

NOSOCOMIAL INFECTION SURVEILLANCE

A detailed microscopic illustration of several bacteria, likely Gram-negative rods, with prominent flagella. The bacteria are rendered in vibrant red and orange colors, contrasting against a dark, textured background with green and blue hues. The flagella are long, thin, and numerous, extending from the bacterial cells.

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CCDR

CANADA COMMUNICABLE DISEASE REPORT

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

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The picture on the cover of this issue illustrates *Clostridium difficile*; the bacteria that cause pseudomembranous colitis and are associated with nosocomial antibiotic resistance (<https://image.shutterstock.com/image-illustration/clostridium-difficile-bacteria-360-degree-600w-1431239777.jpg>).

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CANADA COMMUNICABLE DISEASE REPORT



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ERRATUM

The ID News from the April issue (Vol. 46 No. 4) “Ibuprofen should not be used for managing symptoms, say doctors and scientists” BMJ March 2020, has been removed since it was inconsistent with PHAC, HC, WHO and other scientific stance on this subject.



Healthcare-associated infections and antimicrobial resistance in Canadian acute care hospitals, 2014–2018

Canadian Nosocomial Infection Surveillance Program¹

Abstract

Background: Healthcare-associated infections (HAIs) and antimicrobial resistance (AMR) pose serious threats to the health of Canadians due to increased morbidity, mortality and healthcare costs. Epidemiologic and laboratory surveillance data, collected through the Canadian Nosocomial Infection Surveillance Program, are used to inform infection prevention and control and antimicrobial stewardship programs and policies. The objective of this study was to describe the epidemiologic and laboratory characteristics and trends of HAIs and AMR from 2014 to 2018 using surveillance data provided by Canadian hospitals participating in the Canadian Nosocomial Infection Surveillance Program.

Methods: Data were collected from 70 Canadian sentinel hospitals between January 1, 2014 and December 31, 2018 for *Clostridioides difficile* infection (CDI), methicillin-resistant *Staphylococcus aureus* bloodstream infections, vancomycin-resistant Enterococci bloodstream infections and carbapenemase-producing Enterobacteriaceae. Case counts, rates, outcome data, molecular characterization and antimicrobial resistance profiles are presented. Additionally, hospital-level *Escherichia coli* antibiogram data were collected and are described.

Results: Increases in rates per 10,000 patient-days were observed for methicillin-resistant *S. aureus* bloodstream infections (59%; 0.66–1.05, $p=0.023$) and vancomycin-resistant Enterococci bloodstream infections (143%; 0.14–0.34, $p=0.023$). However, CDI rates decreased by 12.5% between 2015 and 2018 (from 6.16–5.39, $p=0.042$). Carbapenemase-producing Enterobacteriaceae infection rates remained low and stable whereas colonization increased by 375% (0.04–0.19; $p=0.014$).

Conclusion: Ongoing efforts to prevent HAIs and reduce AMR in Canada require consistent, standardized surveillance data from acute care hospitals. Increased collaboration with provincial, territorial and international partners in infection prevention and control, as well as antimicrobial stewardship, will be essential in reducing the burden of observed HAIs (including antimicrobial resistant organisms).

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Keywords: healthcare-associated infections, community-associated infections, antimicrobial resistance, surveillance, *Clostridioides difficile* infection, methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant Enterococci, carbapenemase-producing Enterobacteriaceae, antibiogram, *Escherichia coli*, Canadian Nosocomial Infection Surveillance Program

Introduction

Healthcare-associated infections (HAIs) including antimicrobial resistant organisms (AROs) pose a serious risk to the safety and quality of care delivered to patients globally, including in Canada. HAIs cause significant morbidity and mortality among

patients and result in increased healthcare costs (1–4). A 2017 point prevalence survey among participating Canadian hospitals estimated that 7.9% of patients had at least one HAI; results that are similar to those from a 2016–2017 study by the European

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Centre for Disease Prevention and Control that estimated HAI prevalence among tertiary care hospitals to be 7.1% (5,6). A study conducted in the European Union and European Economic Area in 2015 estimated that 2,609,911 new cases of HAI occur every year, corresponding to an annual burden of 501 disability-adjusted life years per 100,000 general population (7).

Antimicrobial resistance (AMR) is a growing healthcare concern, with increased resistance levels detected in humans worldwide (8). Antimicrobial resistant infections cause at least 50,000 deaths each year across Europe and the United States (US) alone (9). Close monitoring of AMR is vital for detecting and responding to emerging trends and patterns of resistance and thus to effectively controlling and treating HAIs.

In Canada, the Public Health Agency of Canada (PHAC) collects national data on various HAIs and AMR through the Canadian Nosocomial Infection Surveillance Program (CNISP). This program was established in 1995 as a partnership between PHAC, the Association of Medical Microbiology and Infectious Disease Canada and sentinel hospitals across Canada. The goal of CNISP is to help facilitate the prevention, control and reduction of HAIs and AROs in Canadian acute care hospitals through active surveillance and reporting.

Reflecting the core components of infection prevention and control of the World Health Organizations (10), CNISP performs consistent, uniform surveillance to reliably measure HAI burden, establish benchmark rates for internal and external comparison, identify potential risk factors and allow for the assessment of specific interventions to improve the quality of patient care. Data provided by CNISP directly supports the goals outlined in the 2017 Pan-Canadian Framework for Action for tackling antimicrobial resistance and antimicrobial use (11).

In this report, we describe the most recent HAI and AMR surveillance data collected from CNISP participating hospitals between 2014 and 2018.

Methods

Design

Canadian Nosocomial Infection Surveillance Program conducts prospective, sentinel surveillance for HAIs (including AROs) and collects annual hospital-level antibiograms.

Case definitions

Standardized case definitions for healthcare-associated (HA) and community-associated (CA) infections were used. Refer to **Appendix A** for full case definitions.

Data sources

Epidemiologic data: Between January 1, 2014 and December 31, 2018, participating hospitals submitted epidemiologic data on cases meeting the respective

case definitions for *Clostridioides difficile* infection (CDI), methicillin-resistant *Staphylococcus aureus* bloodstream infections (MRSA BSI), vancomycin-resistant Enterococci bloodstream infections (VRE BSI) and carbapenemase-producing Enterobacteriaceae (CPE) infections and colonizations. Community-associated CDI surveillance was launched in 2015 and CA-CDI cases have been included since then. In 2018, 70 hospitals across Canada participated in HAI surveillance and are further described in **Table 1**.

Table 1: Summary of hospitals participating in the Canadian Nosocomial Infection Surveillance Program, by region, 2018

Details of participating hospitals	Western ^a	Central ^b	Eastern ^c	Total
Total number of hospitals	26	28	16	70
Hospital type				
Adult ^d	11	18	8	37
Mixed	12	6	7	25
Pediatric	3	4	1	8
Hospital size				
Small (1–200 beds)	7	6	8	21
Medium (201–499 beds)	13	15	8	36
Large (500+ beds)	6	7	0	13
Admissions and discharge				
Total number of beds	9,277	10,354	3,038	22,669
Total number of admissions	440,400	485,416	103,519	1,029,335
Total number of patient days	3,217,499	3,521,438	926,355	7,665,292

^a Western refers to British Columbia, Alberta, Saskatchewan, and Manitoba

^b Central refers to Ontario and Quebec

^c Eastern refers to Nova Scotia, New Brunswick, Prince Edward Island and Newfoundland and Labrador

^d Seven hospitals classified as “adult” had a neonatal-intensive care unit

Participating hospitals submitted epidemiologic (demographic, clinical and outcome data) and denominator data (associated patient-days and patient-admissions) electronically through the Canadian Network for Public Health Intelligence platform; a secure on-line data entry system. Standardized protocols and case definitions were reviewed annually by expert working groups and annual training sessions were provided for data submission. Data quality within CNISP projects has been evaluated periodically (12,13).

Laboratory data: Patient-linked laboratory isolates were sent to the PHAC’s National Microbiology Laboratory (NML) for molecular characterization and susceptibility testing. MRSA BSI, VRE BSI, CPE and pediatric CDI isolates were submitted year round. Adult CDI isolates were submitted during a targeted two-month period from March 1 to April 30 each year.



Antibiogram data: Hospitals submitted annual hospital-level antibiogram data on all inpatient and outpatient clinical *Escherichia coli* isolates (including blood, urine and other clinical isolates such as respiratory, skin, soft tissue and surgical sites). Duplicate isolates were removed as per Clinical and Laboratory Standards Institute guidelines (14). As of 2018, there was no minimum number of isolates required for hospital reporting (prior to 2018, the minimum cut off for reporting was 30 isolates/hospital).

Statistical analysis: The HAI rates were calculated and represent infections and/or colonizations identified in patients admitted (inpatients) to CNISP-participating hospitals and calculated by dividing the total number of cases by the total number of patient admissions (multiplied by 1,000) or patient-days (multiplied by 10,000). The HAI rates were reported nationally and by region (Western: British Columbia, Alberta, Saskatchewan and Manitoba; Central: Ontario and Quebec; Eastern: Nova Scotia, New Brunswick, Prince Edward Island and Newfoundland and Labrador). The territories did not submit data to PHAC. The Mann-Kendall test was used to test trends over time. Significance testing was two-tailed and differences were considered to be significant at p -value ≤ 0.05 .

Where available, outcome data were reported for HAIs using attributable and all-cause mortality. Attributable mortality was defined as the number of deaths per 100 HAI cases where the HAI was the direct cause of death or contributed to death 30 days after the date of the first positive laboratory or histopathology specimen. All-cause mortality was defined as the number of deaths per 100 HAI cases 30 days following positive culture.

Results

Clostridioides difficile infection

Between 2015 and 2018, the incidence of CDI decreased from 6.16 to 5.39 infections per 10,000 patient-days ($p=0.042$) (Table 2). A decreasing trend was observed in HA-CDI rates (-14.9%, $p=0.042$) and CA-CDI rates (-12.3%, $p=0.174$) (Table S1.1). Regionally, HA-CDI rates have decreased across all regions except in the East. For CA-CDI, Eastern and Central region rates have decreased between 2015 and 2018 while Western rates have remained the same. Adult hospitals have consistently had higher rates of HA and CA-CDI compared to mixed and pediatric hospitals. Attributable mortality decreased from 3.0 to 1.3 deaths per 100 cases from 2015 to 2018.

