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ZOONOTIC DISEASES

SURVEILLANCE

OVERVIEW

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CANADA COMMUNICABLE DISEASE REPORT

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Photo Credit

The photo shows a coyote standing in an open field. The coyote can transmit *Echinococcus* tapeworm to humans via fomites and dogs. This photo was taken by Josée Tremblay at the Experimental Farm in Ottawa, Ontario.

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CCDR
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ZOONOTIC DISEASES

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Surveillance of *Echinococcus* tapeworm in coyotes and domestic dogs in Winnipeg, Manitoba

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Abstract

Background: The *Echinococcus* species, including *E. multilocularis* and *E. canadensis*, are tapeworms that primarily infect canids such as dogs, foxes and coyotes, but which can also infect humans. In humans, *E. multilocularis* can cause alveolar echinococcosis; a serious condition that mimics metastatic malignancy and has a poor prognosis. It is known that coyotes in rural Manitoba are infected with *Echinococcus* species, but it is not known if coyotes in peri-urban areas are also infected.

Objectives: To document and map *Echinococcus* species in wild canids and domestic dogs in Winnipeg, Manitoba (Canada).

Methods: There were 169 fecal samples collected between April 18 and June 1, 2018. These included 44 samples of domestic dog feces, 122 of coyote scat, one of fox scat and two of coyote colonic tissue specimens. Samples were frozen (-80°C) for at least 72 hours to inactivate tapeworm ova. Polymerase chain reaction analyses of *E. multilocularis* and *E. canadensis* were performed on all frozen samples.

Results: *Echinococcus multilocularis*-positive samples were detected in nine (10.6%) of 85 locations, with one positive sample in a suburban Winnipeg dog park and two positive samples in a popular provincial park. No dog samples were positive for *E. multilocularis*; one sample was positive for *E. canadensis*. In contrast, nine coyote samples (7.3%) were positive for *E. multilocularis* and eight samples (6.5%) were positive for *E. canadensis*. The one fox sample was positive for each. Overall, six samples (3.6%) were positive for both infections.

Conclusion: This is the first confirmation of the presence of *E. multilocularis* in coyote feces in the metropolitan area of Winnipeg, Manitoba. In light of the risk this could pose to domestic dogs and human health, periodic surveillance that maps the distribution of this tapeworm could inform the need for additional public health actions.

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Keywords: alveolar echinococcosis, hydatid disease, zoonotic diseases, coyotes, foxes, *Echinococcus* tapeworms, domestic dogs

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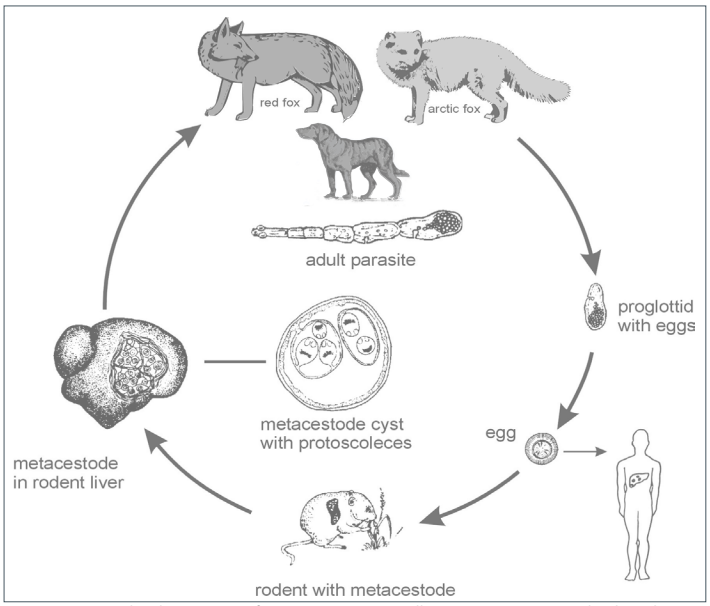
Introduction

Echinococcus species are tapeworms that primarily infect canid species. The two predominant species that have been found in Canada are *E. multilocularis* and *E. canadensis*. The sylvatic lifecycle of *Echinococcus* tapeworms includes coyotes and other canids as definitive hosts and rodents as intermediate hosts. Humans, however, can be incidental (or dead-end) hosts (**Figure 1**). *E. multilocularis* can cause a serious disease in humans: alveolar echinococcosis (1,2). This infection, which behaves like a metastatic malignancy, has a high case-fatality rate and requires radical surgical and long-term anthelminthic treatment (3). Although a more benign infection in humans, *E. canadensis* is also maintained via a sylvatic lifecycle thatincludes wolves, coyotes, and dogs as definitive hosts and caribou, moose and elk as intermediate hosts. In humans, as incidental hosts, the predominant clinical presentation is cystic hydatid disease primarily in the liver, which may require surgical intervention that carries the risk of severe anaphylaxis should cyst rupture occur (2). These two species are not infrequently found together given they share definitive canid hosts. *Echinococcus* species tapeworms are asymptomatic and cause no disease in canids, and they are hard to detect, as the worms are only 1–7 mm in length.

Figure 1: Lifecycle of *Echinococcus multilocularis*



Source: Reprinted with permission from Torgerson PR, Keller K, Magnotta M, Ragland N. The Global Burden of Alveolar Echinococcosis. PLoS Negl Trop Dis 2010;4(6): e722

The World Health Organization and the Food and Agriculture Organization of the United Nations have ranked alveolar echinococcosis as the third most important food-borne parasitic disease of global importance (4). As there is no cost-effective way to eliminate *E. multilocularis* in the sylvatic lifecycle, surveillance is important for human risk assessment.

How humans become infected

Echinococcus multilocularis ova are quite resistant and can survive and remain infective for nearly one year under favorable conditions (5). As the ova are sticky, they can adhere to the fur of dogs, wild vegetation and garden produce that is grown in feces-contaminated soil (2,6,7). Transmission to humans typically occurs when the hand comes in contact with water, soil, fur or objects contaminated with host feces, followed by inadvertent hand to mouth transfer of the ova. Following human ingestion of *E. multilocularis* ova, there is a long clinical latency period; from five to 15 years. Early symptoms include abdominal pain, which is followed by jaundice and eventually by severe hepatic dysfunction (2,8). Alveolar echinococcosis is often mistaken for a neoplastic growth, given its propensity for widespread organ infiltration with metastases (2). *E. multilocularis* may also imitate other diseases, including hepatic carcinoma, cirrhosis and tuberculosis, which may lead to improper diagnostic testing and delayed treatment (3,9,10). Diagnosis is confirmed based on a combination of clinical findings, epidemiological data, imaging, histopathology and/or nucleic acid detection and serology (8). Recommended treatment is radical surgical resection of the parasitic lesion, which in early stages may lead to a complete cure; however, surgical resection can sometimes be incomplete due to the diffuse or undetected spread of the parasite (2,8). As such, post-surgical anthelminthic chemotherapy is recommended for at least two years followed by a minimum of 10 years of close monitoring (8). If untreated, mortality is 90% within 10 years of onset of symptoms (11). Early diagnosis and proper treatment has been shown to improve survival (12).

Echinococcus multilocularis in Canada

Echinococcus tapeworms have been documented in canids in Canada for many years. A study on the prevalence of *E. multilocularis* in Manitoba canid species, performed 40 years ago in Riding Mountain National Park, found that almost one quarter of all coyotes sampled were infected (13). More recently in 2009, an European strain of *E. multilocularis* was discovered in central British Colombia in a domestic dog with no history of travel outside Canada, with further research suggesting the possible establishment of this new strain in the local wildlife (14,15). There may be evidence of a similar strain in the wildlife of Saskatchewan (16). Surveys in Calgary and Edmonton published in 2012 determined that *E. multilocularis* was present in the wild canid populations of those cities (1). Furthermore, in Ontario, recent detections of alveolar echinococcosis in several domestic dogs with no known travel history outside of Ontario suggest that *E. multilocularis* tapeworms may have established a foci in southwestern Ontario as well (17,18).

Echinococcus tapeworms and cases of human alveolar echinococcosis were first reported in the 1930s in Manitoba and Alberta (19). More recently, in November 2017, a pediatric

patient from Manitoba was identified with disseminated alveolar echinococcosis infection (*personal communication November 23, 2017, Dr. Sergio Fanella*). Similarly, in 2018, several human cases of alveolar echinococcosis were detected in Alberta (*personal communication June 5, 2018, Dr. Stan Houston*).

With increasing urbanization and sightings of coyotes in urban and suburban areas, *E. multilocularis* may be brought into close proximity to domestic dogs and humans (20,21). In light of these recent human cases, and the sightings of coyotes in and around Winnipeg (20), a survey of wild canids to look for the presence of *Echinococcus* species was conducted.

The aim of this study was to determine the extent of *Echinococcus* species ova, especially *E. multilocularis*, in coyote, fox and domestic dog feces found in the metropolitan area around Winnipeg, and to perform geospatial mapping to determine at-risk areas.

Methods

Collection sites

The Winnipeg metropolitan area (WMA) was defined as Census Metropolitan Area 602 based on the 2016 census profile from Statistics Canada (22). This consists of the urban area, demarcated by the circumferential perimeter highway surrounding Winnipeg and the peri-urban area that lies outside the perimeter highway and within the WMA. Eighty-five collection sites were identified that covered a wide area of the WMA, including areas frequented by humans and domestic dogs as well as areas with known coyote sightings.

Sample collection

Fecal samples were collected between April 18 and June 1, 2018. Samples from domestic dogs were collected differently from the other canid samples. Dog samples were collected from dog parks or submitted directly by dog owners. Two drop-off locations were offered to volunteers who submitted fecal samples from domestic dogs.

Samples from wild canids (mostly coyotes) were predominantly collected by driving along remote roads near coyote habitat based on local knowledge of coyote sightings. Coyote samples were identified via characteristics of the scat sample including shape, texture, presence of hair and bone belonging to small animals as well as supporting features including coyote tracks, nearby coyote dens and previous sightings (20). Similarly the fox scat sample was differentiated by the local conservation officer by its smaller size and the fact there had been known fox sightings nearby.

All fecal samples were picked up individually with plastic bags, sealed and labelled with date of collection, location of collection [Global Positioning System (GPS) coordinate, postal code or address]. For domestic dog samples, the name and phone number of the dog owner was also noted. Two colon samples from carcasses of coyotes were submitted by local wildlife conservation officers who retrieved the colon from two unique animals. Samples were stored at -80°C for at least 72 hours to inactivate *E. multilocularis* ova. The colonic samples were scraped on the mucosal surface to retrieve fecal matter.

Laboratory testing

Fecal material was stored and transported in sterile fecal containers, kept on ice, and sent with same day delivery to the reference laboratory (IDEXX Laboratories, Inc.) in Markham, Ontario. Fecal samples were processed immediately upon arrival and total nucleic acid extraction was performed using a KingFisher™ Flex Magnetic Particle Processor (Thermo Fisher Scientific, Vantaa, Finland) with proprietary lysis buffer and magnetic glass particles [Roche Diagnostics, Indianapolis, United States (US)]. Real-time polymerase chain reaction (PCR) assays were carried out using total nucleic acid purified from stool samples on a Roche LightCycler 480™ instrument using the manufacturer recommended cycling protocols and PCR reagents (23). Crossing points were calculated using the second derivative maximum-method analysis module with the high-sensitivity algorithm. Real-time PCR tests included PCR primers and a 6-FAM-TAMRA quenched conventional hydrolysis probe was adapted from Isaksson et al. (24).

The target gene for the real-time PCR tests was the mitochondrial gene *rrnL*. Six quality controls, including PCR positive and negative controls, negative extraction controls, environmental contamination control, spike-in internal positive control and pan-bacterial 16 ssrRNA internal sample control, were run to monitor for extraction efficiency, sample matrix inhibitors and cross contamination in the diagnostic runs. This PCR assay specific for *Echinococcus* species is in the process of being validated and peer reviewed. It was used in this study as it had successfully confirmed a clinical case of *E. multilocularis* of a dog in Ontario (*personal communication January 11, 2019, Dr. Roxanne Chan, IDEXX Laboratories, Inc.*).

Analysis

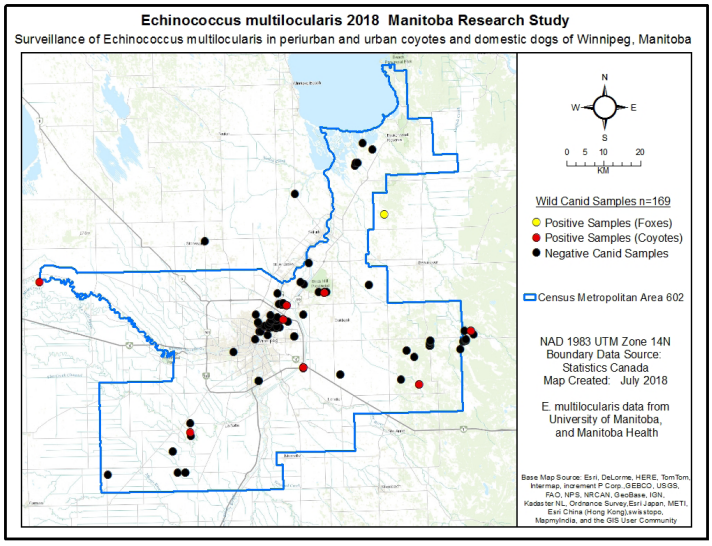
Data were stored in Microsoft Access and analyzed using Centers for Disease Control (Atlanta, Georgia, US) Epi-Info version 7.2.0.1 for descriptive statistics. Geocoding and mapping were done using Environmental Systems Research Institute ArcMap.

Results

In total, 169 samples were collected. This included 122 coyote scat samples, two coyote colon tissue samples, 44 domestic dog fecal samples, of which 34 samples were from unique animals collected directly from dog owners (the other 10 samples were collected from dog parks and may not necessarily be from unique animals), and one fox scat sample.

Echinococcus multilocularis-positive samples were detected in nine (10.6%) of 85 locations, with one positive sample in a suburban Winnipeg dog park and two positive samples in Birds Hill Provincial Park. The other samples appear to be more evenly dispersed across the more rural areas of the WMA. **Figure 2** shows the sites where the samples were collected as well as the location of positive samples of *E. multilocularis*.

Figure 2: Map of the distribution of canid sample collection in the metropolitan area of Winnipeg, indicating *Echinococcus* multilocularis-positive samples



A red dot indicates an *E. multilocularis*-positive sample for coyote scat or tissue, a yellow dot indicates an *E. multilocularis*-positive sample for fox scat and a black dot indicates an *E. multilocularis*-negative canid sample. Blue outline depicts Census Metropolitan Area of Winnipeg; used with permission from Statistics Canada (22)

Of the samples sent for molecular processing, 10 (5.9%) were positive for *E. canadensis* and 10 (5.9%) were positive for *E. multilocularis*, with six (3.6%) coinfections in five coyotes and one fox. *E. multilocularis* was found in 7.3% of all coyote samples, 0% of domestic canine samples and in the single fox sample. *E. canadensis* was found in 6.5% of all coyote samples, 2.3% of domestic dog samples and in the single fox sample (**Table 1**).

Discussion

This is the first confirmation of the presence of *E. multilocularis* in coyote feces in both urban and peri-urban areas of Winnipeg, Manitoba. The distribution of *E. multilocularis* in coyotes appears to be wide, with no hotspots. Although *E. multilocularis* was identified in a popular recreational provincial park and a dog park, no domestic dog samples were positive for this tapeworm. Only one case of the much more benign *E. canadensis* was found in a domestic dog sample.

Limitations of this study include the short duration of surveillance, possible repeated sampling from the same canids and the use of a molecular assay that is still undergoing peer review (23). No characteristics of the domestic dogs were collected, such as if they were outdoor dogs or consumed rodents. The wild canid scat sampling method was targeted and so does not reflect a uniform collection across the entire region. A much larger sample size and longer surveillance timeframe would be required to more fully map the extent of *E. multilocularis* canid infection in the Winnipeg metropolitan area.

Implications and next steps

Our findings indicate a risk of human and domestic dog exposure to coyote feces infected with *E. multilocularis* in the urban and peri-urban areas of Winnipeg.

It is not completely known how often human exposure to the parasite will result in infection leading to alveolar echinococcosis. In 2001, a five-year study in Switzerland was published that showed a high human seropositivity rate to *E. multilocularis*, with no increase in disease rate. One explanation was a potential increased immunity in this population (25). However, a 2007 review found a significant increase in the incidence of alveolar echinococcosis in Switzerland after 2000, and noted this had been preceded by an increase in this infection in the local fox population 10–15 years prior (26). It was thought this reflected the long clinical latency period of alveolar echinococcosis.

Table 1: Number and percent of canid samples infected with *Echinococcus* tapeworms in urban and peri-urban areas of Winnipeg, 2018

Source of stool sample	*Echinococcus multilocularis*			*Echinococcus canadensis*		
	# of samples	# positive stools	% positive	# of samples	# positive stools	% positive
Domestic dog[a]	44	0	0	44	1	2.3
Coyote[b]	124	9	7.3	124	8	6.5
Fox	1	1	100	1	1	100
Total	169	10	5.9	169	10	5.9

Abbreviation: #, number
[a] Of the domestic dog feces samples, 34 were from unique animals, collected directly from dog owners; the other 10 samples were collected from dog parks and may not necessarily be from unique animals
[b] The 124 coyote scat samples are not necessarily from unique animals; hence, several samples could have originated from one coyote

A longer study is now underway to determine if the high prevalence of *E. multilocularis* in the environment is associated with an increased incidence of alveolar echinococcosis in humans (25).

Based on the evidence of *E. multilocularis* in the environment in several provinces and the recent human cases in Alberta and Manitoba, further studies are indicated. To better characterize prevalence and geographic distribution, research with more locations and samples, spatial analysis and in-province molecular diagnostic capabilities are indicated. If warranted, a human seropositivity study of *E. multilocularis* in affected regions could be considered.

This emerging issue is particularly amenable to a One Health approach (27) involving physicians, veterinarians and wildlife experts. Ontario has made *E. multilocularis* infection in domestic dogs and humans reportable, in order to monitor the extent of the infection (28,29). Although currently not notifiable elsewhere, it would be useful to report on the investigation of human alveolar echinococcosis cases, including any travel history (to confirm locally acquired disease versus imported from foreign countries) and information regarding the potential route of exposure to *E. multilocularis* ova. Public education concerning preventative measures to avert domestic dog and human infections may be indicated.

