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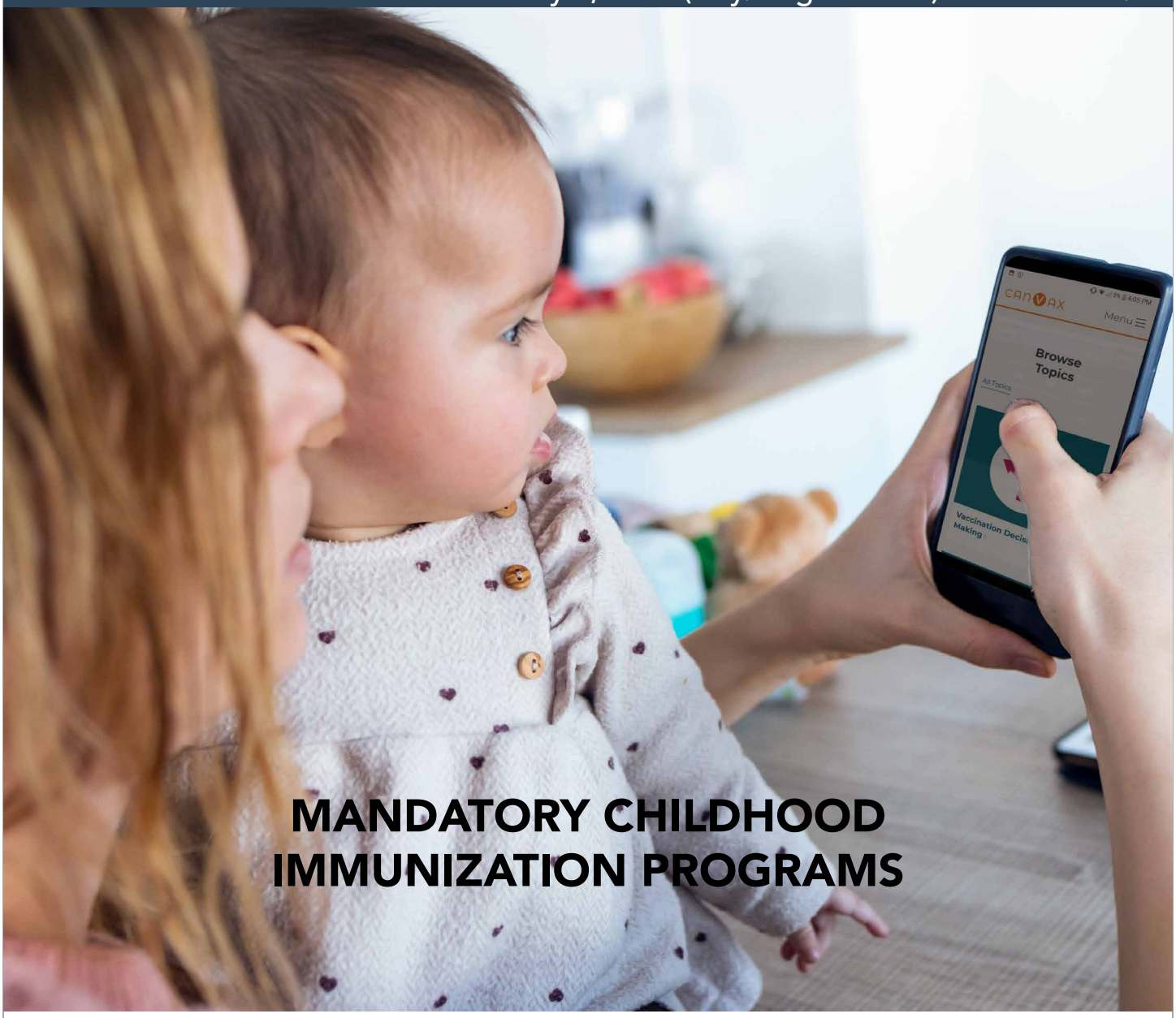

MANDATORY CHILDHOOD IMMUNIZATION PROGRAMS

NEXT ISSUE SEPTEMBER 3, 2020

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CANADA COMMUNICABLE DISEASE REPORT

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The picture on the cover of this issue illustrates a young woman at home, consulting the CANVax website (Canadian Vaccination Evidence Resource and Exchange Centre) on her phone while her infant looks on. This was based on an Envato image that was adapted by Lyal Saikaly (https://elements.envato.com/young-woman-using-her-mobile-phone-while-her-baby--E8Y52LK).

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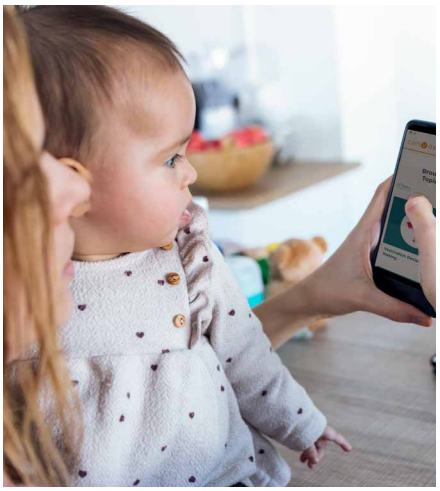

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OUTBREAK REPORT

Mixed community and nosocomial outbreak of *Legionella pneumophila* in Montréal, Québec, 2019

Geneviève Cadieux[1]*, Julie Brodeur[1], Félix Lamothe[1], Cindy Lalancette[2], Pierre A Pilon[1], David Kaiser[1], Éric Litvak[1]

Abstract

Objectives: To describe the investigation of a community-based outbreak of *Legionella pneumophila* serogroup 1, with retirement home and acute care hospital sub-clusters in Montréal, QC, and the key challenges encountered.

Methods: There were 14 cases of *L. pneumophila* serogroup 1 infection with an onset date between June 7 and August 21, 2019. The environmental investigation included sampling of water cooling towers (WCTs) and other potential sources. Sequence-based typing of clinical and environmental isolates was performed. Public health interventions included WCT decontamination orders and communication with clinicians.

Results: Eleven (79%) of the 14 cases were immunosuppressed or immunocompromised. Most (13; 93%) were diagnosed using a urinary antigen test, and five (36%) had a culture. Two sub-clusters were identified: three cases in a retirement home and four cases on an acute care hospital floor. Typing results suggested that the same *L. pneumophila* serogroup 1 may have caused the community outbreak and the two sub-clusters. A matching environmental source was not identified.

Conclusion: Whereas typing of clinical isolates suggested a common environmental source, our investigation failed to identify this source. Future outbreak investigations could benefit from more clinical isolates for typing, local registries of water aerosolization sources other than WCTs, and ongoing access to all WCT routine monitoring results and *L. pneumophila* isolates for typing.

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Keywords: *Legionella, Legionella pneumophila,* Legionellosis, Legionnaires' disease, disease outbreaks, communicable disease control, public health, water microbiology, water quality

Introduction

Legionella sp. infection became reportable in the province of Québec (QC) in 1987. Legionellosis incidence has been increasing since 2006 (1). In 2012, a *Legionella pneumophila* serogroup 1 outbreak in Québec linked to a water cooling tower (WCT) resulted in 183 cases and 13 deaths (1,2). Following this outbreak, the province introduced regulation that requires all WCTs to be registered with the Régie du bâtiment du Québec (RBQ) (3) and undergo routine maintenance and monthly monitoring for *L. pneumophila* (1). WCT sampling must be performed according to provincial guidelines (4), and results must be submitted monthly to the RBQ. The regulation requires WCT owners to take mitigation actions when results are between 10,000 and 999,999 colony-forming units (CFU)/L.

Furthermore, since July 2014, routine *L. pneumophila* monitoring results of 1,000,000 CFU/L or more must be reported to public health, and the reporting laboratory must keep the isolate for three months to facilitate public health investigation. The regulation also enables public health to issue decontamination orders to WCT owners (1,5). Preliminary data on a sample of over 300 WCTs suggest that the concentration of *L. pneumophila* in WCTs has decreased since the regulation was introduced in 2014 (6).

However, although the number of legionellosis cases reported annually ranged from 11 to 19 between 2007 and 2014, the number increased thereafter, to 63 in 2018 and 55 in 2019. In 2018, three spatiotemporal clusters were identified, the largest involving nine cases. Despite extensive investigations, the source of these clusters was never identified. That year, 83 occurrences of *L. pneumophila* at levels of 1,000,000 CFU/L or more involving 70 WCTs were reported to the Montréal public health department (Direction régionale de santé publique de Montréal, or DRSP), of a total of approximately 1,300 registered WCTs in Montréal. Since routine monitoring of WCTs was implemented in 2014, neither a cluster nor a sporadic case of legionellosis has been successfully matched to a WCT in Montréal.

The objective of this report is to describe the investigation of a mixed community and nosocomial outbreak of legionellosis, in spring/summer 2019, in Montréal. Some of the 14 people infected included patients on an acute care hospital ward for immunocompromised and immunosuppressed patients with very limited outdoor exposure. The report highlights the continuing challenges public health faces in identifying and controlling sources of *Legionella* outbreaks in large, densely populated urban areas where there are multiple possible sources of *Legionella*, in spite of a provincial WCT registry and legally mandated monthly routine monitoring for *L. pneumophila.*

Methods

Spatiotemporal cluster detection

A spatiotemporal cluster of three community-acquired cases of legionellosis reported within a period of 27 days was first detected on July 10, 2019, through SaTScan routine daily automated spatiotemporal cluster analysis of local reportable disease data. Manual review of this cluster identified a fourth case reported within a 28-day window; all four cases were infected with *L. pneumophila* serogroup 1.

Case investigation

The provincial legionellosis case definition requires the presence of a compatible clinical presentation and laboratory confirmation of infection from an appropriate clinical specimen (typically a urinary antigen test or sputum culture) (3). All cases reported to the DRSP are investigated using a standard provincial questionnaire (3); data are collected on risk factors (including diabetes, chronic lung disease, cardiovascular disease, chronic renal disease, disease or drug-related compromised immunity, cancer, chemotherapy or radiation in the last six months, smoking, alcohol use); clinical presentation; diagnostic test results; complications; and potential exposures during the incubation period (including travel, health care, spa/pool, decorative fountains, drinking water fountains, grocery stores, greenhouses, water parks, drinking water supply issues, issues with plumbing, equipment that produce aerosols, water heater temperature, dental treatments, occupational and potential workplace exposures). For cases associated with a spatiotemporal cluster or outbreak, detailed information is collected on all sites visited during the incubation period (3). Public health investigators routinely ask treating physicians to consider also ordering a sputum culture for *Legionella* for cases with a positive urinary antigen test.

A confirmed outbreak case was defined as one that met the provincial legionellosis case definition (3); had a culture positive for *L. pneumophila* serogroup 1 with a sequence type consistent with the other outbreak cases; and had resided or worked within 3 km of the cluster's epicentre during their incubation period. A probable outbreak case met the provincial case definition for legionellosis (3); had only a positive urinary *L. pneumophila* serogroup 1 antigen test; and had resided or worked within 3 km of the cluster's epicentre during their incubation period. The usual incubation period of 2–10 days was extended up to 21 days for immunocompromised and immunosuppressed patients; the incubation period for the first four cases that launched the cluster investigation was May 24 to June 28, 2019.

During the case investigation, two sub-clusters were identified: three cases in a retirement home and four nosocomial cases in an acute care hospital. The residents of the retirement home lived on different floors and in different towers. The nosocomial cases had been hospitalized on the same floor for the entire incubation period (more than 21 days).

Environmental investigation

The WCT with *L. pneumophila* serogroup 1 levels of 1,000,000 CFU/L or higher nearest to the epicenter during the incubation period was about 8 km away, so it was more likely that a closer WCT with a lower *L. pneumophila* concentration could be DRSP requested monthly *L. pneumophila* testing results from May through July for all 59 WCTs (38 sites) within this zone from RBQ (3). Manual review of these results identified two WCTs with *L. pneumophila* serogroup 1 concentration below 1,000,000 CFU/L, 16 with missing results and none showing "interfering flora" (which could hide *L. pneumophila*).

After a fifth case of *L. pneumophila* serogroup 1 within the same geographic area was reported on July 12, DRSP issued a public health order to the RBQ to obtain water samples for retesting of the 18 WCTs with abnormal or missing results. The RBQ follows the provincial guideline for WCT sampling (4); the sampling procedure is the same for routine monthly monitoring as for outbreaks: a single 1 L water sample is obtained from a representative site after letting the water run for at least 30 seconds to purge stagnant water.

As more cluster cases were reported, the epicentre and the 4 km radius zone around it were adjusted slightly. DRSP requested the RBQ updated results of routine *L. pneumophila* monitoring for all WCTs located within the zone from on July 19 and 31 and August 12. On August 26, because a source had not yet been identified, DRSP requested that all available isolates from

WCTs located within 12 km of the epicentre and with monthly *Legionella* monitoring results of 1,000,000 CFU/L or more at any time during the cases' incubation period be sent to the laboratory for sequence-based typing.

Concurrently, based on provincial guidance (3) and the scientific literature (7–11), DRSP accessed available databases of built water features and construction sites impeding road circulation as well as satellite images to identify other potential sources of *L. pneumophila* serogroup 1 aerosolization within a 2 km radius of the epicentre. During a field visit on August 7, water and/or biofilm specimens were collected from a high-pressure paint-stripping device and a water hose used for compacting the ground at a nearby excavation site. Water samples from a golf course irrigation system (i.e. sprinklers in three separate areas closest to the cases) were obtained on August 15.

