-based methods can be challenging for informing acute management as growth typically takes 2–3 weeks and may only be positive in the minority of patients with acute pulmonary histoplasmosis (0%–20%) (10).

Recent guidelines suggest testing for histoplasmosis in all patients with community-acquired pneumonia without improvement on empiric antibiotics and exposure to an endemic area, or on initial presentation of community-acquired pneumonia in patients with high risk exposure to bird or bat droppings, or epidemiologic link to histoplasmosis outbreak (12). Practitioners should be aware that local acquisition outside the Great Lakes region is also possible in Canada (11). The urine *Histoplasma* antigen test is recommended as first line, with *H. capsulatum* serology more useful for subacute or chronic presentations (12).

Conclusion

Given the number of Canadian tourists travelling to the Yucatán peninsula and the increasing popularity of visiting cenotes, awareness of the risk associated with this specific exposure should be promoted. Cenote exposure should raise the index of suspicion for histoplasmosis in symptomatic returning travellers.

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EM — Writing–original draft, writing–review & editing
MH — Writing–review & editing
DG — Writing–review & editing
JH — Conceptualization, writing–review & editing

All authors were involved in the clinical care of the patients and review and approval of the final version 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

The authors of this paper do not have any competing interests to declare.

ORCID numbers

Elspeth MacBain — 0009-0009-4097-2641
Michael Hawkes — 0000-0002-4122-0937
David Goldfarb — 0000-0003-0835-9504
Jan Hajek — 0000-0003-1863-4071

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Proposed approaches for public health surveillance: A literature review for the Canadian National HIV Surveillance Program

Anita Robert[1], Wes Martin[1], Leigh Jonah[1], Dana Paquette[2], Joseph Cox[3], Laura H Thompson[1]

Abstract

Background: The National HIV Surveillance Program, managed by the Public Health Agency of Canada, is a passive surveillance system that collects de-identified data on HIV cases in Canada. Regular review of this surveillance system is required to maintain its accuracy, effectiveness and relevance in the face of a changing HIV epidemic. The National HIV Surveillance Program is undergoing a comprehensive review and renewal process with the aim of identifying and implementing potential improvements to meet the information needs of communities, service providers, researchers, provinces and territories and the federal government more effectively.

Methods: A non-systematic literature review was conducted in June to July 2023, with 3,521 articles found and 105 included.

Objective: This literature review aimed to identify proposed approaches for public health surveillance, with an emphasis on HIV surveillance and identify key findings relating to the following themes: surveillance system infrastructure, data collection, ethical considerations and stakeholder relationships.

Results: Key findings from the literature review pertained to standardization and centralization of data collection; collection of demographics, disease staging, social determinants of health and other data elements; and linking surveillance systems to other data sources or other surveillance systems. Additional findings concerned legislative and policy review, privacy strategies, informed consent, ethical surveillance system design, stakeholder consultation at all stages, knowledge translation and ensuring adequate resourcing.

Conclusion: In future work, lessons resulting from the literature review will be combined with evidence from other components of the overall review of Canada's HIV surveillance system. Together, this information will be further assessed and prioritized for possible implementation after consultation with data providers and communities.

Affiliations

[1] Centre for Communicable Disease and Infection Control, Public Health Agency of Canada, Ottawa, ON

[2] Centre for Surveillance and Applied Research, Public Health Agency of Canada, Ottawa, ON

[3] School of Population and Global Health, Department of Global and Public Health, McGill University, Montréal, QC

***Correspondence:**
hass@phac-aspc.gc.ca

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Keywords: HIV, surveillance, diagnosis, review literature as topic, public health practice

Introduction

In 2022, there were 1,833 newly diagnosed HIV cases in Canada (1). Given the persistence of HIV and other sexually transmitted and blood-borne infections (STBBIs) in Canada, the federal government highlighted surveillance systems as a key evidence source to inform programs and policies in its goal to reduce the burden of STBBIs. It committed to strengthening these systems in the Government of Canada's STBBI Action Plan (2024–2030) (2,3). Therefore, high-quality HIV surveillance data remains critical to Canada's STBBI response.

Public health surveillance systems should be updated as proposed surveillance approaches, or the epidemiology of the

condition of interest evolves. The National HIV Surveillance Program compiles data on HIV diagnoses in Canada from various sources: line-listed datasets and case report forms on individual HIV diagnoses reported in the provinces and territories (PT), aggregate data tables on perinatal exposure to HIV from the Canadian Perinatal HIV Surveillance Program, aggregate data tables on positive HIV tests during immigration medical exams provided by Immigration, Refugees and Citizenship Canada (IRCC) and HIV-related mortality data from Statistics Canada. In response to annual data requests sent to the PTs, line-listed datasets and case report forms with data on HIV diagnoses are received, data is cleaned and reformatted to match national HIV surveillance variable formats, PT-specific data is validated, national surveillance data is compiled and reports and infographics are prepared. Additional information on the operation of the surveillance system has been described elsewhere (4). The review and renewal process initiated in 2021 represents the first comprehensive review of the National HIV Surveillance Program. This review and renewal process was undertaken to improve the surveillance system for harmonization of methods related to data reporting and collection across jurisdictions and to better meet community, program and policy engagement and evidence needs. As the epidemiology of HIV has evolved over time, the review and renewal ensure that the National HIV Surveillance Program remains relevant and allows for better alignment of the surveillance system with the goals of the Government of Canada's STBBI Action Plan (2024–2030) (2,3). The National HIV Surveillance Program is undergoing a review and renewal process to identify areas for improvement and implement needed changes to provide better quality data to data users. Along with technical assessments and stakeholder and other key informant consultations, a literature review was undertaken to identify proposed approaches in public health surveillance, emphasizing HIV surveillance systems, to advance HIV surveillance in Canada. This literature review was conducted as an information gathering exercise to identify proposed approaches implemented by other surveillance systems that will be discussed with data providers and community stakeholders for potential implementation during the renewal process. This article reports the findings of the review grouped across the following themes: surveillance system structure and methodology, data collection, ethical considerations and stakeholder consultation.

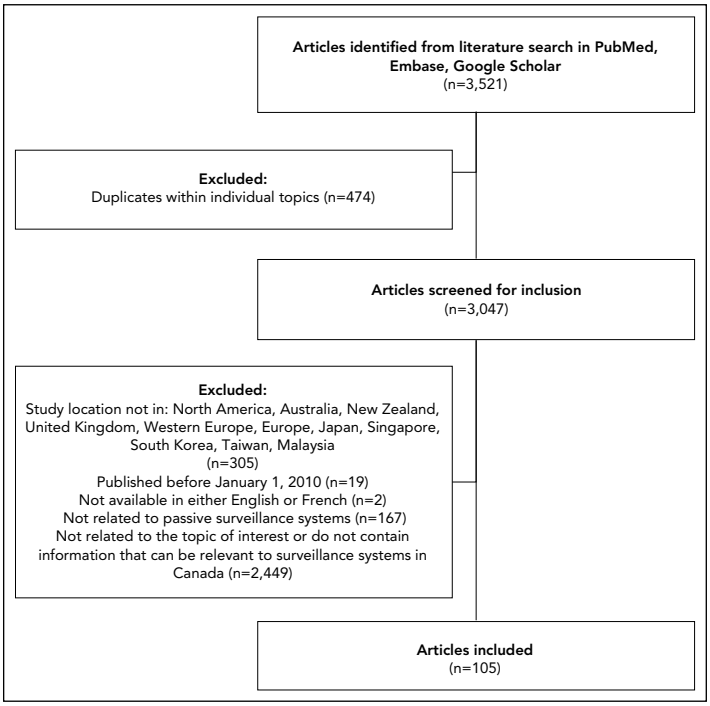
Methods

A general, non-systematic literature review was performed in June to July 2023 to examine proposed approaches in local, provincial and national public health surveillance systems within Canada and globally. Follow-up for newly diagnosed HIV cases in Canada is completed locally, with required reporting to provincial/territorial health authorities and subsequent reporting to the national HIV surveillance program. The National HIV Surveillance Program reports on national trends in new HIV diagnoses stratified by various epidemiological factors. The following topics, determined to be relevant to the National HIV Surveillance Program, were examined: surveillance system processes and methodologies; data reporting methods; data infrastructure; considerations for collection, analysis and use of sociodemographic and epidemiological data; community engagement; ethical considerations; inter-surveillance system linkage; and program and policy engagement.

