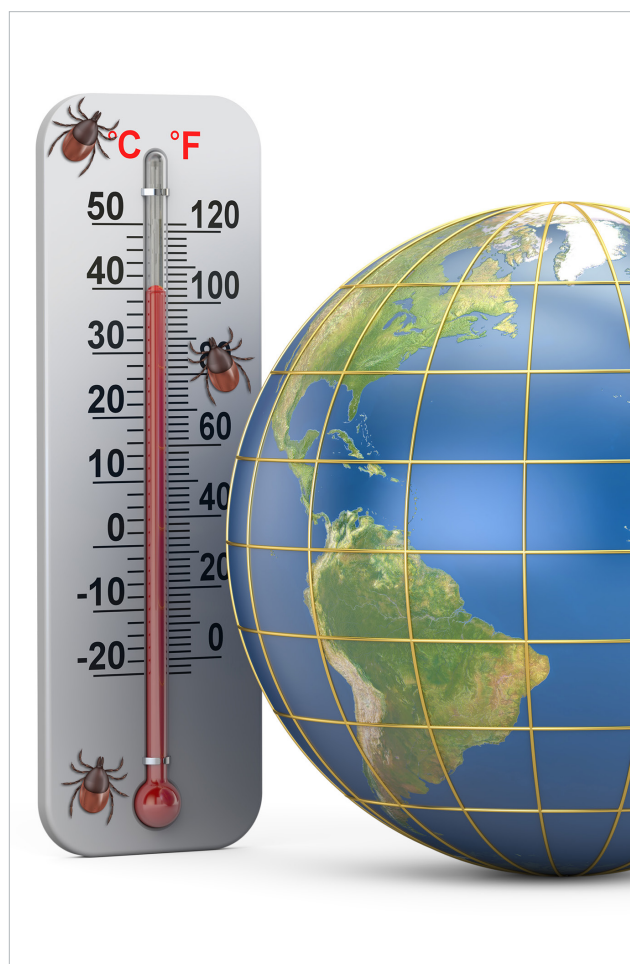


CCDR

CANADA COMMUNICABLE DISEASE REPORT

CLIMATE CHANGE AND LYME DISEASE



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CANADA COMMUNICABLE DISEASE REPORT

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

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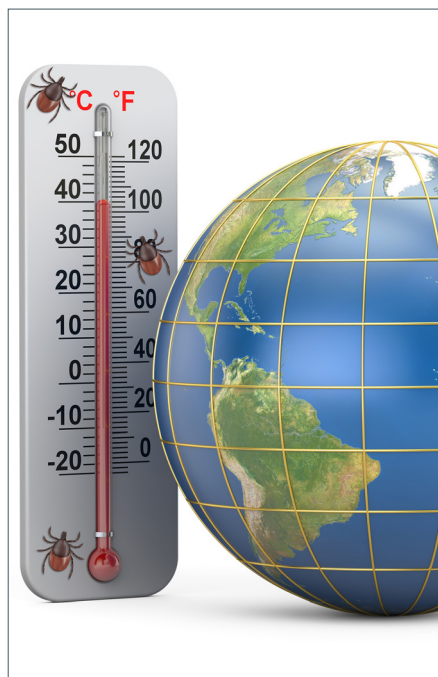
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The continued rise of Lyme disease in Ontario, Canada: 2017

MP Nelder^{1*}, S Wijayasri¹, CB Russell¹, KO Johnson¹, A Marchand-Austin², K Cronin², S Johnson³, T Badiani¹, SN Patel^{4,5}, D Sider^{6,7}

Abstract

Background: Lyme disease is an infection caused by the spirochete *Borrelia burgdorferi* and, in most of North America, is transmitted by the blacklegged tick *Ixodes scapularis*. Climate change has contributed to the expansion of the geographic range of blacklegged ticks in Ontario, increasing the risk of Lyme disease for Ontarians.

Objective: To identify the number of cases and incidence rates, as well as the geographic, seasonal and demographic distribution of Lyme disease cases reported in Ontario in 2017, with comparisons to historical trends.

Methods: Data for confirmed and probable Lyme disease cases with episode dates from January 1, 2012, through December 31, 2017, were extracted from the integrated Public Health Information System (iPHIS). Data included public health unit (PHU) of residence, episode date, age and sex. Population data from Statistics Canada were used to calculate provincial and PHU-specific incidence rates per 100,000 population. The number of cases reported in 2017 by PHU of residence, month of occurrence, age and sex was compared to the 5-year averages for the period 2012–2016.

Results: There were 959 probable and confirmed cases of Lyme disease reported in Ontario in 2017. This was three times higher than the 5-year (2012–2016) average of 313. The provincial incidence rate for 2017 was 6.7 cases per 100,000 population, although this varied markedly by PHU. The highest incidence rates were found in Leeds-Grenville and Lanark District (128.8 cases per 100,000), Kingston-Frontenac, Lennox and Addington (87.2 cases per 100,000), Hastings and Prince Edward Counties (28.6 cases per 100,000), Ottawa (18.1 cases per 100,000) and Eastern Ontario (13.5 cases per 100,000). Cases occurred mostly from June through September, were most common among males, and those aged 5–14 and 50–69 years.

Conclusion: In 2017, Lyme disease incidence showed a marked increase in Ontario, especially in the eastern part of the province. If current weather and climate trends continue, blacklegged ticks carrying tick-borne pathogens, such as those causing Lyme disease, will continue to spread into suitable habitat. Monitoring the extent of this geographic spread will inform future clinical and public health actions to detect and mitigate the impact of Lyme disease in Ontario.

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Keywords: *Borrelia*, epidemiology, expansion, *Ixodes* ticks, public health, range, risk, surveillance

Introduction

Lyme disease is a spirochete infection caused by *Borrelia burgdorferi* and, in much of North America, is transmitted to humans through the bite of an infectious blacklegged tick *Ixodes*

scapularis. The *B. burgdorferi* infection typically begins with a rash and influenza-like symptoms (1–6). In the majority of cases, treatment with antibiotics results in full recovery. However,

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if unrecognized and left untreated, infection can progress to disseminated disease with an increased probability of morbidity, long-term sequelae and post-treatment Lyme disease syndrome (7–9).

Lyme disease case counts in Canada increased by a factor of six from 2009 through 2015, with the majority of cases reported in Ontario (10). This has been associated with an expansion in the geographic range of blacklegged ticks in Canada, including northern regions of Ontario. A driving force behind this expansion is climate change, i.e. an increase in annual cumulative degree days above 0 °C (11–13). Public health officials in Ontario monitor Lyme disease risks by conducting blacklegged tick surveillance and reporting human cases of Lyme disease.

An understanding of Lyme disease epidemiology is essential to inform clinical and public health efforts to increase awareness, prevention, early detection and mitigation efforts. The objective of this study was to identify the number of cases and incidence rates as well as the geographic, seasonal and demographic distribution of Lyme disease cases reported in Ontario in 2017, and compare this to historical trends over the previous five years.

Methods

Study location and population

Ontario has a population of approximately 14.2 million that is largely concentrated in the south of the province (14). Southern Ontario has a moderate, humid, continental climate and mixtures of agricultural, deciduous/mixed forests and built environments (15). In 2017, 36 public health units (PHUs) administered public health services in Ontario, including human Lyme disease case follow-up and blacklegged tick surveillance.

Data collection and analysis

When notified of a new case of Lyme disease, public health professionals conduct follow-up of cases and collect information pertaining to demographics, exposures, symptoms, hospitalizations and deaths. If the case meets the provincial surveillance case definition (**see text box**), then all the data are reported to the provincial integrated Public Health Information System (iPHIS).

For this study, we extracted data from the iPHIS for confirmed and probable Lyme disease cases with episode dates from January 1, 2012, through December 31, 2017, and calculated the number and proportion of cases by PHU of residence, month of occurrence, age and sex.

We used an individual's PHU of residence and earliest episode date in calculating case counts and incidence rates. Episode dates also enabled us to determine seasonality. Episode dates were defined as the date of earliest symptom onset, specimen

Ontario's surveillance case definitions for confirmed and probable cases of Lyme disease (2012–2017): Ontario, Canada (16)

CONFIRMED CASE

- clinician-confirmed erythema migrans greater than 5 cm in diameter in a person with a history of residence in, or visit to, a Lyme disease endemic area or risk area OR
- clinical evidence of Lyme disease with laboratory confirmation by polymerase chain reaction (PCR) or culture OR
- clinical evidence of Lyme disease with laboratory support by serological methods, and a history of residence in, or visit to, an endemic area or risk area

PROBABLE CASE

- clinical evidence of Lyme disease with laboratory support by serological methods, but with no history of residence in, or visit to an endemic area or risk area OR
- clinician-confirmed erythema migrans greater than 5 cm in diameter but with no history of residence in, or visit to an endemic area or risk area

collection or date reported. Due to the incompleteness of data and the possibility of multiple exposure opportunities, we did not attempt to determine if a case was locally acquired (exposure within PHU of residence) or travel related (travel outside of PHU of residence). Population estimates (2012–2016) and projections (2017), obtained from Statistics Canada via IntelliHEALTH Ontario, were used to calculate provincial and PHU-specific incidence rates per 100,000 population. We aggregated Lyme disease incidence rates by PHUs for mapping using a geographic information system, ESRI ArcGIS v10.3 (Environmental Systems Research Institute, Inc., Redlands, California, United States [US]). Incidence rates by PHU were then manually organized into incidence rate classes: 0, 0.1–5.0, 5.1–10.0, 10.1–30.0, >30.0). The 2017 data were compared to the 5-year averages for the period 2012–2016. Descriptive analyses were conducted using Microsoft Excel 2010 and SAS 9.3 (Statistical Analysis System, Cary, North Carolina, US).

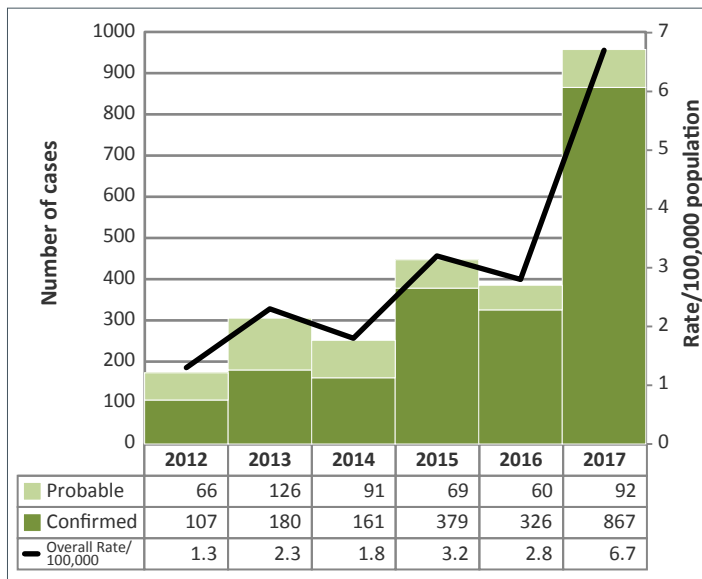
This manuscript reports on routine surveillance activities and not research; therefore, research ethics committee approval was not required. Data are available upon request via Public Health Ontario (PHO) at <https://www.publichealthontario.ca/en/About/Pages/privacy.aspx>.

Results

Case counts, incidence rates and geographic distribution

In 2017, there were 959 confirmed and probable cases of Lyme disease reported in Ontario (Figure 1).

Figure 1: Number of probable and confirmed Lyme disease cases and incidence rate per 100,000 population by year: Ontario, Canada (2012–2017)



The 2017 total was 3.1 times higher than the 5-year (2012–2016) average of 313 (Table 1). The majority of cases in 2017 were reported by Leeds-Grenville and Lanark District (LGL) (n=219, 22.8% of the provincial total), Kingston-Frontenac, Lennox and Addington (KFL) (n=180, 18.8%) and Ottawa (n=180, 18.8%). These three PHUs made up 9.7% of the Ontario population, yet reported 60.4% of the province's Lyme disease cases. In 2017, the LGL case count was 4.6 times higher than the 5-year average; KFL and Ottawa counts were 3.6 and 3.8 times higher than their 5-year averages, respectively.

Table 1: Number of probable and confirmed Lyme disease cases and incidence rates by public health unit: Ontario, Canada (2017)

| Public health unit ^a | Number of cases | % | 5-year average | Incidence per 100,000 population |
|---------------------------------|-----------------|------|----------------|----------------------------------|
| Algoma District (ALG) | 2 | 0.2 | 2.5 | 1.7 |
| Brant County (BRN) | 1 | 0.1 | 2.0 | 0.7 |
| Chatham-Kent (CHK) | 3 | 0.3 | 2.2 | 2.9 |
| City of Hamilton (HAM) | 5 | 0.5 | 6.2 | 0.9 |
| Ottawa (OTT) | 180 | 18.8 | 47.4 | 18.1 |

Table 1: (continued) Number of probable and confirmed Lyme disease cases and incidence rates by public health unit: Ontario, Canada (2017)

| Public health unit ^a | Number of cases | % | 5-year average | Incidence per 100,000 population |
|---|-----------------|------------------|----------------|----------------------------------|
| Durham Regional (DUR) | 46 | 4.8 | 14.2 | 6.7 |
| Eastern Ontario (EOH) | 28 | 2.9 | 17.0 | 13.5 |
| Elgin-St. Thomas (ELG) | 0 | 0.0 | 1.3 | 0.0 |
| Grey Bruce (GBO) | 3 | 0.3 | 2.0 | 1.8 |
| Haldimand-Norfolk (HDN) | 7 | 0.7 | 2.2 | 6.3 |
| Haliburton-Kawartha-Pine Ridge District (HKP) | 17 | 1.8 | 5.2 | 9.3 |
| Halton Regional (HAL) | 13 | 1.4 | 7.4 | 2.2 |
| Hastings and Prince Edward Counties (HPE) | 47 | 4.9 | 18.2 | 28.6 |
| Huron County (HUR) | 1 | 0.1 | 1.7 | 1.7 |
| Kingston-Frontenac and Lennox & Addington (KFL) | 180 | 18.8 | 49.6 | 87.2 |
| Lambton County (LAM) | 1 | 0.1 | 3.0 | 0.8 |
| Leeds-Grenville and Lanark District (LGL) | 219 | 22.8 | 47.8 | 128.8 |
| Middlesex-London (MSL) | 15 | 1.6 | 5.2 | 3.1 |
| Niagara Regional (NIA) | 19 | 2.0 | 9.2 | 4.1 |
| North Bay Parry Sound District (NPS) | 1 | 0.1 | 1.3 | 0.8 |
| Northwestern (NWR) | 2 | 0.2 | 3.2 | 2.5 |
| Oxford County (OXF) | 2 | 0.2 | 1.8 | 1.8 |
| Peel Regional (PEE) | 12 | 1.3 | 5.8 | 0.8 |
| Perth District (PDH) | 1 | 0.1 | 1.3 | 1.3 |
| Peterborough County-City (PTC) | 12 | 1.3 | 2.8 | 8.4 |
| Porcupine (PQP) | 0 | 0.0 | 1.0 | 0.0 |
| Renfrew County and District (REN) | 7 | 0.7 | 3.2 | 6.5 |
| Simcoe Muskoka District (SMD) | 12 | 1.3 | 3.8 | 2.1 |
| Sudbury and District (SUD) | 3 | 0.3 | 1.5 | 1.5 |
| Thunder Bay District (THB) | 0 | 0.0 | 1.0 | 0.0 |
| Timiskaming (TSK) | 0 | 0.0 | 0.0 | 0.0 |
| Toronto (TOR) | 76 | 8.0 | 31.0 | 2.6 |
| Waterloo (WAT) | 7 | 0.7 | 4.2 | 1.3 |
| Wellington-Dufferin-Guelph (WDG) | 9 | 0.9 | 2.4 | 3.1 |
| Windsor-Essex County (WEC) | 7 | 0.7 | 4.0 | 1.7 |
| York Regional (YRK) | 21 | 2.2 | 9.8 | 1.8 |
| Total | 959 | 100 ^b | 313 (average) | 6.7 (average) |

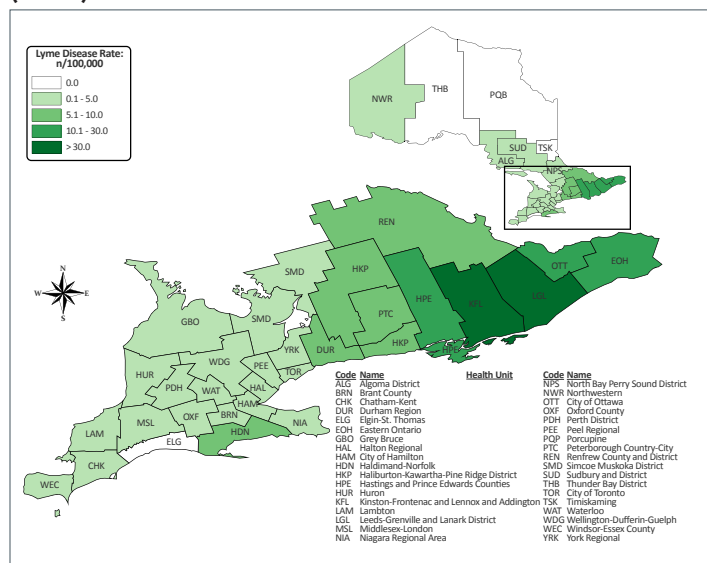
^a 3-letter abbreviation

^b The percentage does not add to 100 percent due to rounding



The highest incidence rates in 2017 occurred in LGL (128.8 cases per 100,000), KFL (87.2 cases per 100,000), Hastings and Prince Edward Counties (HPE) (28.6 cases per 100,000), OTT (18.1 cases per 100,000) and Eastern Ontario (EOH) (13.5 cases per 100,000) (Figure 2).