Separate environmental investigations were also performed for the two sub-clusters of cases at the retirement home and acute care hospital. DRSP reviewed the heated pool and spa maintenance logs and hot water reservoir temperatures at the retirement home. Water samples from the hot water reservoir, heated pool, spa and outdoor decorative fountain and drinking water from the separate apartments of two residents who had become infected were collected on July 25.

The acute care hospital infection prevention and control team investigated potential sources on the affected floor. Water/biofilm samples were collected from sinks, taps and showerheads on July 24 and August 13 and from an ice machine, refrigerator, floor-cleaning machine and outdoor garden hose on August 13.

Laboratory analyses of clinical and environmental specimens

The diagnosing hospital performed the initial analysis of clinical specimens; these specimens or isolates were then forwarded to the provincial public health laboratory for confirmation and typing. On clinical specimens, routine confirmation methods included a locally-developed real-time polymerase chain reaction (PCR) targeting *ssrA*, *mip* and *wzm* genes; on clinical isolates, confirmation was performed using matrix-assisted laser desorption/ionization-time of flight (MALDI-ToF, Bruker, IVD 3,2) and serogroup 1 was identified by agglutination test slide with *L. pneumophila* serogroup 1 antisera (Denka Seiket, Japan). Genotyping was performed by sequence-based typing according to the European Working Group for Legionella Infection (EWGLI) protocol (12,13).

The *Centre d'expertise en analyses environnementales du Québec* (CEAEQ) conducted the culture and quantitative real-time PCR (*L. pneumophila* serogroup 1) analyses of WCT water samples obtained following the public health order. Analyses of environmental samples other than WCTs were performed by different commercial laboratories accredited by the CSA Group (*L. pneumophila* qPCR) and the CEAEQ (*Legionella* culture). All *L. pneumophila* serogroup 1 environmental isolates were forwarded to the provincial public health laboratory for typing.

Interventions

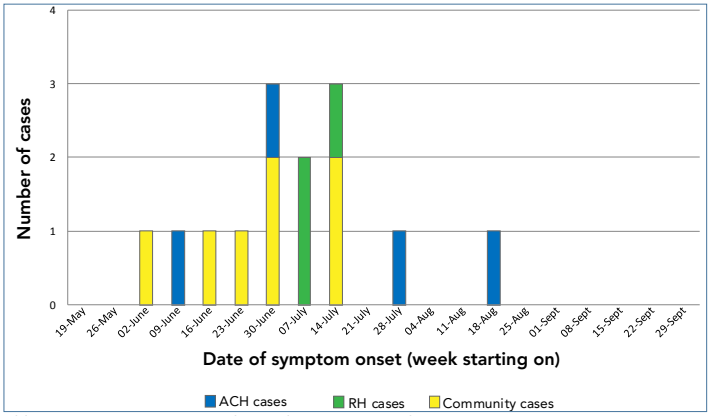
As a precaution, a decontamination order, effective immediately, was issued to all owners/managers of the WCTs that tested positive for *L. pneumophila* (any quantifiable result). The environmental health team from the DRSP followed up with each WCT owner/manager to make sure that decontamination was completed as soon as possible. Decontamination effectiveness was verified through repeat WCT sampling 2 to 7 days later, as per the provincial protocol (4). A public health alert was sent to Montréal clinicians to remind them to test for legionellosis in at-risk patients presenting with pneumonia and to order a sputum culture for *Legionella* to facilitate public health investigation. The outbreak was declared over on October 18, 45 days after the last case was reported to public health.

Results

Epidemiologic investigation

The outbreak comprised 14 cases of *L. pneumophila* serogroup 1, with illness onset between June 7 and August 21, 2019 (**Figure 1** and **Table 1**). Among the 14 cases, ten were male, median age was 68 years, 11 were immunosuppressed or immunocompromised, four required admission to an intensive care unit, two were intubated and one died. Six cases lived in private homes and three in the same retirement home (in different towers and on different floors); four were hospitalized on the same hospital floor for the duration of their incubation period and one lived in an independent living facility for persons undergoing cancer treatment near the acute care hospital.

Figure 1: Epidemic curve for the legionellosis outbreak in Montréal, 2019



Abbreviations: ACH, acute care hospital; RH, retirement home

Thirteen cases were initially diagnosed through a positive urinary antigen test; positive sputum cultures were subsequently obtained for four of them (Table 1). One anuric patient was initially diagnosed through a sputum culture.

Table 1: Outbreak-related *Legionella pneumophila* serogroup 1 cases in Montréal, 2019

Case ID	Date reported	Date of illness onset	Sex	Age group (years)	Risk factors	Urinary antigen test	Sputum/ BAL culture	Complications	Exposure setting
1	2019-06-13	2019-06-07	F	85–89	Chronic lung disease; immunosuppression; cancer; cigarette smoking	Positive	ND	Hospitalized	Private home
2	2019-07-03	2019-06-26	M	25–29	Immunosuppression; cancer	Positive	ND	Hospitalized	Private home
3	2019-07-05	2019-06-30	M	65–69	Diabetes; chronic renal disease; cigarette smoking; alcohol consumption above lower-risk drinking guidelines	Positive	Positive	Hospitalized; ICU stay; intubated	Private home
4	2019-07-09	2019-06-18	M	65–69	Diabetes; immunosuppression; chronic renal disease; cigarette smoking	Positive	ND	Hospitalized; ICU stay	Private home
5	2019-07-12	2019-07-10	F	75–79	Diabetes; cardiovascular disease; chronic renal disease; immunosuppression; cancer; alcohol consumption above lower-risk drinking guidelines	Positive	ND	Hospitalized	Retirement home
6	2019-07-15	2019-07-02	F	30–34	Immunosuppression; cigarette smoking	Positive	ND	Hospitalized	Private home
7	2019-07-19	2019-07-14	F	80–84	Cardiovascular disease; chronic renal disease	Positive	ND	Hospitalized	Private home
8	2019-07-19	2019-07-10	M	75–79	Diabetes; cardiovascular disease; cigarette smoking	Positive	ND	Hospitalized	Retirement home
9[a]	2019-07-22	2019-07-01	M	55–59	Immunosuppression; cigarette smoking	Positive	Positive	Hospitalized	Acute care hospital
10	2019-07-22	2019-07-15	M	60–64	Diabetes; cardiovascular disease; chronic renal disease; immunosuppression	ND (anuric)	Positive	Hospitalized; ICU stay; intubated	Acute care hospital
11	2019-07-22	2019-07-20	M	60–64	Immunosuppression; cancer	Positive	Positive	Hospitalized; ICU stay; death	Cancer care home
12	2019-07-24	2019-07-16	M	70–74	Diabetes; cardiovascular disease; immunosuppression; cigarette smoking	Positive	Positive	Hospitalized	Retirement home
13	2019-08-12	2019-08-03	M	75–79	Diabetes; chronic lung disease; cardiovascular disease; immunosuppression; cigarette smoking	Positive	ND	Hospitalized	Acute care hospital
14	2019-09-03	2019-08-21	M	50–54	Immunosuppression	Positive	ND	Hospitalized	Acute care hospital

Abbreviations: BAL, bronchoalveolar lavage; F, female; ICU, intensive care unit; M, male; ND, not done
[a] Not a resident of Montréal

At 63.8 years (standard deviation: 17.6; median: 68 years), outbreak cases tended to be younger than other 2019 Montréal cases of *L. pneumophila* serogroup 1 infection whose mean age was 69.1 years (standard deviation: 11.7; median: 65 years). A larger proportion had comorbidities including compromised immunity or immunosuppression (see **Table 2**). A detailed review of findings from case investigations did not identify any common exposures between cases other than place of residence.

Environmental investigation

A total of 18 WCTs with abnormal or missing monthly monitoring results were initially sampled by order of the DRSP on July 13–18. Samples were first analyzed for *L. pneumophila* by qPCR, and if positive, by culture (**Table 3**). A positive quantifiable culture result was only obtained for one WCT (WCT-A). Review of updated monthly monitoring results on August 12 identified three WCTs with abnormal culture results in July; the isolates from two WCTs were still available (WCT-B and WCT-C), but the third had already been discarded. A resampling order was issued,

Table 2: Characteristics of *Legionella pneumophila* serogroup 1 cases in Montréal in 2019

Characteristics	Cases linked to this outbreak (N=14)		Other cases in Montréal in 2019 (N=41)	
	n	%	n	%
Age group (years)				
25–34	2	14	0	0
35–44	0	0	0	0
45–54	1	7	3	7
55–64	3	21	16	39
65–74	3	21	10	24
75–84	4	29	5	12
Older than or 85	1	7	7	17
Comorbidities (self-reported)				
Diabetes	7	50	12	29
Chronic lung disease	3	21	6	15
Cardiovascular disease	6	43	21	51
Chronic renal disease	5	36	5	12
Immunosuppression	11	79	6	15
Other risk factors (self-reported)				
Smoking	8	57	27	66
Alcohol consumption above low-risk drinking guidelines[a]	2	14	8	20
Diagnostic test				
Positive urinary antigen test	13	93	40	98
Positive sputum or BAL culture	5	36	5	12
Severity				
Hospitalization	14	100	41	100
ICU admission	4	29	11	27
Intubation	2	14	6	15
Death	1	7	1	2

Abbreviations: BAL, bronchoalveolar lavage; ICU, intensive care unit
[a] Women: >10 drinks/week; men: >15 drinks/week (14)

but the sample tested negative. Twelve other WCTs located 4 to 12 km from the epicentre had routine *L. pneumophila* monitoring results of 1,000,000 CFU/L or more during the combined incubation period of our cases. The provincial public health laboratory conducted typing of all 15 quantifiable *L. pneumophila* serogroup 1 culture isolates.

Samples from all other potential outdoor community sources tested negative for *L. pneumophila* by qPCR. Samples from the retirement home (hot water reservoir, heated pool, spa, outdoor decorative fountain and drinking water) were all negative for *L. pneumophila* by qPCR. All hospital samples taken on July 24

Table 3: Results from culture and sequence-based typing of WCT isolates

WCT	Distance to epicentre (km)	*Legionella* culture result (CFU/L)[a]	Sequence-based typing results						
			flaA	flaA	flaA	flaA	flaA	flaA	flaA
A	1.2	10,000	1	4	3	1	1	1	1
B	1.5	10,000	NA	14	16	16	15	13	2
C	3.5	2,000,000	1	4	3	1	1	1	NA
D	7.1	2,000,000	1	6	3	10	1	1	11
E	7.3	1,000,000	11	14	16	12	15	13	9
F	7.8	2,100,000	1	4	3	1	1	1	NA
G	7.9	3,900,000	1	4	NA	NA	NA	1	NA
H	8.1	3,880,000	11	14	16	12	15	13	9
I	8.3	6,600,000	NA[b]	NA	NA	NA	NA	NA	NA
J	8.5	2,000,000	NA[c]	NA	NA	NA	NA	NA	NA
K	8.8	7,400,000	1	4	3	1	1	1	1
L	9.7	5,600,000	NA[d]	NA	NA	NA	NA	NA	NA
M	9.7	2,000,000	11	14	16	12	15	13	9
N	10.3	1,000,000	1	4	3	1	1	1	1
O	11.5	4,880,000	NA[e]	NA	NA	NA	NA	NA	NA

Abbreviations: CFU, colony-forming units; NA, not available; WCT, water cooling tower
[a] Results shown are for the WCT sample with a positive quantifiable *Legionella* culture on which sequence-based typing analysis was performed; some WCTs had more than one positive quantifiable *Legionella* culture
[b] Isolate was destroyed by the commercial laboratory, in contravention of the provincial regulation that requires all *Legionella* isolates from WCT with levels of 1,000,000 CFUs/L or above to be kept for at least three months
[c] Isolate could not be analyzed due to contamination
[d] Isolate was not sent by the commercial laboratory to the provincial public health laboratory as required by public health; presumed destroyed or lost
[e] Upon reanalysis at the provincial public health laboratory, the isolate was found to be serogroup 2–15 instead of 1; therefore typing was not performed

(15 samples) and August 13–14 (19 samples) either tested negative (25 samples) or had *L. pneumophila* levels below the limit of quantification (9 samples) by qPCR.

Sequence-based typing of clinical and environmental specimens

In total, five clinical isolates were available for typing (**Table 4**); all sequenced alleles matched, suggesting a common source. Four cases had six or seven sequenced alleles, and all sequenced alleles matched each other; two cases from the acute care hospital, one from the retirement home, the other from the

Table 4: Results from sequence-based typing of clinical isolates

Case ID	Exposure setting	Sequence-based typing results						
		flaA	pilE	asd	mip	mompS	proA	neuA
3	Private home	NA	9	2	5	3	20	15
10	Acute care hospital	NA	9	2	5	3	20	15
9	Acute care hospital (same floor)	12	9	2	5	3	20	NA
11	Cancer care home	12	NA	NA	NA	3	NA	NA
12	Retirement home	12	9	2	5	3	20	15

Abbreviation: NA, not available

community. Only two alleles from the cancer care home case could be sequenced; both matched all other cases. The sequence type for the only fully typed case (Table 4, Case ID 12) was a new type, ST2858, in the EWGLI database. Typing results from the WCTs were not a match to the clinical isolates (Table 3).