Distinct search strategies were developed for PubMed, Embase and Google Scholar to address each topic. PubMed and Embase were selected, as their combined use results in a high coverage rate of publications for research (5) and this search was supplemented by Google Scholar due to the large volume of publications included (6). Various search terms were developed for each aspect of the given topic. Search terms used for "surveillance" included: surveillance, monitoring, disease surveillance, passive surveillance, etc. The topics were divided equally across two reviewers responsible for search strategy development, database searches, article screening and assessment for inclusion, article detail extraction and analysis. Given that this was a non-systematic literature review and given the volume of articles identified for screening, each article was only reviewed by one of the two reviewers and no procedure existed for discordant assessments or disagreements between reviewers. Data extraction was completed by entering data into structured evidence tables on citation information, inclusion/exclusion decision, rationale for decision regarding inclusion, notes and the main message for the National HIV Surveillance Program.

Overall, 3,521 articles were identified for screening (**Figure 1**). Articles were assessed for inclusion based on criteria that included relevance, recency and geographic location. By including articles published on or after January 1, 2010, the authors were able to obtain information on improvements to public health surveillance in response to various events over time (i.e., swine flu pandemic, Ebola, COVID-19 pandemic, etc.) and including articles by study location allowed for the extraction of relevant information from jurisdictions with similar public health contexts. Although this literature review was completed as part of the review of the National HIV Surveillance Program, articles related to other conditions were included, as key findings from these articles can also be applied to HIV surveillance. Occasionally, articles with geographic locations outside of the listed regions or published before 2010 were included if reviewers deemed them particularly relevant for Canadian HIV surveillance. Included articles not meeting one or more inclusion criteria are detailed in the **Appendix, Table A1**. Such articles held lessons for the renewal of the National HIV Surveillance Program and met the other relevant criteria for inclusion: contains information that can be relevant to surveillance systems in Canada, related to passive surveillance systems, contains information that is otherwise relevant to surveillance system modernization and available in either English or French. Articles

Figure 1: Flowchart of Article Screening in Literature Review[a]



[a] As literature searches were conducted separately for each topic, the number of duplicates only includes articles identified as duplicated within a particular topic. As articles could be included in multiple themes, the number of duplicates does not include articles appearing under multiple themes

were not restricted by study design. While there was no specific separate search for grey literature, the intention in the use of Google Scholar as a searched database was to capture relevant grey literature Thus, 3,416 articles were excluded across all topics.

Practices were deemed to be "proposed approaches" if their implementation could improve data collection and surveillance system methodology and infrastructure, ensure ethical public health surveillance and improve stakeholder engagement for the National HIV Surveillance Program. Proposed approaches are potential actions for the National HIV Surveillance Program supported by the literature. Although each proposed approach is evidence-based, these have not been vetted for risk or bias. Practices and processes from included articles were grouped into key findings for the National HIV Surveillance Program's renewal. Individual articles could support multiple findings. Thematic analysis was performed using an open-coding system to derive themes through an inductive process, where the main message or key finding for the National HIV Surveillance Program from each included article was derived. Individual main messages were inductively grouped based on similarity to each other into key findings. Key findings were grouped into the four larger themes and subthemes based on surveillance system development, operation and evaluation. The process was conducted manually and no formal qualitative analysis procedure or software was used. The results of this review are separated into "Novel findings," representing potentially new proposed approaches and processes for the National HIV Surveillance Program and "Long standing public health practices," representing practices or processes that have been consistently used in public health surveillance. "Novel findings" were related to modernization and updating surveillance systems and were similar to findings identified from previously completed steps of this review process. "Long standing public health practices" were most often practices for ongoing surveillance system operation and were already in place at other surveillance systems both in Canada and in other jurisdictions.

Results

Key findings

Literature searches were conducted separately for each topic and 3,521 articles were identified across all sources. Article exclusions for duplicates and other reasons are outlined in Figure 1. Overall, 105 articles were included. One third (n=33) were published during or post-COVID-19 pandemic (2020 onwards). The geographic distribution of articles shows that half came from North America (n=52) and 17.1% (n=18) compiled information about multiple countries. Key findings were derived using an inductive approach, where articles included were analyzed to identify any practices or processes potentially applicable to the National HIV Surveillance Program. Post-literature review, the findings were grouped into four key themes: surveillance system structure and methodology, data collection, ethical considerations and stakeholder engagement.

Novel findings

Novel findings were identified related to surveillance system structure and methodology, data collection, ethical considerations and stakeholder consultation. (**Table 1**). Most of the findings were supported by multiple articles, with additional details found in Table 1.

Novel findings regarding surveillance system and methodology addressed real- or near real-time data collection with surveillance system linkage and use of web-based applications in data collection. Web applications have been used in data submission to central agencies (15) and to receive data (16). Timeliness of data has been improved through real-time submissions to central agencies by jurisdictions (9) and institutions (13).

Findings for data collection indicate the need to supplement information from passive surveillance systems with other data sources and collect data on demographic traits, disease staging (e.g., CD4) and the social determinants of health. Disease subtype from laboratory data can supplement routine surveillance (17) and new systems developed by including population databases (21). While data on age, gender, ethnicity, residence, exposure and place of infection is routinely collected for HIV (38), clinical care indicators and social determinants of health data are needed (39).

Table 1: Novel findings by theme and surveillance system stage

Surveillance system stage where relevant	Novel findings	Articles that support findings	Examples of novel findings
Surveillance system structure and methodology			
Surveillance system development	1. Enhance timeliness of data with real-time or close to real-time surveillance for key metrics and data linkage between different surveillance systems (i.e., within the same level, or local surveillance systems to the national surveillance system) to ensure relevance of reporting and ability to respond quickly to transmission clusters (n=8).	Beyrer (2021) (7), Ghosh (2012) (8), Mao (2010) (9), McGill (2023) (10), Moore (2012) (11), Morse (2012) (12), Price (2021) (13), Sullivan (2022) (14)	Mao (2010) (9): Description of the creation of the Chinese national, web-based HIV/AIDS information system. This system provides real-time data on HIV testing, prevention and treatment from provinces. Price (2021) (13): This article discusses the construction of local surveillance systems in the United Kingdom for COVID by linking data from laboratory information management systems with electronic medical records. Data about specimens collected from laboratory information management systems is linked to information about patient admissions and discharges from electronic medical records. This system allows for the real-time monitoring of hospital onset COVID infections.
Surveillance system operation	2. Use web-based application to assist with data collection (n=3).	Cohen (2014) (15), Hood (2017) (16), Mao (2010) (9)	Cohen (2014) (15): Review of the status of the United States (US) National HIV Surveillance System in 2013. This surveillance system uses specialized web application developed by the US Centers for Disease Control and Prevention (CDC) to receive monthly de-identified data submissions from HIV surveillance programs. Hood (2017) (16): A study using HIV epidemiological data and field service data from King County, Washington to assess the impact of misclassification of prior diagnoses on new diagnoses and partners services on linkage to care. Cases in the Laboratory Tracking Database, a database containing electronic laboratory data submissions, are matched to those in the Enhanced HIV/AIDS Reporting System (eHARS), a web-based HIV surveillance data repository, prior to submission.
Data collection			
Surveillance system development	3. Supplemental information obtained through passive surveillance systems with multiple internal or external data sources aside from other existing surveillance systems such as: laboratory data, survey data, clinical data or electronic health records, healthcare system data, testing data and population data (n=28).	Brandwagt (2019) (17), Buchacz (2015) (18), Chapman (2011) (19), Cohen (2014) (15), Ghosh (2012) (8), Goller (2010) (20), Hall (2021) (21), Hood (2017) (16), Jeong (2022) (22), Jones (2011) (23), Jung (2018) (24), Kliewer (2010) (25), Kraut (2023) (26), Leal (2010) (27), Moore (2012) (11), Morse (2012) (12), Newton (2012) (28), Paulukonis (2014) (29), Pierce (2017) (30), Price (2021) (13), Schmidt (2019) (31), Shaw (2011) (32), Sullivan (2022) (14), Tanaka (2021) (33), Weston (2018) (34), WHO (2021) (35), Wijayasri (2016) (36), Willis (2019) (37)	Brandwagt (2019) (17): Discusses the evaluation of the national invasive meningococcal disease surveillance system in the Netherlands, created by linking data from clinical datasets, laboratory datasets and serogroup/subtype data from the national reference laboratory. Data from clinical and laboratory sources are merged with data on serotype and subtype information obtained from further testing at the national reference laboratory. Hall (2021) (21): This article discusses the creation of the HOSTED (Household Transmission Evaluation Database) surveillance system for household COVID19 transmission, developed by merging data from the Second Generation Surveillance System at Public Health England, National Health Service Personal Demographics Service data. The National Health Service Personal Demographics Service dataset has information on the home addresses of people registered with a general physician; unique households are indexed using a Unique Property Reference Number. Data linkage with the Second Generation Surveillance System for COVID occurs in a secure data access environment, generating a pseudonymized dataset for analysis.