Figure 2: Incidence rate of Lyme disease (per 100,000 population) by public health unit: Ontario, Canada (2017)

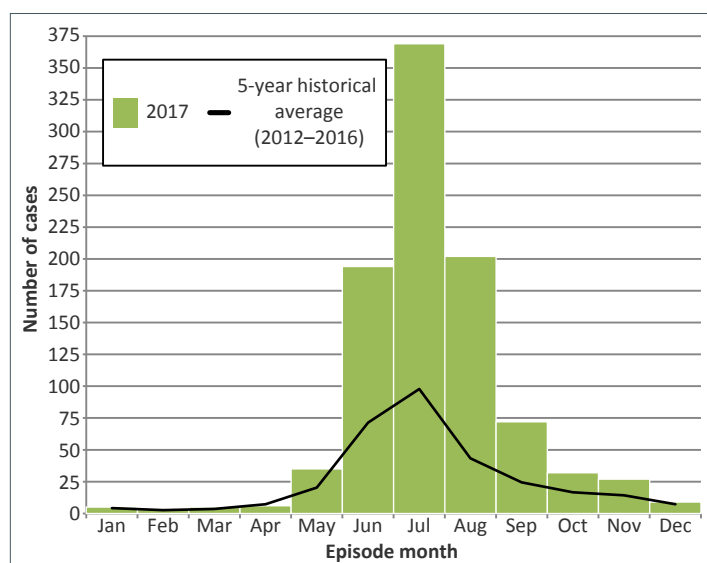


Abbreviations: n, number; > superior to

Seasonality

In 2017, the majority of cases occurred from June through September, with July having the highest number (n=369) (Figure 3). Monthly case counts were above 5-year averages for June (2.7 times higher), July (3.8), August (4.7) and September (3.0).

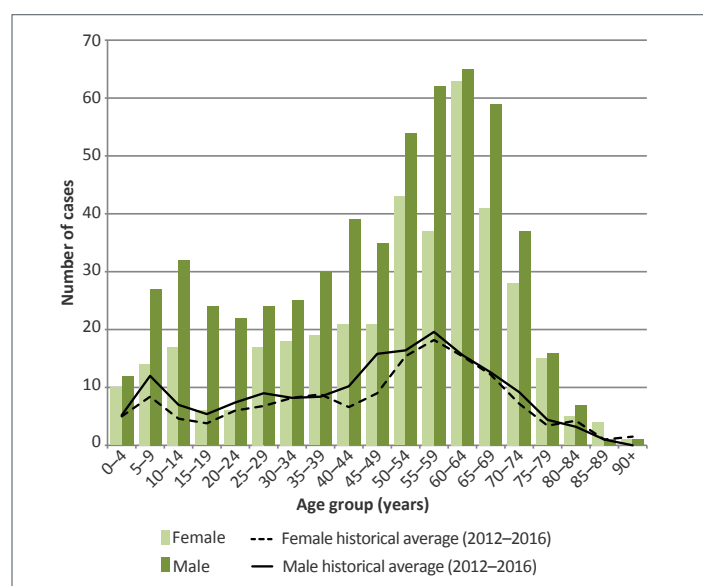
Figure 3: Number of probable and confirmed Lyme disease cases by episode month in 2017, compared to 5-year averages (2012–2016): Ontario, Canada



Age and sex

Lyme disease case counts in Ontario displayed a bimodal pattern in 2017, with relatively higher counts in those aged 5–14 and 50–69 years and relatively fewer in those aged 15–24 years (Figure 4). Over half – 59.8% – of cases were male. The ratio of male to female cases was higher than the 5-year average in most age groups. The male to female ratio was almost two times higher in the 5–14, 35–39, 40–49 and 55–59 year old age groups and was three to four times higher in the 15–19 and 20–24 year age groups.

Figure 4: Number of confirmed and probable Lyme disease cases by age group and sex in 2017, compared to 5-year averages (2012–2016): Ontario, Canada^a



^a Cases with unknown age (n=3) or sex (n=3) were excluded. Age group refers to the age group of the individual at the time of illness

Discussion

Ontario Lyme disease incidence in 2017 was at its highest recorded level since it became a reportable disease in 1988. The increase in Lyme disease incidence in Ontario is not uniform, but is concentrated in the eastern part of the province, which contains more blacklegged ticks and blacklegged ticks with relatively higher *B. burgdorferi* percent positivity (17,18). Consistent with the rest of the Canada and elsewhere, Lyme disease cases were more frequent between June and September, and were more common among those aged 5–14 and 50–69 years and among males.

The strength of our study is that it provides the most up-to-date data available on Lyme disease incidence in Ontario as well as an analysis of the geographic, seasonal and demographic trends in Lyme disease infection.



There are several limitations to consider. First, the true incidence of an infection such as Lyme disease is subject to varying degrees of underreporting due to a variety of factors, such as variable disease awareness, health care-seeking behaviours, clinical diagnoses, reporting behaviours and treatment of clinical early-localized Lyme disease without reporting to the PHU (19,20). Although the degree of provincial underreporting has not been determined, we assume cases reported through passive surveillance skew towards cases confirmed by serology.

Second, the iPHIS is a disease reporting system that allows for ongoing updates to data previously entered. As a result, data extractions from iPHIS represent a snapshot of the database at the time of extraction and may differ from previous or subsequent reports. Third, it was not possible to assess whether *B. burgdorferi* infections were acquired locally or when travelling elsewhere, so the PHU of residence is not necessarily the location of exposure. Nonetheless, the most likely exposure location for a case is near their home or, more broadly, in the PHU of residence (21,22).

Next steps

There are both research and public health implications to these data. Reportable disease databases such as iPHIS, offer an opportunity to explore the epidemiology of Lyme disease in Ontario. For example, research using iPHIS and other health care databases could examine spatiotemporal trends in reporting and treatment of cases with and without laboratory confirmation.

These data have important public health implications in that the identified trends offer an opportunity for better targeting of Lyme disease prevention awareness, such as educational programs for children and parents and the need for protection during summer activities. Summer is associated with the nymph stage of the tick, so increased awareness of the smaller size of the tick at this time may also be useful.

Conclusion

Lyme disease incidence is increasing in Ontario. This trend is likely to continue as climate change progresses and enables blacklegged ticks to survive and propagate in new areas. Ongoing surveillance of both human cases and tick distribution can continue to inform clinical and public health actions to prevent, detect and mitigate the impact of Lyme disease in Ontario.

Authors' statement

MPN – Conceptualization, methodology, analysis, interpretation, writing original draft, review and editing
CBR, DS, KOJ, SW – Conceptualization, methodology, analysis, interpretation, writing original draft (parts), review and editing
A-MA, KC, SJ, SNP, TB – Methodology, analysis, interpretation, review and editing

Conflict of interest

None.

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Ixodes scapularis tick distribution and infection rates in Ottawa, Ontario, 2017

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Abstract

Background: The incidence of Lyme disease has increased in many regions of Canada in recent years, including in Ottawa, Ontario. To date there has been limited active tick surveillance in the region.

Objectives: To estimate both the distribution and density of *Ixodes scapularis* ticks in the city of Ottawa, and the infection rates of ticks with *Borrelia burgdorferi* (that causes Lyme disease) and other tick-borne pathogens.

Methods: Between June and October 2017, tick surveillance was conducted by drag sampling at 23 sites in Ottawa municipal parks, recreational trails and forests. Blacklegged ticks were tested for *B. burgdorferi*, *Borrelia miyamotoi* and *Anaplasma phagocytophilum* using quantitative polymerase chain reaction protocols.

Results: *I. scapularis* ticks were found in 16 of the 23 sites (70%). Recreational trails, conservation areas/forests and the provincial park within the city of Ottawa had significantly higher tick densities than municipal parks ($p < 0.01$). Of the 194 adult and 26 nymphal *I. scapularis* tested, prevalence of infection was 29.5% for *B. burgdorferi*, 0.45% for *B. miyamotoi* and 0.91% for *A. phagocytophilum*.

Conclusion: Almost 30% of *I. scapularis* ticks tested in suburban and rural areas of the city of Ottawa were infected with *B. burgdorferi*, known to cause Lyme disease. Other types of infection, known to cause anaplasmosis and tick-borne relapsing fever, were also detected, although were very rare. Conducting active tick surveillance at the local level may help to inform risk assessment and public health actions.

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Keywords: Lyme disease, surveillance, *Ixodes scapularis*, *Borrelia burgdorferi*, ecology

Introduction

The blacklegged tick (also known as deer tick, *Ixodes scapularis*) is a vector for several pathogens that cause zoonotic diseases, including Lyme disease (1,2). The geographic range of this tick species extends from Texas in the southern United States (US) to parts of central and eastern Canada (3–5). Recent northward spread of *I. scapularis* has been observed in association with ongoing climate and environmental changes, posing an increasing risk to public health (6).

Eastern Ontario has been identified as a region of recent and ongoing tick and Lyme disease expansion (7,8), where environmental factors such as temperature, forest type and microhabitat conditions have been associated with tick occurrence (4,8–10). With recent climate change, the city of Ottawa has become climatically suitable for the establishment of *I. scapularis* populations (6). The number of reported cases of human Lyme disease more than doubled in Ottawa in the last year, from 74 in 2016 to 186 in 2017, associated with exposures both inside and outside of Ottawa (11).



Although ticks are most known for carrying the bacteria that causes Lyme disease, they can also carry other pathogens. For example, ticks can carry *Anaplasma phagocytophilum* that causes anaplasmosis. The first confirmed human case of anaplasmosis in a health unit near Ottawa was reported recently (12). In addition, ticks can carry *Borrelia miyamotoi*, causing an infection sometimes called tick-borne relapsing fever (13,14). Detection is important as these diseases are treatable and full recovery can be obtained when identified and treated early.

Given the recent increase in the number of cases of Lyme disease reported in Ottawa and ongoing expansion of tick populations in eastern Ontario, there was an identified need for surveillance of tick populations to assess the public health risk and inform public health action. Two types of tick surveillance can be used in a given area: passive and active. Passive surveillance involves health care providers and/or the public submitting ticks that had been attached to people (15). Passive surveillance is useful for signalling the presence of potential risk in areas where ticks and tick-borne pathogens are newly emerging. Active surveillance involves field sampling of ticks from the environment either by dragging a flannel sheet over a potentially affected area or collecting and examining (and possibly testing) ticks infesting small mammal hosts such as mice (15). To determine whether tick populations are established, all three life stages of the tick should be detected for two consecutive years (15).

The objective of this study was to estimate the distribution, density and infection rates of ticks in the city of Ottawa.

Material and Methods

Study site

The city of Ottawa is the nation's capital and is situated in eastern Ontario on the south bank of the Ottawa River. It has a population of almost one million people and covers a large geographic area of almost 3,000 km² (16). In addition to the urban core and several suburban districts, the city has abundant green space including conservation areas, parks, trails, wetlands, forests and farmland.

We conducted a survey of 23 sites including nine municipal parks, seven conservation areas and forests, six recreational trails and one provincial park within the city of Ottawa to assess the occurrence and density of *I. scapularis* ticks and rates of infection with tick-borne pathogens (Table 1). Sites were selected based on an ecological niche model of *I. scapularis* (10), with locations chosen across urban, suburban and rural areas of Ottawa.

Sample collection

A team of three researchers with previous field training conducted active tick surveillance using the drag sampling method described by Public Health Ontario (17) at 23 sites: 19 in spring/summer 2017 (June to August) and all 23 sites in fall 2017 (September to October). Ticks were collected by dragging

Table 1: Active tick surveillance sampling sites, Ottawa, Ontario, 2017

| Site ID | Site name | Site type |
|---------|---|------------------------------|
| 1 | Britannia Conservation Area | Conservation area and forest |
| 2 | Rideau River Provincial Park | Provincial park |
| 3 | Rideau River Eastern Pathway | Recreational trail |
| 4 | Beryl Gaffney Park | Municipal park |
| 5 | Dominion Arboretum | Municipal park |
| 6 | Heritage Park | Municipal park |
| 7 | Greenbelt Pathway West | Recreational trail |
| 8 | Pine Grove (Conroy Pit) | Municipal park |
| 9 | South March Highlands Conservation Forest | Conservation area and forest |
| 10 | Morris Island Conservation Area | Conservation area and forest |
| 11 | Stoney Swamp | Conservation area and forest |
| 12 | Petrie Island Park | Conservation area and forest |
| 14 | Meadowbrook Park | Municipal park |
| 15 | Prescott & Russell Recreational Trail | Recreational trail |
| 16 | Pinhey's Point Park | Conservation area and forest |
| 17 | Brown's Inlet Park | Municipal park |
| 18 | Fairmont Park | Municipal park |
| 19 | Carling Campus Northern Access Trail | Recreational trail |
| 20 | Shirley's Bay | Recreational trail |
| 21 | Beacon Hill | Recreational trail |
| 22 | Hog's Back Park | Municipal park |
| 23 | Carp Hill | Conservation area and forest |
| 24 | Greely | Municipal park |

Note: Site 13 was deleted as it was outside the city limits

a 1 metre² white flannel cloth across the forest floor and surrounding vegetation for a total of at least three person-hours at each site, if the size of the area permitted, with less than three person-hours in smaller sites. The drag cloth was checked for ticks every 50 metres and geographic coordinates were recorded using a handheld global positioning system (GPS) device (Garmin eTrex 20x). Adults, nymphs and larvae were maintained alive in plastic vials and transported on ice to the laboratory at the University of Ottawa for species identification and possible testing.

Laboratory testing

All adults, nymphs and larvae were identified by microscopic examination for species verification and sex using standard taxonomic keys (18–20). Adult and nymphal *I. scapularis* ticks were tested for *B. burgdorferi*, *A. phagocytophilum*, and *B. miyamotoi* using quantitative polymerase chain reaction (qPCR) assays, which allow quantification of the amplified DNA molecules according to previously published protocols (13,21). Prior to testing, the qPCR assays established at the University of Ottawa were validated using a panel of test samples provided by the National Microbiology Laboratory (NML) in Winnipeg.



Ticks were dissected and total genomic DNA was extracted using the QIAamp DNA mini kit (QIAGEN Inc., Mississauga, Ontario). A duplex qPCR assay targeting the 23S rRNA and the *msp2* gene was used to identify *B. burgdorferi* sensu lato and *A. phagocytophilum*, respectively. *Borrelia burgdorferi* sensu stricto and *B. miyamotoi* DNA was then confirmed in positive samples by targeting their *ospA* and *glpQ* genes, respectively. Amplification was carried out using the BioRad CFX96 Real-Time PCR Detection System. After amplification and real-time data acquisition, analysis was performed using the CFX Maestro software (BioRad, Hercules, California, US). Subsequent testing by nested PCR and sequencing was performed at NML for samples positive with screening primers but negative with confirmatory assays.

Descriptive analyses

Total tick density was calculated for each site as the total number of adult, nymph and larval *I. scapularis* ticks divided by the total person-hours of sampling, combining data from spring/summer and fall collections. Nymphal density was similarly calculated as the total number of *I. scapularis* nymphs in a given site divided by the total number of person-hours of sampling. Infection rates were calculated as the total number of ticks positive for *B. burgdorferi*, *B. miyamotoi* or *A. phagocytophilum* divided by the total number of ticks tested. Larvae were not tested because

transovarial transmission of *B. burgdorferi* does not occur (13). Differences in tick density by site type were explored using one-way analysis of variance in Stata 15.0 (StataCorp, College Station, Texas, US).