Antimicrobial resistance to moxifloxacin among CDI isolates decreased by 13.7% between 2015 and 2018, with no significant differences between HA and CA-CDI (Table S1.2). While all tested *C. difficile* strains were susceptible to vancomycin, there was a single case of metronidazole resistance in 2018. From 2015

Table 2: *Clostridioides difficile* infection data, Canada, 2015–2018^a

C. difficile infection data	Year							
	2015		2016		2017		2018	
Number of infections and incidence rates								
Number of C. difficile infection cases	4,170		4,008		4,012		3,843	
Rate per 1,000 patient admissions	4.62		4.34		4.28		4.07	
Rate per 10,000 patient-days	6.16		5.77		5.67		5.39	
Number of reporting hospitals	66		67		68		68	
Attributable mortality rate per 100 cases (%) ^b	3.0		2.4		2.3		1.3	
Antimicrobial resistance ^c	N	%	N	%	N	%	N	%
Clindamycin	194	26.0	145	22.1	149	22.0	307	48.7
Moxifloxacin	185	24.8	103	15.7	114	16.9	70	11.1
Rifampin	14	1.9	9	1.4	14	2.1	10	1.6
Metronidazole	0	0.0	0	0.0	0	0.0	1	0.2
Total number of isolates tested ^d	745	N/A	657	N/A	676	N/A	631	N/A

Abbreviations: *C. difficile*, *Clostridioides difficile*; N/A, not applicable

^a All *C. difficile* strains from 2015 to 2018 submitted to National Microbiology Laboratory were susceptible to tigecycline and vancomycin

^b Deaths where *C. difficile* infection was the direct cause of death or contributed to death 30 days after the date of the first positive lab specimen or positive histopathology specimen. Mortality data are collected during the two-month period (March and April of each year) for adults (age 18 years and older) and year-round for children (age one year to less than 18 years old). Among pediatric patients, there was no death attributable to healthcare-associated *C. difficile* infection

^c *C. difficile* infection isolates are collected for resistance testing during the two-month period (March and April of each year) for adults (age 18 years and older) and year-round for children (age one year to less than 18 years old) from admitted patients only

^d Total number reflects the number of isolates tested for each of the antibiotics listed above

to 2018, the proportion of ribotype 027 associated with NAP1 decreased for both HA and CA-CDI, though the decrease was more prevalent among HA-CDI cases (Table S1.3).

Methicillin-resistant *Staphylococcus aureus* bloodstream infections

Between 2014 and 2018, overall MRSA BSI rates increased by 59.1% (0.66 to 1.05 infections per 10,000 patient days, $p=0.023$) (Table 3). An increasing trend in incidence was observed for CA-MRSA BSI (150%, $p=0.05$) and HA-MRSA BSI (27.5%, $p=0.05$) (Table S2.1). In 2018, HA and CA-MRSA BSI rates were highest in Western Canada (0.57 and 0.64 infections per 10,000 patient days, respectively). Among hospital types, HA and CA-MRSA BSI rates remained highest in mixed hospitals compared with adult and pediatric hospitals. All-cause mortality fluctuated from 2014 to 2018; ranging from 16.4% (2017) to 24.9% (2014) (Table 3).

All tested MRSA isolates were susceptible to linezolid and vancomycin (Table 3). Between 2014 and 2018, daptomycin resistance was detected in 12 isolates. Clindamycin resistance among MRSA isolates decreased by 24.1% between 2014



(65.4%, n=221/338) and 2018 (41.3%, n=290/702). Although erythromycin and ciprofloxacin resistance has slowly decreased since 2014, resistance remains high (75.6% and 71.7% in 2018, respectively).

Table 3: Methicillin-resistant *Staphylococcus aureus* bloodstream infections data, Canada, 2014–2018^a

MRSA BSI data	Year									
	2014		2015		2016		2017		2018	
Number of infections and incidence rates										
Number of MRSA bloodstream infections	448		488		604		606		767	
Rate per 1,000 patient admissions	0.48		0.51		0.61		0.61		0.77	
Rate per 10,000 patient-days	0.66		0.7		0.84		0.84		1.05	
Number of reporting hospitals	62		63		64		65		62	
All-cause mortality rate										
Number of deaths	106		95		111		99		144	
All-cause mortality rate per 100 cases	24.9		20.5		19.1		16.4		18.8	
Antimicrobial resistance ^b	n	%	n	%	n	%	n	%	n	%
Erythromycin	305	85.0	318	81.7	418	78.7	455	81.0	531	75.6
Ciprofloxacin	54	87.1	73	81.1	411	77.4	432	76.9	504	71.7
Clindamycin	221	65.4	213	54.8	230	43.3	239	42.5	290	41.3
Tetracycline	18	5.0	14	3.6	31	5.8	35	6.2	50	7.1
Trimethoprim/sulfamethoxazole	6	1.7	6	1.5	11	2.1	8	1.4	14	2.0
Rifampin	2	0.6	2	0.5	10	1.9	9	1.6	6	0.9
Tigecycline	7	1.9	3	0.8	0	0.0	0	0.0	0	0.0
Daptomycin	1	0.3	1	0.3	5	0.9	5	0.9	0	0.0
Total number of isolates tested ^{c-d}	359	N/A	389	N/A	531	N/A	562	N/A	702	N/A

Abbreviations: MRSA, methicillin-resistant *S. aureus*; MRSA BSI, methicillin-resistant *S. aureus* bloodstream infection; N/A, not applicable

^a All MRSA isolates from 2014 to 2018 submitted to National Microbiology Laboratory were susceptible to linezolid and vancomycin

^b Based on the number of cases with associated 30-day outcome data

^c In some years, the number of isolates tested for resistance varied by antibiotic: In 2014, 338 isolates tested for clindamycin, and 62 tested for ciprofloxacin; in 2015, 90 isolates tested for ciprofloxacin

^d Total number reflects the number of isolates tested for each of the antibiotics listed above

Since 2015, community-associated MRSA10 (USA300) has remained the predominant MRSA strain type (46.6% in 2018, n=327/702) while the proportion of community-associated MRSA2 (USA100/800) continued to decrease, representing less than one-third of all strain types identified in 2018 (Table S2.2).

Vancomycin-resistant Enterococci bloodstream infections

From 2014 to 2018, VRE BSI rates have increased by 143% from 0.14 to 0.34 infections per 10,000 patient-days ($p=0.023$) (Table 4). The VRE BSI rates were highest in Central and Western Canada (0.42 and 0.33 infections per 10,000 patient-days respectively) with few VRE BSIs reported in Eastern Canada (0.01 infections per 10,000 patient-days) (Table S3.1). VRE infection was predominantly a healthcare-associated infection, with 95.2% of VRE BSIs reported from 2014 to 2018 acquired in a healthcare facility (Table S3.2). All-cause mortality remained high (31.4%) from 2014 to 2018.

Table 4: Vancomycin-resistant Enterococci bloodstream infections data, Canada, 2014–2018

VRE BSI data	Year									
	2014		2015		2016		2017		2018	
Number of infections and incidence rates										
Number of VRE bloodstream infections	91		89		121		155		243	
Rate per 1,000 patient admissions	0.10		0.10		0.13		0.16		0.24	
Rate per 10,000 patient-days	0.14		0.14		0.18		0.23		0.34	
Number of reporting hospitals	60		57		59		59		62	
Antimicrobial resistance of <i>Enterococcus faecium</i> isolates	n	%	n	%	n	%	n	%	N/n	%
Ampicillin	70	100.0	75	100.0	91	100.0	116	100.0	181	100.0
Chloramphenicol	0	0.0	0	0.0	2	2.2	11	9.5	4	2.2
Ciprofloxacin	70	100.0	75	100.0	91	100.0	116	100.0	181	100.0
Daptomycin ^a	0	0.0	0	0.0	7	7.7	10	8.6	12	6.6
Erythromycin	65	92.9	72	96.0	83	91.2	108	93.1	173	95.6
High-level gentamicin	7	10.0	6	8.0	12	13.2	45	38.8	77	42.5
Levofloxacin	70	100.0	75	100.0	91	100.0	116	100.0	179	98.9
Linezolid	0	0.0	0	0.0	1	1.1	0	0.0	2	1.1
Nitrofurantoin	15	21.4	25	33.3	35	38.5	52	44.8	55	30.4
Penicillin	70	100.0	75	100.0	91	100.0	116	100.0	181	100.0
Synercid	5	7.1	2	2.7	9	9.9	8	6.9	18	9.9
Rifampicin	54	77.1	71	94.7	85	93.4	110	94.8	163	90.1
High-level streptomycin	29	41.4	27	36.0	32	35.2	39	33.6	60	33.1
Tetracycline	38	54.3	44	58.7	46	50.5	66	56.9	108	59.7
Tigecycline	2	2.9	0	0.0	0	0.0	0	0.0	1	0.6
Vancomycin	70	100.0	74	98.7	88	96.7	111	95.7	176	97.2
Total number of isolates tested ^b	70	N/A	75	N/A	91	N/A	116	N/A	181	N/A

Abbreviations: VRE BSI, Vancomycin-resistant Enterococci bloodstream infection;

N/A, not applicable

^a Daptomycin does not have intermediate or resistant breakpoints

^b Total number reflects the number of isolates tested for each of the antibiotics listed above



High-level gentamycin resistance among VRE BSI isolates increased from 10.0% to 42.5% from 2014 to 2018 while daptomycin non-susceptibility was first identified in 2016 (7.7%) and remained stable for 2017 and 2018 (Table 4). Since 2014, the majority (95.7%–100%) of VRE BSI isolates were identified as *Enterococcus faecium*. However, in 2018, three *E. faecalis* VRE BSI isolates were identified (Table S3.3). Among *E. faecium* isolates, sequence type 1478 was first identified in 2013 (data not shown) and increased from 4.0% (for 2014) to 38.7% (for 2018).

Carbapenemase-producing Enterobacteriaceae

From 2014 to 2018, the CPE infection rates remained low and stable (0.04 infections per 10,000 patient-days), while a nearly five-fold increase in colonization rates was observed ($p=0.014$) (Table 5). Regionally, the majority of CPE infections (51.8% $n=57/110$) were identified in Western Canada, followed by Central Canada (45.5%, $n=50/110$) and few CPE infections were identified in Eastern Canada (2.7%, $n=3/110$) (Table S4.1).