Discussion

We investigated a spatiotemporal cluster of 14 *L. pneumophila* serogroup 1 cases reported over a 12-week period from June to August 2019, in Montréal. The outbreak was initially detected through routine daily automated geospatial cluster analysis of reportable disease data. Our epidemiologic investigation identified that outbreak cases tended to be younger, have more comorbidities including compromised immunity or suppression, as compared to non-outbreak cases. No common exposure was identified other than place of residence. Two sub-clusters were identified: three cases resided in the same retirement home and four had been hospitalized on the same acute care hospital floor for their entire incubation period. Typing was performed for five cases; results suggested a common source for all cases. The outbreak was declared over in mid-October, but an environmental source was never identified.

The outbreak investigation benefited from access to monthly *L. pneumophila* monitoring results for all WCTs in the provincial registry and rapid sampling WCT sampling and decontamination (through public health orders). Whereas the outbreak was eventually controlled, our extensive environmental investigations did not identify a source. One potential explanation is that a WCT may harbour multiple *L. pneumophila* serogroups concurrently (15,16) that may change rapidly over time (11) (e.g. between the case's exposure and the sampling of the WCT).

It is not uncommon to fail to identify the source of a *L. pneumophila* outbreak. The Centers for Disease Control and Prevention (CDC) did not find a source for 11 of 17 *L. pneumophila* serogroup 1 outbreaks associated with environmental or undetermined exposures to water in 2013–2014 (17). Similarly, in the United Kingdom, the source was identified in less than 50% of *Legionella* outbreaks (18,19). Recent research suggests that sequence-based typing is insufficient to discriminate between some *L. pneumophila* serogroup 1 (15,20); therefore, it is possible that our outbreak cases were not infected with the same *L. pneumophila* serogroup 1; however, this issue has not been reported for *L. pneumophila* serogroup 1 ST2858.

There were several key challenges in attempting to identify the source of this outbreak. Clinical isolates (i.e. sputum cultures) were available for only a quarter of all cases, thereby limiting our ability to assess which were linked to the outbreak and muddying the search for a common source. The unavailability of environmental isolates from WCTs with *L. pneumophila* monitoring results below 1,000,000 CFU/L, because laboratories are not legally mandated to retain them, also hampered our investigation. Those WCTs had to be resampled, often a few weeks after the initial positive result, sometimes after corrective action, thereby decreasing the probability of re-isolating the same *L. pneumophila* that had been present during the cases' incubation period. There is evidence of *Legionella* outbreaks associated with WCT concentrations of *L. pneumophila* below 1,000,000 CFU/L: a systematic review of all *Legionella* outbreaks attributed to WCTs in 2001–2012 found *Legionella* concentrations below 1,000,000 CFU/L in 4/19 outbreaks (21). A 2017 legionellosis outbreak in the *Mauricie-et-Centre-du-Québec* health region was genetically linked to a WCT that showed "interfering flora" on routine *Legionella* monitoring and had a *Legionella* concentration of 630,000 CFU/L on resampling (1). Given that 11 of the 14 patients in our outbreak were immunocompromised or immunosuppressed, it is possible that the source was a WCT with *L. pneumophila* serogroup 1 levels below 1,000,000 CFU/L.

Another important challenge was the lack of comprehensive databases on potential sources of water aerosolization other than WCTs, for example, decorative water features on public and private properties, public and private construction sites and large-scale irrigation systems. As a result, we could have overlooked a potential source. Also, whereas the RBQ estimates that nearly all WCTs in QC are registered, WCTs on federal buildings are monitored for *L. pneumophila* by a federal agency and results are not reported to the RBQ.

Finally, the provincial sampling protocol involves collecting a single 1 L water sample per WCT, under both routine and outbreak conditions. In contrast, the CDC recommends obtaining five 1 L water samples and three biofilm swabs (from specific areas) per WCT as part of an outbreak investigation (22). Following the CDC's WCT sampling protocol would have likely increased the probability of detecting *L. pneumophila* serogroup 1 in sampled WCTs, thereby increasing the probability of identifying the source of our outbreak.

Conclusion

This report describes a community-based outbreak of *L. pneumophila* serogroup 1 with retirement home and acute care hospital sub-clusters. Whereas typing of clinical isolates suggested a common environmental source, our investigation failed to identify it. Future outbreak investigations could benefit from the availability of more clinical isolates for typing, perhaps adding NAAT to culture (e.g. when antibiotics have already been started); local registries of water features other than WCTs (e.g. fountains) that could potentially aerosolize *L. pneumophila*; ongoing access to all routine WCT monitoring results, rather than public health only being notified of results above a threshold; and access to all recent *L. pneumophila* isolates obtained through routine WCT monitoring (regardless of concentration) for typing. Research is needed to update and summarize *L. pneumophila* environmental sources that have been linked

to cases or outbreaks, as well as to identify *L. pneumophila* thresholds for action that account for the possibility that immunocompromised or immunosuppressed persons may be infected by lower concentrations of bacteria.

Authors' statement

GC co-led the epidemiologic investigation and is the primary author of the manuscript
JB and FL led the environmental investigation, contributed to writing the sections on the environmental investigation and provided feedback on the manuscript
CL oversaw the analyses conducted at the provincial public health laboratory and provided feedback on the manuscript
PAP co-led the epidemiologic investigation and provided feedback on the manuscript
DK oversaw the environmental investigation and provided feedback on the manuscript
EL oversaw the epidemiologic investigation and provided feedback on the manuscript

Competing interests

None.

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The epidemiology of cryptosporidiosis in Ontario, Canada following the introduction of PCR testing in 2018

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Abstract

Background: Cryptosporidiosis is reportable in Ontario, Canada. Detection by polymerase chain reaction (PCR) was introduced by a large community-based laboratory in August 2017, and in 2018, the incidence of reported cryptosporidiosis doubled compared to 2012–2016.

Methods: We assessed cases reported in 2018 for epidemiologic changes since the introduction of PCR testing.

Results: No outbreaks were identified in 2018, and 48% of cases were detected by PCR, suggesting that the observed increase was likely the result of PCR's higher sensitivity compared with previous detection method. From the pre to post-PCR periods, the proportion of female cases increased significantly, due mainly to cases diagnosed by PCR. A significant increase in mean age was also observed among cases diagnosed by microscopy and/or PCR in the post-PCR period.

Conclusion: Our findings highlight the importance of assessing diagnostic methods when evaluating changes in reported rates. The observed changes in incidence will require ongoing monitoring and may require shorter baseline periods for aberration detection.

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Keywords: *Cryptosporidium*, cryptosporidiosis, surveillance, PCR, polymerase chain reaction, epidemiology, outbreak detection

Introduction

Cryptosporidiosis is a diarrheal disease transmitted through fecal–oral contact with infected persons or animals. Although the mode of transmission varies, infection is most acquired through ingestion of drinking or recreational water that has been contaminated with *Cryptosporidium* oocysts (1). Cryptosporidiosis is traditionally diagnosed by microscopic examination of stool specimens and/or enzyme immunoassays for detection of antigens to *Cryptosporidium* spp. However, molecular methods including polymerase chain reaction (PCR) are increasingly used (2,3). In Ontario, Canada, hospital laboratories, the provincial public health laboratory and privately operated community laboratories conduct diagnostic testing for cryptosporidiosis. Privately operated community laboratories diagnose the majority of cases reported. All laboratory-confirmed cases of cryptosporidiosis are reportable in Ontario (4), and reported cases are followed up by local boards of health that collect and report case information centrally to provincial public health officials through the integrated Public Health Information System (iPHIS).

Microscopy has been the main method of detection for cryptosporidiosis in Ontario. In August 2017, a large community-based laboratory with collection centres across the province adopted multiplex PCR testing (5). Recent studies have shown the sensitivity of microscopy to range from 52% to 56% compared to PCR, which has a sensitivity of 100% (6,7).

In this article, we describe our investigation of an increase in reported cryptosporidiosis cases in 2018 with the aim of assessing the magnitude of the increase, determining the role

of PCR testing in the increase and identifying if any shifts had occurred in the epidemiology of cryptosporidiosis since the implementation of PCR testing.

Methods

We conducted this assessment by comparing demographic, risk factor and outcome data from iPHIS for 2018 (the first full year following implementation of PCR testing) with the pre-PCR period of 2012–2016.

We extracted information on age, sex, outcome (hospitalization or death), reported symptoms, reporting laboratory (i.e. community based, hospital or public health) and method of diagnosis [i.e. PCR, microscopy, enzyme immunoassay (EIA) and culture-bacterial] from iPHIS for cryptosporidiosis cases with episode dates from January 1, 2012 to December 31, 2016 (pre-PCR) and from January 1 to December 31, 2018 (post-PCR).

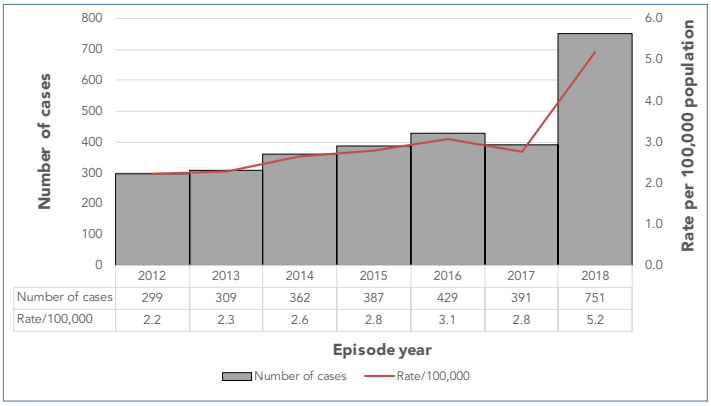
Cases with no diagnostic data, cases diagnosed by PCR in the pre-PCR period and cases that had "culture-bacterial" (which reflect data entry errors) as the method of detection were excluded from all analyses except for overall case counts and rates. Social or behavioural risk factors, including history of travel outside the province, foodborne and waterborne exposures, and animal and person-to-person contact, for cases with episode dates in 2018, were also analyzed to determine whether there were any previously unrecognized outbreaks. All analyses were performed using the statistical package SAS Enterprise Guide version 7.1 ($p<0.05$ considered statistically significant).

Results

Reported cases of cryptosporidiosis increased annually from 299 in 2012 to 429 in 2016, decreased to 391 in 2017 and then increased to 751 in 2018 (**Figure 1**). The annual rate of cryptosporidiosis in Ontario was 2.6 per 100,000 from 2012 to 2016 and 5.2 per 100,000 in 2018 ($p<0.001$). Based on 1,743 cases in the more detailed analysis, detection by PCR accounted for 48% of cryptosporidiosis cases reported in 2018, while detection by microscopy decreased from 99.8% in 2012–2016 to 52% in 2018 ($p<0.001$); EIA was the method of detection for three cases reported during the pre-PCR period (0.2%).

Statistically significant overall and sex-specific increases in mean ages were also observed; the increases in the post-PCR period occurred among cases diagnosed by microscopy and by PCR (**Table 1**). Overall, the proportion of cases among females increased from 48.5% in the pre-PCR period to 55.4% in the post-PCR period ($p<0.009$). Stratification of the post-PCR period showed that this shift in proportion from the pre-PCR period was driven by cases diagnosed by PCR (60.8% in the post-PCR period, $p<0.001$) as the proportion of female cases diagnosed

Figure 1: Number and incidence rate for all confirmed cases of cryptosporidiosis reported, Ontario, Canada, 2012–2018 (n=2,928)[a]



[a] Population Estimates 1986–2017 and Population Projections 2017–2041, Ontario Ministry of Health, IntelliHEALTH ONTARIO, extracted: November 26, 2019

by microscopy in the post-PCR period (50.4%) did not vary significantly from the pre-PCR period (48.5%, $p<0.580$) (Table 1).

From the pre to the post-PCR period, the proportion of hospitalized cases decreased from 5.5% to 2.1% ($p<0.002$). No deaths were recorded in either time period. Method of testing was not related to symptom status, although the proportion of asymptomatic cases was slightly higher among those diagnosed by PCR (2.2%) and microscopy (1.3%) in the post-PCR period relative to the pre-PCR period (0.8%).

Based on the assessed risk factors, no commonalities were reported at the provincial level that suggested the occurrence of any outbreaks among non-travel cases in 2018, or within the health units that had identified localized increases above their usual summer peak in incidence.