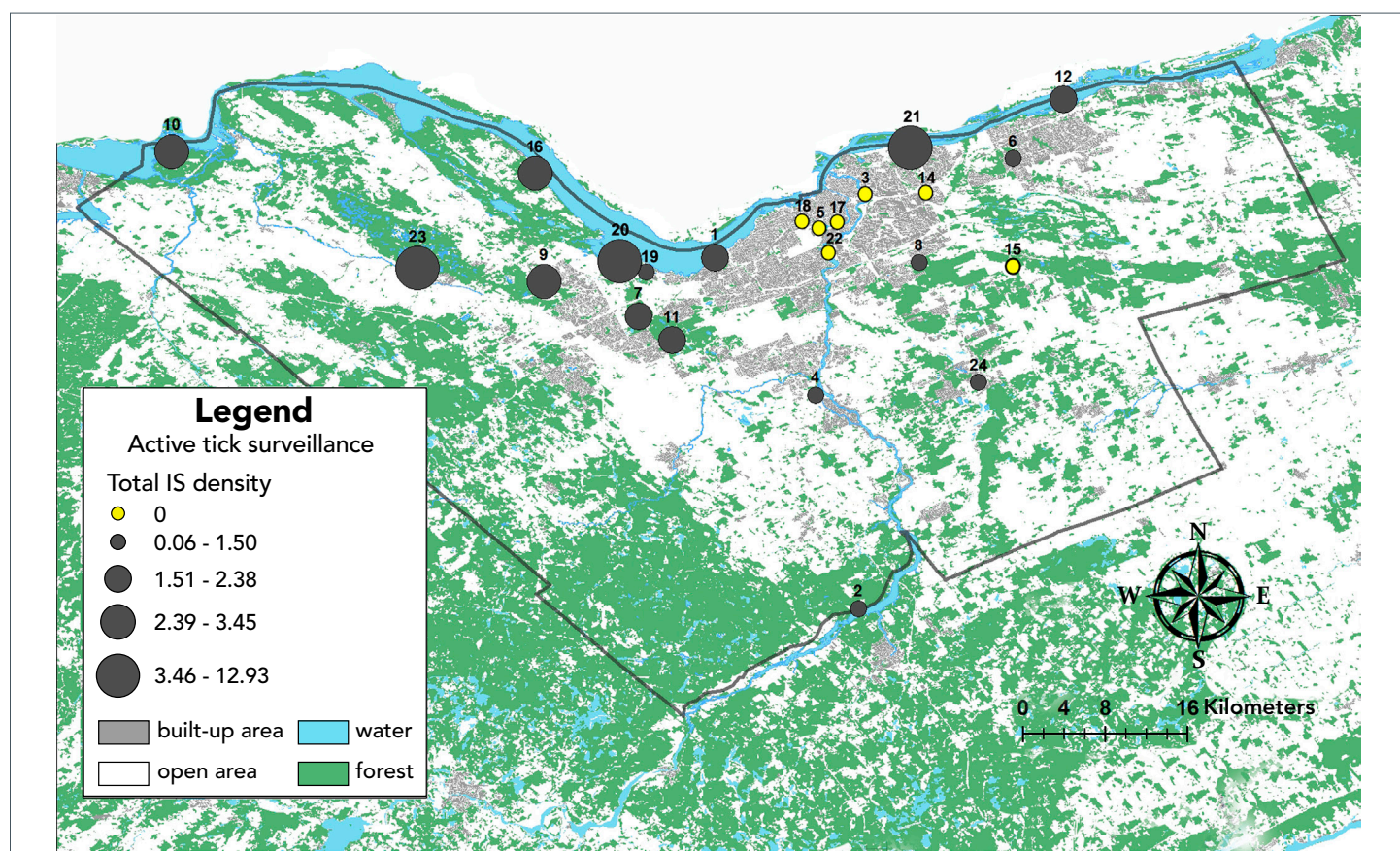
Results

Field sampling

In total, we collected 239 *I. scapularis* ticks, including 194 adults, 26 nymphs and 19 larvae, during 135 person-hours of drag sampling. *Ixodes scapularis* ticks were detected at 16 of the 23 (70%) sites (**Figure 1**). Other tick species were found at three sites: *Haemaphysalis* (n=6) at two sites and *Ixodes marxi* (n=1) at one site.

Overall mean *I. scapularis* density was 2.6 (standard deviation [SD] 4.0) per person-hour in Ottawa sites. Mean tick density differed by type of site, with significantly higher tick density in the recreational trail, conservation area/forest and provincial park sites with a mean (SD) of 4.1 (4.5) compared to the municipal parks mean (SD) of 0.3 (0.5) ($p < 0.01$). Risk areas based on a 5-km radius from sites with tick occurrence were widely distributed around Ottawa, with highest coverage in forested areas of the western region of Ottawa and along the Ottawa River (**Figure 2**).

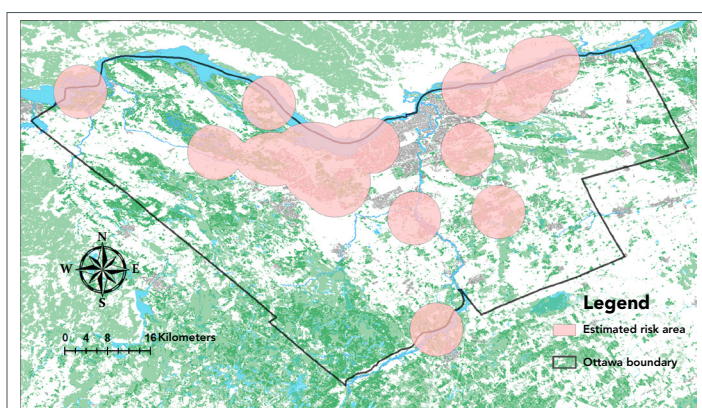
Figure 1: Map of Ottawa illustrating tick density in sites surveyed for active tick surveillance, 2017



Note: The city of Ottawa boundary outlined in black. Density of *Ixodes scapularis* (IS) ticks (number collected per person-hour of drag sampling) is indicated by the size of the circle



Figure 2: Map of Ottawa with estimated risk areas for ticks based on active surveillance, 2017



Note: Risk areas are defined using a 5-km radius from the centre of a location where blacklegged ticks were found by drag sampling and only reflect areas where drag sampling was conducted at 23 sites

Laboratory analyses

All 220 adult and nymphal *I. scapularis* ticks were tested for pathogens. *Borrelia burgdorferi* was detected in ticks from 11 of the 16 sites where *I. scapularis* were found. In total, 65 (29.5%) of all tested ticks were positive for *B. burgdorferi*, and infection

rates varied considerably by site, ranging from 0% to 50% (Table 2). *Borrelia miyamotoi* and *A. phagocytophilum* were detected in two sites in Ottawa representing 0.45% (n=1) and 0.91% (n=2) of the blacklegged ticks tested (Table 2).

Discussion

This study provides a recent picture of the distribution of *I. scapularis* ticks and their infection rates with *B. burgdorferi* and other pathogens of public health significance in urban, suburban and rural areas of the city of Ottawa, where the number of Lyme disease cases have been rapidly increasing. We show that 70% of sampled sites were positive for *I. scapularis* ticks, with highest tick density observed in recreational trails and conservation areas/forests, signalling the potential for human-tick encounter in these sites. Prevalence of infection with *B. burgdorferi* in collected ticks varied considerably, with an average of 29.5% in the 16 Ottawa sites where *I. scapularis* were found.

The study was limited by small numbers of collected ticks (n<30) in the majority of sites within Ottawa, which reduces the robustness of the pathogen prevalence estimates. Therefore, infection rates should be interpreted with caution for these sites.

Table 2: Active surveillance of *Ixodes scapularis* ticks in Ottawa, ON, 2017^a

| Site ID | Person-hours drag sampling (n) | <i>Ixodes scapularis</i> abundance | | | | <i>Ixodes scapularis</i> density per person-hour (n) | | Infection rate (%) | | |
|---------|--------------------------------|------------------------------------|-------|-------|-------|--|-------|--------------------|------------------|------------------|
| | | Adult | Nymph | Larva | Total | Nymph | Total | Bb | Bm | Ap |
| 1 | 8.4 | 15 | 0 | 0 | 15 | 0 | 1.8 | 13.3 ^c | 0 ^b | 0 |
| 2 | 6.9 | 0 | 1 | 0 | 1 | 0.3 | 0.2 | 0 | 0 | 0 |
| 3 | 6.0 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 4 | 11.2 | 1 | 0 | 0 | 1 | 0 | 0.1 | 0 | 0 | 0 |
| 5 | 7.0 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 6 | 7.7 | 1 | 0 | 0 | 1 | 0 | 0.1 | 0 | 0 | 0 |
| 7 | 8.0 | 10 | 6 | 1 | 17 | 1.6 | 2.4 | 43.8 ^d | 0 | 0 |
| 8 | 8.3 | 0 | 2 | 3 | 5 | 0.5 | 0.6 | 0 | 0 | 0 |
| 9 | 7.2 | 23 | 2 | 0 | 25 | 0.6 | 3.5 | 32.0 ^d | 0 | 0 |
| 10 | 8.5 | 25 | 4 | 0 | 29 | 1.0 | 3.4 | 34.5 ^d | 0 | 3.5 ^c |
| 11 | 13.2 | 11 | 11 | 4 | 26 | 1.6 | 2.0 | 31.8 ^d | 0 | 0 |
| 12 | 5.3 | 12 | 0 | 0 | 12 | 0 | 2.3 | 8.33 ^c | 0 | 0 |
| 14 | 3.8 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 15 | 6.3 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 16 | 5.7 | 8 | 0 | 11 | 19 | 0 | 3.4 | 50.0 ^d | 0 | 0 |
| 17 | 4.3 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 18 | 4.4 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 19 | 4.0 | 6 | 0 | 0 | 6 | 0 | 1.5 | 50.0 ^d | 0 | 0 |
| 20 | 4.0 | 46 | 0 | 0 | 46 | 0 | 11.5 | 43.5 ^d | 2.2 ^c | 2.2 ^c |
| 21 | 1.2 | 15 | 0 | 0 | 15 | 0 | 12.9 | 13.3 ^c | 0 | 0 |
| 22 | 1.0 | 0 | 0 | 0 | 0 | 0 | 0 | NA | NA | NA |
| 23 | 1.5 | 18 | 0 | 0 | 18 | 0 | 12.0 | 5.56 ^c | 0 | 0 |
| 24 | 2.0 | 3 | 0 | 0 | 3 | 0 | 1.50 | 0 | 0 | 0 |

Abbreviations: Ap, *Anaplasma phagocytophilum*; Bb, *Borrelia burgdorferi*; Bm, *Borrelia miyamotoi*; NA, not applicable; n, number; ON, Ontario

Note: Site 13 was deleted as it was outside the city limits

^a Only adult and nymphal blacklegged ticks were tested

^b Zeros (green) no infected ticks

^c Infection rate 2–15% (yellow)

^d Infection rate > 20% (red)



Sampling was restricted from June to October due to heavy spring rainfall, which may have limited our ability to detect ticks in some sites. Detection may also have been limited by the use of drag sampling, which has been reported to be 50% sensitive (15), so some sites may have been considered falsely negative for blacklegged ticks because the density of established tick populations was very low.

Given the widespread distribution of *I. scapularis* ticks around the city of Ottawa and the potential for further expansion of tick populations, this study provides an important baseline for monitoring ticks and tick-borne pathogens of public health significance in this region. Although the bacterium causing Lyme disease was the most common type of tick infection, infections causing anaplasmosis and tick-borne relapsing fever were also found, suggesting the potential risk of emergence of these new pathogens in Ottawa.

Further research is needed to better understand the associations between expanding environmental risk in the area and human Lyme disease exposure. Ongoing active tick surveillance is needed over consecutive years. To determine whether tick populations are established, all three life stages of the tick need to be detected for two consecutive years. This information can be used to inform public health actions such as continued public health messaging to health care providers and the public to raise awareness of Lyme disease and other emerging tick-borne infections, associated risks, diagnostic tests as well as both curative and preventive measures.

Authors' statement

MAK – Conception, analysis and data interpretation, writing and editing of this article

RK, AS, CT, BT – Fieldwork and laboratory analysis, analysis and data interpretation, critical revision of this article

AD, LRL – Laboratory analysis, data interpretation, critical revision of the article

Conflict of interest

None.

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A scoping review of Lyme disease research relevant to public health

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Abstract

Lyme disease (LD) is an emerging infectious disease in Canada associated with expansion of the geographic range of the tick vector *Ixodes scapularis* in eastern and central Canada. A scoping review of published research was prioritized to identify and characterize the scientific evidence concerning key aspects of LD to support public health efforts. Prior to initiation of this review, an expert advisory group was surveyed to solicit insight on priority topics and scope. A pre-tested search strategy implemented in eight databases (updated September 2016) captured relevant research. Pre-tested screening and data characterization forms were completed by two independent reviewers and descriptive analysis was conducted to identify topic areas with solid evidence and knowledge gaps. Of 19,353 records screened, 2,258 relevant articles were included in the review under the following six public health focus areas: a) surveillance/monitoring in North America (n=809); b) evaluation of diagnostic tests (n=736); c) risk factors (n=545); d) public health interventions (n=205); e) public knowledge, attitudes and/or perceptions in North America (n=202); and f) the economic burden of LD or cost-benefit of interventions (n=32). The majority of research investigated *Borrelia burgdorferi* (n=1,664), humans (n=1,154) and *Ixodes scapularis* (n=459). Sufficient research was identified for potential systematic reviews in four topic areas: a) accuracy of diagnostic tests; b) risk factors for human illness; c) efficacy of LD intervention strategies; and d) prevalence and/or incidence of LD in humans or *B. burgdorferi* sensu stricto in vertebrate reservoirs or ticks in North America. Future primary research could focus on closing knowledge gaps, such as the role of less studied vertebrate reservoirs in the transmission cycle. Results of this scoping review can be used to quickly identify and summarize relevant research pertaining to specific questions about LD or *B. burgdorferi* sensu lato in humans, vertebrate hosts or vectors, providing evidence-informed information within timelines that are conducive for public health decision-making.

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Keywords: Scoping review, Lyme disease, public health, *Ixodes* ticks, research

Introduction

Lyme disease (LD) is the most common tick-borne infection affecting humans in North America and Eurasia (1). It is a multisystem infectious disease caused by bacteria of the *Borrelia burgdorferi* sensu lato (s.l.) species complex comprising more than 20 genospecies, including the human pathogens *B. burgdorferi* sensu stricto (s.s) in North America and *B. garinii*, *B. afzelii*, *B. burgdorferi* s.s., *B. spielmanii*, *B. bissettii* and *B. bavariensis* in Europe (2,3). In Canada, LD is an emerging issue, and human cases have increased six-fold (from 144 to 917 cases) between 2009 and 2015 as *Ixodes scapularis* and *Ixodes pacificus* ticks' range has expanded (4–6). Predictive

models suggest that factors related to climate change and land use are driving changes in the epidemiology of LD (7–9).

The tick *I. scapularis* is the main vector in northeastern and upper midwestern United States (US) and bordering areas of Canada, while *I. pacificus* is the major vector in western US and western Canada (10,11). The main vector in western Europe is *Ixodes ricinus* (3) while in eastern Europe and Asia it is *I. persulcatus* (12). Immature ticks (larvae and nymphs) require small to medium size vertebrates (rodents, reptiles and birds), while adult ticks feed on medium to large mammals (such as deer) (3,13). Other



human biting tick species share the same geographic location as known vectors of *B. burgdorferi* s.l.; however, these ticks are not competent vectors. Competence is established for some tick species that rarely feed upon humans (e.g., *I. angustus* and *I. spinipalpis*), but they could be contributing to the maintenance of *B. burgdorferi* s.l. transmission cycles involving other vertebrate reservoirs (14,15).

In general, early symptoms of human infection include a characteristic rash, fever, headache and lethargy. If untreated with antibiotics, infection can progress to early disseminated LD (with neurological or cardiac manifestations) and then to late disseminated LD (comprised of neurological manifestations and Lyme arthritis) (16).

Lyme disease is a public health issue in Canada. The number of reported LD cases increased more than six-fold, from 144 in 2009 to 917 in 2015, mainly in Central and Eastern Canada (6). To support evidence-informed decision-making on this emerging public health issue in Canada, synthesis research was prioritized to systematically identify and summarize the global evidence on LD and *B. burgdorferi* s.l. epidemiology, diagnosis, prevention and control. Synthesis research methodologies include scoping reviews on broadly defined questions and systematic reviews and meta-analysis on narrowly defined questions (17–19). Synthesis research methodologies aim to identify and summarize evidence on a topic in a systematic, reproducible and updateable manner (18,19). The objective of a scoping review is to identify the quantity and characteristics of research on a defined topic to understand where evidence saturation and knowledge gaps exist (20–23). The outputs from this study will identify areas where priority systematic reviews could be conducted and those requiring additional research to address knowledge gaps.

The objective of this review was developed with an expert advisory group and aimed to identify and characterize the available literature addressing the following aspects of LD that are relevant for public health: a) surveillance and monitoring to determine the extent of LD in humans and/or *B. burgdorferi* s.s. in vertebrate reservoirs or vectors in North America; b) evaluation of diagnostic tests; c) risk factors reported for LD in humans or exposure to *B. burgdorferi* s.l. and for the occurrence of *B. burgdorferi* s.l. in vertebrate reservoirs or vectors; d) the efficacy of public health intervention strategies to prevent and/or control LD in humans or *B. burgdorferi* s.l. in vertebrate reservoirs or vectors; e) North American public attitudes and/or perceptions towards LD and potential prevention and control strategies; and f) the economic burden or cost-benefit of interventions and potential prevention and control strategies.

Methods

Review protocol, team and expertise

A scoping review protocol, which is available upon request, was developed *a priori* to ensure the synthesis methods

are reproducible and applied consistently in a manner that minimized bias. The review team consisted of individuals with multi-disciplinary expertise in epidemiology, microbiology, veterinary public health, zoonoses, knowledge synthesis and information science.

An expert advisory group of six scientists and public health professionals was established to solicit expert insight on the LD issue, the types of research available and the scope of the review. The expert input defined the literature needed for decision-making, planning and response towards preventing and mitigating the public health risks from LD. The experts were specialists in the ecology of zoonotic diseases, laboratory and field-based surveillance, emerging and vectorborne diseases, molecular biology and veterinary medicine. Input was provided through a questionnaire and consensus meeting (materials are available upon request).

Review question and scope

The scoping review question was developed using a modified version of the Cochrane PICOS/ PECOS (population, intervention/exposure, comparison, outcomes and study design) framework (17). “What is the current state of scientific knowledge on surveillance/monitoring, prevalence and incidence, societal attitudes and/or perceptions in North America and global prevention and control strategies, risk factors and diagnosis of LD in humans and *B. burgdorferi* s.l. in vector and vertebrate reservoirs?” The “populations” of interest were humans, vectors and vertebrate reservoirs. The “interventions/exposures” were the major topic categories: surveillance/monitoring, prevalence and incidence, societal attitudes and/or perceptions in North America (Canada, US and Mexico) and global evaluation of diagnostic tests, prevention and control strategies and risk factors. The “outcomes” were LD or infection/exposure to *B. burgdorferi* s.l. To our knowledge this is the only scoping review with a broad focus on global LD research relevant for public health; a previous scoping review focused only on research from Australia (24).