Conclusion

Echinococcus multilocularis has been documented in Canada for decades in the wild canid population, but human cases have been extremely rare. Over the last two decades, there has been a tendency for wild canids to migrate closer to urban populations, and there have been several recent human cases of alveolar echinococcosis caused by *E. multilocularis*. Although our study did not identify any cross contamination between coyotes and dogs in Winnipeg, the risk of exposure to *E. multilocularis* in urban and peri-urban settings suggests increased awareness and further study would help front line clinicians and public health officials be alert to and monitor this risk.

Authors' statement

CCKT — Project conception, literature searches, study design, field sampling, laboratory investigations, data analysis, writing (original draft, review, and editing)
JB — Project conception, study design, "in kind" laboratory investigations, software support, data analysis, writing (review and editing)
RR — Project conception, study design, software support, spatial data analysis, writing (review and editing)
DD — Project conception, study design, "in kind" laboratory support, data analysis, writing (review and editing)
PJP — Project conception, literature searches, study design, field sampling support, data analysis, writing (review and editing)

Conflict of interest

None.

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The results and conclusions are those of the authors and no official endorsement by Manitoba Health, Seniors and Active Living, or Manitoba Agriculture is intended or should be inferred.

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Human rabies postexposure prophylaxis and rabid terrestrial animals in Ontario, Canada: 2014–2016

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Abstract

Background: The number of rabid terrestrial animals in Ontario has decreased markedly since the 1970s and 1980s. However, the number of recommended rabies postexposure prophylaxis (RPEP) courses has not decreased proportionally. The decision to recommend RPEP for terrestrial animal exposures should be based on a risk assessment that considers the prevalence of rabies in these animals within a jurisdiction, among other factors.

Objective: To explore trends in RPEP recommendations for exposures to terrestrial animals in Ontario in relation to the recency of terrestrial animal rabies cases by public health unit (PHU) jurisdiction.

Methods: RPEP recommendation data for the 36 Ontario PHUs were obtained from the Ontario integrated Public Health Information System and animal rabies data by PHU were obtained from the Ministry of Natural Resources and Forestry. We calculated the annual RPEP recommendation rates for terrestrial animals by PHU for 2014 to 2016, and plotted the 2016 rates in relation to the year of the most recently identified rabid terrestrial animal in the PHU.

Results: Between 2014 and 2016, the annual RPEP recommendation rates for terrestrial animal exposures by PHU ranged from 3.0 to 35.2 per 100,000 persons, with a median of 11.9 RPEP recommendations per 100,000 persons. In 2016, ten PHUs had not identified a rabid terrestrial animal in their jurisdiction for more than 15 years. Five of these PHUs had RPEP recommendation rates above the provincial median.

Conclusion: Along with other factors, consideration of the occurrence of rabies in terrestrial animals in a jurisdiction can assist in the risk assessment of dogs, cats or ferrets that are not available for subsequent observation.

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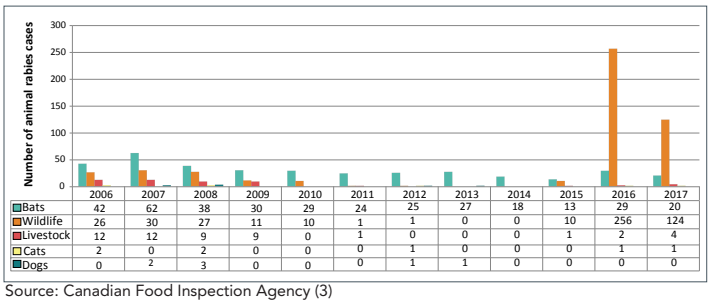
Keywords: rabies postexposure prophylaxis, animal rabies, rabies risk assessment

Introduction

Rabies in humans as a result of exposure to a terrestrial animal has not been identified for over 50 years in Canada (*personal communication, Stevenson B. Ontario Ministry of Natural Resources and Forestry, August 22, 2017*). Nevertheless, given the almost universally fatal effect of rabies infection once symptoms develop, rabies from terrestrial animals continues to be a public health concern. In Ontario, Canada the number of terrestrial animals identified with rabies has been very low in recent years (**Figure 1**) with two exceptions. These exceptions were an epizootic of the raccoon strain of rabies in central west Ontario, which was identified in late 2015 and originated from a translocated raccoon, and an ongoing enzootic of the Arctic fox strain of rabies in south west and central west Ontario (1). The marked decrease in terrestrial animal rabies in Ontario has been attributed to the wildlife rabies vaccination program run by the Ontario Ministry of Natural Resources and Forestry, which began

Figure 1: Animal rabies cases by animal type: Ontario, 2006–2017



	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Bats	42	62	38	30	29	24	25	27	18	13	29	20
Wildlife	26	30	27	11	10	1	1	0	0	10	256	124
Livestock	12	12	9	9	0	1	0	0	0	1	2	4
Cats	2	0	2	0	0	0	1	0	0	0	1	1
Dogs	0	2	3	0	0	0	1	1	0	0	0	0

Source: Canadian Food Inspection Agency (3)

in 1989. As an additional measure to prevent human rabies cases in Ontario, rabies postexposure prophylaxis (RPEP) is publicly funded and readily available (2).

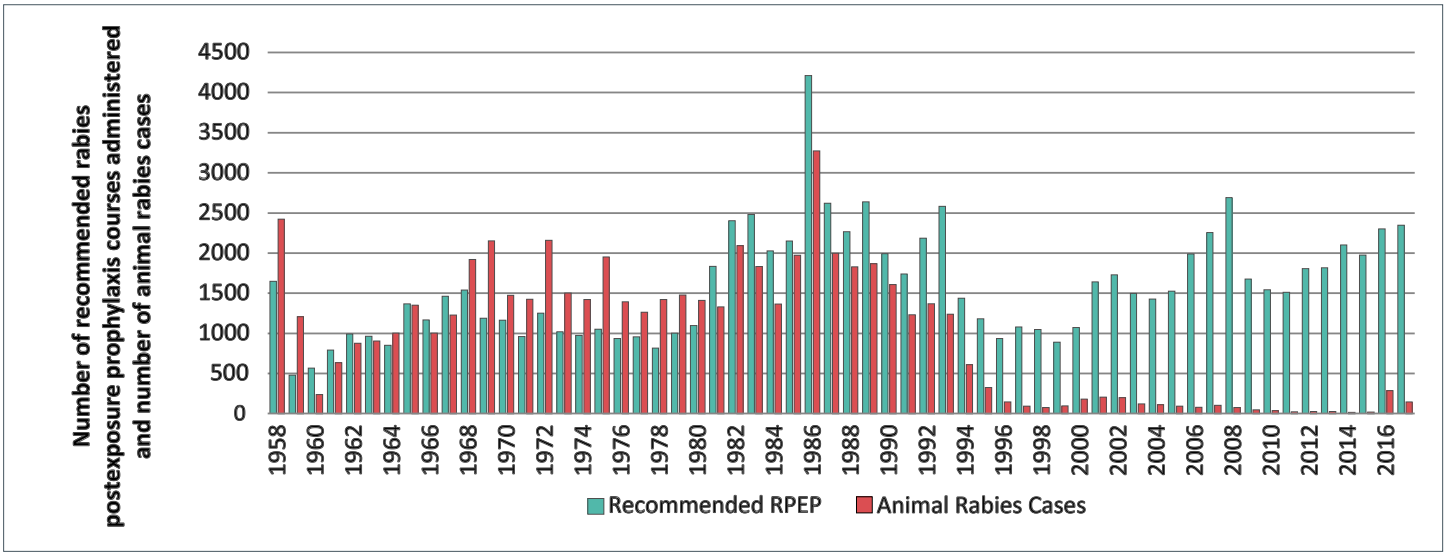
Despite the rarity of human rabies cases in Ontario, and the marked decrease in numbers of rabid terrestrial animals, the annual number of recommended RPEP courses has not decreased proportionally (4–6) (**Figure 2**). Administering RPEP when not indicated incurs the risk of adverse events as well as costs without benefit. One study, in the context of very low incidence of animal rabies cases, calculated that the risk of mortality from an automobile accident en route to receiving RPEP was greater than the risk of mortality from rabies (7).

According to the Ontario *Rabies Prevention and Control Protocol*, the decision to recommend RPEP for terrestrial animal exposures should be based on a risk assessment that considers a number of factors including the prevalence of rabies in these animals within a jurisdiction (8,9). Staff at the 35 public health units (PHUs) in Ontario (36 before May 1, 2018) conduct a risk assessment after a person is exposed to an animal that could carry rabies, although ultimately the health care provider decides whether to recommend RPEP. When a dog, cat or ferret bites or scratches a person, the animal is placed under observation for 10 days by the PHU. If the animal is healthy at the end of the 10-day postexposure period, it is considered not capable of having transmitting rabies at the time of the exposure. In such cases, RPEP is not indicated.

Prior to 2013, Canadian and Ontario guidelines recommended RPEP in all instances when the dog, cat or ferret was not available for a 10-day observation period. In 2013, the guidelines were updated to recommend conducting a risk assessment to determine if RPEP is indicated after exposure to the animal. Elements of the risk assessment for a terrestrial animal that is not available for observation include the type of exposure (i.e. bite, non-bite), the anatomical location of the exposure, the risk of rabies in the animal species involved, the presence of rabies in the area where the incident occurred, and the exposure circumstances (i.e. provoked or unprovoked exposures), as well as the reliability of the injured person's history (8,10,11).

In this article, we explore how local terrestrial animal rabies occurrences relate to the rate of RPEP recommendations by each PHU. For this analysis, we compare 2016 RPEP recommendation rates for terrestrial animal exposures for each PHU to the year in which the last rabid terrestrial animal was identified in each jurisdiction.

Figure 2: Annual number of animal rabies cases (terrestrial animals and bats)[a] and the annual number of rabies postexposure prophylaxis courses administered and/or recommended (including exposures outside of Ontario)[b], Ontario, 1958–2017



Abbreviation: RPEP, rabies postexposure prophylaxis
[a] Rabid animal data for 1958–2013 obtained from published articles (4–6). For 2014–2017, animal rabies case data were obtained from the Canadian Food Inspection Agency (3)
[b] RPEP data for 1958–2013 obtained from published articles (4–6). For 2014–2016, non-nominal RPEP data were extracted from the integrated Public Health Information System (iPHIS) on November 14, 2017, and for 2017, non-nominal RPEP data was extracted from iPHIS on August 23, 2018. Note: RPEP data includes recommendations for both terrestrial animals and bats, whether the RPEP was administered or not, and whether or not the exposure occurred in Ontario or elsewhere

Methods

Data sources

Rabies postexposure prophylaxis data

In Ontario, incidents involving exposure to a potentially rabid animal for which RPEP is recommended (regardless of whether it is administered or not) are entered into the integrated Public Health Information System (iPHIS) by the PHU where the client resides (12). In iPHIS, PHUs are prompted to populate a number of fields with details relating to the incident. These include information about the individual exposed, the circumstances of the exposure, the animal (including whether it is available for observation and its vaccination status, if known), and if RPEP is recommended. An open-text comment section allows adding more details about the case.

iPHIS RPEP data for 2014 to 2016 were extracted on November 14, 2017. Only records with RPEP recommendations for terrestrial animal exposures that occurred in Ontario were included in the analyses. These included exposures to Ontario species that are known rabies reservoirs (i.e. raccoons, foxes and skunks) and bridge vectors (i.e. dogs, cats and livestock, including cattle, horses, sheep, goats and llamas). Excluded were records for exposures that occurred outside of Ontario; to animal species that were not terrestrial animals; or to animal species listed as "unknown" unless details in the comments section indicated that these were terrestrial animals and did not indicate the exposure occurred outside of Ontario.

Population data

Population estimates for each PHU from 2014 to 2016 were obtained from IntelliHEALTH Ontario (13,14).

Animal data

The Ministry of Natural Resources and Forestry provided data on the year of the last confirmed terrestrial rabid animal reported for each PHU as of 2016 (*personal communication, Stevenson B, Ministry of Natural Resources and Forestry, June 29, 2017*).

Analyses

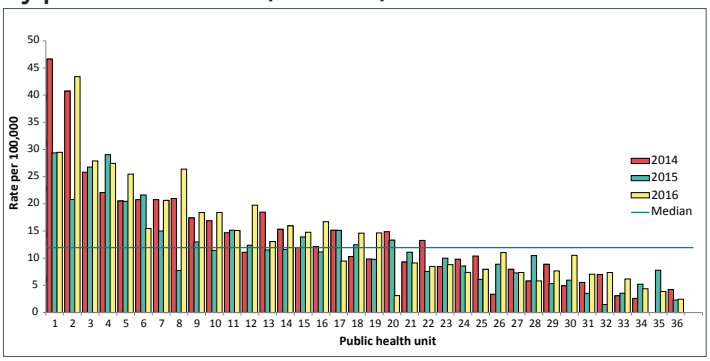
RPEP recommendation rates by PHU were calculated for the years 2014 to 2016. We used each PHU's annual RPEP data for exposures to terrestrial animals as the numerator and the population estimate for that PHU as the denominator, and graphed the results.

The number of years since the last rabid terrestrial animal was identified in each PHU relative to 2016 was also calculated. PHUs were categorized into one of the following five year intervals according to most recent report of a rabid terrestrial animal: 2016 or four preceding years, 6–10 years, 11–15 preceding years and more than 15 preceding years. We graphed 2016 RPEP recommendation rates for exposures to terrestrial animals by PHU, classifying each PHU by their category with respect to the number of years since the last terrestrial rabid animal was identified in that PHU area relative to 2016. Microsoft Excel [version 2010; Microsoft Corporation, Redmond, Washington, United States (US)] was used to analyse the data and generate graphs. Mapping and spatial data preparation of these data were performed using ArcMap (version 10.3; ESRI, Redlands, California, US) geographic information systems (GIS) software.

Results

The annual RPEP recommendation rates for terrestrial animal exposures by PHU for 2014 to 2016 ranged from 3.0 to 35.2 per 100,000 persons, with a median of 11.9 RPEP recommendations per 100,000 persons. The annual rates of RPEP recommendations tended to be fairly consistent, with 10 PHUs having RPEP rates above the median and 15 having rates below the median, for all three years (**Figure 3**).

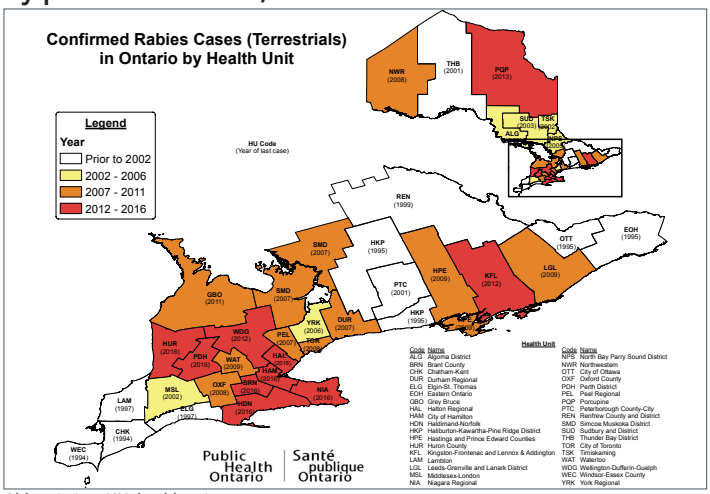
Figure 3: Annual rabies postexposure prophylaxis recommendation rates for terrestrial animal exposures by public health unit[a], Ontario, 2014–2016



[a] Public health units were assigned their number based on the X axis on the average annual three-year rate (2014–2016), in descending order

In 2016, ten PHUs had not identified a rabid terrestrial animal in their jurisdiction for more than 15 years (**Figure 4**). Five of these PHUs had RPEP recommendation rates above the provincial

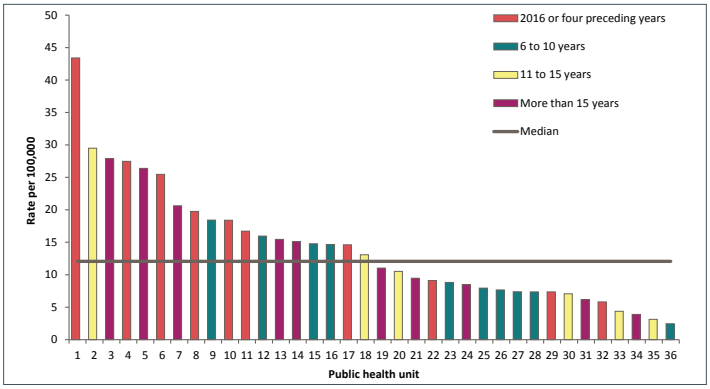
Figure 4: Last confirmed terrestrial animal rabies case by public health unit, Ontario



Abbreviation: HU, health unit

median. Two other PHUs, neither of which had identified a rabid terrestrial animal within the previous 11–15 years, also had RPEP rates above the median (**Figure 5**).

Figure 5: Rabies postexposure prophylaxis recommendation rates for terrestrial animal exposures within Ontario by public health unit[a] for 2016 and number of years since the last terrestrial rabies case relative to 2016



[a] Public health units were assigned their respective number based on the average annual three-year rate (2014–2016) (shown in Figure 3), in descending order

Discussion

Since approximately the year 2000, the number of RPEP courses recommended in Ontario has been high compared to the number of rabid animals, even considering the epizootic in central west Ontario that was identified in late 2015 (Figure 2). Since 2013, risk assessments to determine the need for RPEP have been recommended if a person is exposed to dogs, cats or ferrets that are not available for subsequent observation. Implementation of a risk assessment can potentially optimize the number of courses of RPEP recommended by PHUs, particularly in those PHUs with no recent rabid terrestrial animals.