Conclusion

Our investigation identified a two-fold increase in the incidence of cryptosporidiosis cases in 2018, the first full year after the introduction of PCR testing in August 2017, compared to the pre-PCR period of 2012–2016. However, it remains unclear why the number of cases reported in 2017 decreased despite the introduction of PCR in that year and a gradually increasing trend in the previous five years. As only positive laboratory results are reportable in Ontario, we were not able to assess if the increase in 2018 was due to an increase in the number of cases, an increase in the number of tests ordered or an increase in positivity owing to PCR's higher sensitivity compared with previous detection method. Our investigation of the increase in 2018 also did not identify any common social and behavioural risk factors among domestic cases that were indicative of an outbreak. During the period of increase, clinical indications for testing and surveillance criteria for defining and reporting cases did not change, nor did healthcare providers have the option to

Table 1: Cryptosporidiosis cases reported during the pre-PCR period (2012–2016) compared to cases reported in 2018, overall and stratified by diagnostic method (n=1,743)[a]

Case characteristics	Pre-PCR period (2012–2016)		Post-PCR period (2018)[b]							
	Microscopy (n=1,209) and EIA (n=3)		PCR			Microscopy			Microscopy and PCR		
			n=255		*p* value[c]	n=276		*p* value[c]	n=531		*p* value[c]
Diagnosed (%)	Microscopy (99.8%), EIA (0.2%)		48.0%		–	52%		–	100%		–
Mean age (years)											
Female	23.3		27.3		<0.005	28.4		<0.001	27.8		<0.001
Male	20.9		26.4		<0.002	24.9		<0.011	25.5		<0.001
Total[d]	22.1		26.9		<0.001	26.6		<0.001	26.8		<0.001
Sex, n (%)[d]											
Female	588	(48.5)	155	(60.8)	<0.001	139	(50.4)	<0.580	294	(55.4)	<0.009
Male	620	(51.2)	100	(39.2)	<0.001	136	(49.3)	<0.573	236	(44.4)	<0.010
Hospitalized, n (%)	67	(5.5)	4	(1.6)	<0.008	7	(2.5)	<0.040	11	(2.1)	<0.001
Symptom status[e]											
Asymptomatic, n (%)	9	(0.8)	5	(2.2)	<0.084	3	(1.3)	<0.461	8	(1.7)	<0.129

Abbreviations: EIA, enzyme immunoassay; PCR, polymerase chain reaction, -, no data
[a] Excludes cases diagnosed by PCR in the pre-PCR period (n=7) and cases with no laboratory values or where the diagnostic method was reported as "culture-bacterial" (an inappropriate method of detection that was selected in error during data entry) (n=787)
[b] No cases were diagnosed by EIA in 2018
[c] *P* values based on appropriate tests for proportions (Pearson chi-square and Fisher exact test) and means (*t*-test). The *p* values indicate the probability of finding the observed values for the comparisons between the combined methods of detection in the pre-PCR period and the post-PCR period (PCR, microscopy and PCR and microscopy combined)
[d] Excludes cases where sex was reported as "other" or "unknown"
[e] Excludes cases with no data on symptoms and cases with symptoms that were classified as not clinically compatible with cryptosporidiosis (e.g. cough)

specify their preferred diagnostic method (e.g. microscopy, EIA or PCR) when ordering tests. Given these factors, it is possible that the increase in 2018 resulted, at least partially, from PCR's higher sensitivity, which resulted in the detection of cases that would have otherwise remained undiagnosed by microscopy or EIA.

With the increase in the reported rate of cryptosporidiosis, there was also an increase in the proportion of female cases in 2018, driven by PCR diagnoses. One possible hypothesis is that the baseline test positivity rate for females was lower compared to males and subsequently more affected by the higher sensitivity of PCR testing. In contrast, the increase in mean age among cases diagnosed by both PCR and microscopy in 2018 may reflect an underlying shift in the age distribution of persons tested in 2018 compared to 2012–2016. We would require data on the age and sex of persons that submitted specimens for testing, testing volumes and positivity rates to fully assess these changes in the demographics of cryptosporidiosis cases.

The shift towards fewer hospitalized and more asymptomatic cases after the introduction of PCR testing reflects PCR's higher sensitivity and use in community laboratories that test non-hospitalized patients. Similar trends among microscopy-detected cases were also observed, suggesting that factors other than the introduction of PCR testing may have influenced the shifts in hospital and symptom status in 2018. However, given the small proportions of cases overall that were hospitalized or asymptomatic, caution must be exercised in drawing conclusions from these limited post-PCR data.

Our investigation demonstrated that the traditional approach to examining incidence over time for trends and outbreak detection must be coupled with a review of other data elements such as diagnostic methods and risk factor information, which can indicate whether increases are artifacts, due to increases in sporadic cases or attributable to a specific source. We anticipate that the adoption of PCR testing for diagnosing cryptosporidiosis will occur at different times by the various diagnostic laboratories in Ontario, resulting in staggered increases in incidence. These changes will require continuous reassessment of baseline values for accurate interpretation of trends for aberration detection and timely outbreak detection. With time, we expect the emergence of a more stable and long-standing baseline at a higher incidence rate due to the more widespread use of PCR. As our investigation reflects one year of PCR testing, analysis of additional years of data is required to understand the clinical and public health relevance of cases detected by this method.

Authors' statement

KJ — Data analysis, Writing – review & editing
PT — Data analysis, Writing – review & editing
BW — Data review, Writing – review & editing

YW — Data review, Writing – review & editing
JP — Project administration, Writing – review & editing
MM — Writing – original draft, Writing – review & editing

Competing interests
None.

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RAPID COMMUNICATION

COVID-19 and the increasing need for sex-disaggregated mortality data in Canada and worldwide

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Abstract

In countries most impacted by coronavirus disease (COVID-19), such as Italy and China, surveillance reveals that the number of deaths differ by sex. Preliminary data suggest that while the distributions of cases vary by sex, men represent the larger proportion of deaths in these countries. Analyses of deaths can indicate differential disease progression between men and women more robustly than analyses of cases, as the former are less susceptible to biases of underreporting and bottlenecks in testing. Canada has an enormous opportunity to apply its sex-specific mortality data to conduct comprehensive health and medical research that captures sex-based differences in manifestation of the disease to improve outcomes and prevention methods. During the ongoing pandemic, it is difficult for complete and wholly accurate data of all COVID-19 deaths to be obtained when healthcare and public health personnel are operating at full capacity. However, it is crucial that efforts continue to be made to capture this information and make it accessible, as it can also be applied to inform implementation of more effective and equitable public health and clinical strategies, such as the dissemination of targeted health communication materials and therapy.

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Keywords: COVID-19, coronavirus, sex, gender, infectious disease

Introduction

Many countries, including Canada, have implemented substantial control measures such as physical distancing and travel restrictions to reduce the spread of coronavirus disease (COVID-19), a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease that is highly transmissible through droplets and direct contact (1–3). As of June 10, there were approximately 7.27 million cases of COVID-19 worldwide and 412,013 deaths (5). In Canada, there were 96,653 confirmed cases and 7,897 deaths had occurred as of June 9, 2020 (6).

During the 2002–2003 outbreak of severe acute respiratory syndrome (SARS), a disease also caused by a type of coronavirus, sex-based mortality data indicated that men had a higher case fatality rate than women (7,8). Other studies have also established that sex is linked with response to infectious diseases (9,10). Based on studies of SARS and other epidemic-prone infectious diseases (11), the World Health Organization has encouraged the implementation of sex-based health communication, promotion and primary care strategies.

Early sex-based mortality data from the ongoing COVID-19 pandemic indicates that males account for more COVID-19 related deaths than do females in nearly every country for which such data are available (12). Despite the preliminary observations suggesting that sex plays a role in disease outcome and severity, few countries collect complete sex-disaggregated data on deaths.

Data on COVID-19 cases can be subject to possible biases in symptom reporting and selection bias towards more severe manifestations of the illness due to bottlenecks in testing (13). In contrast, data on COVID-19 deaths are more robust. For instance, in April 2020 the Ontario Ministry of Health guidelines stated that high-risk individuals such as health care workers and persons living and working in congregate living institutions and their close contacts should be tested if displaying symptoms (14). With testing resource availability a likely barrier and women more likely to report bodily symptoms than men (15–18), there may be

a sex-based bias that can result in more men failing to seek or receive adequate care.

Gathering sex-disaggregated mortality data is crucial to providing a better understanding of sex-based disparities in COVID-19 outcome severity and mortality risk (19). Knowing these risks, in turn, can inform more comprehensive research and equitable and effective public health interventions such as targeted health communication and clinical care. Focusing on capturing these data is a feasible start to creating a national dataset that contains disaggregated sex and gender data. This review focuses on the need to gather sex-based data, which can provide insight into the role that biological differences may play in mortality risk. However, gathering gender-based data is also necessary to determine the role of gender-based inequities, norms, and behaviours in mortality risk. Gathering sex-disaggregated mortality data could begin to provide even greater insight into differential disease progression that is associated with behaviours linked with gender norms (12,20).

Current situation

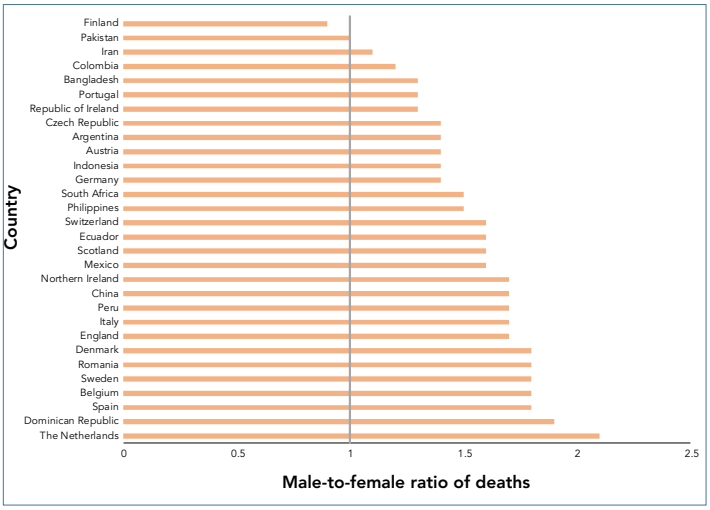
The role of sex in COVID-19 mortality risk

Women form a large proportion of the health workforce and are at greater risk of exposure to SARS-CoV-2 (21). This is reflected in their greater representation among confirmed COVID-19 cases in Canada (6). Unlike in most other countries, women also represent a larger proportion of deaths among confirmed cases. On the global scale, early studies suggested sex-based immunological differences as a possible partial explanation for the greater number of male deaths related to COVID-19 (22,23). Various studies based on populations in China found that the presence of certain medical conditions, such as those for which smoking is a risk factor, which disproportionately affect men (24), may increase the risk of severe COVID-19 illness and outcomes (25,26). Studies in populations with different ethnic and genetic backgrounds are needed to better understand sex-based differences in the expression of angiotensin-converting enzyme 2 (ACE2)—which has increased expression with smoking and is the receptor of SARS-CoV-2—and how this relates to COVID-19 mortality risk (27). The observation that Canada's mortality data does not follow the global trend of men having greater mortality risk may be attributable to other factors specific to Canada. For instance, although sex may play a role, other demographic variables such as age and other genetic factors may also contribute to mortality risk. The interplay between these factors in affecting COVID-19 mortality risk is unknown. In terms of responses to COVID-19, some studies using sex-based case data found major public health interventions such as travel restrictions and social distancing to be associated with equally improved control of the outbreak among both sexes (28,29). However, the effects of public health interventions and policy on mortality risk by sex is unknown.

Trends in sex-disaggregated mortality data

As of June 10, 2020, sex-disaggregated data for COVID-19-related deaths were available for various countries (20). While the male-to-female ratio of confirmed cases varied by country, males represented a larger proportion of deaths among confirmed cases in all but two of these countries (**Figure 1**). Meanwhile, there were several highly affected countries for which the ratio of male-to-female deaths among confirmed COVID-19 cases could not be confirmed, including the United States and France.

Figure 1: Male-to-female ratio of deaths among confirmed cases of COVID-19 in the thirty countries with the most deaths outside of Canada, where the data were available, June 10, 2020



Because sex-disaggregated mortality data on the global scale is somewhat incomplete, establishing the role that sex may play in COVID-19 mortality risk is challenging. The Government of Canada's data suggest that Canada's distribution of deaths by sex does not follow the trend that has been observed in other highly affected countries (6). Among the deaths reported as of June 9, 2020, the male-to-female ratio of deaths among confirmed cases was 0.85. This observation may be attributable to factors such as sex-based age distribution, long-term care facility resident distribution, and frontline health workforce distribution (30,31). It also warrants exploration of possible sex-based disparities in the Canadian context pertaining to areas such as public health interventions, healthcare access, and disease progression.

The Public Health Agency of Canada houses a dataset that includes sex information of COVID-19 deaths; this dataset is made available publicly in an aggregated format (6). The disaggregated line list is obtained from the provinces and territories but may be missing or lagging information due not only to challenges in data collection as the result of the pandemic but also to already existing data collection issues

exacerbated by the pandemic. This obstacle may prevent complete and up-to-date information from being recorded and passed on to the federal government for timely dissemination. Nevertheless, it is important that this information continue to be captured as best as possible as it can inform research and the public health response. Furthermore, COVID-19 cases admitted to the intensive care unit (ICU) experienced longer durations between symptom onset to hospitalization than non-ICU cases (32). Therefore, health promotion efforts that encourage men to use health services earlier and more effectively may be a practical intervention to implement.

Recommendations

Despite local, provincial and national-level institutions operating at full capacity and the challenges that might come with resource and personnel availability in some regions during a pandemic, it is recommended that efforts continue to be made to capture sex-disaggregated COVID-19 mortality data in Canada and worldwide. An effective collaboration between provinces and government would also be a catalyst for the achievement of this goal in Canada. We acknowledge the efforts being made by Statistics Canada, the Public Health Agency of Canada, Health Canada and other federal partners, working closely with provinces, territories and coroners to provide more comprehensive and timely death statistics. Sex-disaggregated data would allow for sex-based analyses to be incorporated into research pertaining to the health behaviours and outcomes surrounding COVID-19 (33) that serve to inform clinical care and health communication and to reveal how public health interventions differentially affect men and women. In terms of clinical care, improved outcomes such as reduced mortality could be seen with sex-based medical interventions if disease progression differs between men and women. In terms of public health interventions, implementing strategies such as sex-based, targeted health communication messages could be more effective in instilling prevention principles among male and female audiences. In order to gain a more comprehensive and clearer understanding of how sex and COVID-19 mortality are related, it is recommended that all countries strive to collect sex-disaggregated mortality data and make these data accessible. While we describe the rationale and advocate for the capture of comprehensive sex-disaggregated data, we have not explored the issue of gender. It is also important that gender-disaggregated data be captured as it can reveal the role of gender-based inequities, norms, and behaviours in COVID-19 mortality risk.