Table 5: Carbapenemase-producing Enterobacteriaceae data, Canada, 2014–2018^a

CPE data	Year									
	2014		2015		2016		2017		2018	
Number of infections and incidence rates										
Number of CPE infections	22		19		20		19		30	
Infection rate per 1,000 patient admissions	0.03		0.02		0.02		0.02		0.03	
Infection rate per 10,000 patient-days	0.04		0.03		0.03		0.03		0.04	
Number of CPE colonizations	23		36		76		108		130	
Colonization rate per 1,000 patient admissions	0.03		0.04		0.08		0.12		0.14	
Colonization rate per 10,000 patient-days	0.04		0.05		0.12		0.16		0.19	
Number of reporting hospitals	57		58		57		58		59	
Drugs tested for antimicrobial resistance										
Antibiotics ^b	n	%	n	%	n	%	n	%	n	%
Piperacillin-Tazobactam ^c	59	89.4	75	98.7	117	95.9	159	96.4	209	95.0
Cefotaxime	59	88.1	71	87.7	147	90.7	168	89.8	196	86.3
Ceftazidime	59	88.1	69	85.2	139	85.8	160	85.6	191	84.1
Meropenem	63	94.0	69	85.2	140	86.4	159	85.0	198	87.2
Ciprofloxacin	49	73.1	64	79.0	134	82.7	138	73.8	157	69.2
Amikacin	17	25.4	22	27.2	42	25.9	32	17.1	42	18.5
Gentamicin	34	50.7	40	49.4	62	38.3	64	34.2	78	34.4
Tobramycin	42	62.7	40	49.4	75	46.3	71	38.0	100	44.1
Trimethoprim-sulfamethoxazole	45	67.2	59	72.8	103	63.6	113	60.4	142	62.6

Table 5: Carbapenemase-producing Enterobacteriaceae data, Canada, 2014–2018^a (continued)

CPE data	Year									
	2014		2015		2016		2017		2018	
Drugs tested for antimicrobial resistance (continued)										
Antibiotics ^b	n	%	n	%	n	%	n	%	n	%
Tigecycline	11	16.4	13	16.0	32	19.8	18	9.6	29	12.8
Total number of isolates tested ^d	67	N/A	81	N/A	162	N/A	187	N/A	227	N/A
Carbapenemases identified										
Carbapenemases	n	%	n	%	n	%	n	%	n	%
KPC	33	49.3	28	34.6	84	51.6	86	46.0	120	52.9
NDM	15	22.4	28	34.6	44	27.2	53	28.3	57	24.1
OXA-48	5	7.5	13	16.0	21	13.0	33	17.6	30	13.2
SME ^e	5	7.5	3	3.7	4	2.5	2	1.1	4	1.8
NDM/OXA-48	2	3.0	1	1.2	4	2.5	5	2.7	6	2.6
GES	1	1.5	5	6.2	0	0.0	1	0.5	1	0.4
IMP	1	1.5	0	0.0	0	0.0	0	0.0	3	1.3
NMC	2	3.0	0	0.0	2	1.2	4	2.1	2	0.9
VIM	3	4.5	3	3.7	2	1.2	3	1.6	2	0.9
Other	0	0.0	0	0.0	1	0.6	0	0.0	2	0.9
Total number of isolates tested	67	100	81	100	162	100	187	100	227	100

Abbreviations: CPE, carbapenemase-producing Enterobacteriaceae; GES, Guiana extended-spectrum β -lactamase; IMP, active-on-imipenem; KPC, *Klebsiella pneumoniae* carbapenemase; NDM, New Delhi metallo- β -lactamase; OXA-48, Oxacillinase-48; N/A, not applicable; NMC, not metalloenzyme carbapenemase; SME, *Serratia marcescens* enzymes; VIM, Verona integron-encoded metallo- β -lactamase

^a Includes data for all CPE isolates submitted

^b All isolates were resistant to ampicillin, and all but one to cefazolin. All carbapenemase-producing organism isolates were screened for the *mcr*-type gene which is an acquired gene associated with colistin resistance

^c The denominator for this drug was adjusted as MIC values were not given in all cases due to vitek algorithms

^d Total number reflects the number of isolates tested for each of the antibiotics listed above

^e Only found in *Serratia marcescens*

Whereas, the majority of CPE colonizations (80.7%, $n=301/373$) were identified in Central Canada, followed by Western Canada (19.3%, $n=72/373$), while no colonizations were reported in Eastern Canada (Table S4.2). Thirty-day all-cause mortality was 14.8% ($n=16/108$) among CPE-infected patients and 26.7% ($n=8/30$) among those with CPE bacteremia. Among all CPE cases reported from 2014 to 2018, 41.3% ($n=203/492$) reported travel outside of Canada and of those, 86.1% ($n=161/187$) received medical care while abroad.

From 2014 to 2018, reductions in antimicrobial resistance for CPE isolates were observed for amikacin, gentamicin, and tobramycin while all others remained stable (Table 5). The predominant carbapenemases identified in Canada were *Klebsiella pneumoniae* carbapenemase (KPC), New Delhi metallo- β -lactamase (NDM), and Oxacillinase-48 (OXA-48); however, the distribution of carbapenemases varies by region with NDM dominant in Western Canada (59.1%, $n=101/171$) and KPC dominant in Central Canada (60.4%, $n=330/546$). Among submitted isolates from 2014 to 2018, the most



commonly identified carbapenemase-producing pathogens were *K. pneumoniae* (25.4%–37.3%), *E. coli* (14.7%–29.9%), and *Enterobacter cloacae* complex (11.1%–18.9%) (Table S5).

Antibiogram

From 2015 to 2018, *E. coli* antibiotic non-susceptibility rates among all specimen types tested remained relatively stable (Table 6). In 2018, the antibiotics with the highest non-susceptibility rates were ampicillin (43.0%), trimethoprim/sulfamethoxazole (22.6%), ciprofloxacin (19.6%) and amoxicillin-clavulanate (16.3%). Carbapenem resistance remained low: meropenem (0.4% non-susceptible) and ertapenem (0.2%).

Discussion

In this surveillance we have shown that infection rates in Canada (including both HA and CA cases) reported via CNISP decreased for CDI (12.5% decrease from 2015 to 2018) but increased for MRSA BSI and VRE BSI (59% and 143%, respectively, from 2014 to 2018). Although CPE infection rates remained low, colonizations increased nearly five-fold from 2014 to 2018. Globally, the overall burden of CDI has been decreasing since 2004, with Canadian rates following a similar pattern. The CDI rates are higher in North America compared with other regions (15).

Table 6: Number of *Escherichia coli* isolates tested and percent non-susceptible, 2015–2018^{a,b}

Antibiotic classes	Year							
	2015		2016		2017		2018	
	# isolates tested	% non-susceptible	# isolates tested	% non-susceptible	# isolates tested	% non-susceptible	# isolates tested	% non-susceptible
Penicillins and penicillin combinations								
Ampicillin	66,756	43.7	52,198	44.0	66,583	40.2	62,983	39.6
Amoxicillin clavulanate	56,200	16.8	43,516	16.6	60,428	14.9	58,243	16.7
Piperacillin-Tazobactam	59,085	5.3	49,956	4.7	61,723	4.5	59,770	5.2
Cephalosporins								
Cephalothin	ND	N/A	17,504	46.9	9,072	42.2	1,877	12.1
Cefazolin (for systemic use)	40,291	19.1	23,048	25.2	29,347	19.3	40,440	24.9
Cefazolin (marker for oral use)	ND	N/A	19,300	22.7	9,078	28.6	11,902	15.2
Cefuroxime	ND	N/A	496	7.0	2,363	16.2	5,783	31.1
Cefoxitin	ND	N/A	26,162	9.4	14,174	6.5	22,076	7.1
Ceftriaxone	57,215	8.5	42,157	9.2	56,138	7.9	61,377	9.4
Cefotaxime (pediatric)	ND	N/A	3,870	8.6	578	3.0	389	10.3
Carbapenems								
Ertapenem	ND	N/A	34,501	0.5	38,789	0.4	36,129	0.3
Imipenem	ND	N/A	31,535	0.3	28,037	0.4	11,971	0.8
Meropenem	44,299	0.5	37,875	0.1	41,955	0.1	58,491	0.3
Fluoroquinolones								
Ciprofloxacin	64,548	18.4	52,179	18.9	66,396	18.3	62,267	19.8
Levofloxacin	ND	N/A	10,550	19.4	ND	N/A	ND	N/A
Aminoglycosides								
Gentamicin	51,714	7.7	52,207	8.0	64,351	7.5	62,992	8.5
Tobramycin	40,654	7.4	47,441	8.9	61,572	8.1	61,640	7.4
Amikacin	ND	N/A	34,905	0.1	35,095	0.2	23,672	0.6
Other								
Trimethoprim/sulfamethoxazole	66,760	22.3	48,672	23.1	66,442	20.8	44,001	22.7
Nitrofurantoin	62,020	4.9	39,943	2.9	45,356	2.8	47,985	3.0
Fosfomycin	ND	N/A	12,911	0.1	17,584	2.5	15,776	0.8
Number of hospitals ^c		21		50		70		65

Abbreviations: ND data not collected; N/A, not applicable

^a All patient types include inpatients and outpatients, all specimen types include urine, blood and any other source (e.g. wound, respiratory, etc.)

^b Antibiogram data collection was a pilot project in 2015

^c Includes hospitals that do and do not participate in Canadian Nosocomial Infection Surveillance Program



Decreasing moxifloxacin resistance (11.1% in 2018) in Canada was associated with declining ribotype 027 prevalence, and remained lower than previously published data in Europe (35.8%) and the US (38.0%) (16–18). Estimates of HA-CDI rates from tertiary care hospitals in Europe and Australia showed lower rates of HA-CDI compared with Canada (19,20). Decreased Canadian CDI rates suggest improvements in infection prevention and control practices in hospitals, such as hand hygiene compliance, environmental cleaning, antibiotic stewardship and increased awareness of infection (21).

An increase in the rates of MRSA BSI, attributed to the increase in CA-MRSA BSI rates, is raising concerns as these infections are associated with a mortality rate higher than 20% among admitted patients (22). As MRSA resistance trends are closely tied to the prevalence of epidemic strains, the decrease in the proportion of strain types that are identified as CMRSA2 is driving down clindamycin resistance among isolates (23). The incidence of MRSA BSI in 2017 was lower than the rates reported by South Korea (0.84 versus 1.6 infections per 10,000 patient days) (24). In a US study, reported medium-sized US hospital-onset MRSA BSI rates between 2016 and 2017 were slightly lower than were healthcare-associated 2017 MRSA BSI rates in Canada (0.45 versus 0.47 infections per 10,000 patient-days), but rates for large US hospitals were higher (0.54 versus 0.42 infections per 10,000 patient-days) (25).

The increase in VRE BSI rates in Canada is a concerning trend as hospitalized patients with VRE bacteremia have a higher risk of mortality and longer length of stay when compared with vancomycin-susceptible *Enterococcus* bacteremia (26). This increase may be due to differences in infection control practices across acute care hospitals, with some hospitals discontinuing the practice of admission screening and use of contact precautions for infected and colonized patients (27).

Laboratory surveillance of VRE isolates revealed an emerging strain, ST1478, associated with daptomycin non-susceptibility and high-level gentamicin resistance. First identified in Australia (28,29), *pstS* negative sequence types emerged in Canada primarily through the identification of ST1478 and may be associated with increased rates of VRE BSI (30). Further investigation is ongoing to understand the emergence and transmission dynamics of this novel strain in Canada.

Defined as antibiotics of last resort by the World Health Organization, carbapenems are now threatened by the emergence of carbapenem-resistant organisms (31). While observed CPE rates are low in Canada, colonizations increased nearly five-fold from 2014 to 2018. Changes in screening practices may have contributed to the increase in reported colonization rates and will be collected moving forward (13). National surveillance suggests increases in CPE are driven by local nosocomial transmission as well as travel and healthcare from endemic areas, as has been reported in Ontario (32). There

is continued need for the coordination of infection control measures and surveillance to prevent further transmission of CPE in Canadian acute care hospitals.

Antibiogram data has confirmed that antibiotic susceptibility to *E. coli* has changed minimally in Canada from 2014–2018. Standardized, routine reporting on AMR data through CNISP contributes to crucial international collaborative initiatives such as the World Health Organization Global Antimicrobial Resistant Surveillance System (33).