The 2014–2016 annual RPEP recommendation rates for exposures to terrestrial animals in Ontario varied markedly between PHUs, from 3.0 to 35.2 per 100,000 persons. However, in general, each PHU's annual RPEP rate remained relatively consistent over the three study years. A PHU's RPEP rate may be influenced by a number of factors, including the likelihood of human exposures to potentially rabid animals, the likelihood of these exposures being reported to the PHU, and the risk assessment performed by the PHU in consultation with the health care provider. Data are not available to assess the likelihood of exposure to potentially rabid animals by PHU, or the likelihood of reporting these exposures, or how the risk assessment was conducted. Nevertheless, data on confirmed cases of rabid animals within a PHU's jurisdiction, an important factor to consider when conducting a risk assessment, are available. Our analysis found that the recency of the last rabid terrestrial animal did not seem to be associated with the respective RPEP recommendation rates by PHU. Five PHUs had RPEP rates for terrestrial animals above the provincial median despite not reporting a rabid terrestrial animal in more than 15 years.

One possible explanation for the lack of association between RPEP recommendation rates for terrestrial animals and recency of terrestrial animal rabies could be that instead of conducting a risk assessment when an animal was not available for observation, some PHUs automatically recommend RPEP, consistent with the Canadian and Ontario recommendations prior to 2013. Another possible explanation for this lack of association is that the occurrence of terrestrial animal rabies is not heavily weighted when assessing the rabies risk after a terrestrial animal exposure when the animal is not available for observation.

The possibility that rabies may arise from sources outside the PHU's jurisdiction, because of incursions of rabid animals from adjacent areas, translocated rabid animals or adoption of rabid animals, may influence the decision to recommend RPEP, even though these events are infrequent. Incursions from adjacent areas as a possible source of introduction of terrestrial rabies only applies to PHUs that border another province or the US. An epizootic of raccoon rabies from incursion from adjacent areas in the US has not occurred in Ontario for more than 10 years and has never been demonstrated to have originated from neighbouring provinces (15). Four of the five PHUs that had not experienced a rabid animal in their jurisdiction more than 15 years and had RPEP recommendation rates above the median rate did not share a land border with the US.

Translocation of an imported rabid animal that results in an unrecognized epizootic is a concern. In recent years, there has been one recognized instance of translocation of a "hitch-hiking" raccoon that resulted in the current epizootic in central west Ontario (14). Adoption of a domestic animal with rabies has only been reported once in Ontario in recent years, when a puppy was transported from rural Ontario to a flea market in Toronto in 2008. The situation was quickly recognized and the large number of people exposed to the puppy were appropriately managed. In order to protect against rabies, dogs and cats more than three months old that are imported into Canada must be vaccinated (with minor exceptions) (16,17), although on occasion, records have been falsified (18–21).

Another potential source of introduction of rabies into terrestrial animals comes from bats, which are known to carry rabies in Ontario. From 2000 to 2018, rabies strain typing in Ontario has identified 11 terrestrial animals with bat strain rabies: skunk (2001, 2004, 2016, 2018); cat (2002, 2004); fox (2003, 2009); raccoon (2002); bovine (2009); dog (2012) (*personal communication, Gagnon R, Ministry of Natural Resources and Forestry, March 20, 2018*). There is no evidence of transmission between animals based on the lack of identified clustering of any animals in time. In addition, a literature search revealed only one article that described the transmission of bat strain rabies among terrestrial animals, in skunks in Arizona (22). The transmission

of bat strain rabies from terrestrial animals to humans also appears to be very rare: only three articles, all from South America, definitively identified the transmission of bat strain rabies to four humans via cats (23–25). These bats were vampire bats (*Desmodus rotundus*), which feed on mammalian blood, increasing the probability of infection in terrestrial animals; bats in Ontario feed on insects.

Limitations

There are a number of limitations in our analyses by PHU. As previously mentioned, we cannot assess other factors that may affect RPEP rates, such as the extent of human exposure to terrestrial animals and subsequent reporting to PHUs. PHUs frequently do not enter information on RPEP recommendations when it is not actually administered. Further, it is possible that the exposure occurred outside of the PHU's geographical boundary. With regard to rabid terrestrial animals, the data are limited by the extent of surveillance in the particular geographic area. In general, animals are tested for rabies when there has been a potential human exposure or during epizootics. It is therefore possible that rabid terrestrial animals in a PHU jurisdiction may be missed.

An additional limitation is that our analysis considered the timing of the last rabid terrestrial animal but did not consider the incidence rates at the time of that last rabid animal (i.e. it did not consider if there was one rabid animal versus multiple rabid animals) and we did not incorporate the recency of terrestrial animal rabies in adjacent PHUs into the analysis, both of which are factors that may impact the risk assessment.

Conclusion

Human rabies acquired from terrestrial animals has not occurred for more than 50 years in Canada. Canadian and Ontario guidelines recommend a risk assessment be conducted when a person is bitten or scratched by a dog, cat or ferret that is not available for a subsequent 10-day observation period. Consideration of the timing of the most recent rabid terrestrial animal in the geographic area is an important factor in determining the need for RPEP in the risk assessment.

RPEP administration rates for terrestrial animal exposures by PHU tend to be fairly consistent within each PHU when measured over a three-year period. Of the ten PHUs that had not had a rabid terrestrial animal in their area for more than 15 years, five had RPEP recommendation rates for terrestrial animal exposures above the provincial median RPEP recommendation rate. Along with other factors, consideration of the occurrence of rabies in terrestrial animals in a jurisdiction can assist in the risk assessment of dogs, cats or ferrets that are not available for observation.

Authors' statement

DM — Conceptualization, analysis and interpretation of data, drafting and revising the paper
LF — Analysis and interpretation of data, drafting and revising the paper
SJ — Analysis and interpretation of data, drafting the paper
SB — Analysis and interpretation of data, revising the paper
BW — Conceptualization, interpretation of data, drafting and revising the paper

Conflict of interest

None.

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OVERVIEW

Toxoplasma gondii: How an Amazonian parasite became an Inuit health issue

SJ Reiling[1], BR Dixon[1]*

Abstract

Toxoplasma gondii is a protozoan parasite that originated in the Amazon. Felids (mammals in the cat family) are the only definitive hosts. These animals shed large numbers of infectious oocysts into the environment, which can subsequently infect many intermediate hosts, including birds, mammals and, possibly, fish. Human *T. gondii* seroprevalence is high in some parts of the Canadian Arctic and is associated with adverse health consequences among Inuit population. Since the range of felids does not extend to the Arctic, it is not immediately obvious how this parasite got from the Amazon to the Arctic. The objectives of this overview are to summarize the health impacts of *T. gondii* infection in Inuit in Canada's North and to consider how this infection could have reach them. This article reviews the prevalence of *T. gondii* infection in terrestrial and marine animals in the Canadian Arctic and discusses their potential role in the foodborne transmission of this parasite to humans. Two distribution factors seem plausible. First, felids in more southern habitats may release infectious oocysts into waterways. As these oocysts remain viable for months, they can be transported northward via rivers and ocean currents and could infect Arctic fish and eventually the marine mammals that prey on the fish. Second, migratory terrestrial and marine intermediate hosts may be responsible for carrying *T. gondii* tissue cysts to the Arctic, where they may then pass on the infection to carnivores. The most likely source of *T. gondii* in Inuit is from the consumption of traditionally-prepared country foods including meat and organs from intermediate hosts, which may be consumed raw. With climate change, northward migration of felids may increase the prevalence of *T. gondii* in Arctic wildlife.

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Keywords: toxoplasmosis, marine mammals, fish, climate change, migratory birds

Introduction

Toxoplasma gondii infection in humans

Toxoplasma gondii is a protozoan parasite that can infect virtually all birds and mammals (1). Although this parasite originally evolved in the Amazon region of South America (2,3), it now infects an estimated two billion people worldwide, with foci of high prevalence in Latin America, Eastern/Central Europe, the Middle East and South-East Asia and Africa, and lower prevalence in many European countries and both Canada and the United States (4). Humans may become infected via three transmission routes:

- Ingestion of tissue cysts by eating fresh raw meat or organs of an infected intermediate host
- Ingestion of sporulated oocysts, which may persist for months or years in soil or water
- Congenitally, from mother to fetus, if a pregnant woman has acute toxoplasmosis (5)

During the initial infection phase of an intermediate host, including in humans, *T. gondii* replicates rapidly and spreads throughout the tissues, including the brain (acute toxoplasmosis). In humans, symptoms may be subtle, and otherwise healthy individuals may not notice that they have become infected. Eventually, parasite replication slows down, and the protozoa cluster together in tissue cysts (latent toxoplasmosis). People with latent toxoplasmosis who become immunocompromised may develop reactivated toxoplasmosis, in which the dormant parasites in the tissue cysts will start replicating again. This reactivation can cause severe flu-like symptoms, blurred vision or toxoplasmic encephalitis. Latent toxoplasmosis has also been linked to changes in cell signaling pathways that may lead to neurological disorders including schizophrenia, epilepsy, Alzheimer's disease and Parkinson's disease (6–11). Furthermore, a positive association has been made between *T. gondii* infection and increased risk-seeking behaviour in humans (12,13).

Congenital transmission may lead to stillbirth or severe neurological complications.

Socioeconomic factors may have a significant impact on human exposure to this parasite. Factors influencing the seroprevalence in humans include proximity to infected domesticated or wild reservoir hosts, access to clean drinking water, urban versus rural lifestyle, types of food consumed, food preparation (raw vs freezing/cooking/drying) and hygiene (washing hands and rinsing fresh produce) (14).

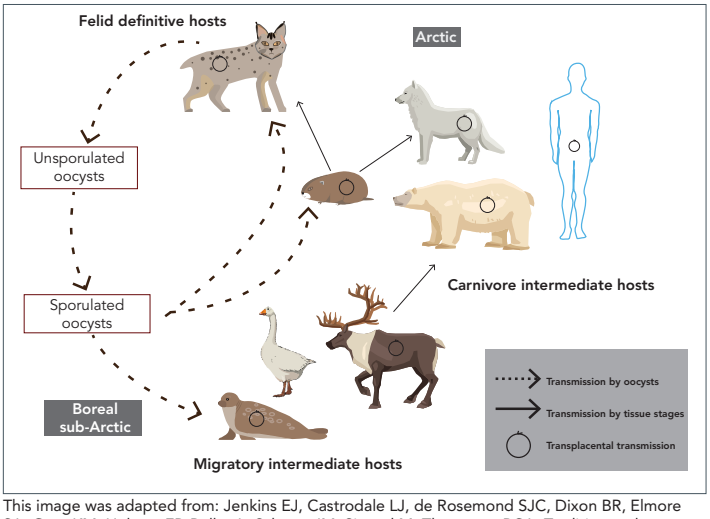
T. gondii from the Amazon to the Arctic

Toxoplasma gondii evolved in the Amazon rainforest (2,3). It is very common in the Amazon region and Indigenous populations of the Amazon River basin have the highest known infection rate worldwide: along the upper Rio Negro, *T. gondii* seroprevalence is greater than 90% (15). Despite its worldwide distribution, only in the Amazon is *T. gondii* characterized by a high level of genetic diversity and the presence of many unique genotypes (3). Analysis of the gene flow of unique genotypes indicated that a small number of ancestral lineages gave rise to the existing diversity of *T. gondii* (2). The primary hypothesis for the worldwide spread of *T. gondii* is that shipping traffic facilitated the travel of domestic cats and infected intermediate hosts to other continents (1). The parasite reproduces in the small intestine of the felid definitive hosts, and millions of oocysts are shed into the environment (5,14). How *T. gondii* spread from the Brazilian rainforest to the Canadian Arctic is not known. In this article, the Arctic boundaries are defined as described by the Conservation of Arctic Flora and Fauna (CAFF), which is the biodiversity group of the Arctic Council. The only wild felid that lives in the Canadian North is the Canada lynx, which has a *T. gondii* seroprevalence of 14% (16); however, the lynx's range does not extend north of the treeline (the boreal forest or subarctic). In addition, there are few domestic cats in Canadian Arctic communities. Thus, while the presence of infected felids may explain the spread of *T. gondii* throughout most of North America, it does not explain the parasite's presence in the Arctic; and, despite the scarcity of potentially infected felids, *T. gondii* is still present in a wide variety of Arctic animals.

To complete the parasite's lifecycle, oocysts that are shed by the felid definitive hosts need to sporulate (**Figure 1**) and be ingested by intermediate hosts, which are potential prey for felids and which include virtually all warm-blooded animals. *Toxoplasma gondii* invades the intermediate host's tissues and disseminates throughout the body, including the brain (1). However, intermediate hosts do not produce oocysts; thus, the mechanism (or mechanisms) of the geographical spread of *T. gondii*, in the absence of a definitive host, is still unknown.

The objective of this review is to highlight the incidence of this parasite in the Canadian Arctic and its impact on Inuit populations, and to consider how this parasite arrived and became endemic in an environment that lacks definitive hosts.

Figure 1: Lifecycle of a *Toxoplasma gondii* in Canada's North



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Toxoplasma gondii in the Arctic

T. gondii infection in Canadian Inuit

Toxoplasma gondii infections were first reported in Inuit in the 1980s (17–19). More recent studies showed that *T. gondii* seroprevalence in Inuit in the Canadian North varies greatly depending upon the region (17). *Toxoplasma gondii* seroprevalence in adults in three Canadian Inuit regions was reported at 8% in Nunatsiavut, 28% in Nunavut and 60% in Nunavik (20–24). There are not enough data to determine whether *T. gondii* prevalence in Inuit is stable or has changed over the decades.

Traditionally prepared "country foods" have great cultural significance for Inuit and in general are regarded as safe and nutritious for most people. However, it appears that *T. gondii* infection is related to the harvest and consumption of "country foods", especially meat and organs, which may be consumed raw (19,25). A correlation between *T. gondii* seroprevalence and different hunting practices and dietary habits has been debated (26–29). In contrast to Inuit communities, neighboring Cree communities, who usually cook their meat, were found to have a *T. gondii* seroprevalence of only 5% (29). It has been demonstrated that either thoroughly cooking meat, or freezing meat for several days, kills the pathogens present in the tissue cysts (30).

While toxoplasmosis is often asymptomatic in healthy individuals, pregnant women with acute toxoplasmosis are at risk of transmitting the parasite to the developing fetus. In 1987, an outbreak of toxoplasmosis was reported in pregnant women in Nunavik (19). Infection was associated with skinning of animals and consumption of raw caribou meat (19).

T. gondii in the absence of definitive hosts

A study from Svalbard, Norway suggested that the role of oocysts in the transmission of *T. gondii* to Arctic terrestrial animals has been overemphasized (31). The Svalbard archipelago is free from any wild or domestic cats, which eliminates the spread of infectious *T. gondii* oocysts into the environment (31). The absence of *T. gondii* oocysts in Svalbard is supported by findings that non-migratory birds and herbivores were seronegative for *T. gondii* (31). However, carnivores (foxes) were found to be *T. gondii*-positive. Thus, migrating birds may have introduced *T. gondii* to Svalbard, and local carnivores were subsequently infected by eating infected prey. Thus, it is possible for *T. gondii* to be transmitted from one intermediate host to another (e.g. bird to carnivore) without the need of sexual reproduction of the parasite in a felid definitive host. This transmission cycle between multiple intermediate hosts may explain the prevalence of *T. gondii* in the Arctic, including the Canadian Arctic, especially in non-felid carnivores. This hypothesis is supported by findings that all tested migratory birds and local carnivores in Svalbard were *T. gondii*-positive (31).

Canadian Arctic terrestrial animals

Regardless of the source of infection (environmental oocysts vs tissue cysts from infected prey), numerous mammals and birds in Canada's North have been reported to have tested positive for *T. gondii* (**Table 1**). Birds worldwide have been shown to be susceptible to *T. gondii* infection (31) and in Canada, migratory birds, such as geese, overwinter in areas where felids are common and where infectious *T. gondii* oocysts are likely to be found in high numbers in the environment (32–34). *Toxoplasma gondii* has been detected in the three tested geese species, with the highest prevalence reported in Ross's geese (34.5%) and the lowest in Canada geese (5.8%). Of the ptarmigan species tested, only one rock ptarmigan was found to be *T. gondii*-positive, possibly due to low exposure to oocysts in their arctic, subarctic and alpine tundra habitats.

Canadian Arctic rodents and lagomorphs showed no prevalence for *T. gondii*. Nearctic brown lemmings were negative, as were Arctic hares and snowshoe hares (Table 1). The only route of *T. gondii* transmission for non-migratory herbivores would be via ingestion of soil, plants or water contaminated with infectious oocysts. The absence of *T. gondii* prevalence in rodents and lagomorphs in the Canadian Arctic support the hypothesis that non-migratory Arctic herbivores have little to no exposure to infectious *T. gondii* oocysts (31).

The *T. gondii* exposure of ungulates varied between species. Caribou had a *T. gondii* prevalence of 11.3%, while the subspecies barren-ground caribou had a prevalence of 36.8%. It is unclear why barren-ground caribou were found to have such a high *T. gondii* prevalence. Muskox had a *T. gondii* prevalence of only 4.6% (Table 1).

Table 1: Birds and terrestrial mammals that have been tested for *Toxoplasma gondii* in the Canadian Arctic[a]

Common name (References)	Latin name	Number tested	Number positive	Percent positive
Birds				
Rock ptarmigan (35)	*Lagopus muta*	25	1	4.0%
Willow ptarmigan (35)	*Lagopus lagopus*	24	0	0.0%
Ross's goose (36,37)	*Chen rossii*	357	123	34.5%
Lesser snow goose (36,37)	*Chen caerulescens*	354	110	31.1%
Canada goose (35,38)	*Branta canadensis*	240	14	5.8%
Mammals				
Rodents				
Nearctic brown lemming (37)	*Lemmus trimucronatus*	84	0	0.0%
Lagomorphs				
Snowshoe hare (35)	*Lepus americanus*	8	0	0.0%
Arctic hare (35)	*Lepus arcticus*	2	0	0.0%
Ungulates				
Barren-ground caribou (39)	*Rangifer tarandus groenlandicus*	117	43	36.8%
Caribou (35)	*Rangifer tarandus*	97	11	11.3%
Muskox (35,40)	*Ovibus moschatus*	348	16	4.6%
Carnivores				
Arctic fox (41)	*Vulpes lagopus*	39	17	43.6%
Canada lynx (16,35)	*Lynx canadensis*	173	44	25.4%
Wolverine (42)	*Gulo gulo*	41	17	41.5%
Grey wolf (35)	*Canis lupus*	37	7	18.9%
Black bear (35,43)	*Ursus americanus*	43	16	37.2%

[a] including seasonally Arctic animals

The prevalence of *T. gondii* in carnivores was high in all species tested, as is to be expected even if the parasite's prevalence in their prey is relatively low. In Canada, *T. gondii* prevalence was found to be 43.6% in Arctic foxes, 25.4% in Canada lynxes, 41.5% in wolverines, 18.9% in grey wolves and 37.2% in black bears (Table 1).