Table 1: Novel findings by theme and surveillance system stage (*continued*)

Surveillance system stage where relevant	Novel findings	Articles that support findings	Examples of novel findings
Data collection (*continued*)			
Surveillance system development (*continued*)	4. Include: race and/or ethnicity data, CD4 count and/or HIV staging, gender, sexual orientation data, residence data, socioeconomic data elements (i.e., income, poverty level, educational), data elements related to migration (i.e., country of infection or country of origin, immigration) and additional variables (i.e., insurance, coverage, incarceration status, occupation, homeless, pre-exposure prophylaxis [PrEP], reason for test) (n=12).	Dickson (2015) (38), Ford (2012) (39), Newton (2012) (28), Rice (2017) (40), Rossi (2017) (41), Schmidt (2019) (31), Sullivan (2022) (14), Cohen (2014) (15), Croxford (2022) (42), Beltran (2011) (43), Beyrer (2021) (7), WHO (2021) (35)	Dickson (2015) (38): Overview of the epidemiology of HIV and AIDS in Aotearoa New Zealand since the inception of the surveillance system. This surveillance system collects data on age at diagnosis, gender, ethnicity, usual residence, likely means of infection, place of infection and initial CD4 cell count. Ford (2012) (39): Identifies critical data and indicators related to HIV care and access to services, looks at the impact of the US National HIV/AIDS Strategy and looks at the data systems that capture key data. This report recommended collection of clinical care indicators, mental health, substance use, housing indicators, food insecurity, demographic and other social determinant of health data (i.e., income, reimbursement for medical services, etc.).
Ethical considerations			
Surveillance system development	5. Design surveillance system and associated infrastructure considering ethical principles including equity and accessibility (n=5).	Aiello (2020) (44), Coltart (2018) (45), Molldrem (2020) (46), Moran-Gilad (2017) (47), Samuel (2018) (48)	Aiello (2020) (44): Outlines principles related to public health surveillance systems involving the internet and social media. Public health surveillance systems must be designed considering the following ethical principles: non-maleficence, beneficence, respect for autonomy, equity and efficiency. Coltart (2018) (45): A review article that examined ethical issues in global HIV phylogenetic research. Risk-benefit assessments, with a special focus on key populations likely to be identified, should be conducted prior to designing, conducting and reporting phylogenetic studies. The rights and interests of individuals participating in these studies and the populations they represent need to be protected with clinically relevant results returned as soon as possible. Awareness regarding the social, legal, human rights and other aspects of society are needed with special focus on the effect of this research on criminalization and violence toward impacted populations (i.e., key populations). Risk mitigation strategies must be implemented to ensure that data cannot be re-linked for harmful purposes, training on privacy and confidentiality and including measures for ongoing monitoring and redress in cases of data misuse. True informed consent from participants is needed. Community engagement during the design, conduct and analysis of research is needed to ensure that projects are relevant to communities affected. Communication should be clear and understandable with special focus on sensitizing groups, such as communities, law enforcement and public health, to phylogenetic research and its implications. Equitable data sharing with governance structures to ensure accountability to communities is also required.

Table 1: Novel findings by theme and surveillance system stage (*continued*)

Surveillance system stage where relevant	Novel findings	Articles that support findings	Examples of novel findings
Ethical considerations (*continued*)			
Surveillance system development (*continued*)	6. Automate processes for data privacy and enhanced security with data anonymized, pseudonymized or using alternative identifiers in the event of data linkage (n=16).	Blais (2014) (49), Boes (2020) (50), Bublitz (2019) (51), Campo (2020) (52), Cauchi (2022) (53), Fan (2010) (54), Jeong (2022) (22), Johnson (2018) (55), McKerr (2015) (56), Ndeikoundam Ngangro (2022) (57), Polemis (2020) (58), Rivière (2018) (59), Sáez-López (2019) (60), Severi (2023) (61), Strobel (2019) (62), Trifirò (2014) (63)	Boes (2020) (50): Discusses the review of the national hepatitis B surveillance system in Germany. Physicians and laboratories report hepatitis B diagnoses to the local public health authorities, which report to state health authorities. Data is pseudonymized at reporting to state health authorities, which then submit data to the Robert Koch Institute. McKerr (2015) (56): An evaluation of Taiwan's national dengue surveillance system as part of the National Disease Surveillance System (NDSS). This system has an active component amongst travellers at ports of entry and a passive component amongst patients presenting for care at their healthcare providers, laboratory testing, notification to local health departments and subsequently the NDSS. Data is anonymized and extracted from the NDSS.
Stakeholder consultation			
Surveillance system operation	7. Community engagement and community-led monitoring throughout surveillance cycle (n=4).	Lee (2009) (64), Sullivan (2022) (14), Sweeney (2013) (65), WHO (2021) (35)	Lee (2009) (64): Commentary that proposes a US national privacy protection standard for public health data. Prior to the use or release of potentially identifiable data, affected community groups should informed and provided the opportunity to provide input in decision making processes. Sweeney (2013) (65): Review of ethical considerations for using HIV surveillance data to facilitate HIV medical care. Prior to piloting a new program, community-based organizations were engaged in the development of strategies for the use and scale-up of HIV surveillance data.
	8. Consult with stakeholders on the development of specific information products with reporting in a sensitive/respectful manner that does not allow for the direct identification of affected individuals (n=8).	Burkom (2021) (66), Cauchi (2022) (53), Goldstick (2021) (67), Hargrove (2018) (68), Marshall (2017) (69), Marzano (2023) (70), Severi (2023) (61), Simonsen (2016) (71)	Marshall (2017) (69): Examines the development of the Prevent Overdose Rhode Island (PORI) website. This website aimed to use public health surveillance data to provide information on drug overdoses to stakeholders and help direct those at risk to treatment. Prior to launching the web application, community and other stakeholders were sent email surveys. Over a hundred comments were received regarding how to improve the website. The next phase of evaluation will involve focus groups and user testing sessions to target content for audience. Marzano (2023) (70): Reviews a real-time suicide surveillance system in Great Britain. Police forces submit forms with information on demographics, life events, mental health problems, previous police contact and circumstances surrounding death (i.e., time, date, location and method) to the British Transport Police. Involvement of police forces in the surveillance system has been controversial, due to previous history of criminalizing suicides. Further, reporting should be conducted in a respectful and anonymized manner.