Consistent and uniform surveillance that helps to inform infection control practices and antimicrobial stewardship programs are essential to reducing the rates of infection and AMR, both of which cause substantial increases in healthcare costs, morbidity and mortality (15).

Strengths and limitations

The main strength of CNISP surveillance data is the active collection of standardized, detailed, epidemiologic and laboratory-linked data from 70 sentinel hospitals across Canada. However, it is primarily large, tertiary acute care hospitals that participate in CNISP, and these hospitals may not fully represent the general Canadian inpatient population. The CNISP is currently undergoing a recruitment process in order to increase representativeness and coverage of Canadian inpatient beds, especially in Northern, rural community and indigenous populations.

The CNISP data, although standardized, may be sensitive to changes in hospital participation infection prevention and control practices and the application of surveillance definitions.

Next steps

Continued recruitment of hospitals into the CNISP network with a 2020 goal of 33% national acute-care bed coverage from all ten provinces and three territories will improve the quality and representativeness of HAI estimates in Canada. To address gaps in surveillance data, detailed hospital screening practice surveys will be conducted annually to better interpret changes in HAI rates. Additionally, steps have been taken to gauge interest in the surveillance of non-acute care settings within the CNISP network such as long-term care facilities. Epidemiologic and laboratory-led working groups were also formed to investigate new and emerging pathogens such as *Candida auris* and VRE BSI ST1478. Lastly, future CNISP antibiogram data aims to report on a broader range of patient and specimen types as well as reporting resistance data on *K. pneumoniae*, *pseudomonas*, *acinetobacter* and *S. aureus*.

Conclusion

Ongoing efforts to prevent HAIs, including AROs, and to reduce AMR in Canadian acute-care hospitals require standardized surveillance and consistent infection prevention and control practices. Data presented in this article indicate rates of



MRSA BSI, VRE BSI and CPE colonizations increased substantially between 2014 and 2018 while rates of CDI decreased. These findings indicate a need for continued vigilance to prevent morbidity and mortality attributable to HAIs and AROs in the inpatient population. As new pathogens emerge, and resistance to last-resort antibiotics is identified, PHAC's continued partnership with acute-care hospitals and collaboration with provincial, territorial and international partners in infection prevention and control as well as antimicrobial stewardship are essential to reducing the burden of HAIs and AROs in Canada.

Authors' statement

Canadian Nosocomial Infection Surveillance Program hospitals provided expertise in the development of protocols in addition to epidemiological data and lab isolates. National Microbiology Laboratory completed the laboratory analyses and contributed to the interpretation and revision of the paper. Epidemiologists from Public Health Agency of Canada were responsible for the conception, analysis, interpretation, drafting, and revision of the paper.

Conflict of interest

None.

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Appendices

Appendix A: Surveillance case definitions and eligibility criteria, 2018

***Clostridioides difficile* infection (CDI)**

A “primary” episode of CDI is defined as either the first episode of CDI ever experienced by the patient or a new episode of CDI, which occurs greater than eight weeks after the diagnosis of a previous episode in the same patient.

A patient is identified as having CDI if:

- The patient has diarrhea or fever, abdominal pain and/or ileus AND a laboratory confirmation of a positive toxin assay or positive polymerase chain reaction (PCR) for *C. difficile* (without reasonable evidence of another cause of diarrhea) OR
- The patient has a diagnosis of pseudomembranes on sigmoidoscopy or colonoscopy (or after colectomy) or histological/pathological diagnosis of CDI OR
- The patient is diagnosed with toxic megacolon (in adult patients only)

Diarrhea is defined as one of the following:

- More watery/unformed stools in a 36-hour period
- or more watery/ unformed stools in a 24-hour period and this is new or unusual for the patient (in adult patients only)

Exclusion:

- Any patients younger than one year
- Any pediatric patients (aged one year to younger than 18 years) with alternate cause of diarrhea found (i.e. rotavirus, norovirus, enema or medication, etc.) are excluded even if *C. difficile* diagnostic test result is positive

CDI case classification

Once a patient has been identified with CDI, the infection will be classified further based on the following criteria and the best clinical judgment of the healthcare and/or infection prevention and control practitioner.

Healthcare-associated (acquired in your facility) CDI case definition

- Related to the current hospitalization
 - The patient’s CDI symptoms occur in your healthcare facility three or more days (or ≥ 72 hours) after admission
- Related to a previous hospitalization
 - Inpatient: The patient’s CDI symptoms occur less than three days after the current admission (or less than 72 hours) AND the patient had been previously hospitalized at your healthcare facility and discharged within the previous four weeks

- Outpatient: The patient presents with CDI symptoms at your emergency room (ER) or outpatient location AND the patient had been previously hospitalized at your healthcare facility and discharged within the previous four weeks
- Related to a previous healthcare exposure at your facility
 - Inpatient: The patient’s CDI symptoms occur less than three days after the current admission (or less than 72 hours) AND the patient had a previous healthcare exposure at your facility within the previous four weeks
 - Outpatient: The patient presents with CDI symptoms at your ER or outpatient location AND the patient had a previous healthcare exposure at your facility within the previous four weeks

Healthcare-associated (acquired in any other healthcare facility) CDI case definition

- Related to a previous hospitalization at any other healthcare facility
 - Inpatient: The patient’s CDI symptoms occur less than three days after the current admission (or less than 72 hours) AND the patient is known to have been previously hospitalized at any other healthcare facility and discharged/transferred within the previous four weeks
 - Outpatient: The patient presents with CDI symptoms at your ER or outpatient location AND the patient is known to have been previously hospitalized at any other healthcare facility and discharged/transferred within the previous four weeks
- Related to a previous healthcare exposure at any other healthcare facility
 - Inpatient: The patient’s CDI symptoms occur less than three days after the current admission (or < 72 hours) AND the patient is known to have a previous healthcare exposure at any other healthcare facility within the previous four weeks
 - Outpatient: The patient presents with CDI symptoms at your ER or outpatient location AND the patient is known to have a previous healthcare exposure at any other healthcare facility within the previous four weeks

Healthcare-associated CDI but unable to determine which facility

The patient with CDI DOES meet both definitions of healthcare-associated (acquired in your facility) and healthcare-associated (acquired in any other healthcare facility), but unable to determine to which facility the case is primarily attributable to.



Community-associated CDI case definition

- Inpatient: The patient's CDI symptoms occur less than three days (or less than 72 hours) after admission, with no history of hospitalization or any other healthcare exposure within the previous 12 weeks
- Outpatient: The patient presents with CDI symptoms at your ER or outpatient location with no history of hospitalization or any other healthcare exposure within the previous 12 weeks

Indeterminate CDI case definition

The patient with CDI does NOT meet any of the definitions listed above for healthcare-associated or community-associated CDI. The symptom onset was more than four weeks but less than 12 weeks after the patient was discharged from any healthcare facility or after the patient had any other healthcare exposure.

Methicillin-resistant *Staphylococcus aureus* (MRSA)

MRSA surveillance inclusion criteria

MRSA case definition:

- Isolation of *S. aureus* from any body site
AND
- Resistance of isolate to oxacillin
AND
- Patient must be admitted to the hospital
AND
- Is a "newly identified MRSA case" at a Canadian Nosocomial Infection Surveillance Program (CNISP) hospital at the time of hospital admission or identified during hospitalization.

This includes:

- MRSA infections identified for the first time during this hospital admission
- Infections that have been previously identified at other NON-CNISP hospitals (since we want newly identified MRSA cases at CNISP hospitals)
- Infections that have already been identified at your site but are new infections. This can only be identified if the previously identified case has another strain. This means the person was exposed again to MRSA and acquired another strain of it from another source (a new patient identifier is assigned only if confirmed with a different strain type)
- MRSA infection identified at a new (different) site in a patient with a MRSA infection identified in a previous surveillance (calendar) year
AND
- Meets the criteria for MRSA infection as determined using the January 2017 Centers for Disease Control and Prevention/National Healthcare Safety Network (CDC/NHSN) surveillance definitions for specific infections, and in accordance with the best judgment

MRSA surveillance exclusion criteria:

- MRSA infections previously identified at other CNISP sites
- Emergency, clinic, or other outpatient cases who are NOT admitted to the hospital
- Infections readmitted with MRSA (unless it is a different strain or a new/different site of MRSA infection)

Healthcare-associated (HA) case definition:

Healthcare-associated is defined as an inpatient who meets the following criteria and in accordance with the best clinical judgement of the healthcare and/or IPC practitioner:

- Exposure to any healthcare setting (including long-term care facilities or clinics) in the previous 12 months
OR
- Patient is on calendar day 3 of their hospitalization

Community-associated case definition:

- MRSA identified on admission to hospital (Calendar day 1 = day of hospital admission) and/or the day after admission (day 2)
AND
- Has no previous history of the organism
AND
- Has no prior hospital, long-term care admission or other exposure to a healthcare setting (rehab, clinics) in the past 12 months
AND
- Has no reported use of medical devices

MRSA clinical infection

MRSA infection is determined using the 2016 CDC/NHSN surveillance definitions for specific infections, and in accordance with the best judgment of the healthcare and/or IPC practitioner. https://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf

The MRSA infection would be considered HA if all elements of a CDC/NHSN site-specific infection criterion were present on or after the third calendar day of admission to the facility (the day of hospital admission is calendar day 1). The MRSA infection would be considered CA if all elements of a CDC/NHSN site-specific infection criterion were present during the two calendar days before the day of admission, the first day of admission (day 1) and/or the day after admission (day 2) and are documented in the medical record.

MRSA bloodstream infection (bacteremia)

To be considered a MRSA bloodstream infection the patient must have MRSA cultured (lab-confirmed) from at least one blood culture.



Vancomycin-resistant Enterococci (VRE)

VRE infection case definition:

- Isolation of *Enterococcus faecalis* or *faecium*
AND
- Vancomycin MIC >8 µg/ml
AND
- Patient is admitted to the hospital
AND
- Is a “newly” identified VRE-infection at a CNISP facility at the time of hospital admission or identified during hospitalization

VRE infection is determined using the January 2017 CDC/NHSN definitions/criteria for infections, and in accordance with the best judgment of the infection prevention and control practitioner. These criteria should be met at the time of the culture that yielded VRE, or within 72 hours of the culture.

https://www.cdc.gov/nhsn/pdfs/pscmanual/17pscnosinfdef_current.pdf

Exclusion criteria:

- Previously identified at other CNISP sites (to avoid duplicate reporting to CNISP)
- Identified through emergency, clinic, or other outpatient areas
- Readmitted with VRE (UNLESS it is a different strain)

Healthcare-associated is defined as an inpatient who meets the following criteria and in accordance with the best clinical judgement of the healthcare and/or infection prevention and control practitioner:

- Exposure to any healthcare setting (including long-term care facilities or clinics) in the previous 12 months
OR
- Patient is on calendar day 3 of their hospitalization

Carbapenemase-producing Enterobacteriaceae (CPE)

Any patient admitted to a participating CNISP hospital with a hospital laboratory confirmation (and subsequent confirmation by the National Microbiology Laboratory) that tested/screened positive for a least one potential carbapenem-reduced susceptible Enterobacteriaceae, from any body site that meets the Clinical & Laboratory Standards Institute criteria.