Search strategy

A comprehensive search strategy, adapted to the specific requirements of each database, was implemented without limits in the following bibliographic databases on September 13, 2013 and updated on September 27, 2016: Centre for Agriculture and Bioscience (CAB) Abstracts, Scopus, PubMed, BIOSIS, PsycINFO, APA PsycNet, Sociological Abstracts, and EconLit. These databases were chosen to ensure appropriate breadth across multiple disciplines. The original search of BIOSIS (via web of knowledge) could not be updated as the database is no longer available. The search algorithm was optimized in Scopus.

The following search terms were used: (lyme OR borrelia) AND (host OR sentinel OR landscaping OR vector OR vectors OR monitor OR monitoring OR surveillance OR reservoir OR reservoirs OR prevalence OR educate OR education OR barrier OR barriers OR intervene OR intervention OR incidence OR



rate OR prevent OR prevention OR control OR risk OR risks
OR attitude OR attitudes OR perception OR perceptions OR
detection OR diagnostic).

The capacity of the electronic search to identify all relevant primary research was confirmed by hand-searching reference lists from two primary research papers (25,26), Practice Guidelines by the Infectious Diseases Society of America (10), one systematic review (27), three narrative reviews (28–30) and four European conference proceedings (31–34).

A search for grey literature on the websites of government and research organizations worldwide was conducted in February 2014, to complement the electronic database search. Only government and research reports and theses/dissertations were considered for inclusion in the review as grey literature.

Relevance screening and inclusion criteria

Citation titles and abstracts were screened using an *a priori* designed form consisting of two questions: whether the citation described primary research on LD or *B. burgdorferi* s.l. and whether it was relevant to one or more aspects of the research question. Primary research was considered original research where authors generated and reported their own data. Articles in English, French and Spanish were included while other languages were excluded due to limited translation resources.

Data characterization and extraction

Complete articles of potentially relevant citations were reviewed using a data characterization and utility (DCU) form consisting of 20 questions designed *a priori* and available upon request. These questions aimed to confirm article relevance, data utility and allow extraction of the main article characteristics to properly classify the study methodology, population(s), laboratory tests, objectives and outcome characteristics. This could result in one study meeting one, two or more categories.

Scoping review management, data charting and analysis

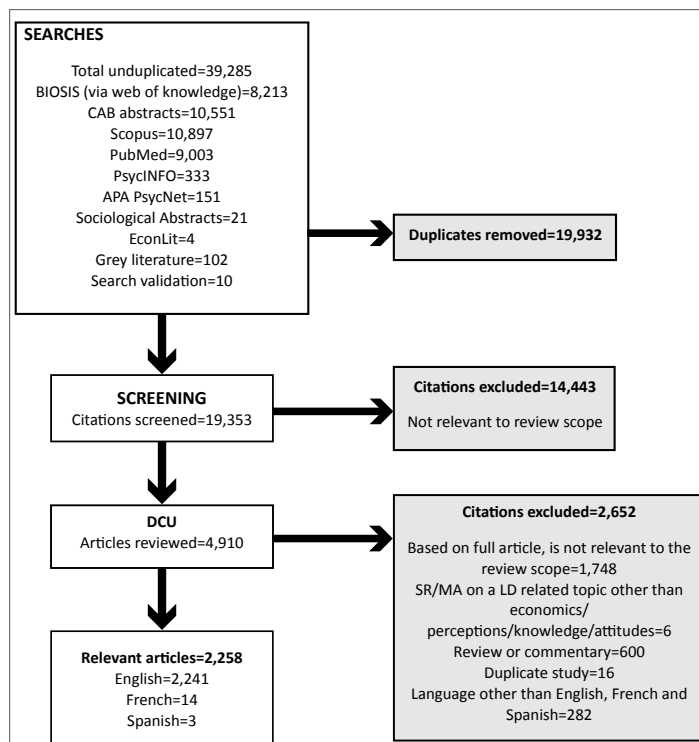
The search results were imported, de-duplicated and managed in reference management software (RefWorks 2.0; ProQuest LLC, Bethesda, Maryland, US). The scoping review was managed in a web-based electronic systematic review management platform (DistillerSR, Evidence Partners, Ottawa, Ontario, Canada). Two reviewers independently completed all steps of the scoping review. Eight reviewers pre-tested the relevance screening tool with 50 abstracts ($\kappa > 0.8$) and the DCU form using three articles. Discrepancies between reviewers were examined and following discussion the form was updated to increase clarity and relevance of questions. The protocol and a reviewer guideline were used to standardize reviewer answers and help resolve conflicts. Resolution of conflicts between reviewers was reached by consensus or by consultation with a third reviewer. Data collected in the DCU form were exported into Excel

spreadsheets (Microsoft Corporation, Redmond, Washington, US), formatted and analyzed descriptively (frequencies and percentages) to facilitate categorization and charting.

Results

The search identified 19,353 abstracts and titles and 4,910 full papers screened for relevance (**Figure 1**). The scoping review included 2,258 relevant articles (full list provided in the [Supplementary References](#)) (35). The majority of the included research was published after 1990 (91.4%; $n=2,064$) and of those (82.8%; $n=1,869$) were journal articles (**Appendix 1**). Included articles were in English ($n=2,241$), French ($n=14$) and Spanish ($n=3$); 282 potentially relevant articles were excluded from the review because they were in other languages (e.g., German, $n=75$ articles; Russian, $n=53$; and Polish, $n=43$). The excluded studies represent an unknown language bias for some focus areas: the evaluation of diagnostic tests ($n=131$); risk factors ($n=94$); interventions ($n=64$); and economic evaluations of the burden of LD ($n=7$). There was a high proportion of North American research (70.8%; $n=1,597$); this likely results from non-North American exclusions under surveillance and public attitudes and/or perceptions categories in addition to the language exclusions.

Figure 1: Flow diagram of articles through scoping review

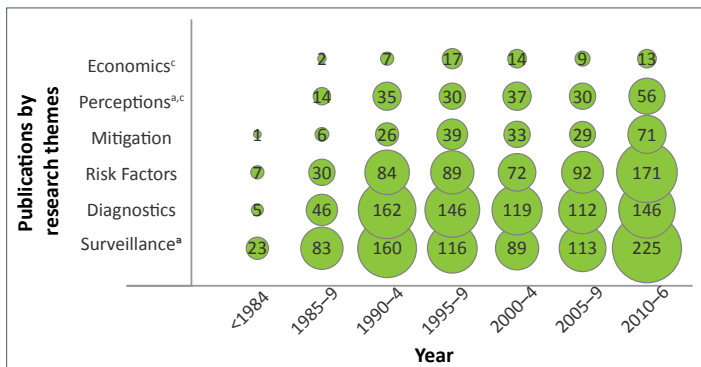


Abbreviations: CAB, Centre for Agriculture and Bioscience; DCU, data characterization and utility; LD, Lyme disease; SR/MA, systematic review/meta-analysis



Research activity across the six focus areas has changed over time (Figure 2) starting with the earliest relevant paper by Steere et al., 1977 that described an outbreak of Lyme arthritis, mainly in children (36).

Figure 2: Bubble plot of research themes by publication year (N=2,258)^{a,b}



Note: Bubble plot of the major Lyme disease or *B. burgdorferi* s.l. research themes by publication year (N=2,258)

^a Included studies are only from North America

^b Article may be included in more than one category, so numbers are >2,258

^c This includes the qualitative research on the topic

Legend: The size of the bubble is proportional to the volume of research noted in each bubble

Since then, the majority of LD research has focused on surveillance (n=809), diagnostic tests (n=736) and identification of risk factors (n=545) on all sample population categories (Table 1). The least amount of primary research has been on the economic burden or cost-benefit of interventions for LD (n=32).

Table 1: Heat chart of the number of studies for each of the six focus areas of Lyme disease by population category (N=2,258)

| Study focus | Total studies ^a | Human Studies | Vertebrate reservoirs | Vectors |
|--|----------------------------|------------------|-----------------------|------------------|
| Surveillance and monitoring in North America | 809 ^c | 283 ^d | 448 ^d | 432 ^d |
| Accuracy of diagnostic tests | 736 ^c | 546 ^d | 158 ^e | 89 ^e |
| Risk factors | 545 ^d | 262 ^d | 202 ^d | 297 ^d |
| Public health interventions | 205 ^d | 72 ^e | 98 ^e | 106 ^e |
| Attitudes and/or perceptions in North America | 202 ^d | 202 ^d | 0 ^e | 0 ^e |
| Economic burden and cost-effective interventions | 32 ^{b,e} | 32 ^e | 0 ^e | 0 ^e |

Note: Heat chart of the number of studies underpinning each of the six focus areas of Lyme disease or *B. burgdorferi* s.l. research included in this scoping review (n=2,258) by population category

^a Numbers do not add up horizontally or vertically to "total studies" as an article can cover two or more study themes

^b These 32 are primary studies – the number in the bubble chart includes reviews and commentaries used in the qualitative piece

^c Heat rate 809–736 (red)

^d Heat rate 202–546 (yellow)

^e Heat rate 1–158 (green)

The 2,258 papers were compared not only by publication year (Figure 1) and study focus groups (Table 1), but also by pathogen, host and vectors (Appendix 2). The number and percentage of papers attributed to the different species of the *B. burgdorferi* s.l. complex are presented as well as the populations studied. The three most investigated human pathogens were *B. burgdorferi* s. (73.7%; n=1,664), *B. afzelii* (9.7%; n=220) and *B. garinii* (9.7%; n=219). Common host species categories included humans (51.2%; n=1,154), rodents (22.5%; n=508) and dogs (10.1%; n=228). Frequently investigated vectors included *I. scapularis* (20.3%; n=459), *I. ricinus* (6.6%; n=149) and *Dermacentor variabilis* (5.0%; n=112). Many non-*Ixodes* tick species (e.g., *D. variabilis*) and one *Ixodes* species (*I. cookei*) are incompetent or inefficient vectors of *B. burgdorferi* s.l. (37), but were sampled and tested in studies of tick range and habitat because their range overlaps with the known vectors.

Surveillance and monitoring in North America

Epidemiological surveys or surveillance and monitoring programs (Table 2) and their results in North America represented 35.9% of articles (n=809) and provided results for one or more population categories; humans with LD 12.6% (n=283) or *B. burgdorferi* s.s. infection in vertebrate reservoirs (19.8%; n=448) or vectors (19.1%; n=432). Seven articles provided an evaluation of

Table 2: Summary of surveillance/monitoring studies in North America (n=809)

| Surveillance type/monitoring approach | Vectors (n=432) | | Vertebrate reservoirs (n=448) | | Humans (n=283) | |
|---------------------------------------|-----------------|----------------|-------------------------------|----------------|----------------|----------------|
| | n ^a | % ^a | n ^a | % ^a | n ^a | % ^a |
| Active | | | | | | |
| Targeted sampling ^b | 364 | 84.3 | 308 | 68.8 | 121 | 42.5 |
| Using sentinel animals | 63 | 14.6 | 102 | 22.8 | 11 | 3.9 |
| Passive | | | | | | |
| Physician/veterinarian reporting | 50 | 11.6 | 41 | 9.2 | 135 | 48.1 |
| Public reporting/submission | 31 | 7.2 | 21 | 4.7 | 16 | 5.6 |
| Syndromic surveillance | 0 | 0.0 | 3 | 0.7 | 24 | 8.4 |
| Other | 0 | 0.0 | 1 ^c | 0.2 | 2 ^d | 0.7 |
| Laboratory-based ^e | 10 | 2.3 | 24 | 5.4 | 61 | 21.4 |
| Evaluation of surveillance methods | 0 | 0.0 | 2 | 0.4 | 7 | 2.5 |

Abbreviation: n, number

Note: Summary of surveillance/monitoring approaches and surveys on the burden of LD in humans or *B. burgdorferi* s.s. in vectors or vertebrate reservoirs captured in the scoping review (n=809)

^a Article may be included in more than one category, so numbers are >809 and percentages will not equal 100%

^b Includes both formal surveillance programs and epidemiological surveys

^c Hunter-killed deer

^d Hospital records

^e Only laboratory test submissions are identified; patients who do not seek medical attention or seek medical attention but are not tested will not be captured by this type of surveillance system



surveillance programs for humans (38–44), two for vertebrate reservoirs (45,46) and none for vector surveillance programs.

Studies include both formal surveillance programs with ongoing (routine) active collection and analysis of data, as well as epidemiological surveys that actively collect and analyse data over a specific and/or defined time period. Laboratory-based surveillance differs from population-wide surveillance and passive physician reporting schemes in that only laboratory test submissions are identified by this type of surveillance. Patients who do not seek medical attention or seek medical attention but are not tested will not be captured by this type of surveillance system.

Accuracy of diagnostic tests

A large number of studies, 32.6% (n=736), evaluated the accuracy of diagnostic and/or screening tests for *B. burgdorferi* s.l. infection or exposure (Appendix 1). Of these, 546 articles evaluated tests for humans, 158 for vertebrate reservoirs and 89 for vectors. More information on this is available in a separate publication (47).

Risk factors

Risk factors related to human or host exposure to ticks, acquiring LD in humans or *B. burgdorferi* s.l. infection in hosts or ticks were reported in 24.1% (n=545) of included articles (Table 3). One or more risk factors were significant in most of these articles (n=425 of the 545 articles). The most frequently evaluated potential risk factors were related to geography (region, type of development; 13.0%; n=294), and landscape features (e.g., presence of leaf litter, elevation, woodland type; 9.2%; n=207).

Table 3: Summary of risk factors studies (n=545)

| Risk factor category ^a | Human (n=262 studies) ^a | Vertebrate reservoirs (n=202 studies) ^a | Vector (n=297 studies) ^a |
|--|--|---|---|
| Host demographic factors ^a | | | |
| Age of cases | 111 | 66 | Life stage 14 |
| Gender | 99 | 46 | 7 |
| Other | 28 ^b | 44 ^c | 0 |
| Human behaviours | | | |
| Occupational risk | 108 | - | - |
| Outdoor recreational activities (e.g., picnics, camping) | 65 | - | - |
| Pet ownership | 54 | - | - |
| History/number of tick bites | 34 | - | - |
| Gardening or yard work | 18 | - | - |
| Walking or jogging in woods | 16 | - | - |
| Clearing brush in yard during spring and summer | 10 | - | - |

Table 3: (continued) Summary of risk factors studies (n=545)

| Risk factor category ^a | Human (n=262 studies) ^a | Vertebrate reservoirs (n=202 studies) ^a | Vector (n=297 studies) ^a |
|---|--|---|---|
| Other ^d | 37 | - | - |
| Geographic | | | |
| Region | 83 | 98 | 102 |
| Urban, suburban or rural setting | 33 | 15 | 18 |
| Living in a single family home with yards, attached land or woods | 14 | 0 | 7 |
| Other | 11 ^e | 1 ^f | 14 ^g |
| Month of year | 60 | 97 | 99 |
| Climate | | | |
| Temperature | 22 | 28 | 64 |
| Rainfall/precipitation | 14 | 26 | 35 |
| Relative humidity | 5 | 4 | 26 |
| Other | 5 ^h | 6 ⁱ | 9 ^j |
| Landscape features | | | |
| Woodland type | 28 | 34 | 94 |
| Drainage | 3 | 4 | 3 |
| Vegetation type | 5 | 14 | 0 |
| Birdfeeders | 5 | 0 | 2 |
| Deer on properties | 15 | 4 | 10 |
| Rock walls/wood piles | 4 | 1 | 3 |
| Wooded properties | 9 | 0 | 4 |
| Elevation/slope of land | 11 | 22 | 50 |
| Deer on residential property | 4 | 0 | 8 |
| Presence of moist humus and leaf litter | 8 | 4 | 17 |
| Animal densities | 3 | 2 | 3 |
| Other | 39 ^k | 31 ^l | 75 ^m |

Abbreviation: n, number; -, not applicable

Note: Summary of risk factors investigated for human exposure to ticks or acquisition of Lyme disease, vertebrate reservoir exposure to ticks and *B. burgdorferi* s.l. infection in vertebrate reservoirs or ticks (n=545)

^a Multiple answers were allowed per article in some categories so the sum of articles across risk factor categories is >545

^b Includes household income, race, education and duration of residency

^c Includes specificity for *Borellia* sp., species, body size and breed

^d Includes history of travel to tick-endemic areas, contact with animals, co-morbidities/infections, blood transfusions, pregnancy/fetal exposure, smoking and engagement in at-risk behaviors for tick bites

^e Includes different habitats/ecosystems, size of area, proximity of residence or sites, entomologic risk index, residential development within recently reforested suburban areas and low density residential development

^f Woodland vs household habitats

^g Includes attitude and longitude, different habitats, zones with different deer densities, size and recently deforested

^h Includes type of climate, air pressure and wind speed, monthly soil moisture and growing days

ⁱ Includes growing days and snow depth

^j Includes saturation deficit, snow cover, Mediterranean climate, wind conditions, solar insolation, North Atlantic Oscillation indices, light intensity, cool moist winters and warm dry summers

^k Includes forest cover, proximity to woods, vegetation type, patch size, weeds in yard, vegetable garden, playscapes, fencing, presence of lizards, beaches or dunes

^l Includes vegetation type, soil characteristics, maturity of trees, land use, impact of sudden oak death, vegetation index, presence of lizards and patch size

^m Landscape features (vectors) other: habitat type, forest fragmentation, vegetation index, maturity of trees, land use, patch size, soil characteristics, proximity to forest, impact of sudden oak death, downed wood, beaches or dunes, forestry, density of trees, plant biomass, playscapes, property size



Many studies examined human risk factors related to high risk behaviours (e.g., walking in the woods and gardening; n=32) and demographics (e.g., age and gender; n=213).