Table 1: Novel findings by theme and surveillance system stage (*continued*)

Surveillance system stage where relevant	Novel findings	Articles that support findings	Examples of novel findings
Stakeholder consultation (*continued*)			
Surveillance system operation (*continued*)	9. Provide training to public health stakeholders on the surveillance system (i.e., data collection) and knowledge mobilization initiatives to affected communities, public health professionals, clinicians and other stakeholders to improve public health surveillance of the condition of interest and demonstrate the public health value of the surveillance system (n=7).	Contoli (2016) (72), Crain (2016) (73), Hennenfent (2017) (74), Magee (2011) (75), Paul (2019) (76), Rivière (2018) (59), Smith (2011) (77)	Contoli (2016) (72): Discusses the implementation of PASSI d'Argento in Italy, a behavioural surveillance system monitoring health related behaviours in senior citizens. This surveillance system includes a web-based community of practice that offers workshops, communication tools and a forum for general discussions among stakeholders. Magee (2011) (75): Describes the creation of a training program for the National Tuberculosis Surveillance System, which receives data from all 50 states, the District of Columbia, New York City, Puerto Rico and other US jurisdictions in the Pacific and the Caribbean. The US CDC developed a training course for the National Tuberculosis Surveillance System. This course had a self study and a facilitator led version. Training materials included visual, auditory, reading/writing and movement aspects with self-study modules to be used in the completion of the training course and to serve as reference material to take back to the participants' jobs. Study questions and case studies were included, along with notes, comments and diagrams. Field testing with quantitative and qualitative data from field tests with experts were analyzed and pre-test and post-tests were designed and conducted. Trainers were also trained using the Teach-Back system. As the training program was successful, this was used as a model for similar trainings in other surveillance systems and jurisdictions.
	10. Provide a media toolkit and other knowledge translation tools for community-led social and behavioural change communication (n=1).	Sullivan (2022) (14)	Sullivan (2022) (14): Describes the data visualization tool America's HIV Epidemic Analysis Dashboard (AHEAD). A toolkit for various users (i.e., jurisdictions, community-based organizations, advocacy organizations and federal agencies) was also available.
	11. Consult stakeholders during the development of and ongoing operation of surveillance system infrastructure and implement any feasible changes suggested (n=5).	Dubiniecki (2022) (78), Marshall (2017) (69), Toutant (2011) (79), Yang (2020) (80), Zhang (2017) (81)	Dubiniecki (2022) (78): Discusses the development and implementation of the Canadian Armed Forces Surveillance and Outbreak Management System (CAF SOMS). This system was developed by the National Contact Tracing Team and the Health Informatics Team and included the use of four distinct forms: case details, contagion elicitation, contact notification and contact follow-up. The database was presented to members of the National Contact Tracing Team for review. Perceptions of the system were positive and certain suggestions were acted on immediately. Other feasible suggestions that could not implemented immediately were prioritized for future implementation. Implemented changes received positive feedback. Toutant (2011) (79): Examines the development of SUPREME, a web application to examine the effect of extreme meteorological events on public health. This web application assists public health surveillance by combining data from various datasets including, health, meteorological, demographic, air quality and geospatial data. The article explains how feedback from stakeholder surveys and meetings were used to identify information needs, provincial capabilities and develop specifications for the web application. Based on the given specifications, the web application, SUPREME, was developed.

Abbreviations: AHEAD, America's HIV Epidemic Analysis Dashboard; CAF SOMS, Canadian Armed Forces Surveillance and Outbreak Management System; CDC, Centers for Disease Control and Prevention; HOSTED, Household Transmission Evaluation Database; NDSS, National Disease Surveillance System; PORI, Prevent Overdose Rhode Island; US, United States; WHO, World Health Organization

Findings on ethical considerations included ethical, equitable and accessible surveillance system design and automated processes for data privacy alongside the ethical principles of non-maleficence, beneficence, respect for autonomy, equity and efficiency (44). Risk-benefit assessments, awareness, risk mitigation, community engagement and equitable data sharing (45) are needed in surveillance system design. Automated processes including pseudonymization (50) at data submission and anonymization at data extraction (56) enhance data privacy.

Stakeholder engagement is encouraged throughout the surveillance cycle and surveillance information product development. Training, knowledge mobilization and demonstration of the public health value of surveillance data, use of various knowledge translation tools and implementing changes recommended by stakeholders to the extent feasible are significant parts of surveillance system operation. Implementation included community engagement in decision and strategy making (64,65), as well as surveillance information product development (69,70); provision of resources, workshops (72) and training courses (75); audience specific knowledge translation toolkits (14); and implementation of community suggested changes in the development of technical tools (78,79).

Long standing public health practices

Long standing public health practices were identified applying to surveillance system structure and methodology, data collection, ethical considerations and stakeholder consultation. (**Table 2**). Most practices were supported by multiple articles with additional details found in Table 2.

Surveillance system structure and methodology should include clearly defined roles and responsibilities and pilot testing during surveillance system development. Questionnaires were centralized and standardized during operation. Periodic evaluation was also conducted. Measures to enhance surveillance system structure included: working groups specifying tasks (83) and program-specific responsibilities (84), pilot testing of surveillance systems in data collection settings (85,86), integration (87) and standardization across jurisdictions (9) and periodic evaluations to understand factors affecting accuracy (41) and ensure the relevance of these factors, as high-quality data is needed (15).

Data collection during operation should include resolving duplicates and data quality issues prior to upload onto databases and manually verifying data linkages. Structured queries (19,64) and cross-tabulations (53,62) and manual verification between data sources (19,64) or against raw data, such as medical records (27), also ensure high data quality.

Ethical considerations include legislative and policy review and approval during development. Data sharing agreements, data access monitoring with need-to-know restriction and non-routine project-specific ethics approval were present during ongoing operation. Informed consent from stakeholders was obtained during evaluation. Ethics committee evaluation (49), data protection for legislative compliance (8), minimum data collection for privacy (49), data sharing agreements governing data provision (62), maintaining data access logs (49) with data access limited to authorized individuals (57), simplified oversight processes for extra projects (60) accounting for existing data protection (54) and verbal informed consent during evaluation interviews (56,59) all ensure ethical public health surveillance.

During surveillance system development, inter- and intra-stakeholder relationships should be built and facilitated using various tools. Dedicated resources should be provided for ongoing operation. Consultations during periodic evaluations should be stratified by stakeholder group. Consistent staff (77), formal outreach processes (103), dedicated resources (105), senior guidance and oversight (11) and consultations stratified by jurisdictional level during evaluation (104) supplemented by existing communications (109) improves stakeholder engagement.

Discussion

Several proposed approaches with respect to areas for improvement, such as surveillance system infrastructure and methodology, data collection, ethical public health surveillance and stakeholder engagement were identified through this literature review. As the use of evidence-informed policy and programs is a guiding principle of the *Government of Canada's sexually transmitted and blood-borne infections (STBBI) action plan 2024–2030*, surveillance data has been emphasized as a guide for developing and implementing programs and interventions (2,3). Thus, it is important to periodically review and modernize surveillance systems to ensure their effectiveness. Key attributes of surveillance systems have been defined as follows by the United States Centers for Disease Control and Prevention (CDC), as part of its guidelines on public health surveillance system evaluation to develop effective surveillance systems: simplicity, flexibility, data quality, acceptability, sensitivity, predictive value positive, representativeness, timeliness and stability (112). Findings from the current review show that effective surveillance systems are characterized as standardized across jurisdictions, timely, developed and tested in conjunction with stakeholders and linked to other data sources. Data collection may benefit from including demographic information, disease staging and social determinant of health indicators, supplemented by other data sources as needed and include data quality and duplicate checks. Ethical surveillance system design considers equity and accessibility, privacy issues, legislation and policy review and informed consent. Effective stakeholder engagement is meaningful and conducted at all

Table 2: Long standing practices in public health by theme and surveillance system stage