Carbapenems are a class of beta-lactam antibiotics with broad-spectrum activity recommended as first-line therapy for severe infections caused by certain gram negative organisms and as directed therapy for organisms that are resistant to narrower spectrum antibiotics.

Carbapenem resistance can be due to changes in the permeability of the organism to the antibiotic and/or the up-regulation of efflux systems that “pump” the antibiotic out of the cell, usually concomitant with the presence of an acquired extended-spectrum beta-lactamase or AmpC enzyme or the hyperproduction of intrinsic chromosomally-located beta-lactamase(s). More recently, resistance is increasingly due to the acquisition of enzymes that break down the carbapenems: carbapenemases (e.g. New Delhi metallo-β-lactamase-1, Oxacillinase-48, *Klebsiella pneumoniae* carbapenemase, Verona integrin-encoded metallo-β-lactamase, active-on-imipenem, etc.). These latter subsets of carbapenem-resistant organisms are called carbapenemase-producing organisms (CPOs) and are of particular concern because of their ability to transfer resistance easily across different genera and species of bacteria. They are quickly becoming a public health problem not only because of the ability to cause healthcare acquired infections which have limited treatment options, but because of the potential for colonizing both inpatient and outpatient populations due to their ease of transmissibility, thus, creating a reservoir of bacterial resistance.

The data presented in this report include *Enterobacteriaceae* spp. that are resistant to carbapenems through the production of a carbapenemase. The first positive isolate from an inpatient identified as colonized or infected with CPE is eligible.

Subsequent positive isolates from the same patient in the same calendar year are eligible only if the patient tests positive for a different carbapenemase. If the patient was initially colonized and subsequently develops an infection with the same gene, within the same calendar year, only the infection is eligible for inclusion in surveillance. Data from previous years included in this report have been adjusted to reflect this change in reporting.



Appendix B: List of supplemental tables

Table S1.1: Cases and incidence rates of healthcare-associated and community-associated *Clostridioides difficile* infection by region and hospital type, Canada, 2015–2018

Table S1.2: Antimicrobial resistance of healthcare and community-associated *Clostridioides difficile* infection isolates, Canada, 2015–2018

Table S1.3: Number and proportion of common ribotypes of HA-CDI and CA-CDI cases, Canada, 2015–2018

Table S2.1: Cases and incidence rates of healthcare-associated and community-associated methicillin-resistant *Staphylococcus aureus* bloodstream infections by region and hospital type, 2014–2018

Table S2.2: Number and proportion of select methicillin-resistant *Staphylococcus aureus* strain types identified

Table S3.1: Number of vancomycin-resistant Enterococci bloodstream infections incidence rates by region and hospital type, 2014–2018

Table S3.2: Number of healthcare-associated vancomycin-resistant Enterococci bloodstream infections and incidence rates, 2014–2018

Table S3.3: Number and proportion of vancomycin-resistant Enterococci bloodstream infections isolate types identified, 2014–2018

Table S3.4: Distribution of vancomycin-resistant Enterococci bloodstream (*Enterococcus faecium*) sequence type, 2014–2018

Table S4.1: Number of carbapenemase-producing Enterobacteriaceae infections and incidence rates by region, Canada, 2014–2018

Table S4.2: Number of carbapenemase-producing Enterobacteriaceae colonizations and incidence rates by region, Canada, 2014–2018

Table S5: Number and proportion of main carbapenemase-producing pathogens identified



Canadian Public Health Laboratory Network Best Practices for COVID-19

Respiratory Virus Infections Working Group¹

Abstract

The ability to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of COVID-19, is a foundational component of Canada's containment and mitigation strategies. Laboratory confirmation of COVID-19 cases allows the appropriate clinical management and public health interventions. Whether the local goal is containment or mitigation will depend on local epidemiology of the pandemic. The Respiratory Virus Infections Working Group of the Canadian Public Health Laboratory Network has developed comprehensive Best Practice Guidelines for detection of SARS-CoV-2. Best practices for specimen collection, transportation, testing and biosafety are addressed from the perspective of Canadian public health laboratories to ensure a consistent approach across the country:

1. Population-based testing for COVID-19 should initially be carried out for surveillance
2. Nasopharyngeal swab is the specimen of choice for routine testing
3. Nucleic acid amplification tests (such as real-time reverse transcription polymerase chain reaction) are the method of choice for routine testing of SARS-CoV-2
4. The decentralization of nucleic acid amplification testing for COVID-19 to hospital or other high complexity medical laboratories should be promoted to increase test capacity and meet increased demands
5. In the early stages of the pandemic, positive (approximately 10–20) and negative (approximately 50) tests by a provincial laboratory require confirmation at the National Microbiology Laboratory
6. Co-circulation of other viral agents associated with influenza-like illnesses (e.g. influenza A and B and respiratory syncytial virus) should be monitored as capacity permits, as part of ongoing surveillance
7. Once validated, serological testing may be utilized for assessing the presence/absence of immune response to the SARS-CoV-2 at either the population or individual level for select indications, but is likely to be of limited utility in diagnosis of acute COVID-19 illness

These recommendations will be updated as new information becomes available.

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Introduction

Since the report of the novel coronavirus disease 2019 (COVID-19), caused by SARS-CoV-2 in late December 2019 in Wuhan, Hubei Province of China, the vast majority of countries have now reported laboratory-confirmed cases of COVID-19. Due to the continued spread of COVID-19, the situation was declared a pandemic by the World Health Organization on March 11, 2020 (1).

The clinical presentation of COVID-19, which is caused by SARS-CoV-2, is non-specific and overlaps with other seasonal respiratory viruses, including influenza. The ability to detect

SARS-CoV-2 in patients is critical for surveillance, diagnosis and clinical management of persons presenting with acute respiratory illness (ARI), influenza-like illness (ILI) and severe respiratory illness to support Canada's containment and mitigation strategies.

The purpose of SARS-CoV-2 testing can fall into two broad categories, and will depend on the local epidemiology and goals of public health strategies (containment vs. mitigation):



1) Testing for the purpose of high probability case finding among persons presenting with ARI and ILI and appropriate exposure criteria is critical to ensure COVID-19 cases are identified in a timely fashion to ensure appropriate clinical and public health management can occur during the containment phase of the pandemic. In addition, when local numbers are low, testing will likely support aggressive case-finding strategies for early contact tracing and implementation of self-isolation. Once the virus becomes widespread, testing of community samples should be reserved for community-based surveillance programs, with the remainder of testing focused on hospitalized patients with ARI and those with risk factors for severe disease where the results of the test may influence decisions regarding care and treatment, infection control (including outbreaks), management of close contacts, and to support remote communities. It is important that the above management and prevention decisions should not be delayed pending testing results. Cases of COVID-19 have had co-infections with other viruses including influenza. Testing for influenza should continue for hospitalized patients to help support patient management with antivirals.

2) Population-based surveillance should occur for ongoing identification of COVID-19 cases and facilitate tracking of other common viral agents, such as respiratory syncytial virus, parainfluenza, adenovirus and rhinoviruses, that co-circulate during the influenza season and during other times of the year.

This *Best Practices* guidance should be used in conjunction with relevant provincial and territorial guidelines. The Public Health Agency of Canada will be posting regular updates and related documents (2).

Surveillance

Population-based surveillance is important during different stages of the COVID-19 pandemic. The areas of focus of surveillance will shift as testing priorities are realigned when the health system moves from a containment to mitigation phase. It is important to note that the existing technologies for COVID-19 detection are not sufficient in their performance to be applied as a general population screening tool, and targeted use of testing in populations where pretest probability is highest, or where potential benefit remains highest, remains an important principle of sample selection.

During containment, population-based surveillance is very important, as mildly symptomatic SARS-CoV-2 infection may play some role in community transmission. At this stage, the majority of patients tested for SARS-CoV-2 are ambulatory, with few hospitalized patients meeting exposure criteria to be a suspect case (3). During this time, it is important to conduct surveillance testing on a subset of hospitalized persons, and persons seen in ambulatory settings with ARI/ILI but no specific risk factors for COVID-19. Additional community surveillance should occur at long-term care homes, where the elderly patient population,

often with comorbidities, are at greatest risk for complications and fatal infection. This surveillance could occur by testing an appropriate selection (as guided by outbreak control authorities) or all respiratory outbreak samples for SARS-CoV-2.

During mitigation, it is presumed that there will be widespread circulation of the virus throughout different sectors of the community. During this time, COVID-19 testing will shift to identifying cases among hospitalized patients, who represent the more severely ill. Community testing for SARS-CoV-2 will be less routinely available for ambulatory patients, though should be continued for ambulatory healthcare workers with ILI (and possibly ARI), institutional outbreaks, remote and confined/congregate communities, and may be provided to populations with risk factors for severe disease (e.g. age 60 years or older, presence of comorbidities). Specific screening, sampling, specimen collection and testing guidelines will be developed by the local provincial healthcare system. Ambulatory surveillance programs should continue during a mitigation phase in order to provide some data on community prevalence of SARS-CoV-2, as this will support tracking the progress of the pandemic.

To assist with maximizing use of laboratory testing data to enable COVID-19 surveillance, hospitals or other high-complexity laboratories doing testing should contribute summary testing data to complement the data from testing at their provincial public health laboratory. These data can then help inform a local, provincial and federal snapshot of pandemic activity. Provinces should seek to perform adequate surveillance and case-finding test volumes, which will provide approximately a daily snapshot of disease prevalence in their test jurisdictions. The determination of that minimum volume is based on a number of factors and should be determined in cooperation with biostatistical or epidemiological support.

Surveillance should also be in place to help with the global monitoring of the molecular epidemiology of SARS-CoV-2. This will help establish any geographic differences in strains circulating, and possible clinically relevant genomic variants. Molecular surveillance will also provide data to assist with monitoring for any diagnostic assay primer or probe mismatches to SARS-CoV-2 that might affect the performance characteristics of diagnostic assays. Such efforts should be coordinated across all jurisdictions, and led by World Health Organization-connected facilities such as the National Microbiology Laboratory (NML) in Winnipeg. While further research is necessary, it may inform questions of postinfection immunity and potential for reinfection, as well as assist with vaccine planning and design. While there currently is no specific antiviral therapy for SARS-CoV-2, genomic sequence data may be helpful in predicting resistant phenotypes if effective antivirals are developed.

Seroprevalence studies may also be conducted to assist with documenting the population attack rates from COVID-19 during the pandemic. These would be conducted by performing SARS-CoV-2 serology on a representative set of residual sera



from across all age groups, and repeating this at set intervals over the coming months. The main challenge to conducting this activity is that no commercial assay has been validated for clinical testing at this time, although efforts for validation are underway in Canada, and the utility of such assays on a broad population scale is not yet affirmed.