Canadian Arctic marine mammals

Most pinnipeds in the Canadian Arctic were positive for *T. gondii*, including harbour seals (16.4%), ringed seals (10.7%), bearded seals (10.0%), hooded seals (1.7%) and walrus (14.7%) (**Table 2**).

Toxoplasma gondii was not detected in harp seals and more research may be required to determine if different feeding habits protect them from exposure to infected prey.

Table 2: Marine mammals that have been tested for *Toxoplasma gondii* in the Canadian Arctic[a,b]

Common name (References)	Latin name	Number tested	Number positive	Percent positive
Pinnipeds				
Harbour seal (26)	*Phoca vitulina*	311	51	16.4%
Ringed seal (26,35)	*Phoca hispida*	896	96	10.7%
Harp seal (35,44)	*Phoca groenlandica*	113	0	0.0%
Bearded seal (26)	*Erignathus barbatus*	20	2	10.0%
Hooded seal (44)	*Cystophora cristata*	60	1	1.7%
Walrus (35)	*Odobenus rosmarus*	34	5	14.7%
Bears				
Polar Bear (35,44–47)	*Ursus maritimus*	599	67	11.2%
Cetaceans				
Beluga (35,48)	*Delphinapterus leucas*	69	13	18.8%
Bowhead whale (35)	*Balaena mysticetus*	2	1	50.0%

[a] including seasonally Arctic animals
[b] including Amundsen Gulf, the Gulf of St. Lawrence, Hudson Bay, Labrador Sea and Beaufort Sea

Polar bears are the only ursines that are considered to be marine mammals because of their dependency on the ocean for food and habitat. *Toxoplasma gondii* has been detected in polar bears on the Canadian mainland and the Beaufort Sea, with an overall prevalence of 11.2%.

Two Arctic cetacean species have been tested for *T. gondii*: belugas and bowhead whales (Table 2). *Toxoplasma gondii* prevalence in belugas in the western Canadian Arctic was found to be 18.8% (Table 2). Of the two bowhead whales tested, one animal was *T. gondii*. gondii-positive (35).

T.gondii in Arctic waters

Toxoplasma gondii DNA has been detected in up to 77% of samples of treated and untreated surface water and well water worldwide (49,50). In some regions of Canada, increased rainfall has been associated with elevated numbers of *T. gondii* oocysts in surface waters (51). Most of Canada's rivers flow northward; 39% of Canada's freshwater drains into Hudson Bay and 36% drains into the Arctic Ocean (52). Oocysts that are washed into seawater are known to remain infective for up to two years and may be disseminated with the ocean currents (20,53–55).

It has been hypothesized that fish could be the missing link between oocysts that end up in the watersheds and infection in marine mammals (56). *Toxoplasma gondii* oocysts have been found in the alimentary tract of a wild fish (57) and it was shown that oocysts can remain infectious inside a fish's alimentary tract for several hours (58), thereby providing a possible source of infection for apex predators. To date, experimental infection of fish with *T. gondii* tissue cysts has only been reported in zebrafish and only under tightly controlled conditions (57). *Toxoplasma gondii* has also been reported in a variety of shellfish worldwide (59), and this may provide another source of infection in marine mammals and humans, although this has not yet been documented and confirmed in the Arctic.

To determine if Arctic fish are a potential source of *T. gondii*, we tested muscle tissues of 121 freshwater and euryhaline fish from Nunavik for the presence of *T. gondii* DNA. Fifteen fish (12.4%) tested positive for *T. gondii* using polymerase chain reaction for DNA amplification, followed by Sanger sequencing. Atlantic salmon and Arctic char had a *T. gondii* prevalence of 26.7% and 12.0%, respectively. Other fish species that tested positive for *T. gondii* DNA were lake trout (2.9%) and brook trout (16.7%). *Toxoplasma gondii* was detected in one sculpin (n=1) but it was not found in pike or lake whitefish, possibly due to low sample size (n=2 and 6, respectively) (*Reiling SJ, Boone R, Merks H, Dixon BR. Unpublished data, 2018*). While these are preliminary findings, more fish from the Canadian Arctic are currently being analyzed in our laboratory for the presence of *T. gondii*.

Discussion

There are a number of mechanisms by which *T. gondii* may have been introduced into the Canadian Arctic. *Toxoplasma gondii* may have been introduced via migratory birds and mammals that became infected by ingestion of oocysts (which may persist in soil and water in geographical regions where felids are present), or infected prey, in their southern habitats and carried the infection with them to the North. The parasite could then be transmitted from one intermediate host to another in the Arctic, even in the absence of definitive hosts. In addition, predators, such as Arctic foxes, wolverines and grey wolves, showed high *T. gondii* prevalence, suggesting that carnivory may also be an important route of transmission in the Arctic. Oocysts shed by felids in the south and transported northwards through waterways may be another source of infection in aquatic animals in the Arctic. Until recently, fish had not been known as a potential source for *T. gondii* infection. However, our preliminary findings suggest that *T. gondii* may be present in fish in the Canadian Arctic and could be another source of infection in humans and fish-eating mammals.

Environmental factors that increase *T. gondii* prevalence in animals that are hunted by Inuit for subsistence may pose a growing health threat to Inuit in the Arctic regions of Canada. More research is needed to determine how environmental and socioeconomic changes influence *T. gondii* prevalence in animals and humans in the Canadian Arctic.

Climate change and warmer temperatures may promote forest growth in regions that were previously too cold (60–62). The increasing forest cover could expand the habitat of wild felids, thereby augmenting the release of *T. gondii* oocysts into the environment (20). Higher numbers of oocysts combined with warming temperatures may increase the potential for infection of intermediate hosts, including birds and mammals not yet known to be hosts for *T. gondii* in the Canadian Arctic. This, in turn, may open up new transmission routes to humans who eat traditionally prepared country foods.

Conclusion

Toxoplasmosis has now spread throughout much of North and South America primarily through felids. Despite the absence of felids, *T. gondii* has now extended into Canada's Arctic, and has posed a health risk to Inuit, especially in pregnant women and those with weakened immune systems. The most likely source of *T. gondii* infection in Inuit is through infected intermediate hosts and the consumption of traditionally prepared country foods including meat and organs which may be consumed raw. Preventing infection by cooking or thoroughly freezing fish, meat, and organs and a better understanding of ongoing zoonotic transmission patterns will help to address this risk.

Authors' statement

SJR collected and analyzed the data. SJR and BRD wrote, proofread and approved the manuscript.

Conflict of interest

None.

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Epidemiology of *Clostridioides difficile* infection in Canada: A six-year review to support vaccine decision-making

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Abstract

Background: Two vaccines against *Clostridioides difficile* infections (CDI) are currently in phase III trials. To enable decision-making on their use in public health programs, national disease epidemiology is necessary.

Objectives: To determine the epidemiology of hospital-acquired CDI (HA-CDI) and community-associated CDI (CA-CDI) in Canada using provincial surveillance data and document discrepancies in CDI-related definitions among provincial surveillance programs.

Methods: Publicly-available CDI provincial surveillance data from 2011 to 2016 that distinguished between HA-CDI and CA-CDI were included and the most common surveillance definitions for each province were used. The HA-, CA-CDI incidence rates and CA-CDI proportions (%) were calculated for each province. Both HA- and CA-CDI incidence rates were examined for trends. Types of disparities were summarized and detailed discrepancies were documented.

Results: Canadian data were analyzed from nine provinces. The HA-CDI rates ranged from 2.1/10,000 to 6.5/10,000 inpatient-days, with a decreasing trend over time. Available data on CA-CDI showed that both rates and proportions have been increasing over time. Discrepancies among provincial surveillance definitions were documented in CDI case classifications, surveillance populations and rate calculations.

Conclusion: In Canada overall, the rate of HA-CDI has been decreasing and the rate of CA-CDI has been increasing, although this calculation was impeded by discrepancies in CDI-related definitions among provincial surveillance programs. Nationally-adopted common definitions for CDI would enable better comparisons of CDI rates between provinces and a calculation of the pan-Canadian burden of illness to support vaccine decision-making.

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Introduction

Clostridioides difficile is the most frequent cause of healthcare-associated infectious diarrhea in Canada and other industrialized countries (1). In the United States, it affects more than 300,000 hospitalized patients yearly (2). Symptoms of *C. difficile* infection (CDI) range from mild diarrhea to severe life-threatening inflammation of the colon (3). In Canada, many provinces

initiated CDI surveillance programs following a dramatic increase in incidence and severity in the early 2000s, and in response to CDI becoming a national notifiable disease in 2009 (4). In parallel, the Canadian Nosocomial Infections Surveillance Program (CNISP) network (2), a sentinel network of 67 primarily tertiary teaching hospitals in urban centers, has participated in hospital-acquired and community-associated CDI surveillance (5). Most provinces use hospital-acquired CDI as one of the indicators assessing health system performance and patient safety. The main objective of provincial surveillance programs is to determine the incidence of hospital-acquired CDI and to monitor trends and patterns in CDI over time, in order to prevent and control disease (6–14). However, in 2015, the Canadian Communicable Disease Steering Committee's Antimicrobial Resistance Surveillance Task Group identified several surveillance gaps in CDI surveillance activities, most notably gaps in data from community settings (4,15).

Two *C. difficile* vaccines are currently in phase III trials worldwide (16,17). To enable decision-making on the potential use of these vaccines in public health programs, considering the Erickson-DeWals-Farand analytical framework (18) and methods of the National Advisory Committee on Immunization (19) for immunization programs decisions in Canada, national disease epidemiology is a critical factor. Although the Public Health Agency of Canada provides annual national healthcare-associated CDI surveillance reports, the data are primarily derived from large, tertiary acute care hospitals and may not be representative of all hospital types and jurisdictions (5,20). There has never been a study conducted systematically on provincial CDI surveillance programs in Canada. Additionally, since healthcare—and thus hospital-acquired infection—is under provincial/territorial jurisdiction, discrepancies in definitions, surveillance methodologies, available laboratory diagnostics and variation in the validation of surveillance programs may exist, hence rendering inter-provincial/territorial comparison difficult.

The objectives of this study were to determine the epidemiology of hospital-acquired CDI (HA-CDI) and community-associated CDI (CA-CDI) as it pertains to Canada, using provincial surveillance data from 2011 to 2016 and to document discrepancies in CDI-related definitions among the provincial surveillance programs.

Methods

Study population

The study population included fiscal-year *C. difficile* infection surveillance in Canada from 2011 to 2016 at the provincial/territorial level. All of Canada's provinces and territories were potential participants in the study. To be included, the jurisdiction needed to have a surveillance system that distinguished between HA-CDI and CA-CDI.

Definitions

The definitions related to CDI have been well-described (6–14). For the purpose of this study, definitions for HA-CDI and CA-CDI used included the most common descriptions shared by the ten provinces (**Text box**). The HA-CDI and CA-CDI definitions, case classification, population surveilled, denominator definition and sources, and laboratory confirmation requirements were extracted separately from provincial protocols for comparison. Surveillance definitions varied from province to province and type of discrepancies were summarized.

Definitions

Hospital-acquired Clostridium difficile infection (HA-CDI)

HA-CDI was defined as:

- a primary CDI case in an inpatient, with symptom onset at least 72 hours, or more than three calendar days, after admission to the reporting facility

OR

- a primary CDI case, with symptom onset in the community or occurring less than 72 hours or less than or equal to three calendar days after admission to the reporting facility, who was discharged from the reporting facility in the four weeks prior to the current hospitalization (6–14)

Community-associated Clostridium difficile infection (CA-CDI)

CA-CDI was defined as:

- a CDI case with symptom onset in the community

OR

- occurring less than or equal to 72 hours or less than or equal to three calendar days after admission to a healthcare facility, provided that symptom onset was more than four weeks after the patient was discharged from any healthcare facility

Data collection

Data were extracted from provincial public reports retrieved from the Internet in July 2018. Data missing (i.e. number of HA-CDI cases and total inpatient days for Nova Scotia) were requested via email directly from the provinces (i.e. Nova Scotia's Freedom of Information and Protection of Privacy Act) in June/July 2018, with answers received in July 2018. For more specific data on the search strategy, please refer to **Appendix A**. All data were published or requested through legal access with the consent of the province.

Statistical analysis

When available, HA-CDI incidence rates per 10,000 inpatient-days, pooled HA-CDI incidence rates per 10,000 inpatient days, CA-CDI incidence rates per 100,000 population and CA-CDI proportions (%) were recorded. If no incidence rates existed in the provincial reports, the HA-CDI incidence rates and CA-CDI incidence rates were calculated from available data. Pooled HA-CDI incidence rates for the entire study period were calculated for each province. The CA-CDI proportions were generated for provinces with numbers of CA-CDI cases and total CDI cases available. Both HA-CDI incidence rates and CA-CDI incidence rates were examined for trends.

Pooled HA-CDI incidence rates and HA-CDI incidence rates were generated based on the following formula: (total number of HA-CDI cases/total inpatient days) x 10,000. Other than provinces with available total inpatient-days data used for calculating incidence rates, the denominator of that formula was back-calculated using the following formula: (number of HA-CDI cases/HA-CDI rate) x10,000. Similarly, CA-CDI incidence rates were computed using the following formula: (total number of CA-CDI cases/mid-year population) x 100,000 (mid-year data from July 1). The CA-CDI proportions were calculated using the following formula: total number of CA-CDI/total number of CDI cases reported in the province x 100%.

Results

Based on the inclusion criteria, the study included nine of the 10 provinces and no territories. One province was excluded because its surveillance system did not distinguish between HA-CDI and CA-CDI. The territories were excluded as they did not have existing CDI surveillance programs.

Hospital-acquired incidence rates

The HA-CDI incidence rates by year and province and pooled HA-CDI incidence rates are presented in **Table 1** with additional detail in **Appendix B**. The HA-CDI incidence rates by year indicated that, for almost all provinces, trendlines had been decreasing. In contrast, rates in Newfoundland and Labrador had been increasing, rates in Prince Edward Island had been rising slightly and no obvious trends were seen for New Brunswick and Nova Scotia. Pooled HA-CDI incidence rates showed that Quebec and British Columbia had relatively higher rates, at 6.5/10,000 and 5.3/10,000 inpatient-days, respectively, followed by Alberta (3.8/10,000 inpatient-days) and Prince Edward Island (3.0/10,000 inpatient-days) (**Appendix C: Figure C-1**). The other provinces (Ontario, Nova Scotia, Saskatchewan, New Brunswick and Newfoundland and Labrador) each had rates of less than 3/10,000 inpatient-days.

Table 1: Hospital-acquired *C. difficile* incidence rates (cases/10,000 inpatient days) by year and pooled incidence rates (cases/10,000 inpatient days)

Prov.	Fiscal year[a]						Pooled rate[b]
	2011–2012	2012–2013	2013–2014	2014–2015	2015–2016	2016–2017	
AB[c]	4.2	4.1	4.3	3.5	3.6	3.4	3.8
BC[c]	8.1	6.5	4.5	4.2	4.8	4.1	5.3
NB[c]	-	-	2.7	2.4	2.8	-	2.6
NL[c]	1.6	2.0	2.0	2.1	2.6	-	2.1
NS[d]	-	3.2[c]	2.8	2.3	2.7	3.3	2.8
ON[b]	3.5	3.3	3.0	2.6	2.6	2.3	2.9
PE[b]	1.8	3.8	3.7	3.4	2.3	2.9	3.0
QC[b]	7.3	7.2	7.2	6.8	5.9	4.6	6.5
SK[c]	-	3.0	2.5	3.2	2.3	2.8	2.7

Abbreviations: AB, Alberta; BC, British Columbia; *C. difficile*, *Clostridioides difficile*; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; Prov., Province; QC, Quebec; SK, Saskatchewan; -, empty cells indicate data were unavailable or calculations could not be performed

[a] The fiscal year started April 1 of that year and ended March 31 of the year after, with the exception of Quebec 2011, when the year started August 14, 2011 and ended August 25, 2012

[b] Rates were calculated

[c] Rates were gathered directly from the reports

[d] For Nova Scotia 2012–2013 fiscal year, only data for the fourth quarter were available

Community-associated incidence rates

Only Alberta, British Columbia, Newfoundland and Labrador, Prince Edward Island, Quebec and Saskatchewan had publicly-accessible CA-CDI data. Alberta was excluded from this part of the study, since it posted only rates and utilized a unit that was different from the one used in this study (per 100,000 population versus per 1,000 admissions).

The CA-CDI incidence rates and CA-CDI proportions for provinces are presented in **Table 2** with additional detail in Appendix B. In contrast to the HA-CDI incidence rates trends, the CA-CDI incidence rates of all five provinces examined (with the exception of Prince Edward Island) increased (**Appendix C: Figure C-2**). For Newfoundland and Labrador and Prince Edward Island, there were marked increases in CA-CDI incidence rates from 2012–2013 to 2014–2015. The same trend was also seen for CA-CDI proportions in British Columbia and Quebec. Even though the CA-CDI proportions in Newfoundland and Labrador were declining over the time period of the study, and the proportion seemed to be increasing in Prince Edward Island, the overall CA-CDI case counts in both provinces still represented a large portion of the total CDI cases reported.

Discrepancies

In the process of data collation and analysis, discrepancies among provincial surveillance definitions of CDI case classification, surveillance populations and rate calculation were detected, which impeded comparison of CDI rates between provinces. The fundamental issue was that each province defined and complied with its own protocol, leading to highly varied numerators (number of CDI cases) and denominators (total inpatient-days). A summary of discrepancies with examples are shown in **Table 3**. For a more detailed description of the different definitions by provincial surveillance programs, refer to **Appendix D**. We were unable to use the Canadian Institute for Health Infomation (CIHI) Management Information System (MIS) database to estimate the denominators due to the differences in total inpatient days between CIHI and provincial surveillance programs. The differences between the data in the CIHI MIS database and denominators adopted by provinces varied plus or minus 5% to 10%. We were unable to match denominators that fit the definitions of provinces from the CIHI database. For detailed differences between denominators estimated from the CIHI MIS database and those used by provinces, and the calculations used to extract the denominators, please refer to Appendix B.