Public health interventions

Intervention efficacy to prevent tick exposure, LD in humans or *B. burgdorferi* s.l. infection in vertebrate reservoirs or vectors was reported in 9.1% (n=205) of included articles. Vaccination (3.5%; n=78), was the most evaluated type of intervention for humans (n=26), dogs (n=25), horses (n=1) or animal models using rodents, birds, chickens, embryonated chicken eggs and Rhesus monkeys (n=28) (Table 4). Chemical control measures were reported in 2.5% (n=56) of articles, including treatment of vertebrate hosts, use of persistent acaricides and spraying of acaricides or desiccants on vegetation. A range of personal protective measures for humans were also evaluated in 2.7% of articles (n=62).

Table 4: Summary of intervention categories (n=205)

| Intervention | n ^a | % ^a |
|---|----------------|----------------|
| Vaccination | | |
| Vaccination of humans | 26 | 12.7 |
| Dogs | 25 | 12.2 |
| Horses | 1 | 0.5 |
| Animal models for vaccine development ^b | 28 | 13.7 |
| Chemical control measures | | |
| Use of persistent acaricides | 17 | 8.3 |
| Rodent-targeted tick-control device use | 15 | 7.3 |
| Spray or broadcast acaricides or desiccants to vegetation | 13 | 6.3 |
| Other ^c | 11 | 5.4 |
| Personal protective measures for humans ^d | 62 | 30.2 |
| Public education to decrease risk of Lyme disease infection | 19 | 9.3 |
| Landscape features and modifications ^e | 18 | 8.8 |
| Other ^f | 28 | 13.7 |

Abbreviation: n, number

Note: Summary of intervention categories that were evaluated for the prevention of tick exposure or LD in humans or *B. burgdorferi* s.l. infection in vertebrate hosts or vectors (n=205)

^a Article may be included in more than one category so numbers are >205 and percentages will not equal 100%

^b Includes rodents, birds, embryonated chicken eggs and Rhesus monkeys

^c Includes treatment of tick hosts with acaricides

^d Includes checking for ticks during/after outdoor activity, wearing long pants and/or lightly-coloured clothing or clothing treated with permethrin insecticide, wearing repellents, avoidance of high risk areas, tucking pants into socks, bathing after spending time outdoors, wear long-sleeved shirt/hat and parental skin inspection

^e Includes fencing, burning/clearing vegetation, frequent mowing, leaf-litter clearing, small scale landscaping, branch trimming, presence of a mulch or gravel dry barrier where lawns abut woods

^f Includes culling deer, biological control of ticks, prophylaxis for humans, checking pets for ticks, unspecified interventions to lower tick abundance, removal of lizards, orally administering an antibiotic to rodents

Attitudes and/or perceptions in North America

Public knowledge, attitudes and/or perceptions towards LD and potential prevention and control strategies in North America were reported in 8.9% (n=202) articles. The general public (n=68)

and/or physicians (n=32) were usually the target populations and the research aim was to assess knowledge of LD (n=131), perception of severity and vulnerability to LD (n=73), protective/risky behaviors (n=73) and knowledge and attitudes towards protection measures (n=56) (Table 5). Within this literature, there are examples of how well-designed and relatively

Table 5: Articles reporting on public knowledge, attitudes or perceptions in North America (n=202)

| Characteristic | n | % ^a (n=202) |
|---|-----|---------------------------|
| Publication date | | |
| Before 1990 | 14 | 6.9 |
| 1990–1994 | 35 | 17.3 |
| 1995–1999 | 30 | 14.9 |
| 2000–2004 | 37 | 18.3 |
| 2005–2009 | 30 | 14.9 |
| >2010 | 56 | 27.7 |
| Document type | | |
| Journal article | 137 | 67.8 |
| Book chapter | 16 | 7.9 |
| Other ^b | 49 | 24.3 |
| Study type | | |
| Primary research, quantitative | 76 | 37.6 |
| Primary research, qualitative | 8 | 4.0 |
| Primary research, mixed methods | 3 | 1.5 |
| Book chapter/review/commentary | 115 | 56.9 |
| Study design | | |
| Observational study | 74 | 85.1 ^c |
| Cross-sectional | 66 | 75.9 |
| Cohort | 2 | 2.3 |
| Case-control | 2 | 2.3 |
| Prevalence survey | 3 | 3.4 |
| Surveillance or monitoring program | 1 | 1.1 |
| Experimental study | 9 | 10.3 |
| Controlled trial | 7 | 8.0 |
| Quasi experiment | 2 | 2.3 |
| Qualitative study | 6 | 6.9 |
| Mixed methods | 1 | 1.1 |
| Study location | | |
| United States | 182 | 90.1 |
| Canada | 27 | 13.4 |
| Stakeholder populations investigated for contextual information | | |
| General public | 68 | 33.7 |
| Physicians | 32 | 15.8 |
| Other medical or public health professionals | 16 | 7.9 |
| Lyme disease experts/researchers | 12 | 5.9 |
| Government personnel | 9 | 4.5 |
| Children/students | 7 | 3.5 |
| Outdoor workers | 6 | 3.0 |
| Veterinarians | 3 | 1.5 |
| Other ^d | 11 | 5.4 |
| Method of contextual data collection | | |
| Quantitative questionnaire or survey | 75 | 37.1 |
| Analysis of documents | 25 | 12.4 |
| Qualitative interview | 15 | 7.4 |
| Other ^e | 18 | 8.9 |

**Table 5: (continued) Articles reporting on public knowledge, attitudes or perceptions in North America (n=202)**

| Characteristic | n | % ^a (n=202) |
|---|-----|---------------------------|
| Not specified | 48 | 23.8 |
| Article focus | | |
| Knowledge | 131 | 64.9 |
| Severity/vulnerability | 73 | 36.1 |
| Behaviours | 73 | 36.1 |
| Efficacy of protection measures | 56 | 27.7 |
| Other ^f | 43 | 21.3 |
| Theories of human behaviour used to inform data collection | | |
| Health belief model | 17 | 8.4 |
| Other ^g | 18 | 8.9 |
| Formats used to report quantitative study results | | |
| Prevalence | 33 | 16.3 |
| Measures of association | 27 | 13.4 |
| Ordinal/Likert scale | 22 | 10.9 |
| Model | 19 | 9.4 |
| 2 x 2 data | 18 | 8.9 |
| Continuous outcome | 11 | 5.4 |
| Non extractable | 12 | 5.9 |
| Need for additional studies | 59 | 29.2 |

Abbreviation: n, number

Note: Articles reporting on public knowledge, attitudes or perceptions towards Lyme disease or prevention and control strategies in North America (n=202)

^a Article may be included in more than one category so percentages will not equal 100%^b Includes newspaper, letter to the editor, abstract, thesis, commentary/editorial, government or research report, conference summary, workshop report, poster/slide deck/presentation, book, meeting report and guidelines^c Percent of primary research articles (n=87)^d Includes non-governmental organization personnel, Lyme patients, immigrants, nursery/landscape employees, media, nudists and pet owners^e Includes conference/workshop discussion notes, author's opinion/commentary, focus groups, patient diaries and educational intervention^f Includes vaccination, diagnosis/tests, willingness to pay for protection, Lyme politics/media, patient advocacy/experience, guidelines, expert opinion of risk factors, trust in doctors, and toxic or environmental effects of control measures^g Includes theory of planned behaviour, behaviour motivation, social learning theory (risk compensation, accuracy hypothesis, risk reappraisal hypothesis, preventative belief model, social cognition theory, experimental learning loop, motivated reasoning, dual-processing models, attribution of responsibility)

inexpensive health education messages, grounded on social learning theory, can result in increased protective behaviors and a reduced rate of LD (48–53).

Economic burden and cost-effective interventions

Primary studies of the economic burden of LD or cost-benefit of interventions were reported in 1.4% (n=32) of the articles. These included analysis of the cost of diagnostic tests for LD, health care costs for patients and cost of particular interventions.

Discussion

This scoping review provides an assessment of the quantity and characteristics of the global evidence for six focus areas of LD and *B. burgdorferi* s.l. research on humans, vertebrate reservoirs and vectors, which included surveillance and monitoring in North America, evaluation of diagnostic tests, risk factors,

interventions, public attitudes and perceptions in North America and the economic burden or cost benefit of public health interventions.

Knowledge saturation and gaps

Research and surveillance data have been consistently collected throughout North America since 1995. Most of LD in humans are from passive surveillance of LD case information. A smaller group of epidemiological studies examined exposure to *B. burgdorferi* s.s. by screening apparently healthy populations. Together these data provide some indication of how much exposure is occurring in areas where *I. scapularis* and other competent vectors have become established and where *B. burgdorferi* s.s. circulates. Additionally, epidemiological surveys were frequently conducted to evaluate *B. burgdorferi* s.s. in vertebrate reservoirs and vectors as opposed to data collected through a surveillance program. This information is key to identifying geographic risk status for public health, which aids in the diagnosis of LD in humans and decision-making on appropriate prevention and control strategies (4,54). Identification of *B. burgdorferi* s.s. in vectors and vertebrates also leads to experimental studies to establish competence for transmission and the role different species may play in the maintenance and spread of *B. burgdorferi* s.s. and how this may change the risk of human exposure to *B. burgdorferi* s.s. in different areas. There is sufficient evidence to conduct a systematic review on the historical evidence of the burden of LD and *B. burgdorferi* s.s. in North America, which would allow an examination of how this changes over time. Some knowledge gaps were also noted pertaining to research on the role of migratory birds in the spread of *B. burgdorferi* s.s. to new areas. The contribution of potential vectors and vertebrate reservoirs to the transmission of *B. burgdorferi* s.s. has not been established for all species.

The recommended protocol for LD diagnosis is based on clinical symptoms, a history of exposure to infected ticks and/or travel to an endemic area, which may also be supplemented by diagnostic testing (55). Recommended diagnostic testing in Canada, the US and most European countries includes a two-tiered serologic testing protocol where a positive or equivocal enzyme immunoassay (EIA) screening test is followed by a confirmatory Western blot (55–58). Improvements to LD diagnostic tests, particularly improved sensitivity for testing early stages of LD, is an active research area. Thus, periodic updates to the two recently published systematic reviews on the accuracy of diagnostic tests for humans in North America, prioritized from this scoping review, and Europe is warranted (47,59).

There are many parallels between the significant risk factors studied and the intervention strategies evaluated, particularly for human personal protective measures and outcomes of tick presence or risk of tick exposure and landscape modification. Overall, the quantity of research on each risk factor or intervention was quite small; most authors highlighted additional needed research. Even though there may not be a lot of



research, systematic reviews summarizing evidence on significant risk factors and intervention efficacy would be useful for the development of new prevention and education strategies for public health. Vaccination was the only intervention category for which there were many studies evaluating potential or commercial vaccines for humans, dogs or horses. No further work on this topic is warranted as a systematic review was recently published (60). Lyme vaccines are currently approved and used in dogs, and there has not been a commercial vaccine available for humans since the withdrawal of LYMERix in 2002 (61–64).

Research estimating the economic impact of LD or public attitudes and perceptions compliment many of the other research focuses. Where economic information is useful in placing an issue on the public health agenda and for the justification of allocated resources (1,65), understanding the drivers and barriers to behavior change can determine the success of a public education intervention. This review captured several different types of economic models and data that could be used as a framework to estimate the cost of LD or other outcomes using local cost estimates. Similarly, research investigating public attitudes and/or perceptions towards LD and potential prevention and control strategies provides an in depth understanding of the context and would be a complimentary addition to results from systematic reviews of public health interventions. These include evaluations of knowledge, attitudes, willingness to pay and the impact of public programs on behaviour (e.g., the use of personal protective measures) (26). Several limitations to this research exist: few studies were based on a model of human behavior change, studies were small thus less generalizable and surrogate and subjective outcome measures for behavior change were often used due to difficulties in obtaining objective measurements (66–68).

Limitations of study

Limitations to this scoping review include the language bias noted above and the potential for publication bias if all relevant research is not identified; the impact of these biases on the review results is largely unknown. There may also be limitations in the utility of the review due to the scope, but this depends on the needs of the end user.

This review focuses on the utility of evidence from each focus area and highlights where there is knowledge saturation and gaps in the literature.

Conclusion

This scoping review is an evidence-informed overview of the quantity and characteristics of the research underpinning each focus area; surveillance and monitoring, diagnostic tests, risk factors, interventions, attitudes and perceptions and economic research on LD and *B. burgdorferi* s.l. in humans, vertebrate reservoirs and vectors. The review provides a very broad understanding of what is known and unknown on this topic at this time and the identified knowledge gaps can be used to prioritize funding for future research. The searchable database created during this scoping review will facilitate addressing both

anticipated and unanticipated questions using a systematic review methodology along timelines that are more conducive to decision-making, which is only possible because the relevant research has already been identified and characterized. Thus, several systematic reviews (e.g., on risk factors and interventions for each study population) could be undertaken to provide evidence-informed summaries of information on LD and *B. burgdorferi* s.l. where estimates of specific outcomes are needed for decision-making.

Authors' statement

JG – Conceptualization, methodology, formal analysis, investigation, data collection and curation, writing-original draft, review and editing, visualization, supervision, project administration

IY – Conceptualization, methodology, investigation, review and editing, visualization

SH – Formal analysis, investigation, data collection and curation, review and editing, visualization

MM – Investigation, data collection and curation, writing-review and editing

LW – Conceptualization, methodology, formal analysis, investigation, data collection and curation, writing-original draft, writing-review and editing, visualization

Conflict of interest

None.

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Appendices

Appendix 1: General characteristics of 2,258 included articles

| Characteristic | n | % of total |
|---|--------------------|------------|
| Publication date | | |
| before 1990 | 194 | 8.6 |
| 1990–1994 | 406 | 18.0 |
| 1995–1999 | 398 | 17.6 |
| 2000–2004 | 334 | 14.8 |
| 2005–2009 | 342 | 15.2 |
| >2010 | 584 | 25.8 |
| Document type | | |
| Journal article | 1,869 | 82.8 |
| Conference proceeding/abstract | 183 | 8.1 |
| Government or research report | 79 | 3.5 |
| Thesis | 21 | 0.9 |
| Book chapter | 16 | 0.7 |
| Other ^a | 90 | 4.0 |
| Study location ^b | | |
| North America (Canada, United States, Mexico) | 1,597 ^c | 70.8 |
| Europe | 615 | 27.2 |
| Asia | 57 | 2.5 |
| Central/South America | 7 | 0.3 |
| Australasia | 6 | 0.3 |
| Africa | 3 | 0.1 |
| Study design ^b | | |
| Evaluation of diagnostic test ^d | 736 | 32.6 |
| Observational study | | |
| Cross-sectional | 664 | 29.4 |
| Prevalence surveys | 371 | 16.4 |
| Case study or case-series | 49 | 2.2 |
| Cohort | 47 | 2.1 |
| Case-control | 34 | 1.5 |
| Experimental study | | |
| Controlled trial | 93 | 4.1 |
| Challenge trial | 68 | 3.0 |
| Quasi experiment | 13 | 0.6 |
| Surveillance program | 181 | 8.1 |
| Risk assessment | 11 | 0.5 |
| Qualitative study | 13 | 0.6 |
| Economic model | 8 | 0.4 |
| Disease transmission model | 3 | 0.1 |
| Other ^e | 26 | 1.2 |

Appendix 1: (continued) General characteristics of 2,258 included articles

| Characteristic | n | % of total |
|--|-------|------------|
| Format used to report study results | | |
| Prevalence | 1,278 | 56.6 |
| Dichotomous outcome | 556 | 24.6 |
| Continuous outcome | 358 | 15.8 |
| Measure of association (e.g., odds ratio, relative risk) | 202 | 8.9 |
| Spatial analysis (includes satellite/remote sensing) | 43 | 1.9 |
| Ordinal/Likert scale scores | 33 | 1.5 |
| Model outcomes | | |
| P-values | 265 | 11.7 |
| Sensitivity and specificity | 121 | 5.4 |
| Coefficients/beta parameters | 97 | 4.3 |
| Confidence limits | 96 | 4.2 |
| R ² | 83 | 3.7 |
| Standard error/standard deviation | 77 | 3.4 |
| Sensitivity only | 13 | 0.6 |
| Specificity only | 7 | 0.3 |
| Other ^f | 11 | 0.5 |
| Non-extractable format | 798 | 35.3 |
| Author identified need for more studies (yes vs no) | 806 | 35.7 |

Abbreviations: n, number; R², the coefficient of determination and is the proportion of the variance in the dependent variable that is predictable from the independent variable(s)

^a Other document types include: letters to the journal editor or correspondence, brief communications, newsletters/bulletins, guidelines/policy statements, poster, patent, PowerPoint presentation

^b Multiple answers allowed per article in some categories (i.e., percentages do not add to 100%)

^c Only relevant research from North America on surveillance, and public and health professionals/physicians knowledge, attitudes and/or risk perceptions towards LD and potential prevention and control strategies was characterised, consequently there was considerably more research characterised from North America