Diagnostic testing

During the containment period, efforts will be directed at intense case finding to ensure early identification, early isolation, early diagnosis and early treatment as well as appropriate contact management and follow up. This will include both outpatient (ambulatory) and inpatient settings. Once the epidemiology of the outbreak suggests that containment is not feasible and resources will become strained, the laboratory will support the goal of mitigation and prioritize testing to the following groups of patients: 1) hospitalized patients with all degrees of ARI, including severe respiratory illness and ILI and milder respiratory illness; 2) patients for whom diagnostic testing will assist decisions regarding care, infection control (including outbreaks), or management of close contacts; 3) persons who died of an acute illness in which influenza or another respiratory virus such as SARS-CoV-2 is suspected; 4) healthcare workers with ARI/ILI; and 5) persons living in remote and isolated communities.

In the mitigation phase, when viral circulation in the community is established, testing may only occasionally be performed on outpatients; specific testing algorithms will be decided on by each provincial health system, with a likely focus similar to what is outlined above. Testing is not indicated for clinical management of persons with uncomplicated respiratory infection residing in communities where SARS-CoV-2 is circulating.

Specimen type and collection

The World Health Organization recently reported that SARS-CoV-2 has been detected in respiratory, fecal and blood specimens (4). Preliminary data report virus detection in upper respiratory samples 1–2 days before symptom onset, which persists for 7–12 days in moderate cases and up to two weeks in severe cases. Virus has been cultured from respiratory tract samples up to eight days following symptom onset. Although SARS-CoV-2 virus has also been detected in saliva, its use for diagnostic testing requires further investigations.

Viral ribonucleic acid (RNA) has been detected in feces in up to 30% of patients commencing day 5 after symptom onset, and this continues for up to five weeks in moderate cases. However, it is not clear whether this reflects shedding of infectious virus. While live virus has been cultured from stool in some cases, the role of fecal-oral transmission is not yet well understood.

At this time the focus of testing is on respiratory samples. Early data suggest that lower viral loads can be detected in nasopharyngeal swabs than in throat swabs (5), and as such they are the preferred upper respiratory tract specimen. In addition, they are also the preferred specimen for influenza detection, which can have a similar clinical presentation. Sputum is a useful lower respiratory tract specimen, and can be collected from patients with a productive cough. However, sputum induction is not recommended due to the risk of generating aerosols. Flocked swabs are recommended to collection of nasopharyngeal or nasal/throat specimens.

Alternative collection devices

In the event of a supply chain interruption and an inability to obtain flocked swabs or viral transport media, alternative options such as rayon on plastic or wires can be considered. Consideration to alternatives to viral transport media include phosphate buffered saline or alcohol for stabilization. Wooden swabs are considered inhibitory to nucleic acid-based testing, and therefore unless validated to the contrary, are not recommended. Any alternative specimen collection devices or transport media will require validation for use in clinical testing. Further information on alternative collection kits is available from U.S. Food and Drug Administration (6).

Specimen pooling

Pooling multiple specimens may be considered as a means of increasing throughput during periods of high submissions, and to preserve reagents during times of shortages. If the pool is positive, then each individual specimen within the pool must be retested to determine which specimen is positive. There is a trade-off of decreased sensitivity when specimens are pooled. Any laboratory considering pooling should do their own evaluation of the impact on sensitivity as this will be assay and laboratory specific, and use this to decide on the optimal number to pool in their setting. Work with influenza outbreaks has shown that sensitivity significantly drops if pooling more than four specimens. Laboratories may choose to run only non-critical specimens through a pooling protocol and preserve single specimen testing for patients with more severe illness (e.g. hospitalized patients). As percent positivity increases, the number of specimens within the pool for this to be efficient will need to be reduced; in general, once the test positive rate reaches the 8%–10% range, there is no benefit to pooling any number of specimens (Table 1).

Specimen transport

Specimens should be transported to the laboratory as soon as possible, preferably within 72 hours, on ice packs. If a longer delay is anticipated, specimens should be frozen at -70°C or colder, and transported on dry ice. However, specimens should not be frozen at -20°C, as this may affect the recovery of the virus if culture is required. If -70°C or below/dry ice is not available, specimens should remain at 4°C and be shipped as

**Table 1: Preferred and alternative specimen types**

Nature of illness	Specimen of choice	Alternative specimens
Mild/moderate influenza-like illness	Nasopharyngeal swab Video demonstration of nasopharyngeal swab collection can be accessed at http://www.youtube.com/watch?v=TFwSefezIHU	Deep nasal swab, throat swab or both https://vimeo.com/397169241
Severe respiratory illness	Nasopharyngeal swab AND endotracheal or bronchoalveolar lavage. Sputum (if productive cough)	Sputum, throat swab
Autopsy	Nasopharyngeal swab AND throat swab Lung tissue or other tissues from suspected organ involvement. Specimens should be fresh or frozen at -70°C or below. Do not put into formalin fixative	Not applicable

soon as possible. Specimens should be transported as Transport of Dangerous Goods-defined diagnostic specimens per the usual practice for seasonal influenza specimens, and no enhanced precautions are necessary. See the PHAC SARS-CoV-2 Biosafety Advisory for more information (7).

Specimen tubes should be appropriately labelled and requisition correctly and fully completed, with matching patient names and unique identifiers, and relevant clinical and/or public health required information.

Testing methods

While other methods exist for the detection of SARS-CoV-2, detection methods in clinical laboratories are limited to molecular detection using nucleic acid amplification tests (NAAT) and viral culture.

Nucleic acid amplification tests

At the time of this publication, there are an increasing number of commercial assays available for detection of SARS-CoV-2. Many laboratories are implementing in-house, laboratory-developed tests based on the detection of the RNA-dependent RNA polymerase, envelope and nucleocapsid genes, while others are implementing commercial assays that detect a variety of viral targets. Some laboratories have a pan-beta coronavirus RNA polymerase NAAT, which is then confirmed by nucleic acid sequencing, although most laboratories have moved to real-time methods that directly identify two different genetic targets—gene sequencing is reserved for cases where a single target is indeterminate on the real-time reverse transcription polymerase chain reaction (rRT-PCR) assay and further clarification of the laboratory result is clinically indicated.

As a result of the evolution of the outbreak into a pandemic, and SARS-CoV-2 no longer being a rare laboratory test finding, detection of a single target under well-validated conditions is sufficient for laboratory confirmation of SARS-CoV-2.

Although little data exist on the diagnostic performance of current NAAT tests, based on preliminary data from Canadian laboratories the level of detection tests have excellent analytical sensitivity (95% limit of detection below 10 copies per reaction) and specificity. During level of detection tests validation, laboratories should determine the maximum cycle threshold value for target detection, using the 95% limit of detection generated in their laboratory as a guide. They should also decide whether an indeterminate cycle threshold range for that particular assay is required, and what cycle threshold values to include in the indeterminate range. Patients who initially test negative should be retested if the clinical suspicion of COVID-19 remains high, in particular among hospitalized patients who are not clinically improving. Lower respiratory tract samples should be obtained from patients with evidence of pneumonia to increase clinical sensitivity. Test performance among patients with different severities of illness (e.g. asymptomatic, mild illness, hospitalized) is likely to differ, and these differences have not been well characterized. Routine testing of asymptomatic patients is not recommended. Ongoing evaluation of commercially available tests, as they are developed, will be important to characterize their performance in the clinical setting and throughout the pandemic. Public health laboratories should take appropriate initiatives and help establish additional testing sites in their respective jurisdictions.

Point-of-care molecular testing

Commercial molecular detection assays are, and more will become, licensed by Health Canada for point-of-care (POC) use outside the laboratory. Before facilities in Canada consider using any POC or a non-class III device “off label” for near POC testing, an implementation and quality plan should be made with a clinical or medical microbiologist and an appropriate laboratory medical director. Where possible, a provincial system should be set up for capturing the data generated from POC testing to assist with laboratory surveillance. As with any medical laboratory activities, adherence to any appropriate personal health information, medical laboratory accreditation and medical laboratory licensure regulations and standards must be considered in advance of offering such testing.

Virus isolation

Virus isolation is limited to laboratories that have licensed containment level (CL) 3 capabilities, and will not play a major role in the diagnosis of COVID-19 patients. It will mainly be used to propagate virus for the generation of positive RNA control material required for NAATs. It may also be required to support growth-based serological assays if developed (e.g. microneutralization), vaccine development, and other areas of research.



Serology

Methods for serologic diagnosis are being developed but have not yet been introduced into routine clinical use in Canada or other countries. Several platforms targeting various immunoglobulins (IgM, IgG, IgA) and total antibodies against different SARS-CoV-2 antigens, such as spike protein and nucleocapsid protein, are available for evaluation. Based on available literature, detection of serological response appears to be less reliable in the first week post-symptom onset where sensitivity is low. The sensitivity of detection increases by 14 days post-symptoms onset. Duration of seropositivity postinfection and whether the immune response offers or correlates with protection from reinfection needs to be determined before interpretation relating to immunity can be made.

The role of serology in diagnosis of acute illness and patient management is likely to be of limited utility. Once the dynamics of serological response are better understood, serology may have a role in the following: use in seroepidemiology studies to better understand the proportion undiagnosed in the population over time and provide a more accurate estimate of attack rate; an adjunct to rRT-PCR for diagnostic testing in patients who are rRTP-CR negative, late in the course of their illness, and have significant contact management challenges that would be well-informed by supportive serology; to implement control measures and to effectively manage significantly at-risk populations, including assessing them for serostatus; and once a vaccine is available it may be used to determine, among high-risk populations, who should be prioritized for earlier vaccination.

Two testing modalities are currently available commercially, enzyme-linked immunosorbent assay- (ELISA-) based assays and POC assays. The performance characteristics of both modalities need to be determined; in particular, sensitivity, specificity, positive predictive value and negative predictive value, in addition to the interpretation of positive results.

The ELISA-based methods are amenable to high-throughput processing, appropriate quality control and assurance, are less susceptible to operator subjectivity in interpretation and reporting of their results can be easily integrated into existing laboratory information systems. The ELISA methods are also capable of providing some quantitative estimate of how much antibody is present. They are, however, more labor-intensive, require special equipment, reagents and laboratory expertise and do not provide rapid results. As an estimate of protection of the immune response, ELISA results should be compared with results of virus neutralization assays. However, at present, neutralization assays are not produced commercially and can only be employed in high complexity laboratories capable of tissue and viral culture, limiting their widespread use.

Most POC tests are immunochromatographic and lateral-flow based and as a result, provide easy to read results in as little as 30 minutes without the requirement of extensive training or

specialized equipment. They are particularly beneficial for use in remote areas with limited access to centralized laboratory-based testing and/or limited local laboratory infrastructure. The same guidelines outlined above for POC molecular assays apply to POC serology assays. Use under such conditions requires particular attention and effort to ensure quality control and assurance, such as participation in external quality assessment, to maintain high-quality testing. Similarly, provisions for maintaining appropriate data and quality records of POC test results are necessary before their implementation into routine use.