Table 2: Community-associated *C. difficile* incidence rates (cases/100,000 population) and proportions (%) by year

Province	Fiscal year[a,b]											
	2011–2012		2012–2013		2013–2014		2014–2015		2015–2016		2016–2017	
	Rate	%	Rate	%	Rate	%	Rate	%	Rate	%	Rate	%
BC	16.74	20.84	17.46	24.46	13.86	26.77	14.51	29.82	18.45	29.93	17.78	34.92
NL[c]	17.50	44.39	31.60	51.72	37.90	56.06	33.00	47.41	21.90	32.95	-	-
PE	38.88	61.54	40.67	46.46	51.65	52.45	43.86	52.89	38.83	60.64	40.81	55.96
QC	8.00	11.80	8.63	12.81	9.21	14.30	8.98	14.73	11.01	20.07	10.57	22.82
SK	-	-	5.88	20.98	9.03	27.47	8.46	21.59	7.41	22.58	-	-

Abbreviations: BC, British Columbia; *C. difficile*, *Clostridioides difficile*; NL, Newfoundland and Labrador; PE, Prince Edward Island; QC, Quebec; SK, Saskatchewan; -, data unavailable
[a] Refer to Appendix D for details on rates calculation
[b] Fiscal years started April 1 of that year and ended March 31 of the year after, with the exception of Quebec 2011, when the year started August 14, 2011 and ended August 25, 2012
[c] Rates were collected directly from the NL provincial reports

Table 3: Surveillance discrepancies and examples

Discrepancy	Examples (6–14)
Population under surveillance	The population under surveillance in British Columbia is defined as "inpatients aged one year or older and admitted to acute care facilities", while some provinces monitor "any patient with a laboratory-confirmed CDI in the province". Quebec excludes from surveillance patients in long-term care facilities. Only cases admitted to acute care hospital, from long-term care would be included; it is not clear if the same is done everywhere.
Classification of cases	While some of the provinces only report hospital-acquired CDI or only monitor new cases, some classify CDI cases into more refined categories: the category of "related to reporting facility" is further stratified into "related to current/previous hospitalization"; "another facility" is stratified into "long-term/ambulatory care and non-reporting"; and also, "new" and "recurrent" cases are documented separately. All HA-CDI cases might be classified into a single category or could be separated in two: acute care facility-acquired or long-term care facility-acquired. CA-CDI surveillance: Quebec only reports hospitalized cases; it is unclear what is done elsewhere.
Definition for the cases classifications	Even though the same categories of CDI cases were monitored, they might have different denominators and case definitions. For example, most provinces define HA-CDI as symptoms occurring more than 72 hours after admission, while Manitoba defines HA-CDI as 48 hours after admission.
Denominators used for calculating the rates	In some jurisdictions, patients less than one year of age (or a proxy of that) and/or psychiatric patients were excluded. Meanwhile, some provinces use the total number of inpatient-days regardless of age or area of care. In some instances, the denominator was estimated from other provincial data sources and might be adjusted to fit CDI rate reporting.
Denominators used by the provinces and CIHI MIS database	Unable to generate the denominators used by the provinces using the data available in CIHI MIS database. Some provinces used denominators that were higher than the total inpatient-days showed in CIHI MIS database.

Abbreviations: *C. difficile*, *Clostridioides difficile*; CA-CDI, community-associated *C. difficile* infection; CDI, *C. difficile infection*; CIHI MIS, Canadian Institute for Health Information management information system; HA-CDI, hospital-acquired *C. difficile* infection

Discussion

From 2011 to 2016, the HA-CDI incidence rates in most provinces decreased, which is consistent with the trend reported by the Canadian Antimicrobial Resistance Surveillance System and a study based on the CNISP network (21,22). This reduction in rates might be attributed to infection prevention and control interventions (e.g. hand hygiene, environmental cleaning, patient-dedicated toilets and single-patient rooms), antibiotic stewardship and increased CDI awareness. The reduction in the proportion of NAP1 isolates (22), which has been the predominant strain in Canada associated with increasing rate of severe HA-CDI, may also have played an important role.

On the other hand, despite the possibility of an actual increase in CDI cases, the increased incidence rates could be partly explained by the evolution of circulating strains, which might lead to increased toxigenic potential and survival of the bacteria, or to improvements in surveillance and reporting in the province. Notwithstanding the slightly increasing trend in New Brunswick and Nova Scotia, there were only three years of data available for New Brunswick and only the fourth quarter of 2011–2012 fiscal year data available for Nova Scotia, decreasing our power to conclude on trends of HA-CDI incidence rate in these two provinces.

Even though most CA-CDI cases were reported in admitted patients, trends, not absolute rates, were studied in this article. Therefore, choosing the provincial population or admissions as the denominator had only a minor impact on the results. The five provinces included in the analysis of CA-CDI incidence rates showed a slight, increasing trend. Of the nine provinces, almost all focused only on HA-CDI. However, the observation of these trends in HA-CDI indicated the importance of also monitoring and analyzing CA-CDI in future surveillance activities. Improved surveillance and reporting from the community may explain these trends. Moreover, the mutual effect of decreasing numbers of HA-CDI cases, growing numbers of CA-CDI cases, and increased use of nucleic acid amplification testing may also explain the observed trends. The decrease in HA-CDI cases may results in

an increase in the proportion of CA-CDI cases, even though the overall numbers (HA-CDI plus CA-CDI cases) remain stable, while the increased testing could contribute to the detection of more CA-CDI cases, which were not tested for in the past. In Newfoundland and Labrador and Prince Edward Island, CA-CDI cases still accounted for a relatively high percentage of all CDI cases reported.

The introduction of more sensitive laboratory testing methods, such as polymerase chain reaction, which detects the toxigenic potential but not the actual toxin production, has been associated with increasing numbers of positive tests and earlier detection compared with enzyme-linked immunosorbent assay (23,24). Currently, although all the provinces required clinical validation for the identification of CDI cases, the test methods used for this validation varied. Moreover, laboratory tests and protocols have changed over the years, and the impact of these changes on the accuracy of CDI rates is difficult to assess.

Limitations

There are a number of limitations to consider. Given the shortage of data, we were limited in the analyses that could be performed. Optimally, comparisons between the provinces and stratified analyses, such as incidence rates by age strata, underlying medical conditions and sex, are performed to determine high-risk populations and to provide useful information for cost-effective analyses that could support future CDI vaccine decision-making processes. Unfortunately, these comparisons and analyses could not be performed fully due to the tremendous disparities among the current provincial surveillance systems (Appendix D).

Another limitation was the discrepancy in the denominators (total inpatient-days) used to calculate HA-CDI rates; discrepancies among the provinces and also between the provinces and the CIHI MIS database. The CIHI database was initially considered for providing a relatively accurate estimation of total inpatient-days. This was because these data were reported on the basis of the fiscal year and are representative of the inpatient population during that year. However, it was found that denominators used by the provinces to calculate their provincial CDI rates were different from the denominators in the CIHI MI database. Furthermore, later comparisons showed a divergence between CIHI data and CNISP denominators. One of the reasons for this difference is that the definitions for denominators derived from the CIHI database did not match those used by either the provinces or CNISP. This suggested that total inpatient-days reported to CIHI and those used for provincial CDI rate calculations were derived from different reporting systems. The target population contributing to the total inpatient-days might vary as well. Because it was not clear how the provinces generated the total inpatient-days, these discrepancies cannot be fully explained. Further research and collaboration is needed to identify the cause of and to solve this discrepancy.

It should also be noted that the data retrieved from provinces through this analysis did not include laboratory-linked strain data for CDI cases. This is a major limitation and prevents the monitoring of ecological trends over time with varied CDI strain types.

Although two potential vaccines are currently undergoing clinical trials, it is not yet known how broadly protective these candidate vaccines will be against the various *C. difficile* strains or the potential mutants escaped from being detected by traditional strategy. The CNISP has already revealed important trends in virulent strains and antimicrobial resistance (5,22). However, as previously discussed, CNISP is limited to data primarily from a small sample of large, tertiary acute care hospitals across Canada and thus does not provide a complete picture.

Missing data were an important limitation in our study. Only Quebec provided data of total inpatient-days that met the definition of their CDI surveillance protocol. For the other provinces, although some total inpatient-days data might have appeared in the provincial reports, none matched those used to calculate HA-CDI rates. Although, as demonstrated in this paper, denominators can be estimated by back-calculation, this erodes the reliability and accuracy of data presented.

Next steps

There is a fundamental need for a nationally-adopted CDI surveillance protocol. This type of surveillance would be the single most important way to address the many discrepancies between provinces, arising from highly varied data—numerators (number of CDI cases), denominators (total inpatient-days) and different definitions for populations under surveillance—that make incidence rates difficult to compare and interpret.

To provide national-level epidemiological data to support decision-makers in their recommendations for the implementation of a potential CDI vaccine program, several key elements are needed. First, demographically-stratified incidence rates, including delineation by age and sex, would be useful to determine whether certain at-risk groups would benefit more from the vaccine. A study conducted in Spain (22,25) showed that CDI evolves differently by sex and age group. Second, as mentioned in the CNISP Summary Report (2) and as shown in our study, recurrent and CA-CDI should be monitored to increase the understanding of the burden, risk factors and outcomes of such infections in Canada. Third, the use of a common, nationally-adopted definition for CDI, CDI categories and total inpatient-days is critical; the CNISP CDI case definition (26) could be adopted for this purpose, with standardized data collected and reported. Fourth, a quality assessment system is needed to ensure quality of reported data. Fifth, CIHI could be an ideal partner to provide data for total inpatient-days, given its already well-established data gathering system from provinces. The CIHI is able to provide the general total inpatient-days that fit the

selected definition, allowing for validation of provincial data, and could be an excellent source for stratified inpatient-days. Finally, the ideal solution would be a national online reporting system that includes universal case definitions, and all hospitals across Canada could provide standardized and comparable data that would be accessed and reported via an online platform, allowing for local, regional, provincial and national comparisons. This would not only simplify the study of the epidemiology of different diseases at different levels and make it more feasible to gather case characteristics to gain a complete view of the disease, but it would provide better control of the overall quality of the information as well. In our interconnected open-data era, this would meet the heightened expectation of timely and publicly-accessible surveillance data. One way to do this would be by expanding CNISP, the Public Health Agency of Canada's sentinel surveillance program that uses a data entry platform on the Canadian Network for Public Health Intelligence (CNPHI), but there may be other equally valid means of collecting CDI surveillance data.

Conclusion

In Canada, the rate of HA-CDI has generally been decreasing but the rate of CA-CDI is increasing. There are important discrepancies in CDI-related definitions among provincial surveillance programs that impede comparisons of CDI rates between provinces, and calculating a pan-Canadian burden of illness to support vaccine program decision-making.

Authors' statement

YX — Conceptualization, methodology, formal analysis, investigation, writing—original draft, review and editing
MCT, CF, KK, KA, SRR, AH — Writing—reviewing and editing
CQ — Conceptualization, writing—reviewing and editing, supervision

Conflict of interest

Y Xia has no conflict of interest
MC Tunis, K Amaratunga and A House are employees of the Public Health Agency of Canada
C Frenette and K Katz are co-Chairs of CNISP
SR Rose is a Past-President of Institute of Public Administration of Canada
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Appendices

Appendix A: Data searching strategy

Appendix B: Hospital acquired- and community associated-*Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, and denominator definition and sources

Appendix C: Supplementary data

Appendix D: Data used for calculation of Appendix B

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Appendix A: Data searching strategy

This document summarizes the sources of data used in the study and additional sources of provincial *Clostridioides difficile* infections (CDI) surveillance information for further study. For those not separately indicating the origin of the data used in the study, the data are all derived from the reports mentioned below.

Alberta

- Number of hospital-acquired CDI (HA-CDI) cases, incidence rate of HA-CDI and total inpatient days: Requested via Alberta Research Facilitation (email: Research.Facilitation@ahs.ca)
- IPC Annual Report to Alberta Health (2016): www.albertahealthservices.ca/assets/healthinfo/ipc/hi-ipc-provincial-surveillance.pdf
- CDI Surveillance Protocol: www.albertahealthservices.ca/assets/healthinfo/ipc/hi-ipc-sr-cdi-protocol.pdf
- Quarterly Performance Report: www.albertahealthservices.ca/about/Page833.aspx

British Columbia

- CDI Surveillance Protocol, Quarterly Report and Annual Report: www.picnet.ca/surveillance/cdi/
- Only the most recent reports were listed on the website: to access the archived reports, change the date in the URL of the latest report
- Population Statistics: www2.gov.bc.ca/gov/content/data/statistics/people-population-community/population/population-estimates

Manitoba

- Manitoba Monthly Surveillance Reports: www.gov.mb.ca/health/publichealth/surveillance/episummary/index.html
- Manitoba Annual Summary of Communicable Diseases: www.gov.mb.ca/health/publichealth/surveillance/cds/index.html
- CDI Surveillance Protocol

New Brunswick

- Quarterly Healthcare Associated Infections Surveillance Report: www2.gnb.ca/content/gnb/en/departments/ocmoh/cdc/content/HAI.html
- No CDI Surveillance Protocol was available. Only the most recent report was listed on the website: to access the archived reports, change the date in the URL of the latest report
- New Brunswick Communicable Disease Annual Report: www2.gnb.ca/content/gnb/en/departments/ocmoh/for_healthprofessionals/cdc.html

Newfoundland and Labrador

- Healthcare-associated Infections Annual report: www.health.gov.nl.ca/health/publichealth/cdc/informationandsurveillance.html#currentyear
- CDI Surveillance Protocol: www.health.gov.nl.ca/health/publichealth/cdc/CDI_surveillance_protocol_final.pdf

Appendix A: Data searching strategy (*continued*)

Nova Scotia

- Number of cases of HA-CDI and total inpatient days:
  requested via Freedom of Information and Protection of Privacy Act
  (email: FOIPOP@nshealth.ca)
- CDI (New cases of healthcare-associated *C. difficile* infection that occur in the hospital)
  Quarterly Performance and CDI Surveillance Protocol:
  https://novascotia.ca/dhw/hsq/public-reporting/c-difficile-data-trending.asp
- Annual Notifiable Disease Surveillance Report (overall CDI cases and incidence):
  https://novascotia.ca/dhw/populationhealth/

Ontario

- Number of HA-CDI cases: "clostridium-difficile-infection.xls" document obtained from www.hqontario.ca/portals/0/documents/system-performance/clostridium-difficile-infection.xls by searching "Clostridium difficile" in Public Health Ontario official website www.publichealthontario.ca/en/Pages/default.aspx

Total inpatient days: Requested via @MOH-G-Patient Safety (email: PatientSafety@ontario.ca)

- *C. Difficile* Infections in Hospital Patients Performance Quarterly Report:
  www.hqontario.ca/System-Performance/Hospital-Patient-Safety/C-Difficile-Infections-in-Hospital-Patients
- CDI Surveillance Guideline:
  www.publichealthontario.ca/en/eRepository/PIDAC-IPC_Annex_C_Testing_SurveillanceManage_C_difficile_2013.pdf

Prince Edward Island

- Prince Edward Island (PE) Infection Prevention and Control Program Surveillance Data Summary (only reports for 2015 and 2016 were available):
  www.princeedwardisland.ca/en/topic/reports-and-trends
- PE Infection Prevention and Control Program Surveillance Data Summary (2014):
  www.gov.pe.ca/photos/original/cpho_ipc_ar2014.pdf
- PE Infection Prevention and Control Program Report (2011):
  www.gov.pe.ca/photos/original/DHW_IPC2011.pdf
- CDI Surveillance Guideline:
  www.princeedwardisland.ca/sites/default/files/publications/c_diff_infection_guideline.pdf
- Population Statistics:
  www.princeedwardisland.ca/sites/default/files/publications/pt_pop_rep_1.pdf

Quebec

- Diarrhées à Clostridium difficile (DACD) Annual Surveillance Report and Protocol:
  www.inspq.qc.ca/infections-nosocomiales/spin/dacd
- Population Statistics:
  www.stat.gouv.qc.ca/statistiques/population-demographie/structure/qc_1971-20xx.htm

Saskatchewan

- CDI Surveillance Annual Report and Protocol:
  www.ehealthsask.ca/services/resources/Pages/Communicable-Disease.aspx
- Population Statistics:
  www.saskatchewan.ca/government/government-data/bureau-of-statistics/population-and-census

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements

Table B-1: Definitions of hospital-acquired *Clostridioides difficile* infections

Province	Definition
Alberta (1)	For a primary, **symptomatic case**, the patient's symptom meeting CDI case definition occur in a hospital more than or equal to 72 hours after admission OR For a primary, **insufficient info case**, the positive *C. difficile* test date more than or equal to 72 hours after admission OR A patient is readmitted to an Alberta Health Services/Covenant Health facility under surveillance within four weeks of discharge from a facility where the admission was more than or equal to 72 hours AND The patient's symptoms meeting CDI case definition occur in a hospital within 72 hours of readmission
British Columbia (2)	A CDI case occurring more than 72 hours or more than three calendar days (the day of admission counted as the first calendar day, the same hereinafter) after admission to an acute care facility cases identified on or after the fourth calendar day of hospitalization will be classified as HCA) OR A CDI case with symptom onset in the community or occurring fewer than or equal to 72 hours or fewer than or equal to three calendar days after admission to an acute care facility, provided that the patient was admitted to a healthcare facility (including acute care and long-term care) **for a period of more than or equal to 24 hours or at least overnight** stay in the past four weeks before onset of CDI symptoms
Manitoba (3)	Patient's initial symptoms occur more than **48 hours** post-admission to a healthcare facility OR A patient, who has been discharged from the current healthcare facility within the preceding four weeks, who **develops an onset of *C. difficile*-acquired disease that requires readmission to the same healthcare facility**
New Brunswick (4)	Same as Canadian Nosocomial Infections Surveillance Program 2014 definition. Cannot be found online
Newfoundland and Labrador (5)	A case in which symptoms occur at least 72 hours or more after the current admission OR Symptoms occur in a patient who has been hospitalized at a hospital and discharged within the previous four weeks
Nova Scotia (6)	The patient's CDI symptoms occur in your healthcare facility three or more days after admission, with day of admission being day one OR The patient's CDI symptoms occur less than three days after admission and are seen in a patient who had been hospitalized at a healthcare facility and discharged within the previous four weeks
Ontario (7)	Onset of symptoms more than 72 hours after admission OR The infection was present at the time of admission but was related to a previous admission to the same facility within the last four weeks and the case has not had *Clostridium difficile*-associated disease in the past eight weeks
Prince Edward Island (8)	Symptoms were not present on admission (onset of symptoms more than 72 hours after admission) and there was no admission to an acute care or long term care facility in the last four weeks (if the patient/resident was in another facility in the past four weeks, the case may be attributed to that facility) Not mentioned in the guideline or other reports
Quebec (9)	Patients hospitalized on a short-term care unit of the reporting facility AND diagnosed with CDAD three days and more (so starting on D4) after admission (admission=D1) OR Long-term or psychiatric patients hospitalized in short-term units three days or more after admission (D4) • Excluded: patients hospitalized on registered psychiatric, neonatal and children's complete long-term care units