^d Enzyme-linked immunosorbent assay (ELISA), enzyme immunoassay (EIA) or immunofluorescence assay (IFA), Western blot, polymerase chain reaction (PCR) tests, culture and microscopy were most frequently reported

^e Includes spatial analysis, predictive models, cost effectiveness, risk models and longitudinal correlation

^f Includes simulation model, percentage of total surveyed, presence or absence, behaviour results, percent reduction, percentage of control, genomic information and tick bite reduction ratio



Appendix 2: Summary of primary research articles on *B. burgdorferi* s.l, host species and vectors (N=2,258)

| Pathogen, host and vector | Number of studies ^a | % ^a |
|---|--------------------------------|----------------|
| <i>Borrelia burgdorferi</i> s.l. species (n=1,808) | | |
| <i>burgdorferi</i> s.s. | 1,664 | 73.7 |
| <i>garinii</i> | 219 | 9.7 |
| <i>afzelii</i> | 220 | 9.7 |
| <i>burgdorferi</i> s.l. ^b | 118 | 5.3 |
| <i>valaisiana</i> | 57 | 2.5 |
| <i>miyamotoi</i> | 53 | 2.3 |
| <i>lonestari</i> | 44 | 1.9 |
| <i>bissetti</i> | 31 | 1.4 |
| <i>spielmanii</i> | 25 | 1.1 |
| <i>lusitaniae</i> | 22 | 1.0 |
| <i>Borrelia</i> spp. | 18 | 0.8 |
| <i>andersonii</i> | 12 | 0.5 |
| <i>anserina</i> | 10 | 0.4 |
| Other ^c | 128 | 5.7 |
| Host species (n=1,841) | | |
| Humans | 1,154 | 51.2 |
| Rodents | | |
| Mouse | 261 | 11.5 |
| Voles | 78 | 3.5 |
| Rat | 59 | 2.6 |
| Chipmunk | 51 | 2.3 |
| Squirrel | 50 | 2.2 |
| Other ^d | 9 | 0.4 |
| Dogs (companion) | 228 | 10.1 |
| Deer | 138 | 6.1 |
| Birds | 76 | 3.4 |
| Horses | 60 | 2.7 |
| Shrew | 44 | 1.9 |
| Farm animals ^e | 35 | 1.5 |
| Raccoons | 32 | 1.4 |
| Rabbits | 28 | 1.2 |
| Cats (companion) | 26 | 1.2 |
| Lizards | 22 | 1.0 |
| Opossums | 17 | 0.8 |
| Other ^f | 75 | 3.3 |
| Vectors (n=789) | | |
| <i>Ixodes scapularis</i> | 459 | 20.3 |
| <i>Ixodes ricinus</i> | 149 | 6.6 |
| <i>Dermacentor variabilis</i> | 112 | 5.0 |
| <i>Ixodes ipacificus</i> | 104 | 4.6 |

Appendix 2: (continued) Summary of primary research articles on *B. burgdorferi* s.l, host species and vectors (N=2,258)

| Pathogen, host and vector | Number of studies ^a | % ^a |
|---------------------------------------|--------------------------------|----------------|
| Vectors (n=789) | | |
| <i>Amblyomma americanum</i> | 92 | 4.1 |
| <i>Haemaphysalis leporispalustris</i> | 46 | 2.0 |
| <i>Ixodes dentatus</i> | 32 | 1.4 |
| <i>Amblyomma maculatum</i> | 27 | 1.2 |
| <i>Dermacentor occidentalis</i> | 26 | 1.2 |
| <i>Dermacentor albipictus</i> | 27 | 1.2 |
| <i>Ixodes spinipalpis</i> | 24 | 1.1 |
| <i>Ixodes cookei</i> | 24 | 1.1 |
| <i>Rhipicephalus sanguineus</i> | 18 | 0.8 |
| <i>Ixodes muris</i> | 20 | 0.9 |
| <i>Ixodes angustus</i> | 18 | 0.8 |
| <i>Ixodes persulcatus</i> | 16 | 0.7 |
| <i>Ixodes texanus</i> | 12 | 0.5 |
| <i>Ixodes affinis</i> | 13 | 0.6 |
| Other ^g | 207 | 9.2 |

Abbreviations: n, number; s.l., sensu lato; spp., species

^a Multiple answers allowed per article in some categories (i.e. percentages do not add to 100%)

^b Article reported *B. burgdorferi* s.l.

^c Other *Borrelia* species: *B. americana*, *B. bavariensis*, *B. coracae*, *B. hermsii*, *B. japonica*, *B. parkeri*, *B. recurrentis*, and *B. turicatae*. The species in bold are not associated with LD but were captured in our search and included for completeness. In five studies only "presence of spirochetes" was reported. Twenty-two other species were investigated in only one study (details are not reported here)

^d Including woodchucks and other rodents types (investigated in only one study)

^e Including cattle, sheep and goats

^f Including bears, feral pigs and cats, fox, coyotes, Mustelidae family (weasels, otters and minks), Rhesus monkeys, skunks, moose, elk, wild sheep, bats, wolves, moles and other animals (investigated in only one study)

^g Other "possible" vectors investigated in primary studies included the following: *Amblyomma* species: *A. cajennense*, *A. inornatum*, *A. longirostre* (Koch); *Dermacentor* species: *D. andersoni*, *D. marginatus*, *D. nigrolineatus*, *D. parumapertus*, *D. reticulatus*; *Ixodes* species: *I. auritulus*, *I. baergi*, *I. brunneus*, *I. hearlei*, *I. hexagonus*, *I. jellison*, *I. kingi*, *I. marxi*, *I. minor*, *I. neotomae*, *I. sculptus*, *I. trianguliceps*, *I. woodi*, *I. uriae*; *Haemaphysalis* species: *H. concinna*, *H. qinghaiensis*, *H. punctata*; *Rhipicephalus* species: *R. annulatus*, *R. bursa*, *R. turanicus* and *R. (Boophilus) microplus*



Results of a population screening intervention for tuberculosis in a Nunavik village, Quebec, 2015–2016

R Dion^{1*}, M Brisson², JF Proulx², H Zoungrana²

Abstract

Background: A small village in Nunavik, Quebec experienced a tuberculosis (TB) outbreak in 2012–2013 and then a resurgence in 2015–2016. Cases were still occurring, despite the fact that contact tracing had already been conducted on one quarter of the population. A decision was taken to conduct large-scale screening of the population for TB.

Objective: To describe the results of a population-based TB screening intervention designed to identify individuals with latent TB infection (LTBI) or active TB requiring treatment.

Methodology: The history of TB infection (either active TB or LTBI, defined as a positive tuberculin skin test result of at least 5 mm induration) and treatment (considered adequate if at least 80% of prescribed doses were taken) were determined. Those who were two years of age and older and had not been included in contact tracing after June 1, 2015 were included for TB screening (n=1,026 eligible individuals). Screening included a nurse assessment, tuberculin skin test (TST) for those with previous negative TST or of unknown status and chest X-ray for the others.

Results: Of the eligible individuals in the affected village, 1,004 (98%) participated in the screening. Of these, 30% had a history of previous TB infection. A TST screening was administered to 71% of the participants, 10% of whom had positive results. Assessments were performed on 425 participants and 385 underwent a chest X-ray. Fifty-two cases of previously diagnosed active TB and three cases of new active TB were documented. In addition, there were 247 individuals with LTBI who had been previously identified (191 were found to have had adequate LTBI treatment, 56 were found to have had inadequate LTBI treatment) and 69 were identified with *de novo* LTBI. In addition, 633 participants were found to have no TB infection. There were 125 participants who were referred for LTBI treatment. Follow-up information was available for 120 and 85 (71%) of these completed the treatment.

Conclusion: Within this northern village, which had persistent TB transmission despite classic control measures, population-based screening had a high degree of coverage and was an effective way to detect additional cases of individuals with active TB and those with LTBI.

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Keywords: tuberculosis, Inuit, screening, tuberculin skin test, chest X-ray, latent tuberculosis infection, tuberculosis prophylaxis

Introduction

The incidence rate of tuberculosis (TB) among the Inuit is almost 300 times that of non-Aboriginals born in Canada (1,2). The determinants of TB and the challenges associated with TB

control in Inuit communities include poverty, food insecurity, overcrowded housing, unstable access to culturally-adapted health care, low levels of education, smoking, alcohol and

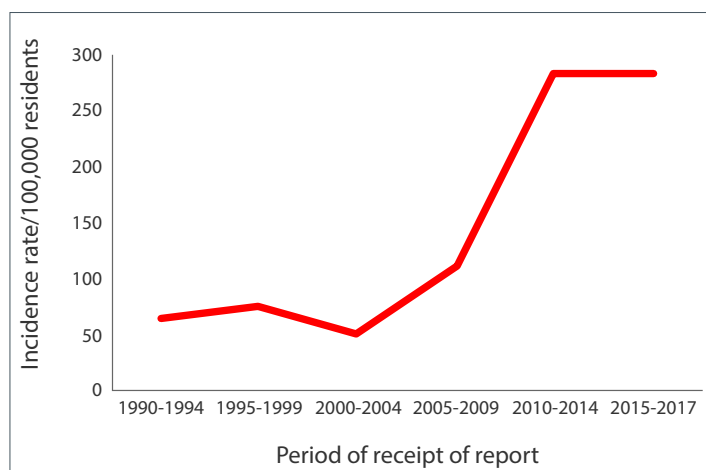


drug abuse and a high prevalence of several chronic medical conditions (2,3).

This paper focuses on a recent outbreak of TB in one village in Nunavik, Quebec. Nunavik comprises the northern third of the province of Quebec and is one of the four Inuit regions in northern Canada. Together, these four regions comprise the Nunangat region. The well-established challenges of dealing with TB in remote Inuit populations were similar to those seen in this village. Socio-economic characteristics of this village are typical of most Inuit communities. The vast majority (99.5%) of the population of the village is of Aboriginal (in this case, Inuit) ancestry, and the population is relatively young (35.5% was 14 years of age or younger in 2016) (4). The housing conditions are poor, with 52% of the housing described as overcrowded and 24% of the housing requiring major repairs (5). Tobacco use throughout Nunavik is high, with 67% reporting regular use in 2012 (6). In 2012, 55% of Inuit in the Nunangat region who were 25 years of age or older reported food insecurity. A high percentage of household expenditures in Nunavik were on food (42%) and for low-income households this proportion was even higher. Food insecurity and expense are especially common in the smaller and more remote communities, since planes are the only means of transport linking the villages in all seasons (7–9).

As a result of these challenges, and despite efforts by the public health authorities, the incidence rate of TB has been on the rise in Nunavik since 2008 (Figure 1).

Figure 1: Five-year mean incidence rate of tuberculosis in Nunavik, QC, 1990–2017^a



Abbreviation: QC, Quebec

^a Sources: Cases of tuberculosis: *Maladies à déclaration obligatoire* system (notifiable infectious diseases database), Quebec (June 29, 2018). Population: *Institut de la statistique du Québec* (ISQ). Population estimates and projection by socio-sanitary region, 1981 to 2036 (updated February 25, 2016). The mean incidence rate from 2015 to 2017 was calculated over three years

The Nunavik village in this study had an outbreak of 31 cases of TB in 2012–2013. This was not a village previously known for TB; no cases had been identified from 1990 to 2006, only one case per year had been identified in 2007 and 2008 and

no cases had been identified in 2009. However, a few cases had been identified in the two years prior to the outbreak (five cases in 2010 and eight cases in 2011). Following a concerted public health response, the 2012–2013 outbreak was considered under control in 2014. However, June 2015 saw resurgence, and by September 19, 2015, the cumulative number of detected cases since the beginning of that year was 22. In response to this, the Nunavik Department of Public Health (DPH) and the Inuulitsivik Health Center (IHC) conducted contact tracing that included almost one quarter of the population. In addition, on the recommendation of the *Comité sur l'immunisation du Québec* (CIQ), bacillus Calmette-Guérin (BCG) vaccination was reintroduced for children younger than two years of age (*Groupe de travail sur le vaccin BCG. Avis sur la pertinence de la réintroduction du vaccin BCG au Nunavik pour le contrôle d'une recrudescence de la tuberculose. Document de travail. p 1–86. INSPQ; 2015. Unpublished document*).

Despite this extensive contact tracing, additional TB cases were subsequently reported, indicative of persistent transmission.

In light of the fact that new cases were being detected outside of contact tracing, the DPH decided to implement a population-based TB screening program. Beginning on October 19, 2015, the intervention was carried out in collaboration with various stakeholders and partners, including DPH, IHC, the Nunavik Regional Board of Health and Social Services (RBHSS), the Institut national de santé publique du Québec (INSPQ), the Canadian Field Epidemiology Program of the Public Health Agency of Canada (PHAC) and the First Nations and Inuit Health Branch (FNIHB) at Health Canada (HC). The objectives of the intervention were to enhance community awareness, knowledge and response to TB, detect individuals with active TB and provide prompt treatment to interrupt transmission and detect individuals with new or incompletely treated latent tuberculosis infection (LTBI) and offer LTBI treatment.

The purpose of this article is to describe this population-based screening intervention and identify the additional number of cases of active TB and LTBI it detected, and how many received treatment.

Methodology

Population

The target population included all village residents of at least two years of age after August 15, 2015, who had not already been included in the contact tracing undertaken since June 1, 2015. The population database consisted of a combination of the municipality's census files, the Municipal Housing Bureau's household counts, IHC medical records and the DPH's contact tracing files. From the database, a list of individuals to include in the intervention was established and



the values of certain fields on the screening questionnaire were pre-filled.

Definition of terms

A tuberculin skin test (TST) with a positive result (at least five mm induration), in the absence of active TB, was classified as LTBI. This threshold was selected in the context of the ongoing village outbreak. LTBI was further classified as recent (less than two-year interval between a negative and a positive TST at screening, with a difference of at least six mm between both results), new (undetermined date, no previous TST or previous negative TST at least two years previous) or old (positive TST from at least two years previous). Recent and new LTBI were grouped as *de novo* LTBI. LTBI was assessed as adequately treated if there had been at least an 80% completion of the prophylaxis treatment (number of doses taken divided by the number of doses prescribed). Previous TB infection was defined either as active TB, if the diagnosis was validated as confirmed or probable based on surveillance case definitions (10), or LTBI documented in the past. Suspected active TB was defined by the presence of any of the following symptoms or clinical signs: unusual cough for equal to or greater than two weeks; persistent fever; significant weight loss (or absence of or delayed weight gain in a growing person); or hemoptysis. A non-specific clinical abnormality was defined as clinical manifestation non-suggestive of active TB but requiring follow-up with a nurse to check for persistence and, if necessary, a medical assessment. Contact tracing was defined as the follow-up of persons in contact with TB cases to identify and treat any secondary cases of TB or LTBI, in order to offer treatment (3).

Data collection

A standardized questionnaire and user guide was developed for data collection that included the following sections: demographic information; history of TB infection (including active TB or LTBI); clinical nurse assessment; TST (administration and results); chest X-ray; and medical assessment.

A clinical algorithm for the screening procedure was developed by the DPH in collaboration with partners, including pneumologists from the *Réseau universitaire intégré de santé* at McGill University, Montreal, QC. The screening procedure was then conducted by the Nunavik nurses and included the following steps:

- verification and completion of pre-existing clinical data, medical file number as unique identifier and demographic information (including house civic number);
- verification of history of active TB (with most recent year of onset), of TST and last TST result, diagnosis of LTBI, administration of preventive treatment and its completeness;
- questions on the presence of symptoms and clinical signs suggestive of active TB;
- administration of TST to individuals without a history of TB infection and without symptoms or clinical signs suggestive of active TB;

- reading and documentation of TST results 48–72 hours after its administration;
- referral of individuals with a history of active TB or LTBI and those with a TST screening result of at least five mm for chest X-ray;
- questions on recent exposure (since January 1, 2015) to a hospitalized case of active TB;
- follow-up in the presence of non-specific clinical abnormalities;
- immediate referral to clinical physicians of individuals with symptoms or clinical signs suggestive of active TB for diagnosis and medical follow-up, as appropriate; and
- referral to clinical physicians of individuals with a history of TB infection, or a TST at screening of at least five mm, for diagnosis and decision on next steps.

Screening and referral

The TST test was administered according to the *Quebec Immunization Protocol* (11); those that had not been read or had been read more than 72 hours after administration were retaken. The subject was either discharged (normal clinical evaluation and negative TST) or referred to a clinical physician.

Screening started in the secondary school and then continued by neighbourhood and household with people brought to the village's Local Community Service Center (CLSC), with the help of municipal transportation services.

Analysis

The data were entered into a Microsoft Access 2007 (Redmond, Washington State, US) file and validated by the DPH. The CLSC's medical records were reviewed at the conclusion of the intervention. Finally, records of individuals identified as candidates for prophylaxis were matched with a database of LTBI treatment follow-ups. The data were analyzed using Epi Info™ 7.1.5.2 (Centers for Disease Control and Prevention, Atlanta, Georgia, US) (12) and SPSS 23 (IBM Analytics, Armonk, New York, US) (13) software.