External quality assurance

Any laboratory implementing testing for SARS-CoV-2 should do so according to the medical laboratory regulations in place in their jurisdiction. As is required for other microbiology clinical tests, they must be enrolled in available external quality assessment programs that can be accessed provincially, nationally and/or internationally. This is particularly important when providing testing for an emerging pathogen such as SARS-CoV-2. The development and provision of standardized serology panels to support implementation and proficiency testing will be key to the successful implementation of serology assays in Canadian laboratories.

Detection of other respiratory viruses

The emergence of COVID-19 comes at a time when many regions in the Northern Hemisphere are experiencing their respiratory virus season and there are data to suggest that co-infections can occur; however, the clinical implications of co-infection on patient outcomes are not clear. It is expected that with wide spread circulation of the virus, the diagnostic capacities of laboratories may be exceeded and will require the suspension of some services or the use of contingency plans thus making it unrealistic to expect broad routine testing for the other viruses. However, the detection of influenza, particularly in patients requiring hospitalization or those with comorbidities putting them at risk for complications, should continue to help guide patient management with anti-influenza agents.

Biosafety considerations

The SARS-CoV-2 is a risk group (RG) 3 pathogen. Propagation or culture of the virus is restricted to laboratories that have federally licensed CL3 facilities. The SARS-CoV-2 is transmitted from respiratory droplet spread and, as such, respiratory specimens would be considered potential sources of virus. Although there are limited data that suggest SARS-CoV-2 can be detected in blood and stool, there are no data at this time that suggest these are a source of infection. Non-propagative diagnostic activities using specimens that do not result in the



concentration or extraction of the pathogen, such as routine chemistry, hematology or urinalysis can continue using standard precautions. Respiratory specimens from patients with suspect COVID-19 can be safely handled in CL2 facilities with additional precautions including the following: a lab coat, gloves, and eye protection are worn when handling primary specimens; centrifugation of primary specimens is carried out in sealed safety cups, or rotors, that are loaded/unloaded in a Class II biological safety cabinet (BSC) or other primary containment device; a certified Class II BSC, or other primary containment device, is used for procedures that may produce infectious aerosols including pipetting; and respiratory protection that provides a level of filtration of 95% or greater (e.g. N95) is worn where aerosol generating activities cannot be contained within a BSC or other primary containment device.

It is recommended that laboratories perform a local risk assessment on activities involving specimens from COVID-19 patients to determine if additional precautions are required.

Virus culture should not be conducted on respiratory specimens in a CL2 laboratory when a novel or emerging pathogen is suspected as they are RG 3 pathogens. Virus culture, if required, may be considered if the specimen has been tested for these pathogens and is negative by rRT-PCR.

Disinfection

Based on currently available evidence, chemical disinfectants that are effective against enveloped viruses are suitable for decontamination of SARS-CoV-2, provided they are used according to manufacturer's recommendations. Particular attention should also be given to the correct contact time (e.g. 10 minutes), dilution (i.e. concentration of the active ingredient) and expiry date of the working solution preparation. Such effective disinfectants include sodium hypochlorite (bleach), 70% ethanol, 0.5% hydrogen peroxide, quaternary ammonium compounds and phenolic compounds. It is possible other biocidal agents may be less effective (e.g. 0.05%-0.2% benzalkonium chloride, 0.02% chlorhexidine digluconate).

Sodium hypochlorite (bleach) at a concentration of 1,000 ppm (0.1%) is recommended for general surface disinfection and 10,000 ppm (1%) for disinfection of blood spills.

See the PHAC SARS-CoV-2 Biosafety Advisory (7) and WHO Laboratory Biosafety Guidance Related to the Novel Coronavirus (2019-nCoV): Interim Guidance (4) for more information.

Authors' statement

The Respiratory Virus Infection (ReVI) Working Group of the Canadian Public Health Laboratory Network (CPHLN) is dedicated to providing leadership and guidance on topics

related to respiratory viral pathogens, including laboratory response to emerging respiratory viruses. The ReVI Working Group is comprised of leaders from public health laboratories across Canada.

Conflict of interest

None.

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

Respiratory Virus Infections Working Group¹

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<https://doi.org/10.14745/ccdr.v46i05a03>

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

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Introduction

Point-of-care (POC) serology testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes COVID-19, detect the human antibody response to infection rather than the virus itself. Most POC serology tests are qualitative immunochromatographic (lateral-flow) based assays that detect immunoglobulins M and/or G in blood from a finger prick and can provide results in less than 30 minutes. While there is widespread interest in adopting POC serology tests for SARS-CoV-2, there are currently significant limitations to this testing modality, including the lack of understanding of the immunological response in COVID-19, limited clinical validation data and variability in performance among different POC tests.

Current position for use of point-of-care serology testing for acute diagnostics

The POC serology tests for SARS-CoV-2 have not currently been validated for use as a diagnostic tool for acute infection and none is approved by Health Canada to date. In general, these antibody tests often do not become positive until a week or more after symptoms have started and, therefore, are not suitable for diagnosis of acute SARS-CoV-2 infection at this time. We recommend that nucleic acid detection (e.g. real-time polymerase chain reaction, PCR) remains the first-line test for the diagnosis of acute SARS-CoV-2 infection, as advised by the World Health Organization (1).

Key points relating to point-of-care serology testing

- It can take 7–12 days after symptom onset for antibodies to SARS-CoV-2 to develop; therefore, the use of POC serology tests in the early phase of infection can result in false-negative results at a time when patients are most infectious (i.e. a negative result does not rule out infection) Since POC serology tests do not detect virus, a positive or negative

- result does not determine whether a person is infectious
- Positive results may reflect either a past or present infection with SARS-CoV-2
- False-positive results may occur if these kits cross react with antibodies from recent or past exposure to other coronaviruses, including human seasonal coronaviruses (HKU1, NL63, OC43, 229E), severe acute respiratory syndrome coronavirus 1 (SARS-CoV-1) or Middle East respiratory syndrome coronavirus (MERS-CoV). Other infections, as well as non-infectious conditions (e.g. rheumatoid factor-positive diseases) may also cause false-positive results. All kits considered for use need to be thoroughly evaluated for such cross reactivity before being used clinically
- False-negative results may occur in elderly and immunocompromised patients

Where point-of-care serology testing could be used

At present, the use of serology in the diagnosis of acute SARS-CoV-2 infection and patient management is likely to be of limited utility. However, once the dynamics of the serological response in COVID-19 are better understood, serology will play an important role in the public health response. A key aspect of the use of serology testing is understanding whether antibody production correlates with protective immunity and what the duration of that protection is. The ease of use and quick turnaround time of POC assays make it an ideal testing modality in 1) remote areas with limited access to centralized laboratory-based testing and/or local laboratory infrastructure and



2) situations that would benefit from immediate triaging.

Examples of the latter include the following:

- seroepidemiology—used to better understand the proportion of undiagnosed in the population over time and to provide more accurate data of attack and mortality rates
- informing targeted diagnostic testing strategies (using PCR testing), where priority would be given to populations/areas with no evidence of immunity
- detecting seroconversion and assessing immunity in healthcare workers and other essential/frontline workers
- as an adjunct to PCR for diagnostic testing in patients who are PCR-negative and in the late course of their illness to implement control measures and to effectively manage patients
- testing high-risk populations exposed to SARS-CoV-2 to assess their risk of developing infection
- detecting seroconversion as a surrogate for effectiveness of control measures
- determining, once a vaccine is available, who should be prioritized for earlier vaccination
- supporting clinical trials that are assessing novel therapies, such as the use of neutralizing antibodies

Important considerations for implementing point-of-care serology testing

- A well validated test, which has been evaluated against a gold standard (viral neutralization assays or another laboratory-based serological assay), is required. Performance characteristics (sensitivity, specificity, positive and negative predictive values, cross-reaction to other coronaviruses) should be established using sera from 1) patients infected with SARS-CoV-2, 2) other respiratory viruses, including seasonal coronaviruses, and 3) healthy controls
- Adequate training of healthcare workers to administer the test and interpret the result will be required
- Risk of infection with SARS-CoV-2 and bloodborne infections for the operator must be assessed
- Provisions must be in place to ensure the capture of 1) testing data for individual patient records and surveillance purposes and 2) requirement for participation in external quality assessment to maintain high-quality testing

Conclusion

Based on currently available information, the Canadian Public Health Laboratory Network recommends that SARS-CoV-2 POC serological assays not be used for clinical testing in any capacity at this time. As more information becomes available on test performance, and assays are validated against gold standard

serological methods, clinical application of POC assays will be reevaluated. Molecular testing, such as real-time PCR, remains the primary test method for laboratory confirmation of acute SARS-CoV-2 infection and diagnosis of COVID-19.

Authors' statement

The Respiratory Virus Infection Working Group of the Canadian Public Health Laboratory Network (CPHLN) is dedicated to providing leadership and guidance on topics related to respiratory viral pathogens, including laboratory response to emerging respiratory viruses. The Respiratory Virus Infection Working Group is comprised of leaders from public health laboratories across Canada.

Acknowledgements

The Respiratory Virus Infection Working Group would like to thank members of the Canadian Public Health Laboratory Network (CPHLN) Secretariat, S Radons Arneson and D Marcino, for coordination of document synthesis. We would also like to thank the Laboratory Directors Council of the CPHLN for review of the document.

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Laboratory-confirmed COVID-19 in children and youth in Canada, January 15–April 27, 2020

Dana Paquette¹, Christopher Bell¹, Maxime Roy¹, Lindsay Whitmore^{1*}, Andrea Currie¹, Chris Archibald¹, Diane MacDonald¹, Jennifer Pennock¹

Abstract

Understanding the epidemiology of COVID-19 among children and youth in Canada will help to inform public health measures in settings where children gather. As of April 27, 2020, provinces and territories provided the Public Health Agency of Canada with detailed information on 24,079 cases, of which 3.9% (n=938) were younger than 20 years of age. The detection rate per 100,000 population was lower in this age group (11.9 per 100,000), compared with those aged 20–59 years (72.4 per 100,000) and 60 and older (113.6 per 100,000). The median age among those younger than 20 years of age was 13 years, and cases were distributed equally across male and female genders. Among provinces and territories with more than 100 cases, 1.6% to 9.8% of cases were younger than 20 years of age. Cases in this age group were more likely to be asymptomatic: 10.7% compared with 2.4% in those aged 20–59 years and 4.1% in those aged 60 and older. Children and youth experienced severe outcomes less often, but 2.2% (n=15/672) of cases within this age group were severe enough to require hospitalization. Based on available exposure information, 11.3% (n=59/520) of cases aged younger than 20 years had no known contact with a case. Canadian findings align with those of other countries.

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Keywords: COVID-19, youth, children, Canada, surveillance

Introduction

As of April 27, 2020, there were 47,327 COVID-19 cases reported in Canada. With the growth in new cases slowing, provincial, territorial and federal governments are planning how and when to ease some public health measures including the timing and parameters for reopening schools, daycares and other settings where children gather. To inform such decisions, it is important to understand the epidemiology of COVID-19 among children and youth in Canada.