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements (*continued*)

Table B-1: Definitions of hospital-acquired *Clostridioides difficile* infections

Province	Definition
Quebec (9) (*continued*)	OR Patients hospitalized or not in the reporting facility and diagnosed with CDAD up to four weeks after their release from a short-term care unit of the reporting facility whatever the length of hospitalization OR Patients transferred to a residential and long-term care centre or private residence providing care and diagnosed with CDAD up to four weeks after their release from a short-term care unit of the reporting facility whatever the length of hospitalization whether they are re-admitted to the reporting facility or not OR Patients transferred to a general hospital specialty clinic (other participating short-term care centre) or rehabilitation centre, participating in monitoring or not, and diagnosed with CDAD less than three days (so D1, D2 or D3) after their admission/registration in emergency (D1) • Excluded: patients transferred to a short-term care centre or rehabilitation centre, participating in monitoring or not, and diagnosed with CDAD three days and more after admission (so starting on D4) after their transfers (these cases will then be attributed to the centre to which each patient was transferred)
Saskatchewan (10)	The patient's CDI symptoms began more than or equal to three days after admission to the reporting healthcare facility OR The patient's symptoms began in the community or fewer than three days after admission to the reporting facility AND The patient was admitted to the reporting facility for a period of more than or equal to three days in the past four weeks

Abbreviations: *C. difficile*, *Clostridioides difficile*; CA-CDI, community-associated CDI; CDAD, *Clostridium difficile* associated diarrhea; CDI, *Clostridioides difficile* infections; n/a, data not available
Note: Bolded text reflect subtle differences between provinces

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements (*continued*)

Table B-2: Provincial definitions of community-associated *Clostridioides difficile* infection

Province	Definition
Alberta (1)	**Any primary CDI case not meeting the criteria for the hospital-acquired or healthcare-associated** will be considered community acquired
British Columbia(2)	A CDI case with symptom onset in the community or occurring within fewer than or equal to 72 hours or fewer than or equal to three calendar days after admission to an acute care facility, provided that the patient was not admitted to any healthcare facility (including acute care and long-term care) for **a period of more than or equal to 24 hours or at least overnight stay** in the past four weeks before onset of CDI symptoms
Manitoba (3)	Patient does not meet either nosocomial case definition
New Brunswick	n/a
Newfoundland and Labrador (5)	A case with symptom onset in the community or three calendar days or less after admission to a healthcare facility, provided that symptoms onset was more than four weeks after the last discharge from a healthcare facility
Nova Scotia	n/a
Ontario	n/a
Prince Edward Island (8)	Symptom onset in the community or fewer than 72 hours after being admitted to an acute care or long term care facility, and symptom onset was more than four weeks post-discharge from an acute care/long term care facility Not mentioned in the guideline or other reports
Quebec (9)	Patients hospitalized on a short-term care unit of the reporting facility and diagnosed with CDAD less than three days (so D1, D2 or D3) after admission/registration in emergency and having no connection with the care environment (hospital, residential centre or ambulatory services included in categories 1b, 1c, 1d and 2) within the preceding four weeks (28 days)
Saskatchewan (10)	CDI symptoms began in the community or fewer than three days after admission to a healthcare facility, provided that symptom onset was more than four weeks after the patient was discharged from any healthcare facility CA-CDI cases do NOT need to be entered into the CDI Electronic Report Form—might underestimate the number of CA-CDI cases

Abbreviations: *C. difficile*, *Clostridioides difficile*; CA-CDI, community-associated CDI; CDAD, *Clostridium difficile* associated diarrhea; CDI, *Clostridioides difficile* infections; n/a, data not available
Note: Bolded text reflect subtle differences between provinces

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements (*continued*)

Table B-3: Case Classification in the regular reports

Province	Case classification
Alberta (11)	Hospital-acquired infections
British Columbia (12)	HA-CDI • HCA with reporting facility, new cases • HCA with another facility, new cases • HCA with reporting facility, relapse • HCA with another facility, relapse Community-associated CDI Unknown
Manitoba (13)	Total CDI cases
New Brunswick (4)	CDI attributed to reporting hospital (definition see HA-CDI) CDI attributed to reporting hospital but does not meet the criteria of the first classification CDI attributed to another acute care facility CDI attributed to long term care or non-acute care facility Unknown
Newfoundland and Labrador (14)	CDI in acute care facilities CDI in long term care facilities Healthcare-associated (not hospitalized cases) CDI Community-associated CDI
Nova Scotia (15)	Healthcare-associated CDI in the reporting facility * Not mentioned new/recurrent case
Ontario (16)	New hospital acquired CDI in the reporting facility
Prince Edward Island (17)	New cases of healthcare-associated CDI in long term care, acute care and other, respectively New cases of community-associated CDI Other
Quebec (18)	Case associated with current hospitalization in the reporting facility Case associated with previous hospitalization in the reporting facility Case associated with ambulatory care of the reporting facility Case associated with long-term care unit of the reporting facility Case associated with a stay in a non-reporting facility Case of community origin, not associated with care environment
Saskatchewan (19)	CA-CDI (2012–2015) HA-CDI • Community-onset HA-CDI and Healthcare-onset HA-CDI • Recurrent HA-CDI and Primary HA-CDI (primary acute HA-CDI and primary long term care HA-CDI)

Abbreviations: *C. difficile*, *Clostridioides difficile*; CA-CDI, community-associated CDI; CDI, *Clostridioides difficile* infection; HA-CDI, hospital-acquired CDI; HCA, healthcare-associated

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements (*continued*)

Table B-4: Provincial Surveillance—Population Surveilled

Province	Population
Alberta (1)	All individuals admitted to Alberta Health Services and Covenant Health acute and acute tertiary rehabilitation care facilities, where inpatient care is provided 24 hours/day, seven days a week, who are more than or equal to one year of age
British Columbia (2)	Inpatient one year or older admitted to acute care facilities Inclusion criteria: • Patients admitted to the Emergency Department awaiting placement • Patients in alternative level of care bed • Patients in labour and delivery beds Exclusion criteria: • Outpatient visits to clinics in the acute care facility • Emergency room patients not admitted to an acute care inpatient ward • Patients in extended care beds or in mental health beds housed in the acute care facilities • Inpatient younger than one year of age In the case that *mental health inpatients are NOT excluded* from the population under surveillance for CDI in your health authority, the cases of CDI identified among mental health inpatients should be collected and included in your CDI data submission
Manitoba (3)	Patients, residents and clients
New Brunswick (4)	Patients who have been hospitalized (no protocol)
Newfoundland and Labrador (5)	Any patient with laboratory-confirmed CDIs in the province Not specified in the protocol
Nova Scotia (6)	To be included in the surveillance, a patient with healthcare-associated CDI must be: • One year of age or older • Admitted to the acute care hospital Long-term care and awaiting-placement patient on acute-care wards are to be included. Patients admitted to hospital, but who remain in the Emergency Department once admitted, are included. Patients who are discharged after the date of the positive culture but before the results are available are included Exclusion criteria: • Emergency, mental health units, psychiatric or withdrawal management units and ambulatory clinic or other outpatient cases. Patients who were discharged in the previous four weeks and return to the emergency department or outpatient clinic with a new onset of CDI, but are not readmitted, are NOT included
Ontario (7)	Total number of new nosocomial (i.e. hospital acquired) CDI cases Inclusions: • All publicly-funded hospitals • Inpatient beds • Laboratory-confirmed CDI cases Exclusion criteria: • Patients younger than one year of age
Prince Edward Island (17)	All cases of CDI in Health Prince Edward Island facilities Not specified in the guideline

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements (*continued*)

Table B-4: Provincial Surveillance—Population Surveilled (*continued*)

Province	Population
Quebec (9)	For each administrative period for each facility must be included in monitoring for all categories of CDAD cases meeting the definition: • all hospitalized patients with a CDAD diagnosis (see exclusions) • all hospitalized patients with a CDAD diagnosis more than eight weeks after the end of treatment of a previous CDAD episode • all patients not hospitalized at the time of CDAD diagnosis but who were hospitalized in the reporting facility during the four weeks preceding the diagnosis Excluded from monitoring: • all non-hospitalized patients with a CDAD diagnosis **AND** who have not been hospitalized in the reporting facility during the four weeks before the diagnosis; a CDAD recurrence is defined as the reappearance of symptoms less than eight weeks after the end of treatment for the last episode diagnosed (with positive lab test or by physician); a repeat diagnosis does not necessarily require a new positive lab test; a case recurring more than eight weeks after the end of treatment for the last episode is considered a new case, and that case should be included in monitoring Note: the system automatically excludes patients in [hotel] ([measure] 37), neonatal and children's care (measure 38) and psychiatric beds (measure 53); patients in residential and long-term care centre beds (mission/class 400) are also excluded
Saskatchewan (10)	Only patients or residents admitted into a hospital or long-term care facility at the time the CDI diagnosis is made, OR who had been acute care inpatients/long-term care residents in the four weeks prior to diagnosis are included for surveillance Inclusion criteria • One year of age and older • Admitted to an acute care unit (this includes patients awaiting placement on acute care units, patients admitted to your facility but who remain in the emergency room once admitted, 'outpatients' in ER who have been there for more than three days, and patients who are discharged after the date of diagnosis, but before the laboratory results are received) • In a mental health inpatient ward/unit • Residents in long-term care facilities • Patients who were discharged from a healthcare facility in the previous four weeks and return to an outpatient unit/facility with a new onset of CDI Outpatient units may include, but are not limited to, the following: • Cancer centre • Dialysis unit • Emergency room (not admitted) • Physician clinic or office

Abbreviations: *C. difficile*, *Clostridioides difficile*; CDAD, *Clostridium difficile* associated diarrhea; CDI, *Clostridioides difficile* infection

Appendix B: Hospital-acquired and community-associated *Clostridioides difficile* infections: definitions, case classification in provincial reports, population surveilled, denominator definition and sources and laboratory confirmation requirements (*continued*)

Table B-5: Definition and source of denominators used to calculate rates

Province	Denominator
Alberta (1)	The data are abstracted from Admission, Discharge and Transfer Data using a standard methodology and is provided to Infection Prevention and Control. Inpatient admissions and inpatient days cannot be excluded for inpatients younger than one year of age; therefore, **as a proxy, the Neonatal Intensive Care Unit denominators and newborn denominators in maternal or labour and delivery units are excluded**
British Columbia (2)	Total number of inpatient days collected from the patient information systems by the respective health authority
Manitoba (13)	Denominator used is total population, not total inpatient days
New Brunswick (4)	Days spent in a hospital for all patients, regardless of medical condition Derived from the report, no protocol available
Newfoundland and Labrador	Not mentioned in the guideline or reports
Nova Scotia (6)	The total number of days that patients are in hospital ("patient days") on the units on which surveillance for CDI is conducted. This is collected on a quarterly basis. Excluded from "patient days" are dedicated long-term care, mental health/psychiatric or withdrawal management units, and patients younger than one year of age. Denominator data should be collected using the health information systems of the respective authority
Ontario (7)	Total number of inpatient days Inclusions: • **All publicly funded hospitals** • Inpatient beds Exclusions: • Patients younger than one year of age
Prince Edward Island	Not mentioned in the guideline or reports
Quebec (9)	Based on the number of patients and their length of stay in the facility or care unit
Saskatchewan (10)	The appropriate denominator used to determine CDI rates is 'patient/resident days'. Denominator data **(estimated from other provincial data sources)** is provided to regional Infection Control Professionals (ICPs). The ICPs **may change** these numbers if they are not reflective of the current situation (e.g. due to bed closures), or if the ICPs are able to **refine** the estimate provided. Some ICPs have submitted exact denominator data for their region and others have allowed the **estimated provincial data** to be used. However, given that the denominator is based on 10,000 patient days, the discrepancy between the actual denominator and the estimate would have to be fairly large to make a significant difference in the rate

Abbreviations: CDI, *Clostridioides difficile* infection; ICP, Infection Control Professionals
Note: Bolded text reflect subtle differences between provinces

Table B-6: Laboratory confirmation requirements

Province	Laboratory confirmation requirements
Alberta (11)	Laboratory-confirmed positive *Clostridium difficile* test (by polymerase chain reaction or toxin assay)
British Columbia (12)	The presence of *C. difficile* toxin A and/or B (positive toxin, or culture with evidence of toxin production, or detection of toxin genes)
Manitoba (13)	Positive *C. difficile* toxin, culture with evidence of toxin production or histological/pathological diagnosis of *C. difficile*-associated disease

Abbreviation: *C. difficile*, *Clostridium difficile*
Note: No data available for New Brunswick (4), Newfoundland and Labrador (14), Nova Scotia (15), Ontario (16), Prince Edward Island (17), Quebec (18) or Saskatchewan (19)

Appendix B: Footnotes

1. Alberta Health Services Infection Prevention and Control. Clostridium difficile Infection (CDI) Provincial Surveillance Protocol. AHS 2018. www.albertahealthservices.ca/assets/healthinfo/ipc/hi-ipc-sr-cdi-protocol.pdf
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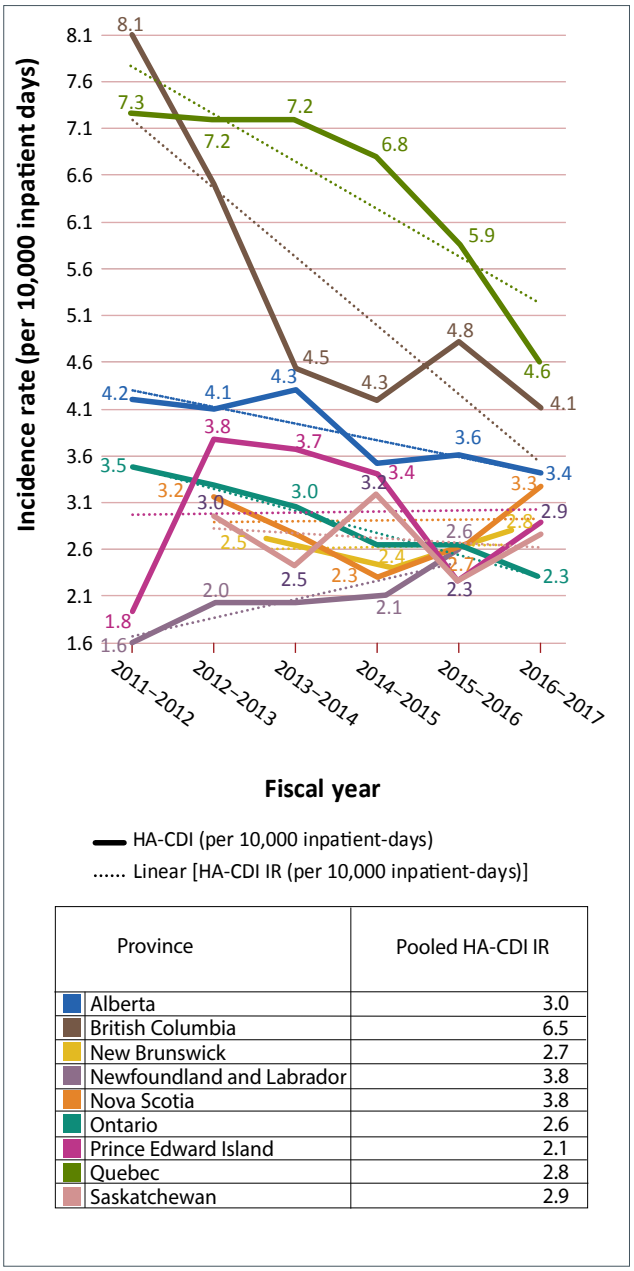
Appendix C: Supplementary data

Figure C-1: Hospital-associated *Clostridioides difficile* infection incidence rates (cases per 10,000 inpatient days)