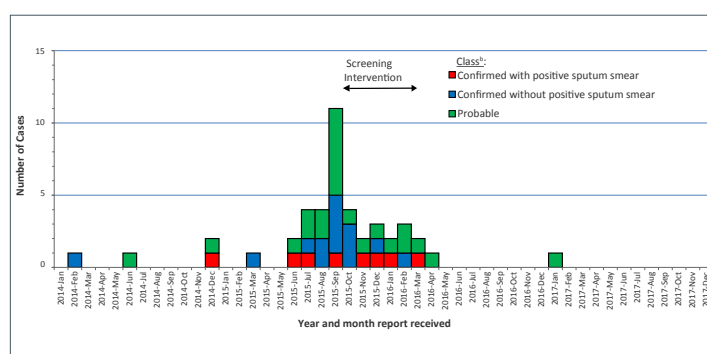
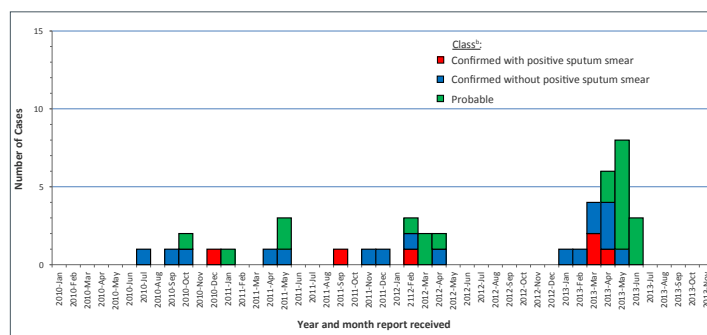
Results

The total population of the village was estimated to be 1,477 (*Agence de la santé publique du Canada*. Shane A, Born J. Dépistage de la tuberculose en milieu scolaire et dans la population au Nunavik, Québec, du 6 octobre au 13 novembre 2015. p 1-38. ASPC; 2015. *Unpublished report*). Two groups were excluded from the TB screening: 69 children younger than two years of age who had received BCG vaccine; and 350 individuals who were already covered by the contact tracing. A further 32 individuals were removed for various reasons (including 18 individuals who were living outside the village and 14 who were hospitalized or incarcerated). Thus, the final number of eligible individuals was 1,026. Of these, two refused to participate and 20 could not be reached.



Clinical evaluations were conducted on the remaining 1,004 from October 19, 2015 to March 21, 2016 (Figure 2).

Figure 2: Number of confirmed and probable cases of tuberculosis in a village in Nunavik, QC, by date of notification, 2010–2017^a



Abbreviation: QC, Quebec

^a Source: *Maladies à déclaration obligatoire* system, Quebec (June 29, 2018)

^b According to the current Quebec surveillance case definitions (10)

Ninety individuals (73.8% of the student population of 122, or 9.0% of the total study group) were screened in schools and 914 (91.0%) were screened in households.

Of the 1,004 participants, 531 (52.9%) were male and 473 (47.1%) were female. Their ages ranged from 20 months to 85 years (mean: 27.0 years; median: 23.0 years), with a similar distribution across both sexes. Six individuals were children younger than two years of age whose parents had previously refused the BCG vaccination.

Fifty-two (7.8%) of the 667 persons for whom the information was available had a history of active TB. The year TB was diagnosed was available for 44 of the cases and ranged from 1955 to 2015. Six hundred and seven people had a record of a previous TST result in their file; 282 (46.5%) of these individuals were TST-positive and of those 235 (83.3%) had a result of at least 10 mm (Table 1).

Table 1: Distribution of previous tuberculin skin test results in Nunavik, QC

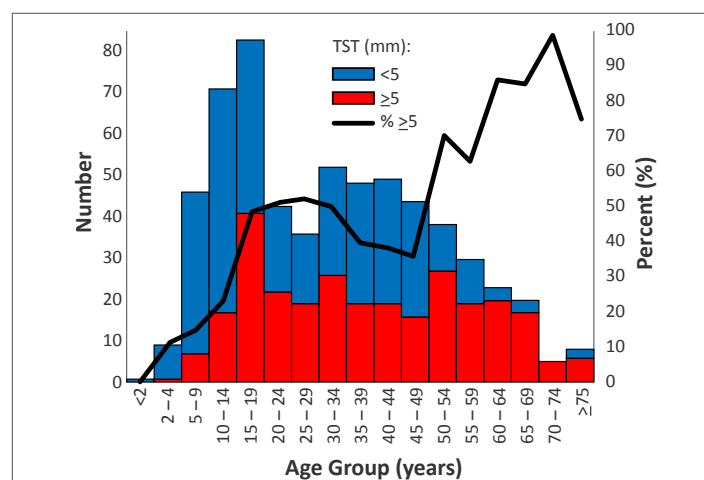
| TST result (mm) | Number | Percent (%) |
|-----------------|--------|--------------------|
| 0 | 281 | 46.3 |
| 1 to 4 | 44 | 7.2 |
| 5 to 9 | 47 | 7.7 |
| ≥10 | 235 | 38.7 |
| Total | 607 | 100.0 ^a |

Abbreviations: mm, millimetre; QC, Quebec; TST, tuberculin skin test; ≥, superior or equal to

^a Does not quite add up to 100% due to rounding

The proportion of positive results was similar by sex but varied by age, with the maximum among individuals 50 years of age or older, followed by young adults and then adolescents (Figure 3).

Figure 3: Previous tuberculin skin test results: Number at least 5 mm or less than 5 mm and proportion at least 5 mm, by age group in Nunavik, QC (n=607)



Abbreviations: mm, millimetre; n, number; QC, Quebec; TST, tuberculin skin test; <, inferior to; ≥, superior or equal to

LTBI treatment was considered adequate in 191 (77.3%) of the 247 individuals who had an earlier positive TST and for whom information was available. Including active TB and positive TST (non-mutually exclusive values), 297 (29.6%) of the 1,004 participants had a history of TB infection.

In addition, 47 (4.7%) participants reported one or more symptoms or clinical signs suggestive of active TB, but none of them had been diagnosed with TB.

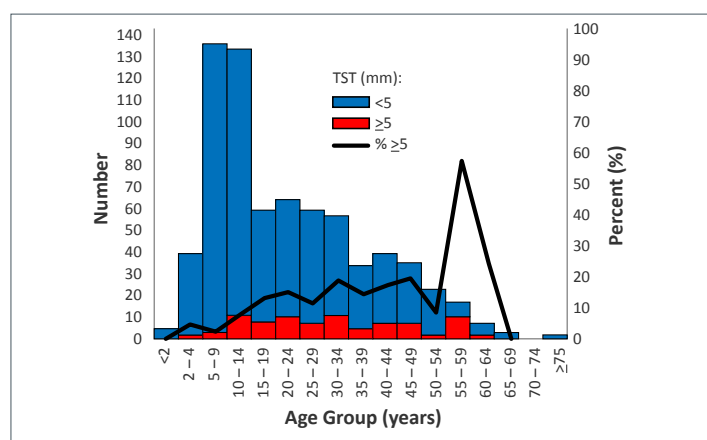
A screening TST was performed on 713 (71.0%) of the 1,004 participants, 10 of whom were mistakenly redone on individuals who had a positive prior TST; 85 (11.9%) people had a positive result. Of those, 60 (70.6%) had a result of at least 10 mm (Table 2).

**Table 2: Distribution of screening tuberculin skin test results in Nunavik, QC, 2015–2016**

| TST result (mm) | Number | Percent (%) |
|-----------------|--------|-------------|
| 0 | 562 | 78.8 |
| 1 to 4 | 66 | 9.3 |
| 5 to 9 | 25 | 3.5 |
| ≥10 | 60 | 8.4 |
| Total | 713 | 100 |

Abbreviations: mm, millimetre; QC, Quebec; TST, tuberculin skin test; ≥, superior or equal to

Although the proportion of positive results was similar for males and females, it varied by age, peaking among individuals in the 55 to 64-years age group (Figure 4).

Figure 4: Screening tuberculin skin test results: Number at least 5 mm and less than 5 mm and proportion at least 5 mm, by age group in Nunavik, QC (n=713)

Abbreviations: mm, millimetre; n, number; QC, Quebec; TST, tuberculin skin test; <, inferior to; ≥, superior or equal to

The time interval between the administration of the TST and its reading was two days for 650 (91.3%) and three days for 62 (8.7%) of the 712 individuals for whom the dates were known, and were therefore in accordance with the recommended interval for all subjects.

A chest X-ray was performed on 385 (38.3%) participants. The results were reported as abnormal for 103 (26.7%). A detailed report was available for 96 people; one case with active pulmonary TB was diagnosed with a cavitary lesion. A medical assessment was carried out on 394 (39.2%) of participants.

The information was verified and recorded in the clinical records, as of November 12, 2016 (Table 3). There were 55 active TB cases, including 52 previously diagnosed cases and three new cases (two confirmed and one probable) detected by the screening. There were 316 individuals with LTBI, including 247 who had been previously diagnosed, of which 191 (77.3%) had received adequate treatment and 56 (22.7%) who had incomplete treatment, and 69 with *de novo* LTBI. In addition, 633 participants were found to have no TB infection.

Table 3: Summary of tuberculosis screening outcomes in a village in Nunavik, QC, 2015–2016

| Status | Number of subjects |
|-------------------------------|--------------------|
| Active TB | 55 |
| • previously diagnosed | 52 |
| • newly detected by screening | 3 |
| LTBI | 316 |
| • <i>de novo</i> | 69 ^a |
| • previously diagnosed | 247 |
| - adequately treated | 191 |
| - incomplete treatment | 56 ^a |
| No TB infection | 633 |
| Total | 1,004 |

Abbreviations: LTBI, latent tuberculosis infection; QC, Quebec; TB, tuberculosis

^a These 125 individuals were considered candidates for TB prophylaxis; it was offered to 68 of the 69 people with *de novo* LTBI. Information on preventive treatment follow-up was available for 120 (96.0%) of these 125 candidates (see Table 4)

Of the 125 participants who were offered LTBI treatment (including 62 *de novo* and 56 with a history of incomplete treatment) records were found for 120 (96.0%) (Table 4). Of those, 85 (70.8%) received adequate LTBI treatment; the majority of which (94%) was rifampin, self-administered daily for four months.

Table 4: Summary of latent tuberculosis infection treatment outcomes in a village in Nunavik, QC, 2015–2016

| LTBI treatment outcome | Number | Percent (%) |
|--|--------|------------------|
| Completed (took at least 80% of prescribed doses) | 85 | 70.8 |
| Received but degree of completeness unknown | 2 | 1.7 |
| Started but lost during follow-up (moved from the village) | 1 | 0.8 |
| Refused or discontinued by the patient | 13 | 10.8 |
| Discontinued by nursing staff | 16 | 13.3 |
| Discontinued for an unknown reason | 3 | 2.5 |
| Total | 120 | 100 ^a |

Abbreviations: LTBI, latent tuberculosis infection; QC, Quebec

^a Does not quite add up to 100% due to rounding

Source: latent tuberculosis infection treatment follow-up database, Nunavik Department of Public Health (June 26, 2018)

The epidemic curve (Figure 2) indicates that the last case of the 2015–2016 TB outbreak occurred in April 2016, for a total of 39 cases, none of whom died. One sporadic case was reported in January 2017 and two cases were reported in May 2018 (*data not shown*).

Discussion

Almost the entire population of this Inuit village in Nunavik was assessed for TB, either by contact tracing or by population-based screening. This large-scale intervention, which involved TB screening of over 1,000 individuals, was launched in response to the ongoing spread of the infection despite following the traditional approach to TB control, as outlined and advocated in the *Canadian Tuberculosis Standards* (3) and *Quebec's Guide*



d'intervention contre la tuberculose (14). As a result, three (8%) of the 39 new active TB cases that were identified during this outbreak were detected by population-based screening. Without this screening these three cases would not have been identified or would only have been identified later. These cases didn't present symptoms suggestive of TB at the time of their clinical assessment.

A strength of this intervention was that 98% of eligible subjects were screened, which is a remarkable achievement. The high rate of participation was obtained thanks to village engagement, stakeholder involvement and the support of various partners and stakeholders.

This study had two main limitations. The first limitation involved uncertainties about the population data used to determine the subgroup to screen. When the population database was created, none of the available lists was complete. However, by comparing multiple lists it was possible to obtain reasonable approximations for this population. The second limitation involved the lack of consistency and completeness in data collection and entry. The screening questionnaires were not always complete as some information was recorded elsewhere, such as in the medical charts, and some questions and variables were ambiguous or poorly defined. There were many stakeholders involved, which made information sharing difficult. Fortunately, reviewing the information contained in the clinical records helped to improve the accuracy of the data.

Although some elements of the process were evaluated, the impact of the intervention in terms of TB cases avoided was not assessed, as this depends on many other factors. However, a pool of individuals with *de novo* or past LTBI inadequately treated was identified. These people were then offered prophylaxis to avoid developing the disease and, in turn, becoming infectious.

In terms of next steps, an integrated regional TB surveillance system is currently being developed, which will increase the ability to document TB outbreaks and support contact tracing and follow-up of TB treatment and prophylaxis (15).

Conclusion

Population-based screening to address an ongoing TB outbreak in a remote village in Nunavik, Quebec was able to reach 98% of the eligible population. It was able to identify those individuals who needed treatment and the majority of those who needed it successfully completed their treatment. Such a widespread intervention was possible because of the ability of the villagers and the professional, municipal and village stakeholders to effectively support this village-based action.

This intensive effort identified new requirements for data collection, storage and access, and many of these will be resolved by the new integrated regional TB surveillance system.

Such a surveillance system will facilitate the assessment of the impact of TB prevention and control programs in the future.

Authors' statement

RD – Conceptualization, methodology, software, validation, official analysis, data conservation, writing of the first draft, display

MB – Conceptualization, methodology, software, validation, official analysis, surveys, resources, data conservation, writing of the first draft, review and revision of the final version, supervision, project administration

JFP – Conceptualization, methodology, resources, review and revision of the final version, supervision, project administration

HZ – Conceptualization, methodology, validation, surveys, writing – review and revision of the final version

Conflict of interest

None.

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Outbreak of *Salmonella* Chailey infections linked to precut coconut pieces — United States and Canada, 2017[†]

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Abstract

Foodborne salmonellosis causes an estimated one million illnesses and 400 deaths annually in the United States (US). During March–May 2017, an outbreak of 19 cases of *Salmonella* Chailey associated with precut coconut pieces from a single grocery store chain occurred in the United States and Canada. The chain voluntarily recalled precut coconut pieces. This was the first time that coconut has been associated with a *Salmonella* outbreak in the United States or Canada. In recent years, salmonellosis outbreaks have been caused by foods not typically associated with *Salmonella*. Raw coconut should now be considered in investigations of *Salmonella* outbreaks among fresh food consumers.

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Keywords: *Salmonella* Chailey, foodborne outbreak, raw coconut, gastroenteritis

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Introduction

Foodborne salmonellosis causes an estimated one million illnesses and 400 deaths annually in the United States (US) (1). In recent years, salmonellosis outbreaks have been caused by foods not typically associated with *Salmonella*. On May 2, 2017, PulseNet, Centers for Disease Control and Prevention (CDC)'s national molecular subtyping network for foodborne disease surveillance, identified a cluster of 14 *Salmonella* Chailey isolates with a rare pulsed-field gel electrophoresis (PFGE) pattern. On May 29, Canadian health officials informed CDC that they were also investigating a cluster of five *Salmonella* Chailey infections in British Columbia with the same PFGE pattern. Nineteen cases were identified and investigated by CDC, US state health departments, the Public Health Agency of Canada, and the British Columbia Centre for Disease Control. Isolates from all cases were highly related by whole genome sequencing (WGS). Illness onset dates ranged from March 10 to May 7, 2017. Initial interviews revealed that infected persons consumed various fresh foods and shopped at

grocery chain A; focused questionnaires identified precut coconut pieces from grocery chain A as a common vehicle. The Canadian Food Inspection Agency (CFIA) and the US Food and Drug Administration (FDA) conducted a traceback investigation that implicated a single lot of frozen, precut coconut as the outbreak source. Grocery chain A voluntarily removed precut coconut pieces from their stores. This action likely limited the size and scope of this outbreak.

Epidemiologic Investigation

A case was defined as infection with *Salmonella* Chailey with the outbreak PFGE pattern with illness onset during March 10–May 7, 2017, and highly related by WGS to other cases. Nineteen cases were identified: 14 in seven US states (one case each in Colorado and Kansas, two each in Oregon, Pennsylvania, Utah, and Washington, and four in Texas) and five cases in British Columbia, Canada (**Figure**).



OUTBREAK REPORT

Infected persons ranged in age from <1 to 87 years (median = 57 years), including two aged <5 years; nine persons were female. Among 17 persons for whom information on hospitalization was known, three were hospitalized; no deaths occurred.