Surveillance system stage where relevant	Practice	Articles that support practices	Examples of practices
Surveillance system structure and methodology			
Surveillance system development	1. Delineate clear roles and responsibilities (n=3).	Gulaid (2012) (82), Kodan (2021) (83), O'Brien (2012) (84)	Kodan (2021) (83): Describes the process of implementing a maternal death surveillance system in Suriname as experienced by healthcare providers, committee members and public health experts. A working group oversaw the clear delineation of roles and responsibilities by specifying tasks. O'Brien (2012) (84): Compares surveillance of transfusion-transmissible infections across the blood donation systems of five high income countries. Canada's and France's surveillance systems had differentiated responsibilities across programs and surveillance systems.
	2. Pilot test new data collection applications or systems in collaboration with other programs during surveillance system development (n=4).	Brady (2020) (85), Karp (2017) (86), Mao (2010) (9), Sweeney (2013) (65)	Brady (2020) (85): Discusses the pilot testing of a voluntary community-based testing surveillance system for HIV in Ireland, with testing data submitted by clinics to the Health Protection Surveillance Centre. A steering group, including government and non-government organizations, was developed to oversee the development of the system including the development of a minimum dataset. Organizations were surveyed to develop database protocols and data collection tools. Karp (2017) (86): Examines the National Antimicrobial Resistance Monitoring System (NARMS) in the US. This surveillance system receives data on retail meat from the US Food and Drug Administration (FDA) and food animals from the United States Department of Agriculture (USDA) in addition to data on human illness from the US Centers for Disease Control and Prevention (which receives data from state and local public health units). Data from the surveillance system is used as part of risk assessment in drug approvals the creation of risk management strategies using data on resistance trends, types and pathogen prevalence. Pilot studies were conducted on farms to assess data and sample collection processes and lessons learned were used in the development of antimicrobial resistance in food animal surveillance programs.
Surveillance system operation	3. Centralize and standardize data collection with standardized questionnaires and forms (n=7).	Kebisek (2021) (87), Lee (2009) (64), Mao (2010) (9), Mohammed (2016) (88), O'Brien (2012) (84), Weston (2018) (34), Zhang (2012) (89)	Kebisek (2021) (87): Describes the process of conducting near real-time COVID-19 surveillance among the US Army population during the first year of the pandemic through the integration of several Department of Defense surveillance systems. Mao (2010) (9): Describes the creation of the Chinese national, web-based HIV/AIDS information system. Data collection on HIV testing, prevention and treatment is standardized across provinces.
Surveillance system evaluation	4. Conduct periodic evaluations of surveillance system (n=5).	Cohen (2014) (15), Lee (2009) (64), Petty-Saphon (2019) (90), Rossi (2017) (41), Trepka (2016) (91)	Cohen (2014) (15): Reviews the status of the US National HIV Surveillance System in 2013. The surveillance system will continue to evolve in response to the need for high-quality data and the findings from this evaluation. Rossi (2017) (41): Reviews the factors that influence the accuracy of infectious disease monitoring in migrants in Europe. The improvement of existing surveillance systems was recommended after this review.

Table 2: Long standing practices in public health by theme and surveillance system stage (*continued*)

Surveillance system stage where relevant	Practice	Articles that support practices	Examples of practices
Data collection			
Surveillance system operation	5. Resolve duplicates and data quality issues prior to upload into database (n=3).	Chapman (2011) (19), Jung (2018) (24), Strobel (2019) (62)	Chapman (2011) (19): Examines the development of the Virginia Vital Events and Screening Tracking System (VVESTS), which is created by merging the Virginia Congenital Anomalies Reporting and Education System (VaCARES) (passive surveillance system) and the Virginia Early Hearing Detection and Intervention Program (VEHDIP). As duplicate records are a challenge, these records are assessed by querying for combination of variables. Strobel (2019) (62): Examines the evaluation of the Intellectual Disability Exploring Answers (IDEA) surveillance system in Western Australia, which was created by merging data from the Department of Education Western Australia and the Disability Services Commission (DSC). The surveillance system can be linked to administrative data as necessary. Data quality is assessed by cross-checking data across different systems and conducting cross-tabulations as needed.
	6. Manually verify data linkages (n=2).	Chapman (2011) (19), Leal (2010) (27)	Chapman (2011) (19): Examines the development of the VVESTS, which is created by merging the VaCARES (passive surveillance system) and the VEHDIP. Data linkages are manually reviewed for accuracy. Leal (2010) (27): Examines the creation of a surveillance system for bloodstream infection in Calgary, which was created by merging regional laboratory data with data from hospital administrative databases. Regional laboratory data was merged with hospital administrative databases. Medical records were manually reviewed to verify data linkages.
Ethical considerations			
Surveillance system development	7. Review relevant legislations specific to the condition under surveillance (i.e., criminalization), their implications, privacy policies/ legislations, other relevant legislations and obtaining the needed approvals to design surveillance systems in compliance with these laws and policies (n=13).	Abecasis (2018) (92), Blais (2014) (49), Bublitz (2019) (51), Campo (2020) (52), Condell (2016) (93), Fritsch (2019) (94), Ghosh (2012) (8), Hoppe (2022) (95), Leitner (2018) (96), Marzano (2023) (70), Ndeikoundam Ngangro (2022) (57), Scaduto (2010) (97), Trifirò (2014) (63)	Blais (2014) (49): Discusses the evaluation of the Québec Integrated Chronic Disease Surveillance System (QICDSS). This surveillance system was created by linking several databases: the health insurance registry, hospitalization database, vital statistics death database, physician claims database and pharmaceutical services databases. The QICDSS creation process was evaluated by government bodies with legal ownership of databases, the public health ethics committee and *Commission d'accès à l'information du Québec*. Ghosh (2012) (8): Reviews the National Tuberculosis Surveillance System in the US, created by linking epidemiological data submitted by state and territorial public health departments with laboratory data from the National Tuberculosis Genotyping Service. Compliant with federal legislation, identifying information is not stored and user credentialing is also maintained.
Surveillance system operation	8. Create data sharing and use agreements with surveillance partners with variables and additional sources limited to purposes of surveillance system for privacy reasons (n=3).	Blais (2014) (49), Ghosh (2012) (8), Strobel (2019) (62)	Blais (2014) (49): Discusses the evaluation of the QICDSS. This surveillance system was created by linking several databases: the health insurance registry, hospitalization database, vital statistics death database, physician claims database and pharmaceutical services databases. Only relevant variables were used in the creation of the QICDSS. Strobel (2019) (62): Examines the evaluation of the IDEA surveillance system in Western Australia, which was created by merging data from the Department of Education Western Australia and the DSC. Variable collection is limited for privacy reasons. Data sharing agreements governing data provision from data sources are present.

Table 2: Long standing practices in public health by theme and surveillance system stage (*continued*)

Surveillance system stage where relevant	Practice	Articles that support practices	Examples of practices
Ethical considerations (*continued*)			
Surveillance system operation (*continued*)	9. Restrict data access and sharing on need-to-know basis for data integrity and privacy with access monitored using logs (n=4).	Blais (2014) (49), Ghosh (2012) (8), Marzano (2023) (70), Ndeikoundam Ngangro (2022) (57)	Blais (2014) (49): Discusses the evaluation of the QICDSS. This surveillance system was created by linking several databases: the health insurance registry, hospitalization database, vital statistics death database, physician claims database and pharmaceutical services databases. Data access is logged and limited to the team working within the surveillance system. Ndeikoundam Ngangro (2022) (57): Discusses the feasibility of an automated surveillance system for sexually transmitted infections in France. Sexually transmitted infections clinics submit data to *Santé Publique France* through a web portal. Data access is limited to authorized personnel.
	10. Seek ethics approvals for specific projects outside of routine surveillance (i.e., manuscripts) (n=2).	Fan (2010) (54), Sáez-López (2019) (60)	Fan (2010) (54): Describes the development of the Alberta Real Time Syndromic Surveillance Network (ARTSSN), a real-time surveillance system obtaining data from several different databases simultaneously: Health Link calls, emergency department visits, school absenteeism, laboratory reports and online forms. Research uses of the data must be approved with the process simplified due to the pseudonymization of data. Sáez-López (2019) (60): Discusses the evaluation of Portuguese influenza surveillance system, which has a sentinel and non-sentinel component. The non-sentinel component operates by having laboratories associated with the Portuguese Laboratory Network for the Diagnosis of influenza infection. Approval for specific projects is granted by the Health Ethic Committee of National Institute of Health Doutor Ricardo Jorge.
	11. Obtain informed consent from individuals consulted as part of surveillance system evaluation (n=3).	Johnson (2018) (55), McKerr (2015) (56), Rivière (2018) (59)	McKerr (2015) (56): This article is an evaluation of Taiwan's national dengue surveillance system as part of the National Disease Surveillance System (NDSS). This system has an active component amongst travellers at ports of entry and a passive component amongst patients presenting for care at their healthcare providers, laboratory testing, notification to local health departments and subsequently the NDSS. Verbal informed consent was obtained from those interviewed. Rivière (2018) (59): Summarizes an evaluation of the surveillance of bovine tuberculosis in France. Passive surveillance is conducted on specimens killed by hunters and dead or dying animals with data submitted to local veterinary services and the National Hunting and Wildlife Office. There is also an active surveillance component on living specimens with data submitted to the local veterinary services. Verbal informed consent was obtained prior to interviews.
Stakeholder consultation			
Surveillance system development	12. Build stakeholder relationships with each other and with surveillance system based on ongoing communication with stakeholders using tools such as communication plans including multiple methods of communication (n=16).	Asburry (2019) (98), Burkom (2021) (66), Cauchi (2022) (53), Contoli (2016) (72), Crain (2016) (73), Dawson (2016) (99), European Food Safety Authority (2023) (100), Huot (2019) (101), Johnson (2018) (55), McGill (2023) (10), Rivière (2018) (59), Schönfeld (2018) (102), Schwartz (2022) (103), Smith (2011) (77), Strobel (2019) (62), Takla (2012) (104)	Smith (2011) (77): Examines the implementation of a surveillance system model for child maltreatment developed by the US CDC. Numerous data sources are used, such as: death certificates, homicide files, medical examiner records, child protective services records, child welfare registries and Child Death Review Team (CDRT) reports. Respondents indicated that personal collaborative relationships between stakeholders were essential. However, frequent staff turn over and low meeting attendance were identified as hindrances in developing these relationships. Schwartz (2022) (103): Outlines the development of a COVID19 surveillance system in Memphis, US. The surveillance system combined regional laboratory COVID19 testing and epidemiological data with electronic medical records, social determinant and environmental data. The surveillance system included standard operating procedures for team meetings and community outreach in addition to a formal community outreach leadership team.