Conclusion

Early data from the COVID-19 pandemic suggest that men represent the larger proportion of COVID-19 deaths in most countries. Currently, Canadian response to the COVID-19 pandemic has included policies and public health efforts that consider various aspects of SARS-CoV-2, such as its infectivity and routes of transmission. However, there is an opportunity to curb the number COVID-19-related deaths and severe outcomes by incorporating the role of sex in mortality risk into more comprehensive and relevant research and to develop a more effective response that can include targeted health communication and clinical care. It is therefore essential that these data continue to be collected, made accessible and applied in Canada and other affected countries in a timely manner during the ongoing COVID-19 pandemic.

Authors' statement

AL — Methodology, investigation, writing – original draft
RE — Conceptualization, writing – review and editing, supervision
NA — Writing – review and editing
CA — Writing – review and editing
IGJ — Writing – review and editing
MH — Writing – review and editing

Competing interests

None.

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A retrospective analysis of the start of the COVID-19 epidemic in Canada, January 15–March 12, 2020

Public Health Agency of Canada COVID-19 Surveillance and Epidemiology Team[1]

Abstract

We describe the epidemiology of COVID-19 at the start of Canada's epidemic from January 1 to March 12, 2020, before governments at all levels implemented aggressive community-based public health measures. During this time, 153 laboratory-confirmed cases were reported in Canada. Due to delays inherent in the diagnosis and reporting process, these cases represented a small subset of the 1,360 confirmed cases subsequently reported, whose symptom onset occurred on or before March 12. More than half (57.8%) of these 1,360 cases had a history of international travel or were linked to a case that had travelled, most commonly from countries where few cases had been reported at that time. Community transmission, marked by cases that could not be traced back to another case, was first noted on February 20 and increased steadily thereafter. This descriptive analysis indicates that COVID-19 was spreading internationally and in Canada more broadly than was initially detected by surveillance systems from January to mid-March 2020. To limit the impact of future waves, an expanded surveillance system is now being implemented with multiple data streams to provide a more complete picture of the epidemic, including early signals of cases and clusters. Improved access to laboratory testing and expanded contact tracing are critical elements to detect and isolate cases early, including those with mild symptoms.

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Keywords: epidemic, COVID-19, Canada, retrospective analysis, epidemiology

Introduction

Following reports of severe pneumonia with an unknown etiology in Wuhan, China in December 2019 and subsequent confirmation that these illnesses were caused by a novel coronavirus on January 7, 2020, the federal, provincial, territorial and local governments in Canada implemented enhanced public health surveillance and took progressive public health action to prevent transmission of the disease inside their borders. These efforts included, and were not limited to, activating intergovernmental public health emergency response plans, implementing progressively more restrictive border measures, and establishing and expanding testing capacity. Early efforts focussed on containment at source, in order to slow importation to Canada and prevent spread domestically.

Canada's first imported case was reported on January 25, 2020 but it was not until mid-March that daily case counts started climbing. By June 2, 92,151 cases had been reported across 12 provinces and territories. Though daily case counts were on the decline at the time of writing, the disease continues to spread in some areas and settings, and no vaccine currently exists for this novel coronavirus. Evidence-based public health measures are vital to control the epidemic in Canada. Understanding the early epidemiology of COVID-19 in Canada will inform the strengthening of public health surveillance systems, allow for the implementation of appropriate public health measures, and increase understanding of impacts across different groups (e.g. women and men, different age groups).

This rapid communication describes the epidemiology of COVID-19 in Canada from January 1 to March 12, 2020. March 12, 2020 is significant because this date marks the beginning of aggressive public health measures implemented by federal, provincial and territorial jurisdictions to limit the transmission of COVID-19 (e.g. school closures, closure of non-essential businesses and strict border controls) in Canada.

Situation

Importation

Based on information received from provinces and territories as of April 17, 2020, 1,360 laboratory-confirmed cases were reported with an illness onset between January 1 and March 12, 2020. Case characteristics are summarised in **Table 1**, including cases by sex and age. During this period, more than half (57.8%) of the cases were related to international travel: 52.2% (n=710) had a history of international travel and 5.6% (n=76) were linked to cases who had travelled. Of the 710 cases with a history of international travel, 703 cases provided specific information on countries visited. More than a third (34.7%) of these cases had transited through or arrived from the United States, and almost 20% had arrived from either the United Kingdom or France (**Table 2**). Notably, only 1.4% of cases had arrived from China even though China was the epicenter of the COVID-19 pandemic throughout January and February (1,2).

Table 1: Characteristics of COVID-19 cases with illness onset from January to March 12, 2020 (N=1,360)

Case characteristics[a]	Frequency	
	n	%
Province/territory		
ON	533	39.2
QC	312	22.9
BC	250	18.4
AB	166	12.2
MB	24	1.8
NS	18	1.3
NB	17	1.3
SK	32	2.4
NL	1	0.1
PE	2	0.2
YT	2	0.2
Repatriated traveller	3	0.2
Gender[b]		
Female	670	49.5
Male	684	50.5
Age group (years)		
0–19	52	3.9
20–39	368	27.8
40–59	510	38.5
60–79	341	25.8
80 and older	53	4.0
Hospitalized (includes ICU)	195	17.5
ICU admissions	81	10.3
Deaths	27	2.5

Abbreviations: AB, Alberta; BC, British Columbia; ICU, intensive care unit; MB, Manitoba; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; ON, Ontario; PE, Prince Edward Island; QC, Quebec; SK, Saskatchewan; YT, Yukon Territory
[a] Missing data for gender (six cases), age (36 cases), hospitalized (246 cases), ICU admissions (573 cases) and deceased (280 cases) were not included in the calculation of percentages
[b] Provinces and territories may define gender differently and some may be referring to biological sex

Table 2: Countries visited by cases of COVID-19 in Canada who reported international travel in 14 days prior to symptom onset, January to March 12, 2020 (N=703)

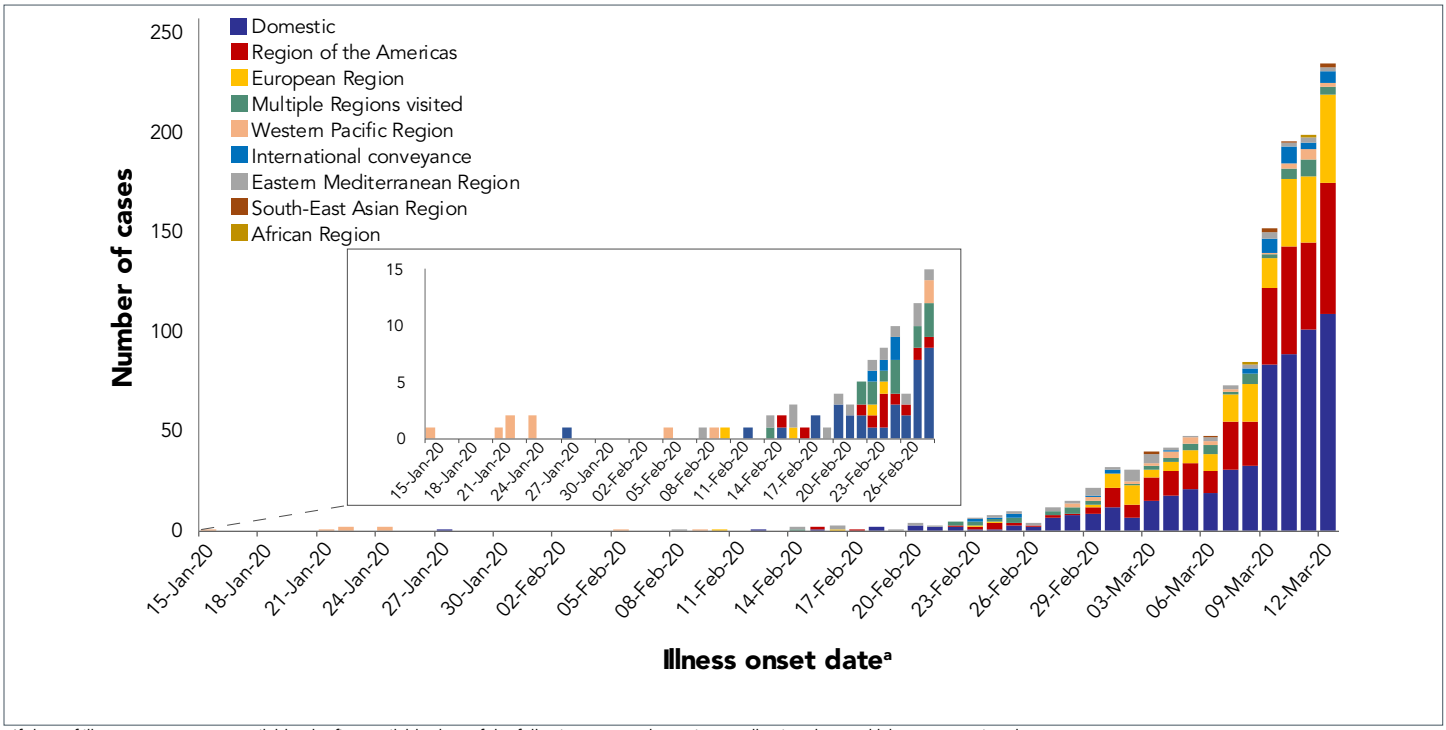
Country(ies)[a,b]	n	%
United States	244	34.7
United Kingdom	67	9.5
France	64	9.1
International conveyance (cruise)	47	6.7
Germany	45	6.4
Mexico	35	5.0
Iran	34	4.8
Egypt	33	4.7
Spain	29	4.1
Switzerland	24	3.4
Austria	22	3.1
Portugal	21	3.0
Philippines	20	2.8
Cuba	19	2.7
The Netherlands	19	2.7
Italy	17	2.4
China	10	1.4

[a] Cases reported all countries visited in 14 days prior to symptom onset, therefore proportions do not total 100%
[b] Of the 710 cases that had travelled internationally, 703 provided information on country

Cases that travelled were categorized according to World Health Organization (WHO) region(s) (3) visited to examine trends over time (**Figure 1**). In the first three weeks of the epidemic (weeks of January 12 to January 26, 2020), there were seven cases and all were either travellers arriving from China (Western Pacific Region) or their close contacts. In early February, four cases were reported with a travel history to the Eastern Mediterranean Region, the European Region and the Americas. Cases with a travel history from these regions occurred despite small numbers of cases being reported within these regions at the time [nine cases in the Eastern Mediterranean Region, 46 cases in the European region and 15 cases in the Americas (excluding Canada)] (4). In the last two weeks of February, a total of 99 cases had transited through or arrived from countries in the Americas. This occurred despite a total of only 65 cases reported within countries of the Americas (excluding Canada) by the end of February (2).

A number of border and travel health measures were implemented during this period (i.e. travel health notices, enhanced symptom screening and public health messaging at ports of entry and requesting arriving international travellers from certain jurisdictions to self-isolate for 14 days). The implementation of measures specific to individual countries was guided, in part, by the number of COVID-19 cases and the type of transmission that was reported by the WHO and individual

Figure 1: Laboratory-confirmed COVID-19 cases in Canada by date of illness onset and region of travel for cases reporting international travel, January 15 to March 12, 2020 (N=1,275)



[a] If date of illness onset was not available, the first available date of the following was used; specimen collection date and laboratory testing date

countries. The type of transmission was categorized by the WHO as imported cases only, local transmission (transmission occurred within the country with few cases not related to known chains of transmission) or community transmission, defined as the inability to relate a large number of confirmed cases to chains of transmission (2). At the time, with the exception of China, all imported cases to Canada were from countries assessed by WHO as countries with imported cases only or local transmission with no community transmission. In retrospect, it is clear that what was reported globally was only the tip of the iceberg and that the true extent of the global spread of the disease was not known at the time. Using lessons learned from the first wave of COVID-19, additional data sources and indicators will be included in the risk assessments that are used to inform various border and travel health measures such as the timely posting of travel health notices.

Early detection

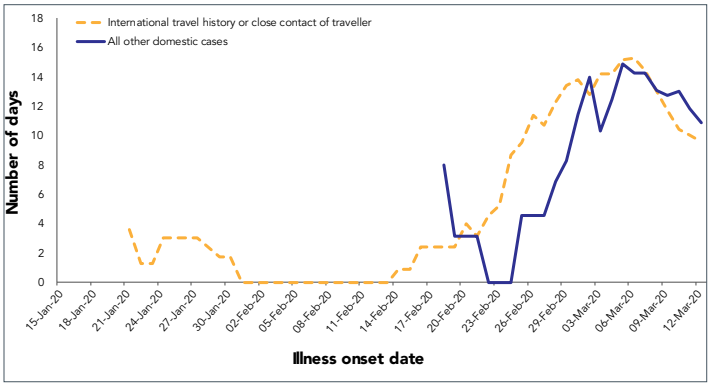
Early detection of cases is vital to implementing effective public health measures at all jurisdictional levels (local, provincial, territorial and federal). During the start of the epidemic, the median number of days between illness onset and case report date (as noted by local public health) differed significantly by type of exposure ($p<0.05$). Cases linked to international travel and those that were linked with a known case had a slightly lower number of median days between illness onset and reporting compared to cases that could not be linked to a known case (**Table 3**). In other countries, differences have been noted between those whose infections were acquired internationally compared to domestically (5,6). These differences in Canada and elsewhere were likely due to a higher index of suspicion for those with risk factors that were known at the time. The number of days between illness onset and case report date increased over time, as the number of cases that could not be linked to other cases also increased. This delay began to decrease for cases with illness onset in early March (**Figure 2**).