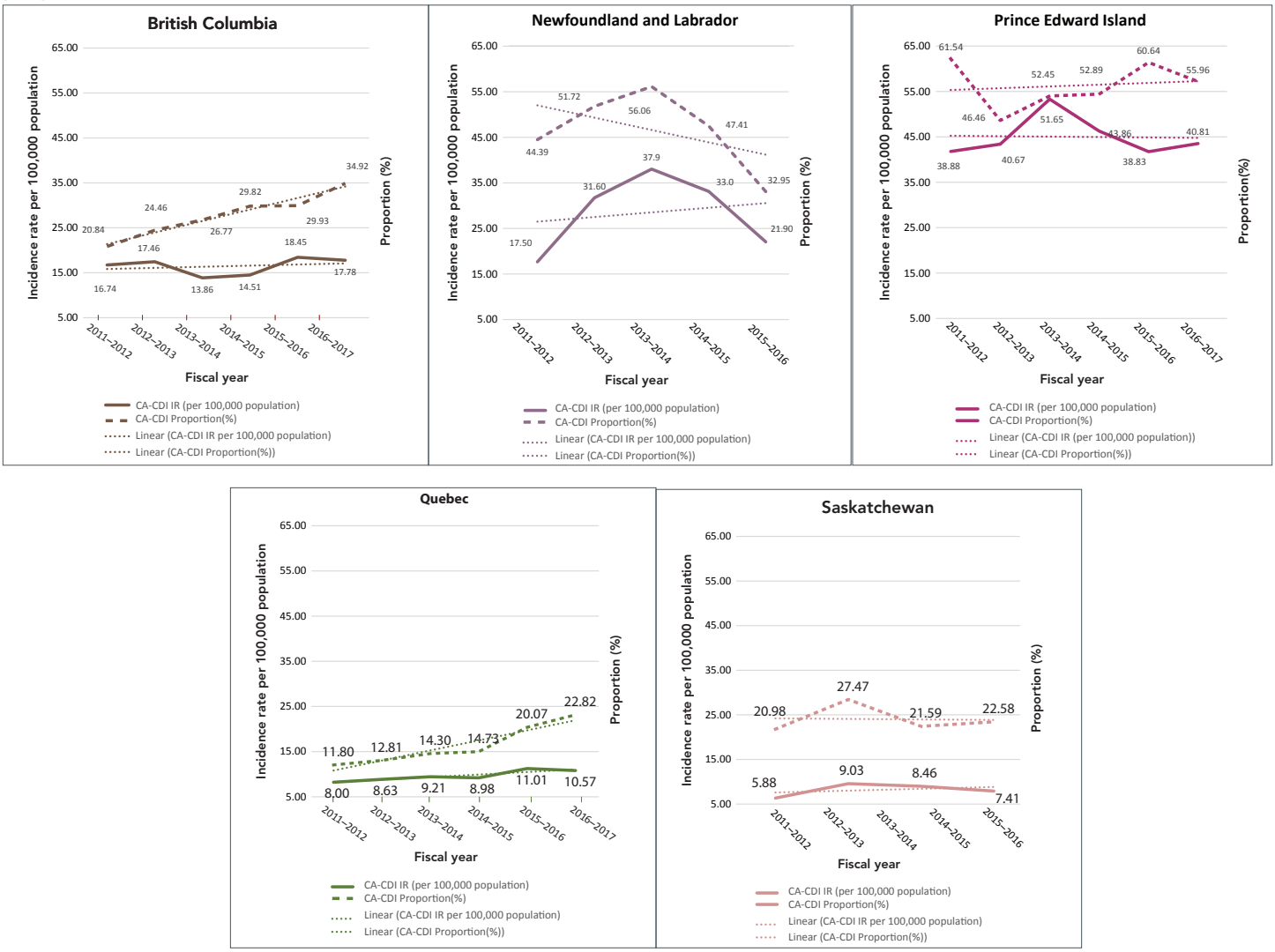


Province	Pooled HA-CDI IR
Alberta	3.0
British Columbia	6.5
New Brunswick	2.7
Newfoundland and Labrador	3.8
Nova Scotia	3.8
Ontario	2.6
Prince Edward Island	2.1
Quebec	2.8
Saskatchewan	2.9

Abbreviations: CA-CDI, community-associated *Clostridioides difficile* infection; IR, incidence rates

Appendix C: Supplementary data

Figure C-2: Community-associated *Clostridioides difficile* infection incidence rates (per 100,000 population) and proportions (%)



Abbreviations: CA-CDI, community-associated *Clostridioides difficile* infection; IR, incidence rates
Note: Prince Edward Island includes only new CA-CDI cases. Trendlines are dotted

Appendix D: Detailed data for hospital and community-acquired *Clostridioides difficile* infections

Table D-1: Data for hospital-acquired *Clostridioides difficile* infections: 2011–2017

Year	Type of data	Provinces								
		AB	BC	NB	NL	NS[a]	ON[b]	PE[c]	QC	SK
2011–2012	rate	4.2	8.1	n/a	1.6	n/a	**3.5**	**1.8**	**7.27**	n/a
	Number of cases	1,200	2,212	n/a	71	n/a	**3,555**	26	3,778	n/a
	TID	2,846,938	2,733,174	n/a	**443,750**	n/a	10,223,096	141,552	5,196,485	n/a
	CIHI TID	**2,883,600**	**2,616,700**	n/a	479,600	n/a	10,261,500	137,900	n/a	n/a
2012–2013	rate	4.1	6.5	n/a	2.0	**3.2**	**3.3**	**3.8**	**7.2**	3.0
	Number of cases	1,166	1,835	n/a	89	61	**3,356**	55	3,794	184
	TID	2,857,501	2,825,727	n/a	**445,000**	192,430	10,258,361	143,690	5,240,187	**613,333**
	CIHI TID	**2,928,400**	**2,653,200**	n/a	485,700	n/a	10,345,000	143,700	n/a	1,010,300
2013–2014	rate	4.3	4.5	2.7	2.0	**2.8**	**3.0**	**3.7**	**7.2**	2.5
	Number of cases	1,263	1,309	228	97	210	**3,086**	52	3,689	213
	TID	2,929,444	2,883,121	**844,444**	**485,000**	744,868	10,174,367	140,766	5,136,300	**852,000**
	CIHI TID	**2,996,200**	**2,709,000**	804,400	500,100	**925,300**	9,254,300	140,700	n/a	960,700
2014–2015	rate	3.5	4.2	2.4	2.1	**2.3**	**2.6**	**3.4**	**6.8**	3.2
	Number of cases	1,065	1,206	208	107	195	**2,707**	47	3,455	296
	TID	3,059,257	2,903,390	**866,667**	**509,524**	831,901	10,274,057	139,350	5,091,013	**925,000**
	CIHI TID	**3,120,000**	**2,731,100**	830,600	511,400	**943,600**	9,199,000	139,300	n/a	969,300
2015–2016	rate	3.6	4.8	2.77	2.6	**2.7**	**2.6**	**2.3**	**5.9**	2.3
	Number of cases	1,091	1,423	238	127	216	**2,645**	31	2,979	217
	TID	3,058,834	2,943,047	**859,206**	**488,462**	803,310	10,260,427	133,640	5,046,574	**943,478**
	CIHI TID	**3,111,200**	**2,765,100**	747,600	494,000	**907,100**	9,203,700	131,200	n/a	941,900
2016–2017	rate	3.4	4.1	n/a	n/a	**3.3**	**2.3**	**2.9**	**4.6**	2.8
	Number of cases	1,043	1,190	n/a	n/a	266	**2,388**	43	2,330	265
	TID	3,098,415	2,908,197	n/a	n/a	813,469	10,345,978	150,116	5,022,104	**946,429**
	CIHI TID	**3,219,300**	**2,799,400**	n/a	n/a	**912,100**	9,387,400	146,900	n/a	956,700
Pooled	rate	**3.8**	**5.3**	**2.6**	**2.1**	**2.8**	**2.9**	**3.0**	**6.5**	**2.7**
	Number of cases	**6,828**	**9,175**	**674**	**491**	**948**	**17,737**	**254**	**20,025**	**1,175**
	TID	**17,850,38**	**17,196,656**	**2,570,317**	**2,371,735**	**3,385,978**	**61,536,286**	**849,114**	**30,732,663**	**4,280,240**

Abbreviations: AB, Alberta; BC, British Columbia; CIHI, Canadian Institute for Health Information; n/a, data not available; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; QC, Quebec; SK, Saskatchewan; TID, total input days

[a] For the 2012–2013 fiscal year, only data for Q4 were available

[b] Number of cases in Ontario were aggregated from monthly data

[c] Total inpatient days of Prince Edward Island were an approximation for using inpatient days (excludes psychiatric) derived from "Health PEI Annul Report". Case counts for each fiscal year were provided by the Prince Edward Island Department of Health and Wellness

Notes:

1. If there was a discrepancy between the data in the report of that year and the same kind of data in the latest report, data in the latest reports were used. For example, if the rate reported in the 2011 report was different from the rate of 2011 in the 2016 report, the rate in the 2016 report was used
2. Data unbolded indicate that the data were collected directly from the reports or provided by the province. Data bolded indicate that the data were estimated
3. Rates were calculated using TID estimated from provincial data
4. CIHI TID were derived from CIHI Management Information System database and calculated according to the provincial surveillance protocols:
   - Alberta: Overall TID - Extended care/chronic TID, unable to extract TID for patients less than one year old
   - British Columbia: Overall TID - Extended care/chronic TID - Rehabilitation - Psychiatric TID, unable to extract TID for patients less than one year old
   - New Brunswick: Overall TID
   - Newfoundland and Labrador: Overall TID
   - Nova Scotia: Overall TID - Extended care/chronic TID, unable to extract TID for patients less than one year old
   - Ontario: Overall TID, unable to extract TID for patients less than one year old
   - Prince Edward Island: TID (excludes psychiatric)
   - Quebec: Data not available
   - Saskatchewan: Overall TID, unable to extract TID for patients less than one year old

Appendix D: Detailed data for hospital and community-acquired *Clostridioides difficile* infections

Table D-2: Data for community-associated *Clostridioides difficile* infections: 2011–2017

Year	Type of data	BC	NL	PE	QC	SK
2011–2012	Number of CA cases	753	91	56	641	-
	Total	3,613	205	91	5,431	-
	Population	4,499,139	-	144,038	8,007,656	-
	Rate	**16.74**	17.50	**38.88**	**8.00**	-
	Percentage	**20.84**	**44.39**	**61.54**	**11.80**	-
2012–2013	Number of CA cases	794	165	59	698	64
	Total	3,246	319	127	5,448	305
	Population	4,546,290	-	145,080	8,085,906	1,088,030
	Rate	**17.46**	31.60	**40.67**	**8.63**	**5.88**
	Percentage	**24.46**	**51.72**	**46.46**	**12.81**	**20.98**
2013–2014	Number of CA cases	636	199	75	751	100
	Total	2,376	355	143	5,251	364
	Population	4,590,081	-	145,198	8,151,331	1,106,838
	Rate	**13.86**	37.90	**51.65**	**9.21**	**9.03**
	Percentage	**26.77**	**56.06**	**52.45**	**14.30**	**27.47**
2014–2015	Number of CA cases	674	174	64	737	95
	Total	2,260	367	121	5,004	440
	Population	4,646,462	-	145,915	8,210,533	1,122,653
	Rate	**14.51**	33.00	**43.86**	**8.98**	**8.46**
	Percentage	**29.82**	**47.41**	**52.89**	**14.73**	**21.59**
2015–2016	Number of CA cases	866	115	57	909	84
	Total	2,893	349	94	4,529	372
	Population	4,694,699	-	146,791	8,254,912	1,133,165
	Rate	**18.45**	21.90	**38.83**	**11.01**	**7.41**
	%	**29.93**	**32.95**	**60.64**	**20.07**	**22.58**
2016–2017	Number of CA cases	846	-	61	880	-
	Total	2,423	-	109	3,856	-
	Population	4,757,658	-	149,472	8,321,888	-
	Rate	**17.78**	-	**40.81**	**10.57**	-
	Percentage	**34.92**	-	**55.96**	**22.82**	-

Abbreviations: BC, British Columbia; CA, community-associated; NL, Newfoundland and Labrador; PE, Prince Edward Island; QC, Quebec; SK, Saskatchewan; -, no data
Note: Data unbolded means data collected directly from the reports or provided by the province, otherwise, the data were estimated

A public health enhanced surveillance system for a mass gathering event

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Abstract

Background: From June 7 to June 9, 2018, a G7 Summit was held in the Canadian province of Quebec. This international political mass gathering event posed a number of potential risks to public health.

Objective: To assess three additional monitoring strategies to detect public health threats during a mass gathering event.

Intervention: In addition to routine public health monitoring, a partnership was created and three monitoring strategies were put in place three days before, during and six days after the G7 event: the analysis of data on the presenting complaint and discharge diagnosis from 11 emergency departments in the area using the logiciel Early Aberration Reporting System; the daily polling of key health partners with an online questionnaire; and the analysis of calls to Info-Santé, a government-run telephone consultation service for the public regarding health and social issues.

Results: Emergency room data produced 78 alerts from the presenting complaints and 39 alerts from the discharge diagnoses. Of these 117 alerts, two were investigated (one in the respiratory and one in the neurological-muscular categories) and no other interventions were required. With a few exceptions, all of the health partners completed the online survey each day and no signal of concern was generated. Compared with historical data, no increase or differences in calls to Info-Santé were detected during the monitoring period.

Conclusion: The three additional monitoring strategies developed to detect events of public health importance during the 2018 G7 Summit in Quebec were successful in gathering timely data for analysis. Close collaboration and good participation from the different partners were essential to this project. However, because no public health event occurred, it was not possible to determine whether the enhanced surveillance system had sufficient speed and sensitivity for timely detection and response.

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Keywords: mass gathering event, surveillance, syndromic surveillance, public health, epidemiology

Introduction

From June 7 to June 9, 2018, the prime minister of Canada hosted a G7 Summit in La Malbaie and Québec, Quebec (1). Seven internationally protected persons and their delegations (approximately 3,200 people), 3,200 journalists, thousands of demonstrators, 1,000 to 2,000 police officers, 1,000 service members from the Canadian Armed Forces and approximately 12,000 people from a number of non-G7 countries invited as part of the Outreach Program were expected to attend.

In preparation for this event, experts in emergency management were consulted, and the literature (2–9), including lessons learned from the Summit of the Americas in 2001 (10), was reviewed. A number of monitoring initiatives previously applied

during sporting (3,11–19), religious (5,20,21) and artistic events (22,23) have been described previously. However, there was less detailed information available about surveillance during political events, especially those that are at risk for violent demonstrations or acts of terrorism (24,25).

In advance of the event, a number of potential public health threats were identified and prioritized for monitoring: rapid spread of certain infectious diseases; violence associated with demonstrations and use of crowd-control agents; potential for chemical, biological, radiological, nuclear or explosive (CBRNE) terrorist threats; and presence of suspicious packages (26). Although the probability of these threats was considered low (11–16,27), an enhanced surveillance system was needed to quickly detect potential public health threats (28–31), as well as a rapid intervention plan for each of these threats.

Routine public health surveillance in Quebec relies on the mandatory reporting of notifiable diseases by physicians and laboratories, and on the passive reporting of perceived or real public health threats by various partners, including clinicians, government departments and local municipalities (32). However, these routine surveillance activities lacked the necessary sensitivity and timeliness to rapidly detect and respond to priority public health threats during the G7 Summit (33). To address this, the Direction de santé publique (DSPublique) of the Centre intégré universitaire de santé et de services sociaux de la Capitale-Nationale (Public Health Department of the Nationale Capital Integrated University Health and Social Services Centre) developed an enhanced surveillance system that included activities for the period from June 4 to June 15, 2018 (three days before, three days during and six days after the event). The goal of the enhanced surveillance system was to develop a surveillance capacity that met the goals of early detection and acceptability to all participating partners.

The purpose of this article is to describe the development and outcome of three monitoring strategies that were part of the enhanced surveillance system during the 2018 G7 Summit, and to consider the implications of these strategies for public health surveillance during future mass gathering events.

Establishing partnerships

Approximately six months before the event, a DSPublique project team began the development of an enhanced surveillance system. All of the region's emergency departments (ED) already had in place electronic records for both presenting complaints (those given by patients to the triage nurses when they came into the ED) and medical discharge diagnoses (those given by a physician when the patient left the ED). Not all these data are usually available to the DSPublique, and they had not been previously used for public health surveillance. The EDs of six university hospital centres and five regional hospital centres within the event perimeter or nearby were invited to collaborate for this event. To ensure access to these data, additional partners from other Integrated University Health and Social Services Centre departments collaborated with the DSPublique project team.

To receive daily reports from key partners, five organizations likely to detect the targeted threats early were approached: the Centre antipoison du Québec (Quebéc Poison Control Centre); the region's ambulance services; the Laboratoire de santé publique du Québec (Quebec Public Health Laboratory); and the Bureau du coroner (Quebec Coroner's Office). Info-Santé (a public telephone consultation service for health and social issues) was a key partner that provided daily reports and contributed data for enhanced surveillance. Three temporary clinics were set up for the event and also submitted daily reports.

In addition to the partners who directly contributed to the enhanced surveillance system, the region's clinicians were informed of the project's progress stage-by-stage through the emergency management structure, which was put on alert for the event. The Public Health Agency of Canada provided support, deploying two field epidemiologists for planning, analyzing data and producing reports. All the enhanced monitoring activities were timed to allow for rapid analysis and dissemination of results, decision-making and response. A daily report summarizing the results was prepared and distributed to the DSPublique, partners and decision-makers. Two versions (short and detailed), adapted to the target audiences, were available.

Enhanced monitoring activities

To enhance the sensitivity and timeliness of the surveillance system, while ensuring it remained acceptable to all partners, the following three monitoring activities were added to Notifiable Disease reporting and passive reporting for the period from June 4 to June 15, 2018:

- Monitoring trends in presenting complaints and discharge diagnoses at ED
- Requesting daily reports from key partners
- Monitoring trends in calls to Info-Santé

Monitoring trends from emergency departments

For the ED electronic data, presenting complaints were recorded by the triage nurse following a patients' arrival, and medical discharge diagnoses were recorded when the patient was ready to leave the ED. All univserity hospital patients were identified with a unique identifier number. These data were available the day after the visit. Electronic record data from all ED visits in the area surrounding the G7 Summit were incorporated into the enhanced surveillance system. This approach was acceptable to clinical partners because these data were already available

for other purposes. However, it did create a slight increase in workload, as reminders were sent if there were entry delays.

The discharge diagnoses were identified according to the International Classification of Diseases, 10th revision (ICD-10) as per the Quebec guidelines (34). Selected presenting complaints and discharge diagnoses were sorted and analyzed by category (see **Appendices 1** and **2**). A few discharge diagnoses were also analyzed individually; these included either a notifiable disease or a diagnosis for which a public health response may be indicated for a single case, such as measles (see last column in Appendix 2). Two clinicians—one specializing in CBRNE emergencies and the other in clinical toxicology—validated the choices.

The number of cases in each category was analyzed using the Centers for Disease Control and Prevention's Early Aberration Reporting System (35) software, which detects alerts or aberrations in the number of cases based on short-term historical data (ten days). All the generated alerts were compared with historic data for the period of April to July 2013–2017. A daily analysis of the previous day's data was conducted, by emergency department and for all emergency departments combined. Age group, municipality of the cases and details on the presenting complaints and diagnoses were used when available. A team evaluation and decision were made regarding whether or not to further investigate each alert that was generated.