Table 2: Long standing practices in public health by theme and surveillance system stage (*continued*)

Surveillance system stage where relevant	Practice	Articles that support practices	Examples of practices
Stakeholder consultation (*continued*)			
Surveillance system operation	13. Ensure that the surveillance system is sustainable, ongoing and well resourced with the ability support the participation of all stakeholders in the surveillance system (n=15).	Asburry (2019) (98), Crain (2016) (73), Dawson (2016) (99), Ehlman (2021) (105), Fedorowicz (2010) (106), Hennenfent (2017) (74), Jermacane (2019) (107), Johnson (2018) (55), McGill (2023) (10), Moore (2012) (11), Paul (2019) (76), Schönfeld (2018) (102), Smith (2011) (77), Wijayasri (2016) (36), Wong (2022) (108)	Ehlman (2021) (105): Discusses the evaluation of the National Electronic Injury Surveillance System. Coders in emergency departments complete data entry in the system, sending data to the Consumer Product Safety Commission, which submits data to the US CDC. Issues identified with the surveillance system include multiple approvals, updates and training required when the system is updated, data completion, issues with laptops and staff turnovers and the need to replace sites if any drop out of surveillance system. Moore (2012) (11): Describes the evaluation of the US Department of Defense Serum Repository and Defense Medical Surveillance System, linking laboratory data with demographic data to create a surveillance system for the health of the military. Recommendations included: setting and communicating priorities for resources, strengthening and resourcing organizational oversight, distinct chain of command for receiving guidance and resource from policymakers in addition to adequate staffing to meet user needs.
Surveillance system evaluation	14. Stratify consultations based on different groups and include the following in surveillance system evaluation: surveys, focus groups and/or meetings and interviews (n=15).	Ehlman (2021) (105), Fedorowicz (2010) (106), Halliday (2013) (109), Hennenfent (2017) (74), Jermacane (2019) (107), Johnson (2018) (55), Kunze (2022) (110), Paul (2019) (76), Pratt (2020) (111), Rivière (2018) (59), Schönfeld (2018) (102), Smith (2011) (77), Takla (2012) (104), Yang (2020) (80), Zhang (2017) (81)	Halliday (2013) (109): Describes the surveillance system evaluation of the Australasian Maternity Outcomes Surveillance System. In this surveillance system, monthly data requests are emailed to maternity unit data collectors who can either submit data or submit a nil report through web-based reporting. Data collected would then be accessed by study investigators for research and dissemination. In addition to conducting an anonymous online survey of stakeholders, documentation from advisory and project meetings in addition to official correspondence were reviewed to identify previous concerns, questions, comments and feedback. Takla (2012) (104): Discusses an event-specific surveillance system developed for the FIFA women's world cup in Germany in 2011. The local district where the world cup was held would report to the Robert Koch Institute (national health authority) through state health authorities, with infectious disease notifications being provided daily. The national health authority would provide feedback and summary reports to the ministry of health, district and state health authorities twice weekly in addition to phone conferences with key stakeholders as needed. Results from the evaluation were stratified across district vs. state health authorities.

Abbreviations: ARTSSN, Alberta Real Time Syndromic Surveillance Network; CDC, Centers for Disease Control and Prevention; CDRT, Child Death Review Team; DSC, Disability Services Commission; FDA, Food and Drug Administration; IDEA, Intellectual Disability Exploring Answers; NARMS, National Antimicrobial Resistance Monitoring System; NDSS, National Disease Surveillance System; QICDSS, Québec Integrated Chronic Disease Surveillance System; US, United States; USDA, United States Department of Agriculture; VaCARES, Virginia Congenital Anomalies Reporting and Education System; VEHDIP, Virginia Early Hearing Detection and Intervention Program; VVESTS, Virginia Vital Events and Screening Tracking System

stages of public health surveillance, integrating various methods and programs.

The positive impact of modernizing national HIV surveillance systems was noted previously in the United States, since it updated its National HIV Surveillance System in 2013 with enhancements, such as improvements in data collection on sexual orientation, gender identity, social determinants of health and improved data deduplication procedures to enhance data quality (113). This update has resulted in an increased capacity to rapidly respond to HIV clusters and support ongoing viral suppression through "data-to-care" activities (113). Although the National HIV Surveillance Program in Canada presents information on the epidemiology of HIV on a national level, the program does not have a centralized database with consistent data standards and relies on data received from thirteen PTs. This affects the timeliness of surveillance data, impacting the relevance of data used to inform evidence-based policies and programs for HIV prevention and treatment. As the data for the Canadian National HIV Surveillance Program is provided by the PTs, data linkages to additional data sources for other social determinants of health data is not available. As such, proposed approaches included incorporating a centralized database, data quality procedures and additional data sources and social determinant of health data collection as part of the National HIV Surveillance Program renewal. Furthermore, it is important to

update the National HIV Surveillance Program to better address the burden of HIV in Canada. It is anticipated that the potential renewal of the program in Canada will result in improved data collection and quality, providing key evidence needed to meet the federal government's commitments under its STBBI action plan (2,3), improved public health outcomes and improved outcomes for those diagnosed and living with HIV.

The proposed improvements to surveillance system infrastructure and methodology may improve the simplicity, timeliness and stability of the National HIV Surveillance Program as data standardization across jurisdictions simplifies data submission, which in turn could improve timeliness and stabilizes data submission processes. Proposed approaches for ethical surveillance system design may result in improved ethical surveillance practices and subsequently increase the acceptability of the surveillance system. Improving stakeholder engagement using the proposed approaches could improve the acceptability as stakeholders may be more likely to engage with the surveillance program.

Although numerous proposed approaches addressed various areas of improvement, not all findings from this literature review may be applicable to national HIV surveillance in Canada. For instance, a real-time HIV surveillance system (35) may not be needed at the national level, as provincial, territorial and local public health units would be primarily addressing HIV outbreaks or clusters, as opposed to the National HIV Surveillance Program and the national program serves to provide a national overview of HIV epidemiology, instead of localized data.