Table 3: Number of days between date of illness onset and case report date (N=727)[a]

Exposure category	n	Median number of days	25th percentile	75th percentile
International travel history	400	9	6	15
Domestically acquired—Linked to a traveller	49	7	5	11.5
Domestically acquired—Linked to a domestic case	134	8	6	14
Domestically acquired—Could not be linked	87	11	10	18
Domestic—Contact information not specified	57	11	8	19

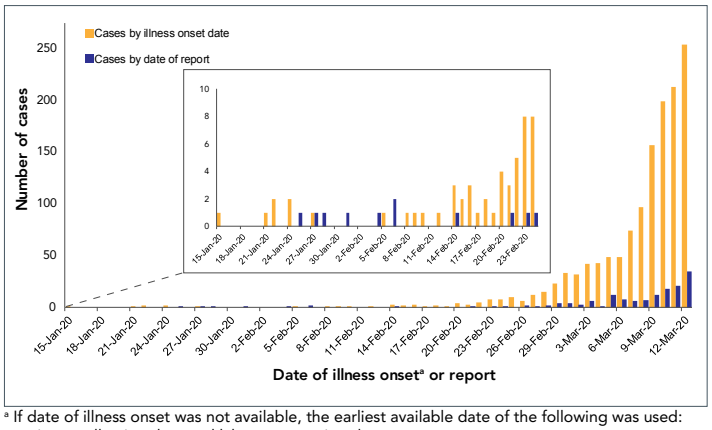
[a] Dates needed to calculate days from illness onset to case report date were missing for 633 (46.5%) cases

Figure 2: Number of days between illness onset date and case report date (seven day moving average) for COVID-19 cases by exposure, January 15 to March 12, 2020 (N=727)



At the provincial, territorial and federal levels, timely information on cases is needed to develop, implement and evaluate programs and policies to limit transmission. Due to the length of time between illness onset and reporting of cases, provinces and territories had only reported 153 COVID-19 cases as of March 12th, compared to the 1,360 laboratory confirmed cases with actual illness onset during this period (see **Figure 3**). As well, there were likely unreported infections during this period due to limited testing at the time. Results from some countries have indicated the disease was already spreading before the rapid rise in cases was apparent and noted, or in the case of France, even before the first case was reported (7,8).

Figure 3: Number of COVID-19 cases reported daily by provinces and territories compared with those with illness onset[a], January 15 to March 12, 2020



[a] If date of illness onset was not available, the earliest available date of the following was used: specimen collection date and laboratory testing date

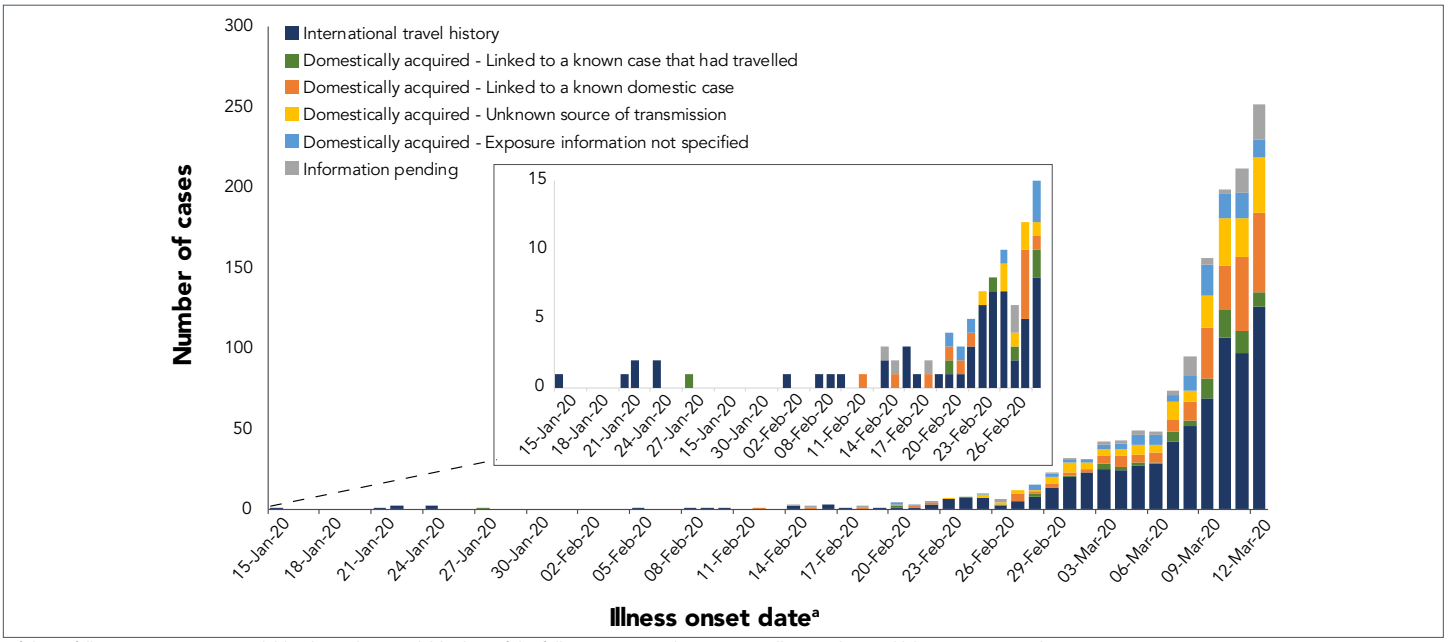
At the start of the epidemic, public health surveillance efforts were informed by the surveillance guidance within the Canadian Pandemic Influenza Plan (9). For example, in the initial stages of Canada's epidemic, detailed information was captured on confirmed cases (10) to allow for a description of the epidemiological characteristics of the cases. These efforts were complemented by provincial and territorial efforts, including enhanced surveillance in certain settings (e.g. testing of individuals with respiratory illness in hospitals). Moving forward, a number of complementary data streams will be integrated, to help strengthen COVID-19 monitoring efforts at the national level and detect early signals of increases in cases or clusters or changes in disease severity. These data streams are expected to include provincial and territorial case-based information, federal and provincial public health laboratory data; hospital, emergency and outpatient data, outbreak information and syndromic surveillance through the "Fluwatchers" app (11), among other data sources. The results of future studies will be used to build on the information gleaned from these surveillance activities, and will provide more detailed information on key populations (e.g. the impact of COVID-19 on racialized communities, health care workers, Indigenous communities, and different groups of women, men and gender diverse people).

Onward transmission

In the first four weeks of Canada's outbreak (weeks of January 12 to February 2), 100% of the cases were related to travel (had travelled, or were linked to a traveller). From the week of February 9 to March 12 between 11% and 40% of cases, by week, were domestic cases that could be traced back to another domestic case. On February 23, the first case became ill who could not be linked to another known case (an indicator of community transmission), after which the number of such cases grew steadily (**Figure 4**). Other countries have similarly experienced a short phase of mostly imported cases, followed by the onset and exponential growth in domestically acquired cases (12).

To prevent onward transmission, at the start of the epidemic, guidelines on infection prevention and control and on public health management of cases and contacts were disseminated to facilities and to public health professionals. Canadians were urged to self-monitor for symptoms, to stay at home when ill and practice frequent and meticulous hygienic measures. Nonetheless, community transmission occurred and the number of such cases increased rapidly. This may reflect a number of factors: Canada was still in its influenza season and individuals may not have sought out testing if they had influenza-like symptoms; the contribution of transmission from individuals with mild symptoms who did not seek out testing or who did not qualify for testing given the testing guidance in place at the time; or transmission from individuals who were pre or asymptomatic (13).

Figure 4: Laboratory-confirmed cases of COVID-19 in Canada by date of illness onset and exposure category, January 15 to March 12, 2020 (N=1,276)



[a] If date of illness onset was not available, the earliest available date of the following was used: specimen collection date and laboratory testing date

Conclusion

At the start of Canada's epidemic, public health measures to limit the spread of COVID-19 were guided, in part, by the epidemiologic data available at the time. In hindsight, it is clear that these data did not provide the full picture in relation to when and where the disease had spread or how and when individuals were capable of spreading the infection to others. As new evidence emerged to expand our knowledge of COVID-19 epidemiology, our case detection protocols, public health measures and other areas of the COVID-19 response were adapted. Moving forward, surveillance systems will likewise continue to be enhanced through the addition of numerous data streams, which will allow for a more complete picture of the epidemiology of COVID-19 and for the early detection of cases and clusters to inform public health action and improved management of COVID-19 in Canada.

Authors' statement

DP — Conceptualization, original draft, review and editing
LL — Data curation, formal analysis, review and editing
LW — Review and editing
AC — Conceptualization, review and editing
KW — Review and editing
MB — Review and editing
DT — Review and editing
CA — Review and editing
JT — Data curation, formal analysis
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None.

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Effective presentation of data in tables and figures

Patricia Huston[1]

Abstract

The presentation of data in tables and figures is a hallmark of scientific publications. Tables and figures are most effective if they reflect two principles and a number of best practices. The first principle is to use tables and figures to highlight the main findings of a study. The second principle is to choose the appropriate format based on the type of data. Tables are most effective for presenting precise data and multiple outcomes. Figures are most effective for presenting trends over time or comparative values. When constructing a table, different populations are identified in columns and then compared according to variables that are identified in rows. This structure enables comparisons between the different study populations. When constructing figures, the independent variable (such as time) is on the horizontal or x-axis and the dependent or outcome variable is on the vertical or y-axis. Good titles for both tables and figures give a concise description of who, what, where, when and how many. Electronic readers can read tables if there are visible row and column lines and there is a single datum per cell; electronic readers can read figures if there is a link to an Excel spreadsheet with the data or if there is a short text description. With these principles and best practices, tables and figures will highlight the key findings of scientific studies in a way that is clear, accessible and memorable.

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Introduction

A hallmark of a scientific study is the presentation of data; yet authors often do not consider how they are going to present their data before starting to prepare manuscripts for publication. Definitive textbooks on this topic are available (1–4), as are articles in other disciplines (5–7). However, these sources generally do not consider international guidelines on ensuring that online publications are accessible to those visually impaired (8). These guidelines have been adopted by scientific publishers worldwide, and knowing how to comply with them prevents the need for subsequent revision.

The objective of this article is to provide researchers with a concise overview of principles and best practices for creating accessible tables and graphs in health research. Information on other types of figures, such as photographs, diagrams and biomedical images, can be found elsewhere (1).

Appropriate use

Tables and figures are often essential in communicating health research. To present data effectively, you need to apply two key principles and certain best practices. The two key principles are to highlight the main findings and to choose the appropriate format based on the type of data. Best practices include conventions for creating titles; structuring tables and figures; and making abbreviations and footnotes accessible so they can be read by those who use electronic readers with text-to-speech technology (9).

The question of how much data to include often arises when starting to prepare research findings for publication. The initial impulse may be to share all that has been gleaned. With the growing trend towards open science and open data, this is now in fact possible: whole datasets are being posted and made accessible online (10). In a scientific publication, however, a clear focus helps readers identify and retain the key findings of a study; too much data can be overwhelming. On the other hand, if readers are presented with too little data, they may get the impression that there is a lack of substance to support the scientific findings.

The best way to get the presentation of data in tables and figures just right is to use these to focus on the main findings, including both the results of the methodology (more on this below) and the main outcome measures of the study. Know that,

as part of assessing whether a manuscript is appropriate for a journal, editors will assess if the information provided by the figures and tables is warranted based on the paper's length and if the manuscript fits within the journal's space limits (11). As a general rule of thumb, medical journal articles typically include three to four tables and figures and often no more than five to seven.

Methods

There are at least three instances when a table or figure showing pertinent information on the methodology is indicated: randomized clinical trials, systematic reviews and studies that involve two or more populations. For randomized clinical trials, the CONSORT statement has identified the need for a flow diagram to show how many people were invited to join the study, how many accepted and were randomized, how many were in each group, and how many dropped out or completed the study (12).

In systematic reviews, the PRISMA statement has identified the need for a flow diagram to show the results of the literature search and the winnowing down of the studies based on inclusion and exclusion criteria (13).

In epidemiologic studies involving two or more groups (such as a nested case–control study), the STROBE statement notes the need to describe the demographic, clinical and social characteristics of study participants, and information on exposures and potential confounders for cases and controls (14); a table is the most efficient way to do this. A table also helps readers assess whether the groups were similar at the start of the study; randomization does not always result in equivalent groups. In both randomized controlled trials and case–control studies, if one group ends up with more co-morbidity, for example, this may bias the results and needs to be taken into account when interpreting the results.

Main outcomes

Key research findings include the main outcome measure and, often, a number of secondary measures that are all linked to the objective of the study. The objective can have several components. For example, if the objective of a study is to examine trends in new HIV cases over a certain period of time by age, sex, geographic location and risk group, each of these areas would be addressed in the results. One would anticipate data in each of these areas to be visually displayed.

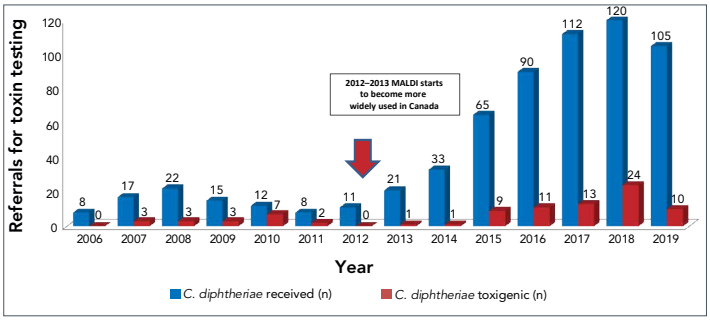
Once you have identified what you want to highlight, the question is "is it best to present the data in a table or a figure?". The answer depends on the type of data you have to present. A trend over time is best presented in a figure. If exact values are important, or there are many, these are best presented in a table (1).