Infected persons in the US were initially interviewed using state-developed questionnaires or CDC's National Hypothesis Generating Questionnaire; both collected information on foods consumed and locations where food was purchased during the 7 days before illness onset. Review of data collected using these questionnaires revealed that among nine persons with information on grocery stores, seven reported shopping at grocery chain A, which comprises health food stores. Other commonly reported foods consumed included oranges (six persons), strawberries (five), tomatoes (four), kale, tuna, zucchini, almonds (three each), and shrimp (two). The tuna and other seafood exposures were noteworthy because a strain with the outbreak PFGE pattern had been isolated from yellowfin tuna imported from Indonesia in 2010. Because of the strong fresh-foods signal from the initial information, open-ended interviews were conducted to obtain more information about foods purchased from grocery chain A and other fresh foods that were not included on the standard National Hypothesis Generating Questionnaire (2) used during the initial interviews. Open-ended, iterative interviews were conducted by a single interviewer to gather more detailed information about foods persons ate before they became ill. Interviews were completed for eight persons, including five who had already been interviewed with a standard questionnaire. One person reported eating precut coconut pieces from grocery chain A, two persons reported drinking coconut water, two reported eating sushi, seven reported eating oranges, and three reported eating seaweed snacks. Because open-ended interviews did not identify a single food item of interest, a focused questionnaire was developed. The focused questionnaire included detailed, open-ended questions about food items purchased from grocery chain A, as well as specific questions asking about consumption of coconut,

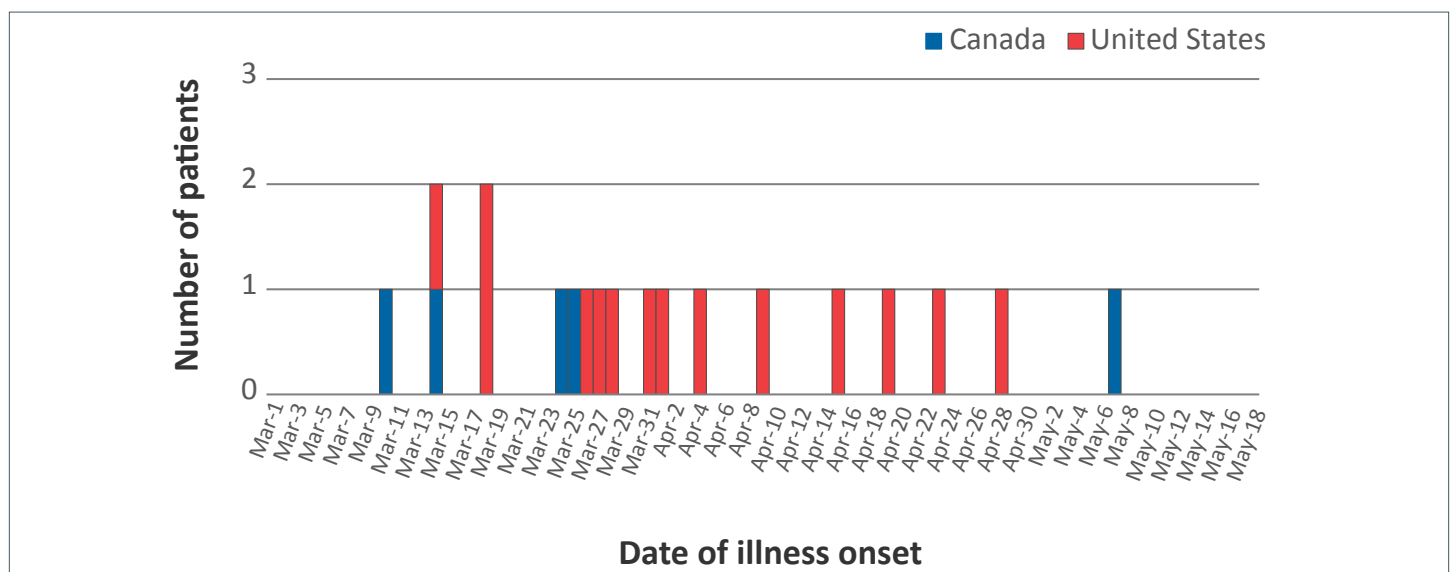
coconut water, other fruits, vegetables, nuts, seaweed, sushi, and other fish.

At the same time, Canadian investigators used a centralized interviewer approach to interview all five infected persons in Canada using a modified version of CDC's focused questionnaire. All five persons reported shopping at grocery chain A locations in Canada and consuming precut coconut pieces purchased there. Eleven infected persons in the US were reinterviewed with the focused questionnaire, and six reported eating precut coconut pieces from grocery chain A. In total, 16 persons in the US and Canada were reinterviewed, and 11 reported consuming precut coconut pieces from grocery chain A.

CDC and the British Columbia Centre for Disease Control requested consumer purchase information from grocery chain A to continue to generate hypotheses while reinterviewing persons. Because grocery chain A did not have a shopper card program, consenting persons were asked to share the purchase dates, total purchase dollar amounts, store location, and the first six digits and last four digits of the credit card used at time of purchase. Grocery chain A used this information to retrieve receipts.

Seven persons provided information to retrieve receipts from six grocery chain A locations in British Columbia, Oregon, and Texas. Receipts were retrieved for all seven persons, four of whom (one person in the US, who initially did not report coconut exposure, and three persons in Canada) had precut coconut pieces listed on their receipts (purchase dates March 7–15, 2017). Another person who did not provide information to retrieve receipts reported purchasing precut coconut pieces on April 13. A total of 12 persons reported eating precut coconut pieces or had receipts verifying the purchase of precut coconut pieces from grocery chain A.

Figure: Number of persons infected with the outbreak strain of *Salmonella* Chailey, by date of illness onset — United States and Canada, 2017 (N=19)





Laboratory investigation

Clinical isolates were characterized by WGS. Whole genome, high-quality single nucleotide polymorphism (hqSNP) analysis (whole genome, high-quality single nucleotide polymorphism analysis was performed using the Lyve-SET hqSNP pipeline (<https://github.com/liskatz/lyve-SET>) indicated that the 19 clinical isolates differed by 0–4 hqSNPs, indicating high genetic relatedness. An additional two *Salmonella* Chailey isolates with the same PFGE pattern from persons in the US and Canada with illness onset dates consistent with this outbreak were excluded, as they differed from the rest of the isolates by approximately 100 hqSNPs. The isolates from yellowfin tuna imported from Indonesia in 2010 were 19 hqSNPs different from the clinical isolates and were also considered to be not closely related genetically.

Inspections and traceback

Canadian officials conducted an inspection at a location of grocery chain A and reported that frozen, vacuum-packed coconut pieces were received at the store every other day. These were thawed at the store and repacked into smaller plastic tubs for sale in the produce area, with a five-day shelf life applied. Grocery store A headquarters communicated to US officials that all of their stores thaw and repack this product in the store. FDA visited three US-based, FDA-regulated firms associated with the import and repackaging of this product and identified no objectionable conditions.

CFIA and FDA conducted a traceback investigation for nine persons in the US and Canada who all reported consuming precut coconut pieces sold by grocery chain A. These locations received product from three distribution centers located in three states that obtained frozen precut coconut pieces from the same US firm. Records collected by FDA and CFIA at grocery chain A locations, distribution centers, and the processor suggested that a single lot of frozen precut coconut pieces imported from Indonesia was the outbreak source. FDA tested environmental and coconut samples from processing and distribution centers, but no *Salmonella* was detected. However, coconut from the suspected lot was not available for testing.

Public health response

Based on the results of the epidemiologic investigation, grocery chain A voluntarily removed thawed, precut coconut pieces from store shelves, which included all precut coconut pieces from the lot identified by the traceback investigation. No public communication was issued, given that this action, combined with the 5-day shelf life of thawed precut coconut pieces, made it unlikely that contaminated precut coconut pieces were still available for purchase or in customers' homes.

Discussion

International collaboration on the epidemiologic and laboratory investigation was important for identifying that the Canadian and US cases were part of the same cluster. This allowed investigators to focus on food purchased at grocery chain A and to identify frozen precut coconut pieces as the outbreak source.

Early communication and collaboration with grocery chain A assisted

the investigation through the collection of detailed purchase history information and facilitated a rapid removal of precut coconut from stores. The timely action of grocery chain A likely limited the size and scope of this outbreak.

In recent years, salmonellosis outbreaks have been caused by foods not typically associated with *Salmonella*. This was the first time that coconut has been associated with an outbreak of *Salmonella* in the US or Canada (3). Cases were reported throughout the US and Canada that were associated with different grocery chain A locations, supplied by different distribution centers. The single lot of imported, precut coconut pieces was processed over many months but remained frozen and minimally manipulated once in the US. Therefore, contamination likely occurred in the country of origin, Indonesia. Furthermore, the frozen yellowfin tuna with the same PFGE pattern was imported from Indonesia in 2010, providing support for the hypothesis that a food product from Indonesia could be the source of the outbreak.

This was a complicated investigation, and it required considerable time and effort by investigators in two countries to identify the food product ultimately responsible for the outbreak. Although no coconut from the suspected lot was available for laboratory sampling, epidemiologic and traceback information indicates that frozen precut coconut pieces were the source of the outbreak. In light of this finding, public health officials might consider raw coconut in investigations of *Salmonella* outbreaks among consumers of fresh foods.

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All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Advancing knowledge and increasing capacity to address climate-driven infectious diseases in Canada

C Lee-Fuller¹, A Magnan¹, S Pharand¹

Abstract

The *Pan-Canadian Framework on Clean Growth and Climate Change* (PCF) was adopted in December 2016. This collaboratively developed federal, provincial and territorial report documents Canada's plans to meet its Paris Agreement commitments and stimulate Canada's economy. This PCF identifies a series of actions that will be addressed through four key pillars: pricing carbon pollution; complementary measures to reduce emissions; adaptation and climate resilience; and enabling economic growth through clean technology, innovation and jobs. Within the PCF, protecting and improving human health and well-being was included as an essential aspect of adaptation and climate resilience. New actions in the PCF included greater federal action to prevent illness from extreme heat events led by Health Canada and to reduce the risks associated with climate-driven infectious diseases led by the Public Health Agency of Canada (PHAC).

Public health and climate change intersect in the area of infectious disease. To deliver on its new commitments in the PCF, PHAC established the Infectious Diseases and Climate Change (IDCC) program, and a new grants and contributions fund. The program has three principal aims: to increase PHAC's capacity to respond to the increasing demands posed by climate-driven infectious diseases; to provide Canadians access to timely and accurate information to better understand their risks and take measures to prevent infection; and to improve the adaptability or resiliency to the health impacts of infectious diseases through surveillance and monitoring, increased laboratory diagnostic capabilities, and access to education and awareness tools. In the first year of the IDCC Fund, a number of projects on monitoring and surveillance and on education and awareness have been approved. In collaboration with our stakeholders as well as governments at all levels and in all provinces and territories, PHAC will continue to work to raise awareness about the effects of climate change on the prevalence of infectious diseases and help Canadians to prepare for the anticipated and unanticipated impacts.

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Keywords: Climate change, infectious diseases, resilience, adaptation, surveillance, education, awareness, capacity

Introduction

In response to the recognized need to take action on climate change, Canada's First Ministers adopted the *Pan-Canadian Framework on Clean Growth and Climate Change* (PCF) in December 2016 (1). This collaboratively developed federal, provincial and territorial report documents Canada's plans to meet its Paris Agreement (2) commitments. The

provincial and territorial governments that support the PCF and the federal government have identified a series of actions that will be addressed through four pillars: pricing carbon pollution; complementary measures to reduce emissions; adaptation and climate resilience; and enabling economic growth through clean technology, innovation and jobs.



The PCF recognizes that addressing climate change is a shared responsibility and that everyone—all levels of government, Indigenous organizations, communities, industry, non-government organizations and individuals across the country—have a role to play. The PCF includes more than fifty concrete actions on climate change, spanning all provinces and territories and all sectors. In addition, it also supports implementation of the 2030 UN Sustainable Development Goals (3).

Within the PCF, protecting and improving human health and well-being is included as an essential aspect of adaptation and climate resilience. Other action areas within this pillar included translating scientific information and traditional knowledge into action, building climate resilience through infrastructure, supporting particularly vulnerable regions and reducing climate-related hazards and disaster risks. The inclusion of health and well-being as a key component of the PCF acknowledged that the burden and impact on Canadian's health is anticipated to increase as changes in climate advance. Unfortunately, the vulnerable and at-risk populations may experience the brunt of these impacts from climate change. For this reason, new actions in the plan include greater federal action to prevent illness from extreme heat events and to reduce the risks associated with climate-driven infectious diseases as well as support to Indigenous communities and Nations to lead health activities.

Health Canada, the Public Health Agency of Canada (PHAC), the Canadian Institutes of Health Research, and its partners were also charged with continuing to advance the science, knowledge and best practices to adapt to climate change. PHAC has a long history of programming in this area and leads on the public health implications of climate change on infectious disease.

The objective of this article is to briefly highlight the role of public health in climate change adaptation and describe the new Infectious Disease and Climate Change (IDCC) program that PHAC has launched, which includes a new grants and contributions fund.

Public health and climate change

Public health plays an important role in raising awareness about the effects of climate change by equipping the public, health professionals, and decision-makers at various levels of government with tools and information to help Canadians to prepare and be more resilient to the impacts. The public health role in addressing climate change requires new partnerships, collaborations through multi-jurisdictional and multi-disciplinary actions.

Public health and climate change intersect in the area of infectious disease. One example of the direct and indirect effects of our changing climate on infectious disease and where our knowledge continues to evolve is vector-borne disease

risks. The shifting of the geographic range, habitats, and seasonality of vector-borne microbes is leading to the expansion of relatively rare infectious diseases to new areas and/or the emergence of diseases not previously present in Canada (4). Recent federal investments at PHAC within both the Centre for Food-borne, Environmental and Zoonotic Infectious Diseases and the National Microbiology Laboratory under the umbrella of the PCF have focused on building greater capacity and understanding to address climate-driven infectious diseases, including vector-borne diseases through enhanced surveillance and monitoring, risk assessments, modelling and laboratory diagnostics, as well as health professional education and public awareness activities (5). This investment reflects the realization that the toll of climate change and inadequate preparation for these changes could be tremendous.

PHAC's Infectious Diseases and Climate Change Program

To deliver on its new commitments in the PCF, PHAC established the IDCC program in 2016. The program builds on previous programming, the areas identified above, and will also help advance some work under the *Federal Framework on Lyme Disease and Action Plan* (6) and Lyme Disease Research Network grant process led by the Canadian Institutes for Health Research (7).

The focus of PHAC's program is on climate-driven zoonotic (including vector-borne diseases), food-borne and water-borne infectious diseases and includes a new grants and contributions fund. The program has three principal aims: to increase PHAC's capacity to respond to the increasing demands posed by climate-driven infectious diseases; to provide Canadians access to timely and accurate information to better understand their risks and take measures to prevent infection; and to improve the adaptability or resiliency to the health impacts of climate-driven infectious diseases through surveillance and monitoring, increased laboratory diagnostic capabilities and access to education and awareness tools.

In August 2017, PHAC launched the IDCC Fund, to provide up to \$2 million annually in grants and contributions funding for projects over 11 years. The Fund provides PHAC with a new vehicle to advance work in Canada on climate-driven infectious diseases and where possible, the One Health approach. Funds are being disbursed through directed, targeted and open solicitations. This Fund includes two priority areas:

- Monitoring and surveillance, and
- Education and awareness.

Surveillance activities will help establish baseline data and monitoring will facilitate better prediction and responses to climate-driven infectious diseases. This will be done by analyzing the movement of infectious diseases (e.g., viruses, bacteria,



parasites, fungi and prion diseases), particularly in underserved communities.

Education and awareness activities will include the development, uptake and/or distribution of materials for use by health professionals and the dissemination of tools and best practices across Canadian communities including vulnerable populations.

The projects that have received IDCC funding approval include health professional organizations, universities, Indigenous communities and provinces advancing work on the human health impacts of climate-driven infectious diseases. These PHAC funded projects will enhance baseline knowledge through field surveillance of tick populations, studies of infectious disease risks in specific regions of Canada and development of new tools, training and resources for health professionals, vulnerable populations, and communities. The announcement of the funded projects is pending.

PHAC is currently preparing for the next IDCC Fund solicitation process—planned for the fall of 2018—for projects to begin in 2019/2020, and for the future years of the program. More detailed information on the focus of this solicitation will be available on canada.ca and via email through program engagement.

Conclusion

The impacts of climate change are becoming more and more evident worldwide. In Canada, the provincial and territorial governments that support the PCF and the federal government have spelled out the critical steps required to respond to these changes. And, there is greater acknowledgement of the need to focus on health and well-being as part of our adaptation measures.

PHAC is committed to addressing the impacts of climate change on infectious diseases, and has identified gaps in knowledge and capacity that need to be addressed in order to better respond to current and future climate-driven increases in infectious diseases. To support the implementation of the PCF, PHAC continues to

increase its knowledge and expertise. It has put in place the new IDCC program that includes a grants and contributions fund.

PHAC will continue to work to advance knowledge and awareness of the effects of climate change and to help Canadians to prepare for and be more resilient to its impacts.

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Corrections for Can Commun Dis Rep 2018;44(9)

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The web version of the September 2018 issue of CCDR did not include the visual abstract “Rat bite fever (RBF) on Vancouver Island: Rare but higher than expected” (1). It has now been added to the web version of the publication. No change was required for the PDF version of the publication.

The infographic “Pertussis (whooping cough) is still a danger to infants” was placed in the PDF version Can Commun Dis Rep 2018;44(9):195 without a citation and was not identified in the Table of Contents. It was also not included in the web version. The infographic is now included in the Table of Contents of the PDF and has been added to both the Table of Contents and the text of the web version; both now have a citation (2).

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- The *influenza treatment recommendations* from the Association of Medical Microbiology and Infectious Disease (AMMI) Canada

Dr. Gemmill will present on prevention of seasonal influenza, types of vaccines available and their effectiveness, new indications and available internet resources. Dr. Evans will present on the burden of seasonal influenza, the trends in recent years and the antiviral treatment recommendations.

The information in this webinar is for frontline healthcare practitioners and public health vaccine providers. Presentations will be followed by a Q&A session.

This webinar will be presented in English. A French transcript will be available online at a later date.

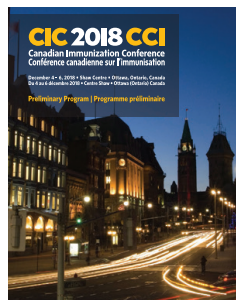
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