Findings from this review were consistent with findings from consultations with data providers and community organizations conducted as part of the National HIV Surveillance Program's review and renewal process and the recommendations in the *Pan-Canadian Health Data Strategy: Toward a world-class health data system* (114). While the need for meaningful community engagement and involvement has been acknowledged previously (115,116), the program's consultations and the Pan-Canadian Health Data Strategy (PCHDS) (114) emphasized the importance of community consultations regarding data collection, interpretation and storage. Regarding data infrastructure and quality, the program's consultations and the PCHDS (114) suggest developing consistent data standards, with the PCHDS advocating for timely data access, health data literacy promotion and data-driven social and technological innovation (114). Furthermore, the program's consultations recommended the collection of information on sex, gender, sexual orientation, race and/or ethnicity and disease staging (e.g., CD4 cell count). The PCHDS proposed prioritizing the following related to data governance: ethical data use, First Nations, Inuit and Metis data sovereignty, oversight, federal leadership and measures to address security and privacy concerns (114). The findings of this review are consistent with the Public Health Agency of Canada's vision for what public health surveillance should look like by 2030, with enhanced surveillance workflows, high-quality data, improved data sharing and linkage, community partnerships and public engagement (117). The National HIV Surveillance Program's ongoing collaboration with data providers and community members to update data management, improve data collection on key variables and stakeholder engagement represents meaningful efforts to advance HIV surveillance in Canada.

This literature review provides a comprehensive overview of current and future proposed approaches in public health surveillance relevant to Canada's national HIV surveillance. It contains evidence gathered from diverse sources over a broad timeframe, encompassing technological advances and surveillance system enhancements in response to public health events. As the epidemiology of diseases change over time, surveillance systems are updated to ensure relevance, resulting in the development and incorporation of new public health practices. The wide timeframe allows for the aggregation of practices gained from experience dealing with various public health events (e.g., COVID-19 pandemic) and technological updates, such as databases incorporating automated data linkage. Including information from a wide range of jurisdictions, with similar surveillance systems or public health contexts, allowed for a wider range of public health practices to be incorporated in this literature review for future discussion. In addition, the inclusion of information on other surveillance systems, instead of solely focusing on HIV surveillance systems, allowed for the inclusion of various practices. These include linked national and state tuberculosis surveillance systems in the United States (8) and additional methods for stakeholder collaboration and communication through resources tailored to stakeholders in a surveillance system examining health related behaviours in senior citizens in Italy (72). With the potential incorporation of these practices, linking the National HIV Surveillance Program to other surveillance systems or data sources could improve data collection on HIV and other relevant indicators. Resources tailored to stakeholders could improve the relevance of surveillance information products such as surveillance reports and infographics, as well as improve stakeholder engagement with the national program. Incorporating grey literature allowed novel and innovative practices found in emerging research to be included. Information can often be found in evidence reviews or reports in addition to published journal articles, such as a World Health Organization report on achieving key goals related to HIV, hepatitis and sexually transmitted infections, outlining various advances, such as case-based surveillance systems enhanced with additional data for improved care (35).

Limitations

This review was limited to information available online (i.e., additional information may be found in internal surveillance protocols and standard operating procedures). There may be additional technical details from these internal documents that

may guide the development and operation of data management systems and other surveillance system tools that may not be accessible for review. While attempts were made to include articles primarily focused on passive surveillance systems, decisions regarding inclusion were sometimes difficult. For instance, articles regarding more recent surveillance systems often included components involving active or sentinel surveillance that supplemented passive surveillance. Additionally, this review was not a systematic review. Therefore, quality of evidence and risk of bias were not assessed. As quality of evidence was not considered and risk of bias was not assessed, evidence presented here could not be weighted based on these factors, rendering all sources as equal. This allows for over emphasis on lower quality and biased sources and under emphasis on higher quality sources with less bias. Despite these limitations, the results of this review provide evidence for improving surveillance practices as the National HIV Surveillance Program seeks to modernize surveillance practices and processes.

In addition to identifying possible directions for improvement of Canada's national HIV surveillance program, this literature review summarizes public health surveillance practices for HIV and other conditions. The potential for applying public health surveillance practices for other conditions to HIV surveillance has been highlighted in this review and it serves as a valuable reference compiling information on proposed approaches to improving surveillance system infrastructure and methodology, data collection, ethical public health surveillance and stakeholder engagement in a single place. As such, this review may be relevant to other surveillance systems looking to review and renew their own systems.

Conclusion

In conclusion, as part of a comprehensive review of Canada's HIV surveillance program, several current and future proposed approaches for surveillance systems were identified. Promising potential innovations include updates to data collection infrastructure, inclusion of new data elements (e.g., CD4 cell count), improving collection of existing data elements (i.e., sex and gender, race and/or ethnicity, HIV exposure information), developing a data governance framework and ongoing engagement with data providers and communities. Next steps include examining ways to validate and operationalize these key findings in collaboration with data providers and affected communities.

Authors' statement

AR — Methodology, investigation, writing–original draft
WM — Methodology, investigation, writing–original draft
LJ — Conceptualization, writing–review & editing, supervision
DP — Writing–review & editing
JC — Writing–review & editing
LHT — Conceptualization, writing–review & editing, supervision

Competing interests

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ORCID numbers

Wes Martin — 0009-0005-2238-2104
Joseph Cox — 0000-0002-7041-1556
Laura H Thompson — 0000-0003-3792-9772

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Appendix

Table A1: Articles included that did not meet one or more inclusion criteria

Article	Inclusion criteria not met	Rationale for inclusion
Kodan (2021) (83)	Study location in: North America, Australia, New Zealand, United Kingdom, Western Europe, Europe, Japan, Singapore, South Korea, Taiwan, Malaysia This study was conducted in Suriname.	This article was included as it outlined the development and operation of a working group overseeing the assignment of tasks and clearly delineating roles and responsibilities. This is relevant during stakeholder collaboration during a potential renewal.
Mao (2010) (9)	Study location in: North America, Australia, New Zealand, United Kingdom, Western Europe, Europe, Japan, Singapore, South Korea, Taiwan, Malaysia This study was conducted in China.	This article was directly related to HIV surveillance and detailed the development of a national web-based HIV/AIDS information system based on real-time data. This is relevant to surveillance structure methodology and infrastructure during a potential renewal.
Zhang (2012) (89)	Study location in: North America, Australia, New Zealand, United Kingdom, Western Europe, Europe, Japan, Singapore, South Korea, Taiwan, Malaysia This study was conducted in China.	This article had discussed the effect of social stigma and political structures on HIV surveillance in China and highlighted the importance of centralized data collection. This is relevant to data collection during a potential renewal.
Lee (2009) (64)	Published on or after January 1, 2010 This article was published in 2009.	This article was a commentary in the United States proposing a national privacy protection standard for public health data and emphasized the importance of community groups providing input in decision making, standardized data collection and periodic surveillance system evaluation. This is relevant during stakeholder collaboration during a potential renewal.

Additional supplementary information on search strategies and included articles is available upon request.
Please contact hass@phac-aspc.gc.ca

Travel-related dengue, Zika and chikungunya in Canada, 2012–2023

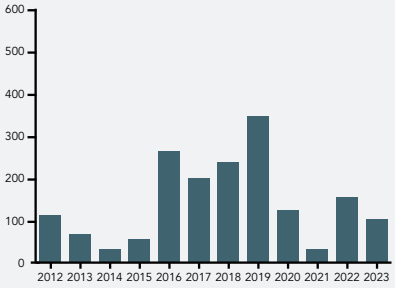
Results from a feasibility pilot study on laboratory-based surveillance

- Dengue, Zika and chikungunya are vector-borne diseases (VBD) spread by mosquitoes that Canadians may encounter during travel abroad[1]. These diseases are not endemic in Canada and are not reportable and/or nationally notifiable, yet hundreds of Canadians returning from travel to endemic regions are diagnosed each year[2,3].
- Laboratory-based surveillance uses routine laboratory requisition and testing data to identify and monitor disease activity.
- The Retro 3 feasibility pilot study used laboratory-based surveillance methods to retrospectively analyse travel-related dengue, Zika and chikungunya among returning Canadian travellers[4]. Data from persons tested at the National Microbiology Laboratory (NML) are presented, however they underestimate total disease burden as vital testing information from provincial public health laboratories are not yet included in this analysis.