Figures

Figures can provide instant information that would otherwise take many sentences to explain. A graph or a histogram easily and memorably shows comparative data or identifies trends over time. For example, a graph is commonly used in surveillance summaries and outbreak reports to show disease incidence.

For graphs, the y-axis identifies the measures of interest (such as rates or the number of cases) and typically begins at zero. The x-axis represents the independent variable, for example, time (by days, months or years) (see **Figure 1**). Such a visual display makes it instantly obvious whether rates are increasing, decreasing or staying about the same. If you need to condense the height of the graph, the y-axis can be a logarithmic scale or you can use a pair of diagonal lines (-- // --) to show that the scale is not continuous.

Figure 1: *Corynebacterium diphtheriae* referrals for toxin testing by year and subset by number of toxigenic strains, 2006–2019 (15)



Abbreviations: *C. diphtheriae*, *Corynebacterium diphtheriae*; MALDI, matrix-assisted laser desorption/ionization spectrometry
Source: Bernard *et al.*, 2019 (15)

Colour can be used to differentiate between different lines in graphs or bars in histograms, but to meet accessibility guidelines, the colours need to be sufficiently different to pass a colour blind test or have an additional design feature to distinguish them. Figures need a legend to identify each line or bar. In Figure 1, the legend identifies the data represented by the red bars and the blue bars; both of these colours passed colour blindness testing.

Tables

Precise outcomes and multiple types of data are best presented in tables. When constructing tables it is useful to consider both structure and the placement of content.

Structure

Authors often wonder what data to note in rows and what data to note in columns. A general principle is dependent or outcome variables are identified in rows and independent variables are

identified in columns (1). For example, if you are comparing the characteristics of two study populations, the study populations would be identified in columns and the different baseline characteristics or outcomes would be presented in rows. English and French is read horizontally and noting the characteristics in columns enables readers to more easily compare the two populations.

Each column needs a heading that describes what is in the column. Headings that span two or more columns are called spanner headings. For example, spanner headings might describe different populations (e.g. "Documented two-dose vaccination," "Documented one-dose vaccination" and "No documentation or no history of vaccination"). Under each spanner heading are two column headings for "n" and "%" (**Table 1**).

Table 1: Names and components of a scientific table[a]

Column heading for stub and row headings		Spanner head				Total	
		n	%	n	%	n	%
Stub heading	Row heading 1	-	-	-	-	-	-
	Row heading 2	-	-	-	-	-	-
	Row heading (n)	-	-	-	-	-	-
Stub heading	Row heading 1	-	-	-	-	-	-
	Row heading 2	-	-	-	-	-	-
	Row heading (n)	-	-	-	-	-	-
Total	-	-	-	-	-	-	100

Abbreviation: -, not applicable
[a] Adapted from Style Manual Subcommittee, 2014 (1)

The far left column heading describes what is in the rows. In the far left of each row are row headings. Stub headings, which organize row headings into groups, can be included. Each row heading describes the data in the cells to the right. Consider the order of the row headings. This may be in chronologic order (e.g. "status on admission," "status at discharge," "status six months post-discharge"); in alphabetical order (such as the names of different countries if you are comparing their incidence of diseases) or geographically (e.g. disease incidence in Canada by province or territory from west to east). Ensure that each spanner, column, stub and row heading accurately describes what is presented in the cells it covers.

Write only one datum per cell and leave no cell empty. The convention used to be to write the "n" value followed by the percentage in brackets in a single cell. As seen in Table 1, these are now written in separate columns in order to be accurately interpreted by electronic readers (8,9). If the datum is zero, write zero. If there are no data, write "ND" (for "no data") or "NA" (for "not applicable") and explain the abbreviation below the table.

Content

Usually numeric results in tables are right justified and numbers are aligned on the decimal point (1). If the total sample size is less than 100, use percentages as whole numbers (i.e. no decimal points) so you do not give the impression of greater precision than is merited (3). Likewise, if the total sample size is less than 20, no percentages need be reported (3). If the units vary in a column (for example, if you are reporting on different blood test results), the units need to be identified in the row headings and the data in each cell may be centred.

When indicated, add a column for a statistical measure of variation, such as standard deviation or standard error of the mean, and another column for the *p* value (11).

In general, the entire study sample should be accounted for (3). If you are missing data for some elements (for example, if a survey participant did not respond to some questions), consider adding a "no response" category so readers can consider how this may affect the overall results. Related to this is that both the actual number (or "n") and the percentage should be given and all the percentages should add up to 100% (3). To demonstrate this, there is often a total in the far right column and/or the bottom row.

Once the table is constructed there are a few finishing touches to consider, for example, how to minimize empty space. For text tables, use abbreviations and symbols to minimize column width, and then adjust column widths so the columns that contain the most information have the largest width. Finally, always double-check the numbers in the table with the original data and ensure any corrections are reflected in the text.

Best practices

There are a number of best practices that cover all the other information that may be associated with tables and figures. This summary is based on the definitive style manual for scientific publications, *Scientific Style and Format* (1), the international *Recommendations for the Conduct, Reporting, Editing and Publication of Scholarly Work in Medical Journals* (15) and the *Web Content Accessibility Guidelines* (8).

Titles

The title of a table or figure should give enough information that it explains the data in the table without having to read the context in the article. Consider each table and figures as a "stand

alone." The title should be concise but complete, and include who and what, when and where and, when indicated, the total sample size. A set of tables or figures containing similar types of information calls for a parallel format for the titles. For example:

- Figure 1: New HIV cases in Canada, 2019, by geographic area (n=)
- Figure 2: New HIV cases in Canada, 2019, by age and sex (n=)
- Figure 3: New HIV cases in Canada, 2019, by risk factor (n=)

Abbreviations, footnotes and references

Abbreviations are generally identified in the line immediately under a table or figure and are listed in alphabetical order (e.g. AST, aspartate aminotransferase; DWI, driving while intoxicated, etc.). Even if abbreviations have been introduced in the text, they should be redefined under a table or figure so that these can be stand alone.

Footnotes are used when more explanation is needed. Footnotes are identified by placing a letter in superscript (beginning with "a" and proceeding in alphabetical order) immediately following the words or numbers that need additional explanation. Numbers are eschewed for footnotes as electronic readers may confuse them with either results or reference numbers. Footnotes are identified sequentially in the same order as one reads—from left to right in rows and from top to bottom. As shown in Table 1, the footnotes are placed sequentially, below the abbreviation line.

References are identified in tables to either show the source of a table or support an assertion in a footnote. References cited only in tables or figure legends should be numbered based on where the table or figure is first cited in the text. For example, Figure 1 above has a reference after the title that keeps the citations in numeric order.

Additional data

If you use data from other published or unpublished sources that are not in the public domain, you need to submit to your publisher written permission from the copyright holder to reproduce these data (11). There is a trend now to move away from copyrighted articles to the public domain, such as with a Creative Commons licence (16). In any case, it is important to identify the source and indicate if any changes were made to the original.

Occasionally, additional tables containing backup data may be appropriate in an appendix or a supplement or they are made available to readers directly by the authors upon request. This is something that is negotiated with the journal editor. When agreed to, a statement is added to the text to inform readers that this additional information is available and where it is located. Additional data are typically included with the manuscript upon submission so that the data are available as part of the peer review process.

Identification in text

Each table and figure in an article should be identified in the text. Tables and figures are numbered in order and the publishing convention is to place them at the end of the paragraph where they are first identified. However, for manuscript submission, most medical journals request that authors place the tables and figures at the end of the manuscript (11). This allows editors and reviewers to focus on the text and the data presentation separately. Tables and figures are placed in the text during layout based on convention, but this may be altered slightly to maintain a pleasing layout to the article. It is useful to know this and avoid making statements like: "See Tables 1–4" as this means the text would normally be followed by four tables, which breaks up the flow of the text and creates formatting challenges on the printed page.

Accessibility

Electronic readers are able to read tables—as long as there is only one datum in each cell—but they are not able to read figures. To accommodate this, either include an Excel spreadsheet (for graphs, histograms and pie charts) or add a text description (for flow diagrams and illustrations). **Table 2** shows an Excel-type table used to identify the data in Figure 1. In the HTLM version of the original publication, the table was hyperlinked to the word "Text Description" found below the figure (15).

Conclusion

Creating effective tables and figures is essential to successfully communicate scientific research. When developed to highlight the main findings of a study and constructed based on best practices, tables and figures help to make the results of a scientific study clear, accessible and memorable.

Table 2: Text description of Figure 1 for people with visually impaired

Species	Toxigenic strains/year														
	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
C. ulcerans received (n)	0	3	1	0	0	0	0	4	5	1	0	1	2	5	22
C. ulcerans toxigenic (n)	0	1	1	0	0	0	0	1	4	0	0	0	1	2	10

Author's statement

PH conceived and wrote the article.

Competing interests

None.

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Considerations for mandatory childhood immunization programs

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Abstract

Outbreaks of vaccine preventable diseases occur even in countries that have unrestricted and relatively equitable accesses to immunizations because vaccine uptake rates are lower than necessary for effective disease control. Vaccine hesitancy is seen in many countries, including Canada, and has led to enacting or strengthening legislation requiring mandatory childhood immunization in some provinces. Although mandatory immunization may seem to be the simplest solution to this issue, it is not always as effective as anticipated. Different countries/states/provinces/territories have used different strategies to encourage parents to fully immunize their children. Definition, scope, flexibility (such as exemptions for medical, religious and philosophical reasons) and framework factors (such as strictness of application and levels of enforcement of the mandate) vary widely between jurisdictions. Surprisingly, no marked differences were seen in vaccination rates between countries that recommended versus mandated them. Unintended consequences of mandatory immunization programs—both good (increased availability of data) and bad ("gaming" of the system and disproportionate impacts on families of lower socioeconomic status) have been reported. Addressing lower vaccine uptake rates is a complex problem that needs a multipronged, more nuanced and tailored approach.

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Keywords: childhood immunization, mandatory, CANVax

Introduction

Outbreaks of vaccine preventable diseases occur even in high-income countries that have unrestricted and equitable access to immunizations. The reason for these outbreaks is that vaccine uptake rates are not where they need to be for adequate control of vaccine preventable diseases. Parents in many jurisdictions, including Canada, have been hesitant about immunizing their infants and children on time and on schedule (1). As a consequence, several countries have discussed, enacted or strengthened mandatory childhood immunization legislation to address this vaccine hesitancy problem (2–4). Mandatory immunization is seen as a "simple" solution to the problem. Historically, three factors appear to act as triggers for the implementation of mandatory childhood immunizations: failure of incentives to achieve desired vaccine uptake rates; response to a vaccine preventable disease outbreak that is difficult to control because of lower than desired vaccine uptake rates; and the push to achieve a vaccine preventable disease elimination goal, such as for polio (5).

Given that queries have also been raised in the press about whether coronavirus disease 2019 (COVID-19) vaccine(s), when available, should be made mandatory for some or all in Canada, this Canadian Vaccination Evidence Resource and Exchange Centre (CANVax) Brief provides an overview and brief discussion of what mandatory childhood vaccination means followed by discussions of scope and framework factors to consider. Also discussed are the reported outcomes, including reports of unintended consequences.

This is the sixth in a series of articles, produced by CANVax, an online database supporting immunization program planning and delivery. This series includes both the identification of existing resources and the description of the new resources developed by a multidisciplinary group of professionals (6). The article is one of a series and shows how the various aspects of vaccine hesitancy that have been considered to date can be applied to fostering vaccine acceptance.

Definition, scope and frameworks of mandatory immunization programs

In 2010, an expert group proposed the definition that a "mandatory" vaccine is one that every child in the country/state/

province/territory must receive by law without the option for the parent to accept or refuse it, independent of whether a legal or economical implication or sanction exists for the refusal (7). Mandatory immunization programs vary widely. There is neither a uniform approach for establishing mandatory immunization programs nor a common scope for such programs. Hence, it is critical when discussing any mandatory program for childhood vaccinations (and/or for other age groups) to understand what that program entailed and what it was hoped that program would achieve.

With respect to childhood immunizations, the scope of the mandate may apply to the entire country (Italy (3) and France (3)) or to specific constituent states, territories or provinces (California, United States (US) (3) and Ontario, Canada (8)), or it may apply more narrowly to a defined subset of the child population (9). Some programs cover most but not all of the World Health Organization (WHO) recommended childhood vaccines (e.g. Italy (3)), another may identify a limited range of vaccines (e.g. France, a specific list (3)) and another only one vaccine (Belgium, polio vaccine (10)). Some may specify an age group or milestone such as on school entry (Italy on enrolment in kindergarten) (3) and California, US, on school entry). With respect to flexibilities, some contain exemptions for medical contraindications only, while others include or previously included exemptions for religious and philosophical reasons (California, US (4) and Australia (11) prior to 2016).

Framework factors, such as strictness of application and levels of enforcement of the mandate, also vary, as can the body responsible for enforcement of the mandatory requirements (California, US) (4). Other programs may not enforce the mandate at all (Serbia). The program may focus on financial incentives to encourage compliance (11) or impose penalties that maybe financial or social (e.g. children can be precluded from daycare (Ontario, Canada (12) and Australia (11)) or school entry (California, US). Individuals may be precluded from access to theme parks (California, (12)) or they may be fined (Slovenia (10)) or even imprisoned (Uganda (13)).