Daily reports from key partners

Key partners included Quebéc's Poison Control Centre, the region's ambulance services, the Quebec Public Health Laboratory, the Coroner's Office, Info-Santé and three temporary clinics. A short, three-question online questionnaire (Voxco Inc. platform) (36) was developed and sent to respondents from partner organizations on a daily basis (before, during and after the event) regarding infectious or environmental health threats. Questionnaires were completed by 10 am regarding information from the previous day.

Monitoring trends for calls to Info-Santé

Electronic data on the reasons for calling Info-Santé were already available to the DSPublique, but had not previously been used for surveillance. The most relevant reasons for calling were selected based on the priority threats (**Table 1**). These reasons were sorted into categories for enhanced surveillance. In each category, the number and percentage of calls were analyzed on a daily basis to detect any increase or change compared with historical data.

Table 1: Monitored reasons for calling Info-Santé by category

Category	Reasons for calling
Cardiovascular	Cardiovascular system manifestations or symptoms
CBRNE/physical/ environmental	Extreme heat
	Intoxications
	Large events
	Environmental health
Cutaneous/lymphatic	Skin and tissue manifestations or symptoms
Extreme	Avian influenza (bird flu)
	Ebola virus
Gastrointestinal	Gastrointestinal system manifestations or symptoms
Infectious	Infectious and parasitic diseases
	Thermoregulation
Neurological/muscular	Nervous system manifestations or symptoms
Ophthalmological/ otorhinolaryngological	Ophthalmic manifestations or symptoms
Respiratory	Influenza-like illness
	Respiratory problems excluding the flu

Abbreviation: CBRNE, chemical, biological, radiological, nuclear or explosive

Results

Emergency department data

During the monitoring period, data were available for both the presenting complaints and the discharge diagnoses. No presenting complaint data were missing. Overall, 27% of diagnosis data were missing during the entire monitoring period, which extended from June 4 to 15. During the G7 Summit (June 7 to 9), however, only 23% of diagnosis data were missing. These missing data were due to patients leaving the ED before a diagnosis was made and delays in the entry of diagnoses into the electronic record.

Emergency department data produced 78 alerts for the presenting complaint categories and generated 39 alerts in the various diagnosis categories. Among these 117 alerts, two were investigated (one for respiratory category and one for neurological-muscular category). No other intervention was required. **Table 2** summarizes the number of alerts per category.

Daily reports and Info-Santé

With a few exceptions, all of the partners completed the survey every day and few reminders were required. One of the three temporary clinics reported two cases of gastroenteritis. Ambulance services reported one case of opioid intoxication. Given that these reports did not exceed the expected frequency and there were no related health threats, none of these reports was investigated.

Table 2: Number of alerts by presenting complaint and discharge diagnosis category from 11 emergency departments in the La Malbaie/Québec region, June 4–15, 2018

Category	Number of alerts	
	Presenting complaints	Discharge diagnosis
Cardiovascular	5	3
CBRNE/physical/environmental	6	4
Cutaneous/lymphatic	6	4
Fever	9	n/a
Gastrointestinal	9	0
Hemorrhagic	8	6
Infectious	n/a	5
Opioid intoxication	n/a	0
Neurological/muscular	8	8
Ophthalmic/Otorhinolaryngological	9	4
Respiratory	5	2
Systemic/dehydration	13	3
TOTAL	78	39

Abbreviations: CBRNE, chemical, biological, radiological, nuclear or explosive; n/a; not applicable

In analyzing the reasons for calls to Info-Santé, neither increases nor differences were detected during the monitoring period in comparison with historical data.

Discussion

A three-pronged enhanced surveillance system, developed to detect events of public health importance during the 2018 G7 Summit in Quebec, was successful in gathering timely data for analysis. Most alerts were generated from the analysis of ED data. The use of historical data made it possible to limit the number of alerts for which an investigation was needed. The use of these data appeared to result in high sensitivity but low specificity.

A strength of this enhanced surveillance system was the close collaboration with a number of different partners. This collaboration was essential to the development of this enhanced surveillance system. The three additional monitoring strategies exhibited a high level of participation by the partners. This was likely because partners understood the importance of the additional monitoring and because only minimal additional time was required by participants. Thus, most data requested from the partners were received in a timely manner.

This work identified the feasibility of our enhanced surveillance system and could inform future public health preparedness for mass gathering events. However, because no public health event occurred, it was not possible to determine whether the enhanced surveillance system had sufficient speed and sensitivity for timely detection and response.

Conclusion

Three additional monitoring strategies developed to detect events of public health importance during the 2018 G7 Summit in Quebec were successful in gathering timely data for analysis. However, further assessment of speed and sensitivity is needed if applied to a future public health surveillance strategy of a mass gathering event.

Authors' statement

HC — Conceptualization, methodology, intervention, analysis and interpretation of data, article writing
AP — Conceptualization, methodology, intervention, analysis and interpretation of data, article review
KHC — Intervention, analysis and interpretation of data, article review
MAB — Analysis and interpretation of data, article review
JV — Conceptualization, methodology, article review
NB — Intervention, analysis and interpretation of data, article review
IGS —Conceptualization, resources, article review
JR — Intervention, analysis and interpretation of data, article review

Conflict of interest

None.

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Appendix 1: Monitored presenting complaints from emergency departments, by category

Category	Presenting complaint
Cardiovascular	Cardiac arrest (non-traumatic)
	Chest pain—cardiac features
CBRNE/physical/environmental	Noxious inhalation
	Chemical exposure
	Intoxication
	Exposure to communicable disease
Cutaneous/lymphatic	Reddened hot limb
	Neck swelling/pain
	Groin pain/mass
	Pruritus
	Rash
	Localized swelling/redness
	Other skin conditions
	Lumps, bumps, calluses
	Burn
Fever	Fever
Gastrointestinal	Diarrhea
	Nausea/vomiting
	Blood in stool/melena
	Jaundice
	Abdominal pain
	Diarrhea and fever
Hemorrhagic	Epistaxis
	Vomiting blood
	Hematuria
	Spontaneous bruising
Neurological/muscular	Difficulty swallowing/dysphagia
	Altered level of consciousness
	Confusion
	Seizure
	Gait disturbance/ataxia
	Extremity weakness/symptoms of cerebrovascular accident
	Headache
	Diplopia
Ophthalmological/ Otorhinolaryngological	Sore throat
	Chemical exposure, eye
	Visual disturbance
	Red eye, discharge
	Photophobia
	Eye pain
	Eye trauma

Appendix 1: Monitored presenting complaints from emergency departments, by category (*continued*)

Category	Presenting complaint
Respiratory	Symptoms of upper respiratory tract infection
	Chest pain—non-cardiac features
	Dyspnea
	Respiratory arrest
	Cough/congestion
	Hemoptysis
	Stridor
	Wheezing—no other complaints
	Cough and fever/Influenza-like illness
Systemic/dehydration	General weakness
	Syncope/pre-syncope
	Oliguria
	Cyanosis

Abbreviation: CBRNE, chemical, biological, radiological, nuclear or explosive

Appendix 2: Monitored discharge diagnoses with ICD-10 code from emergency departments, by category[a]

Category	ICD-10 code	ICD-10 diagnosis	Individual analysis done (Y/N)
Cardiovascular	I20.0	Unstable angina	N
	I20.9	Angina pectoris	N
	I21.9	Acute myocardial infarction	N
	I24.9	Acute ischemic heart disease, acute coronary syndrome (ACS)	N
	I46.9	Cardiac arrest	N
	I95.9	Hypotension	N
	R00.1	Bradycardia	N
	R07.2	Chest pain of unknown cause	N
	R07.3	Anterior chest-wall pain	N
	R07.4	Chest pain	N
	R57.0	Cardiogenic shock	N
CBRNE/physical/ environmental	J68.9	Inhalation of toxic products	**Y**
	T59.9	Toxic effect: gases, fumes and vapours	**Y**
	T62.9	Noxious substance eaten as food	**Y**
	T67.0	Heatstroke and sunstroke	**Y**
	T52.9	Toxic effect: organic solvent	N
	T54.9	Toxic effect: corrosive substance	N
	T58	Toxic effect of carbon monoxide	N
	T60.9	Toxic effect: pesticide	N
	T65.9	Toxic effect: unspecified substance	N
	T66	Effects of radiation	N
	T67.9	Effect of heat and light	N
	T71	Asphyxiation	N
	Y14	Poisoning by and exposure to other and unspecified drugs, medicaments and biological substances, undetermined intent	N
	Y17	Poisoning by and exposure to other gases and vapours, undetermined intent	N
	Y25	Contact with explosive material, undetermined intent	N
	Z20.9	Contact with and exposure to unspecified communicable disease	N
	Z29.9	Prophylactic measure	N
Cutaneous/lymphatic	B05.9	Measles	**Y**
	B09	Viral exanthema	**Y**
	L02.9	Cutaneous abscess, furuncle and carbuncle	**Y**
	I88.9	Nonspecific lymphadenitis	N
	I89.1	Lymphangitis	N
	L03.9	Cellulitis	N
	L13.9	Bullous disorder	N
	L25.9	Unspecified contact dermatitis	N
	L29.9	Pruritus	N
	L50.9	Urticaria	N
	L51.9	Erythema multiforme	N
	L72.9	Cyst of skin	N
	L97	Ulcer of lower limb, diabetic foot ulcer	N
	L98.9	Disorder of skin and subcutaneous tissue	N
	M72.69	Necrotizing fasciitis	N

Appendix 2: Monitored discharge diagnoses with ICD-10 code from emergency departments, by category[a] (*continued*)

Category	ICD-10 code	CD-10 diagnosis	Individual analysis done (Y/N)
Cutaneous/lymphatic (*continued*)	R21	Rash	N
	R22.9	Localized swelling, mass and lump	N
	R59.9	Enlarged lymph nodes	N
	R60.0	Localized edema	N
	T29.0	Burns of multiple regions	N
	T30.1	Burn of first degree	N
	T30.2	Burn of second degree	N
	T30.3	Burn of third degree	N
Gastrointestinal	A05.9	Bacterial foodborne intoxication	**Y**
	A09.9	Gastroenteritis	**Y**
	B19.9	Viral hepatitis	**Y**
	K29.7	Gastritis	N
	K29.9	Gastroduodenitis	N
	K51.9	Ulcerative colitis	N
	K56.7	Ileus	N
	K65.0	Acute peritonitis	N
	K72.9	Hepatic failure	N
	K92.9	Disease of digestive system	N
	R10.4	Abdominal pain	N
	R11.1	Isolated nausea	N
	R11.3	Nausea with vomiting	N
	R17	Jaundice	N
Hemorrhagic	D65	Disseminated intravascular coagulation (DIC)	N
	D68.9	Coagulation defect	N
	D69.6	Thrombocytopenia	N
	D75.9	Blood disease	N
	I62.9	Intracranial hemorrhage (nontraumatic)	N
	K92.0	Hematemesis	N
	K92.2	Gastrointestinal hemorrhage	N
	R04.0	Epistaxis	N
	R31.8	Hematuria	N
	R58	Hemorrhage	N
Infectious	A39.2	Acute meningococcaemia	**Y**
	A21.2	Pulmonary tularaemia	**Y**
	A00.0	Cholera due to *Vibrio cholerae* 01, *biovar cholerae*	N
	A00.1	Cholera due to *Vibrio cholerae* 01, *biovar eltor*	N
	A00.9	Cholera, unspecified	N
	A01.0	Typhoid fever	N
	A01.1	Paratyphoid fever A	N
	A01.2	Paratyphoid fever B	N
	A01.3	Paratyphoid fever C	N
	A01.4	Paratyphoid fever, unspecified	N
	A02.0	Salmonella enteritis	N

Appendix 2: Monitored discharge diagnoses with ICD-10 code from emergency departments, by category[a] (*continued*)

Category	ICD-10 code	ICD-10 diagnosis	Individual analysis done (Y/N)
Infectious (continued)	A02.1	Salmonella sepsis	N
	A02.2	Localized salmonella infections	N
	A02.8	Other specified salmonella infections	N
	A02.9	Salmonella infection, unspecified	N
	A03.0	Shigellosis due to *Shigella dysenteriae*	N
	A03.1	Shigellosis due to *Shigella flexneri*	N
	A03.2	Shigellosis due to *Shigella boydii*	N
	A03.3	Shigellosis due to *Shigella sonnei*	N
	A03.8	Other shigellosis	N
	A03.9	Shigellosis, unspecified	N
	A15.0	Tuberculosis of lung, confirmed by sputum microscopy with or without culture	N
	A15.1	Tuberculosis of lung, confirmed by culture only	N
	A15.2	Tuberculosis of lung, confirmed histologically	N
	A15.3	Tuberculosis of lung, confirmed by unspecified means	N
	A15.4	Tuberculosis of intrathoracic lymph nodes, confirmed bacteriologically and histologically	N
	A15.5	Tuberculosis of larynx, trachea and bronchus, confirmed bacteriologically and histologically	N
	A15.6	Tuberculous pleurisy, confirmed bacteriologically and histologically	N
	A15.7	Primary respiratory tuberculosis, confirmed bacteriologically and histologically	N
	A15.8	Other respiratory tuberculosis, confirmed bacteriologically and histologically	N
	A15.9	Respiratory tuberculosis unspecified, confirmed bacteriologically and histologically	N
	A20.2	Pneumonic plague	N
	A36.0	Pharyngeal diphtheria	N
	A36.1	Nasopharyngeal diphtheria	N
	A36.2	Laryngeal diphtheria	N
	A36.3	Cutaneous diphtheria	N
	A36.8	Other diphtheria	N
	A36.9	Diphtheria, unspecified	N
	A40.9	Streptococcal infection	N
	A41.9	Septicemia	N
	A48.3	Toxic shock syndrome	N
	A49.9	Bacteremia	N
	A80.0	Acute paralytic poliomyelitis, vaccine-associated	N
	A80.1	Acute paralytic poliomyelitis, wild virus, imported	N
	A80.2	Acute paralytic poliomyelitis, wild virus, indigenous	N
	A80.3	Acute paralytic poliomyelitis, other and unspecified	N
	A80.4	Acute nonparalytic poliomyelitis	N
	A80.9	Acute poliomyelitis, unspecified	N
	A96.2	Lassa fever	N
	A98.0	Crimean-Congo hemorrhagic fever	N
	A98.3	Marburg virus disease	N
	A98.4	Ebola virus disease	N
	B03	Smallpox	N

Appendix 2: Monitored discharge diagnoses with ICD-10 code from emergency departments, by category[a] (*continued*)

Category	ICD-10 code	ICD-10 diagnosis	Individual analysis done (Y/N)
Infectious (continued)	B34.9	Viral infection	N
	R50.9	Fever	N
	R57.2	Septic shock	N
Opiod poisoning	T40.1	Poisoning: heroin	N
	T40.6	Poisoning: narcotics	N
	F11.9	Mental and behavioural disorders due to use of opioids	N
Neurological/muscular	A05.1	Botulism	**Y**
	A39.0	Meningococcal meningitis	**Y**
	A86	Viral encephalitis	N
	A87.9	Viral meningitis	N
	F05.9	Delirium	N
	G00.9	Bacterial meningitis	N
	G03.9	Meningitis, unspecified	N
	G04.9	Encephalomyelitis	N
	G24.9	Dystonia	N
	G41.9	Status epilepticus	N
	G44.8	Headache, other	N
	G51.0	Bell palsy	N
	G52.9	Cranial nerve disorder	N
	G61.0	Guillain-Barré syndrome	N
	G62.9	Polyneuropathy	N
	G72.9	Myopathy	N
	G83.4	Cauda equina syndrome	N
	G83.9	Paralytic syndrome	N
	G93.4	Encephalopathy	N
	G95.9	Myelopathy	N
	G96.9	Disorder of central nervous system, unspecified	N
	H53.2	Diplopia	N
	M62.99	Myopathy	N
	R13.8	Dysphagia	N
	R26.88	Abnormalities of gait and mobility	N
	R29.8	Symptoms and signs involving the nervous and musculoskeletal systems	N
	R40.0	Altered state of consciousness	N
	R40.29	Coma	N
	R41.0	Disorientation	N
	R51	Headache	N
	R56.88	Convulsions	N

Appendix 2: Monitored discharge diagnoses with ICD-10 code from emergency departments, by category[a] (*continued*)

Category	ICD-10 code	ICD-10 diagnosis	Individual analysis done (Y/N)
Ophthalmological/ otorhinolaryngological	H16.0	Corneal ulcer	N
	H10.9	Conjunctivitis	N
	H16.9	Keratitis, unspecified	N
	H18.9	Disorder of cornea	N
	H53.9	Visual disturbance	N
	H57.1	Eye pain	N
	H57.9	Disorder of eye and adnexa	N
	J02.9	Acute pharyngitis	N
	J03.9	Acute tonsillitis	N
	J04.0	Acute laryngitis	N
	J05.0	Acute obstructive laryngitis (croup)	N
	J05.1	Acute epiglottitis	N
	R07.0	Pain in throat	N
	S05.9	Injury of eye and orbit	N
Respiratory	J06.9	Acute upper respiratory infection	**Y**
	U04.90	Severe acute respiratory syndrome (SARS) – suspected	**Y**
	J04.1	Acute tracheitis	N
	J04.2	Acute laryngotracheitis	N
	J11.8	Flu/influenza	N
	J18.9	Pneumonia	N
	J20.9	Acute bronchitis	N
	J45.90	Asthma	N
	J69.0	Aspiration pneumonia	N
	J80	Adult respiratory distress syndrome- ARDS	N
	J96.0	Acute respiratory failure	N
	J98.0	Bronchospasm	N
	J98.9	Respiratory disorder, unspecified	N
	R04.2	Hemoptysis	N
	R05	Cough	N
	R06.0	Dyspnoea	N
	R06.1	Stridor	N
	R09.2	Respiratory arrest	N
Systemic/dehydration	E86.0	Dehydration	N
	E87.0	Hypernatraemia	N
	E87.1	Hyponatremia	N
	E87.6	Hypokalemia	N
	E87.8	Disorders of electrolyte and fluid balance	N
	N17.9	Acute renal failure	N
	R23.0	Cyanosis	N
	R53	Malaise and fatigue	N
	R55	Syncope and collapse	N
	R57.1	Hypovolemic shock	N
	R57.9	Shock	N

Abbreviations: ICD-10, International Classification of Diseases, 10th revision; N, No; Y, Yes

[a] Identified ICD-10 diagnoses were subject to a separate analysis

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