DENGUE

1,725 cases[5] | Median age: 35

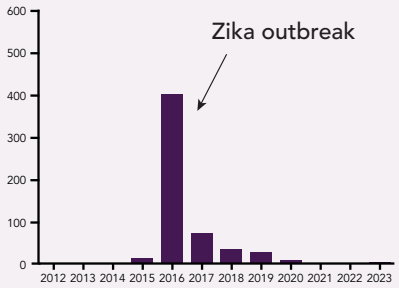
70% women (49% pregnant)



ZIKA

559 cases[5] | Median age: 35

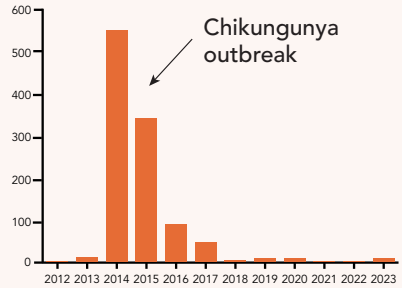
68% women (28% pregnant)



CHIKUNGUNYA

1,065 cases[5] | Median age: 49

63% women (1% pregnant)



The Caribbean[6] was the top travel destination linked with laboratory-based cases of dengue, Zika and chikungunya

- **A total of 3,349 laboratory-based cases of travel-related dengue, Zika and chikungunya were identified among 49,942 persons tested for these diseases at the NML in 2012–2023[7].**
- Disease trends closely aligned with those observed globally and in countries of travel destination.
- Most laboratory-based cases were among women of childbearing age, except for chikungunya, which was more common in older age groups.
- Only 1% of chikungunya and 28% of Zika laboratory-based cases among women reported pregnancy, compared to approximately 50% for dengue[8].

Laboratory data can be leveraged for epidemiologic analyses to monitor long-term trends and detect outbreaks of travel-related VBD. Laboratory-based surveillance of VBD could provide valuable insights into their epidemiology and play a critical role in supporting current surveillance efforts for emerging VBD.

BC Centre for Disease Control
An agency of the Provincial Health Services Authority
Alberta Health Services
Public Health Ontario | Santé publique Ontario

1. Government of Canada. Zika virus: Latest travel health advice. 2023. https://www.canada.ca/en/public-health/services/diseases/zika-virus/latest-travel-health-advice.html. 2. Ogden NH, Gachon P. Climate change and infectious diseases: What can we expect? Can Commun Dis Rep 2019;45(4):76–80. https://doi.org/10.14745/ccdr.v45i04a01. 3. Government of Canada. Dengue fever: Surveillance. 2024. https://www.canada.ca/en/public-health/services/infectious-diseases/viral-haemorrhagic-fevers/dengue-fever/surveillance.html. 4. Public Health Agency of Canada, BCCDC Public Health Laboratory, Alberta Health Services Laboratory Services, Public Health Ontario Laboratory. Retro 3: A feasibility pilot study for the development of a laboratory-based surveillance system for vector-borne diseases. Can Commun Dis Rep 2025;51(5):213. 5. Laboratory-based cases. 6. Travel regions are based on intermediate regions within the United Nations' Statistical Division's M49 classification system. Travel within Canada was excluded. Highlighted box is an approximation of countries/areas within the Caribbean intermediate region. 7. Year is defined as the earliest year among sample collection, sample receipt or symptom onset. 8. This higher proportion for dengue likely reflects Zika testing recommendations for potential travel exposure during pregnancy also leading to dengue testing due to overlapping travel risks, clinical presentations and cross-reactivity, rather than indicating a true higher prevalence of dengue among pregnant women.

Public Health Agency of Canada, BCCDC Public Health Laboratory, Alberta Health Services Laboratory Services, Public Health Ontario Laboratory. Travel-related dengue, Zika and chikungunya in Canada, 2012–2023: Results from a feasibility pilot study on laboratory-based surveillance. Can Commun Dis Rep 2025;51(5):212.

Public Health Agency of Canada | Agence de la santé publique du Canada
Canada

Retro 3: A feasibility pilot study for the development of a laboratory-based surveillance system for vector-borne diseases

Vector-borne diseases (VBD) are rapidly expanding globally[1]. In addition to emerging sporadic domestically-acquired VBD, hundreds of cases occur among Canadian travellers annually[2,3]. Yet, several emerging VBD are not reportable and/or nationally notifiable in Canada.

The Retro 3 pilot study was a collaboration between the Public Health Agency of Canada (PHAC) and participating provincial public health laboratories to assess the feasibility of leveraging routine laboratory data for surveillance of these diseases, through a retrospective analysis of dengue, Zika and chikungunya.

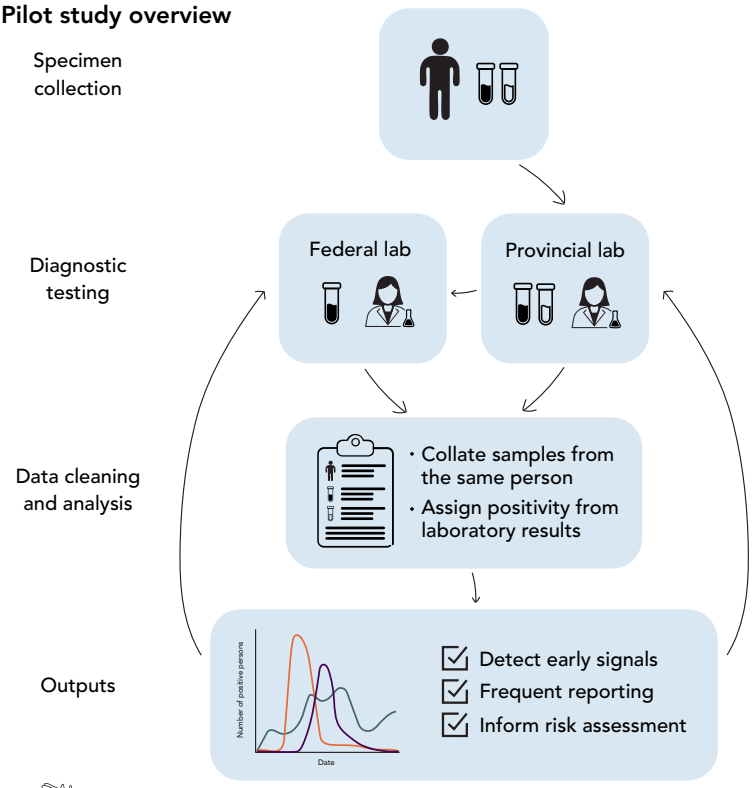
Vision

To identify and monitor early outbreak signals and gather data to assess the long-term trends and epidemiology of VBD of interest

Project objective

To assess the feasibility of leveraging routinely collected national and provincial laboratory data to conduct surveillance on VBD of interest

Pilot study overview



Data sources

- Provincial/national public health laboratory requisition and testing data

Data elements

- Non-nominal sample/person tags, dates, basic demographics, test results for diseases of interest, available travel and clinical data

Data analysis

- Laboratory-based definitions classify individuals as positive or negative for the disease of interest based on diagnostic test results

Feasibility pilot study key findings[4]

- Routine disparate lab data can be linked
- Data quality/completeness are sufficient
- Laboratory-only disease definitions can be used to classify positive persons
- Epidemiological patterns match global trends
- Data gathered allow for basic epidemiological analyses to inform public health initiatives

This feasibility pilot study demonstrated that laboratory requisition and testing data on dengue, Zika and chikungunya can be leveraged to conduct analyses compatible to those from a surveillance system, thus indicating the viability of a laboratory-based surveillance system for such diseases. Such a system would need to remain flexible to expand to other VBD in the future using a phased approach and could ultimately complement existing traditional case-based surveillance efforts and address critical gaps in Canada's VBD monitoring.

Laboratory-based surveillance represents an innovative, collaborative and efficient approach to leverage, integrate and disseminate routine laboratory data to support targeted public health actions and significantly enhance Canada's capacity to detect and respond to emerging VBD threats.

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