There is a wide diversity of approaches to mandatory childhood immunization required by law:

- No enforcement, anyone can opt out without penalty (e.g. France before changes in 2018 (2))
- Opt out due to personal or philosophical objection without penalty (e.g. Ontario before changes in 2016 (14))
- Laws requiring parental education about immunization (rather than immunization itself); opt out with personal or philosophical objection but requires specific forms and notarization but no penalty for noncompliance (e.g. Ontario (8))
- Laws requiring immunization but opt out with personal or philosophical objection that requires specific forms and added effort. There is a penalty for noncompliance and strict enforcement (e.g. Australia before changes in 2016 (11))
- Laws requiring immunization with serious financial penalties or social restrictions; only allowing medical exemptions; strict enforcement (e.g. California, US after 2016 (4,15) and Australia after 2016 (11))

Outcomes of mandatory immunization programs

There are surprisingly few systematic reviews, and very little comparative evidence on the outcomes of mandatory infant and childhood immunization programs. A 2006 report noted no strong difference in vaccination rates between countries that only recommend certain vaccinations and countries that mandate them (16). A 2016 systematic review of outcomes of mandates found only 11 before and after studies, and 10 studies comparing immunization rates in similar populations with and without mandates. Overall, the authors concluded that mandatory immunization was generally helpful to increase vaccine uptake rates, albeit 18 of the included studies originated from one country, the US, with only two from Canada and one from France (17). This review did not assess the impact of mandatory immunization on attitudes toward immunization.

In 2018, a landscape review of the legislative environment for childhood immunization was conducted in 53 countries of the European region (18). Findings of this review showed a diversity of legislative frameworks for immunization (from recommendations to strong mandatory policies) with no clear evidence for the "best approach" to enhance vaccine uptake and acceptance (i.e. uptake rates did not correlate with presence or absence or type of legislation). To interpret the results correctly it is necessary to understand the differences that exist between mandatory immunization programs in a historical and geographical context. The 15 ethnic Republics that composed the former United Soviet Socialists Republic and its communist neighbours all had very strong centralized public health systems with mandatory vaccination that enabled enforcement without question and was associated with high uptake rates. By 2018, however, much had changed with respect to childhood immunization in many of these countries. By 2018, Ukraine had the lowest childhood vaccine uptake rate in the WHO European Region, and Serbia and Poland had experienced protests against mandatory immunizations.

There have not been studies of mandates in high-income countries in jurisdictions with relatively high baseline rates or with mandates for child-care centers. In Belgium and Italy, for example, some vaccines were mandatory for historical reasons and others were not. Non-mandatory vaccines may have been perceived by the public and health care professionals as being less important and less necessary. In Italy, this divergence in the program led to high coverage (all greater than 93%) of the mandatory vaccines (e.g. diphtheria, tetanus, poliomyelitis and hepatitis B) but lower than needed coverage of other

recommended but not mandated vaccines (e.g. measles coverage was 87%) (3). Measles outbreaks led Italy to move to broader mandatory immunization (3).

In Australia, in 2015, due to concerns about uptake rates, the *No Jab No Pay* amendment bill removed the vaccination "conscientious objection" exemption to vaccination requirements (11). By March 2017, these changes were associated with an increase in vaccine uptake among five-year olds from 92.59% to 94.34% (10) but, as noted below, the impact of the change was not uniform across socioeconomic classes.

In Ontario, tightening of the mandatory process required to obtain a philosophical exemption has revealed valuable information, as this newly available record-level data has permitted more detailed analysis (19). In 2016–2017, 2.4% of students had a non-medical exemption to at least one antigen; however, there were also students who were not yet immunized but who had not requested an exemption. Furthermore, having a signed non-medical exemption did not always correlate with non-immunization. The likelihood of having a non-medical exemption and not being immunized was higher for private or other non-government funded schools and specific geographic areas. In addition, older and/or disadvantaged students were less likely to have a non-medical exemption.

Unintended consequences of mandatory immunization programs

Mandatory immunization programs have the potential for unintended consequences. The removal of non-medical exemptions (i.e. personal belief exemptions) has led to an increase in medical exemptions in California, US (20) and Australia (11). Regions with high previous rates of personal exemptions before the instigation of more restrictive laws appear to develop higher rates of medical exemptions. This suggests a "gaming" of the system. Disappointingly, the target population response has been to seek medical exemption rather than to accept immunization.

In Australia, the *No Jab No Pay* mandatory childhood immunization program did increase immunizations as noted above; but disproportionately children and families living in poverty were most negatively affected, leading to equity and justice concerns (11).

An unintended benefit of mandatory programs is the requirement for greater attention to data collection on who is immunized. This was notable in Ontario where time, attention and funds were paid to make the childhood immunization registry functional.

COVID-19 vaccines and consideration for a mandatory approach

While a poll in Canada in late April 2020 reported strong support amongst the general public for making COVID-19 vaccination mandatory (21), this strategy can only be considered when these vaccines become widely available in Canada. Given that a mandatory program has costs both in terms of implementation and monitoring (5), decisions need to rest on what additional benefit is hoped to be achieved. If vaccine uptake is already expected to be high amongst groups deemed necessary for the control of the spread of COVID-19, then the added costs of a mandatory program are likely not justified. In contrast, if the rates of uptake are low and the ease of access and other strategies known to improve uptake have been addressed, then a mandatory approach may be worth pursuing. Careful attention must be paid to whether this will be an incentive or penalty program, how it will be monitored and by whom (5).

Conclusion

There is no standard global approach to mandatory immunizations. Which vaccines are included, which age groups are covered, program flexibility and rigidity (e.g. opportunities for opting out, penalties or incentives and degree of enforcement) all have to be considered. Mandatory immunization for childhood vaccines is no guarantor that the problem of lower-than-desired vaccine uptake rates will be overcome, although it can lead to increased uptake. There were no strong differences in vaccination rates between countries that only recommend certain vaccinations and countries that mandate them. Context matters; different countries have implemented or not implemented mandatory immunization for different reasons, different circumstances and used different approaches. Furthermore, unintended consequences like a reduced acceptance rate of non-mandatory immunizations needs to be anticipated as well as the possibility of vaccine-hesitant individuals gaming the system. Rigid mandatory vaccination requirements may appear, at the first sight, to be the simple solution to improving vaccine uptake rates; however, evidence does not strongly support this conclusion. Mandatory immunization is but one strategy to consider. Addressing lower vaccine uptake rates is a complex problem that needs a multipronged, more nuanced and tailored approach (22).

Authors' statement

NEM — Writing original draft
ED — Writing, review & editing
DG — Writing, review & editing

Competing interests

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CANVax is the first online resource of its kind in Canada to equip public health professionals with access to a centralized resource centre focused on vaccine acceptance and uptake.

https://www.canvax.ca/

ALREADY PUBLISHED IN CCDR

A new resource to summarize evidence on immunization from the Canadian Vaccination Evidence Resource and Exchange Centre (CANVax) – CCDR Vol. 46 No. 1 (January 2, 2020)

Promoting immunization resiliency in the digital information age – CCDR Vol. 46 No. 1 (January 2, 2020)

Optimizing communication material to address vaccine hesitancy – CCDR Vol. 46 No. 2/3 (February 6, 2020)

Motivational interviewing: A powerful tool to address vaccine hesitancy – CCDR Vol. 46 No. 4 (April 2, 2020)

Vaccine acceptance: How to build and maintain trust in immunization – CCDR Vol. 46 No. 5 (May 7, 2020)

Managing immunization stress-related response: A contributor to sustaining trust in vaccines – CCDR Vol. 46 No. 6 (June 4, 2020)

Infectious disease climate change fund

Source: Public Health Agency of Canada. Infectious Disease and Climate Change Fund; PHAC. Ottawa (ON) 2020. https://www.canada.ca/en/public-health/services/funding-opportunities/infectious-diseases-climate-change-fund.html

Public health plays an important role in raising awareness about the effects of climate change by equipping 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 multijurisdictional and multidisciplinary actions (https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2018-44/issue-10-october-4-2018/article-6-lyme-disease-grants-contributions-2018.html). The following projects funded by the Public Health Agency of Canada's (PHAC) Infectious Disease and Climate Change Fund (https://www.canada.ca/en/public-health/services/funding-opportunities/infectious-diseases-climate-change-fund.html) are just a few that are helping to advance knowledge and increase capacity within Canada to address climate-driven infectious diseases, such as Lyme disease.

eTick (Bishop's University)

This innovative project, bringing science into the hands of Canadians, is a bilingual public platform for image-based identification and population monitoring of ticks in Canada. By submitting a tick picture on eTick.ca or through the new eTick mobile app, you can get a species identification by trained personnel within one business day, to know if you or your pet might have potentially been exposed to tick-borne diseases, such as Lyme disease. Once the tick has been identified, your submission will automatically appear as a dot on an interactive distribution map and awareness/education materials. They have recently expanded the eTick (http://etick.ca/) website and launched a new eTick app [available in English and French for iOS (https://apps.apple.com/ca/app/etick/id1501804954?l=fr) and Android (https://play.google.com/store/apps/details?id=com.comit.etick)].

While the website and app are currently available to residents of Newfoundland and Labrador, Nova Scotia, New Brunswick, Québec, Ontario and Saskatchewan, Bishop's University is working to expand its partnership with other Canadian jurisdictions.

Climate-driven vector-borne disease guidelines (Canadian Association of Schools of Nursing)

The Canadian Association of Schools of Nursing have recently released Guidelines for Undergraduate Nursing Education on Climate-Driven Vector-Borne Diseases [available in English and French (https://www.casn.ca/2020/04/guidelines-for-undergraduate-nursing-education-on-climate-driven-vector-borne-diseases/)]. These are national, consensus-based guidelines that offer direction to nursing faculty on curriculum development on climate change and vector-borne diseases (VBDs). The domains and accompanying entry-to-practice learning outcomes in this guideline delineate the key knowledge, skills, and attitudes that all new registered nursing graduates in Canada should possess to support and care for individuals, families, communities, and populations affected by, or at risk of being affected by, climate-driven VBDs.

Early Lyme disease Management in Primary Care (Centre for Effective Practice)

Already the most common tick-borne illness in Canada, the incidence of Lyme disease is increasing due to blacklegged tick population growth (https://www.canada.ca/en/public-health/services/funding-opportunities/infectious-diseases-climate-change-fund.html). Improved diagnosis and treatment of early localized Lyme disease will help keep patients from progressing into later-stage disease. The Centre for Effective Practice has developed a new clinical tool on Early Lyme Disease Management in Primary Care (https://cep.health/clinical-products/early-lyme-disease/) to help health care providers diagnose and treat early localized Lyme disease. A complementary patient resource has also been developed to provide information for patients who have been bitten by a tick or diagnosed with early Lyme disease.

Prairie Climate Centre (University of Winnipeg)

The Prairie Climate Centre is uniquely focussed on translating scientific knowledge for diverse audiences on the Climate Atlas of Canada (https://climateatlas.ca). They proficiently combine sophisticated climate science with visualization tools, compelling narratives, and engaging video content to educate and inform the public about climate change. The Prairie Climate Centre's initial PHAC-funded work has focused on Lyme disease, in which they interviewed experts across the country and created a video, article, and map to serve as Lyme disease and climate change risk communication tools for the general public, frontline health workers, researchers and scientists. These tools were then tested with communities across urban and rural southern Manitoba, and feedback was integrated to further increase their efficacy for diverse audiences. The final tools can be found on the Lyme Disease Under Climate Change (https://climateatlas.ca/lyme-disease-under-climate-change) page of the Climate Atlas.

This work is part of a broader initiative called *Stories of Health and Hope* that will bring together science and storytelling regarding climate change, infectious disease, and how these issues combine to affect public health. Through workshops, interviews, and dialogue this project documents diverse health impacts and adaptations across various sectors/scales and synthesize findings using multi-media approaches and best practices in climate and health communications. These outcomes will be continue to be shared on the Health Topic Page (https://climateatlas.ca/topic/health) on Climate Atlas of Canada.

To learn more about the Infectious Disease and Climate Change Fund, the current funded projects and for future solicitation opportunities please visit this link (https://www.canada.ca/en/public-health/services/funding-opportunities/infectious-diseases-climate-change-fund.html).

Beware the public opinion survey's contribution to misinformation and disinformation in the COVID-19 Pandemic

Source: MacDonald NE, Dubé E, Greyson D, Graham JE. Beware the public opinion survey's contribution to misinformation and disinformation in the COVID-19 Pandemic. https://canvax.ca/brief/beware-public-opinion-surveys-contribution-misinformation-and-disinformation-covid-19

The COVID-19 pandemic has been accompanied by an "infodemic" of misinformation and disinformation. Given the large degree of uncertainty, the complexity of the science, and rapidly evolving knowledge, well-intentioned misinformation is not surprising. As scientists race to understand a new disease, partial information and guesswork fill the gap until reliable research evidence is established. Unfortunately, disinformation, defined as deliberately false or misleading information, can be expected when crises are used as opportunities to make money or to undermine existing institutions, including education and health care systems. Regardless of intention, misleading information can spread rapidly in the era of social media and 24/7 news coverage, aided by the influence of fear, anxiety, and stress on learning, beliefs, and health decisions. It is therefore incumbent on those conducting COVID-19 rapid research, especially research associated with public awareness and knowledge translation, to avoid contributing to the spread of misinformation and disinformation through their work.

COMING THIS FALL 2020!

THE WEBINAR

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