Current situation

Data for this analysis were drawn from laboratory-confirmed cases reported to the Public Health Agency of Canada (PHAC) as of April 27, 2020. Of the 47,327 cases reported up to that date, detailed information was provided to PHAC for 26,876 cases. Of these, 24,723 were laboratory-confirmed and 24,079 included information on age. Among these cases, 3.9% (n=938) were younger than 20 years of age, and form the basis for this analysis.

The rate of laboratory-confirmed COVID-19 cases was lower in individuals under 20 years of age at 11.9 per 100,000 (1), compared with 72.4 per 100,000 for those 20 to 59 years of age and 113.6 per 100,000 for those 60 years of age and older ($p<0.001$). Rates per 100,000 population were consistent (7.1–11.4 per 100,000) across finer age groups for children younger than 15 years of age, while the 15–19 years of age group had a higher rate (20.7 per 100,000) (see **Table 1**). This difference may be due to adolescents being more independent than younger age groups and therefore more able to seek out social contact with peers (2). It is also important to note that observed

Table 1: Age distribution among cases younger than 20 years of age (N=938)

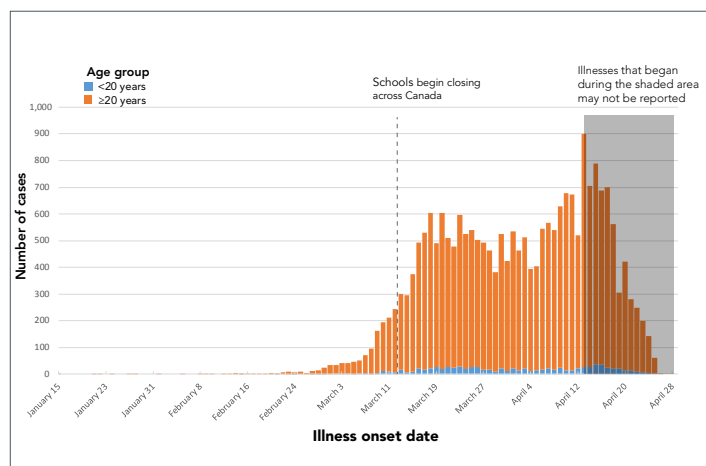
Age group (years)	Frequency		Rate per 100,000
	n	%	
Younger than 1	42	4.5	11.4
1–4	109	11.6	7.1
5–9	152	16.2	7.5
10–14	215	22.9	11.2
15–19	420	44.8	20.7
Total	938	100	11.9



differences in rates across age groups may be due, in part, to differences in laboratory testing patterns by age.

Among the cases younger than 20 years, 50.7% were female and the median age was 13 years. The proportion of cases younger than 20 years reported daily remained fairly consistent over time on the days where cases numbered more than 100 (**Figure 1**), ranging from 2.1% to 6.9%. Information on exposure category was available for 55.4% ($n=520/938$) of cases younger than 20 years for which PHAC received more detailed information. Of these, 20.4% were exposed internationally, 9.6% were contacts of travelers from affected areas, 58.7% were contacts of cases infected in Canada and 11.3% had no known contact with cases. The younger age groups (0 to 4, 5 to 9 and 10 to 14 years) had a lower percentage of cases with no known contact with a case (8.0%, 8.3% and 9.7%, respectively) compared with the 15–19 year age group, in which 15.1% of cases had no known contact.

Figure 1: Epidemiologic curve from January 15 to April 27, by age group^a, (N=22,973)



^a If date of illness onset was not available, the next available date of the following was used: specimen collection date and laboratory testing date

The distribution of cases in the younger than 20 years age category varied significantly across provinces and territories ($p<0.001$) (see **Table 2**), which may reflect differences in the local epidemiology of COVID-19 across provinces and territories and/or differences in laboratory testing criteria across jurisdictions. Among the jurisdictions that reported more than 100 cases (this excludes Yukon, Northwest Territories, Nunavut and Prince Edward Island), in British Columbia, Saskatchewan, Manitoba and Ontario, 5.0% or less of all reported cases were younger than 20 years, while Alberta, Quebec, New Brunswick, Nova Scotia and Newfoundland and Labrador reported a higher proportion of cases in this age group (between 6.8% and 11.1%). At the time of this report, no outbreaks were noted in settings where children gather (e.g. daycares, schools, camps, etc.). This may be due to the early timing of schools and some daycare closures.

Information on whether cases were symptomatic or not was available for 24.7% ($n=5,939/24,079$) of cases for which PHAC

Table 2: Number and proportion of cases younger than 20 years of age, for provinces with more than 100 cases reported (N=937)

Province ^a	Number and proportion of cases	
	n	%
Ontario	328	2.2
Alberta	229	8.1
Quebec	226	7.3
Nova Scotia	85	9.8
British Columbia	25	1.6
Newfoundland and Labrador	22	8.6
Manitoba	10	4.0
New Brunswick	8	6.8
Saskatchewan	4	3.2

^a Yukon, Northwest Territories, Nunavut and Prince Edward Island were excluded as they had fewer than 100 cases for all ages for this time period

received detailed reports. A larger proportion of asymptomatic cases (10.7%) was noted in the younger than 20 years age group, compared with 2.4% in those aged 20–59 years and 4.1% in those aged 60 and older. These proportions are likely underestimates of asymptomatic cases across all age groups, given that, during the time period in question, testing was focused on high risk populations who were symptomatic.

Symptom information was available for 24.6% ($n=5,912/24,079$) of cases for which PHAC received detailed information. Of those who experienced symptoms, the three most common symptoms differed across age groups. The three most common symptoms for those younger than 20 years of age were cough (57.0%), runny nose (41.2%) and headache (39.4%); compared with cough (74.2%), headache (64.3%) and pain (56.0%) for those aged 20–59 years and cough (75.1%), weakness (56.2%) and fever (51.9%) for those aged 60 and older. Other common symptoms in those younger than 20 years of age included fever (36.4%), sore throat (34.3%), weakness (31.8%) and chills (30.6%).

Severe outcomes were less likely to occur in the younger age group. Hospitalization status was available for 57.0% of all cases ($n=13,723/24,079$) for which PHAC received detailed information. Among individuals younger than 20 years of age, 2.2% were hospitalized, compared with 10.4% in those aged 20–59 years and 35.6% among those aged 60 and older. Among those hospitalized, in cases younger than 20 years of age, 13.3% were admitted to the Intensive Care Unit. Across all age groups, these proportions likely overestimate the true proportion of COVID-19 infections that result in severe outcomes, as individuals who experienced more severe symptoms and outcomes may have been more likely to be tested and reported than those who were asymptomatic or had only mild symptoms.

Among those younger than 20 years of age, hospitalization information was available for 71.6% ($n=672/938$) of cases. There



were only 15 hospitalizations in this age group, among which infants younger than one year of age had a higher proportion of hospitalizations than other age groups (see **Table 3**). However, the numbers were small in this age group, and these results should be interpreted with caution. Within the 15 hospital admissions in cases younger than 20 years of age, two cases were admitted to the Intensive Care Unit, and both cases were younger than one year of age. No deaths were reported in individuals younger than 20 years of age as of the date of this report, based on public reporting by province and territory health officials.

Table 3: Hospitalization status for cases younger than 20 years of age (N=672)

Age group (years)	Hospitalized		Not hospitalized	
	n	%	n	%
Younger than 1	4	13.3	26	86.7
1–4	0	0	83	100
5–9	0	0	118	100
10–14	2	1.3	153	98.7
15–19	9	3.1	277	96.9
Total	15	2.2	657	97.8

Conclusion

The data presented in this report add to our knowledge of the epidemiology of COVID-19 among children and youth. Few reports have been published to date, but based on what is available in the published literature and from surveillance reports, the Canadian findings are in line with those from other countries. Fewer cases have been reported among children and youth, compared with older age groups (3–5). A higher proportion of children and youth were asymptomatic, and they experienced different symptoms than adults (6–8). While less severely affected (3–5), hospitalizations still occurred, including among infants (7,9) and, as in the United States, a larger proportion of infants were hospitalized when compared with older children and youth (8).

Based on these and other findings, a significant proportion of cases among children and youth was asymptomatic. Though preliminary studies suggest children are less important sources of SARS-CoV-2 infection than adults, asymptomatic transmission has been noted (10). It will, therefore, be important to maintain key public health measures even as some controls are relaxed. Among these, behaviours such as staying home when ill, maintaining physical distancing, use of non-medical masks and frequent handwashing should continue to be encouraged in this age group to prevent transmission. As well, since higher rates of confirmed infection were observed in those aged 15–19 years, additional efforts to educate and reinforce public health preventative measures, such as physical distancing, may be needed to target this more independent and mobile age group.

To ensure that COVID-19 continues to be monitored in children and youth, plans are underway for enhanced surveillance of the pediatric population. Data will be available through multiple data streams in addition to province and territory case-based reporting. Enhanced surveillance will make use of existing administrative databases and surveillance systems, including the Canadian Institute for Health Information's Discharge Abstract Database, the Canadian Nosocomial Infections Surveillance Program and the Canadian Pediatric Surveillance Program. These data streams will provide complimentary information to monitor trends in severe pediatric cases, identify risk factors associated with disease, and assess the burden of disease within this population.

Authors' statement

DP — Conceptualization, original draft, review and editing

CB — Data curation, formal analysis, review and editing

MR — Data curation, formal analysis

LW — Review and editing

AC — Review and editing

CA — Review and editing

DM — Review and editing

JP — Review and editing

Conflict of interest

None.

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PREVENT THE SPREAD OF COVID-19

CORONAVIRUS DISEASE (COVID-19): HOW TO CARE FOR A PERSON WITH COVID-19 AT HOME—ADVICE FOR CAREGIVERS

Link contact

- One care provider should provide care.
- Do not care for anyone who has COVID-19, such as a roommate, family member, or friend, unless you are wearing a mask and gloves.
- If you must care for someone with COVID-19, wear a mask and gloves at all times.
- If you must care for someone with COVID-19, wear a mask and gloves at all times.
- If you must care for someone with COVID-19, wear a mask and gloves at all times.

Protect yourself

- Avoid contact with anyone who has COVID-19.
- These people should wear a mask and gloves at all times.
- If you must care for someone with COVID-19, wear a mask and gloves at all times.
- If you must care for someone with COVID-19, wear a mask and gloves at all times.
- If you must care for someone with COVID-19, wear a mask and gloves at all times.

WHAT IT IS

COVID-19 is an illness caused by a coronavirus. It is spread from person to person, usually through droplets that are released when someone coughs or sneezes.

SYMPTOMS

Symptoms may be very mild or more serious. They may take up to 14 days to appear after exposure to the virus.

PREVENTION

COVID-19 is spread from person to person, usually through droplets that are released when someone coughs or sneezes.

IF YOU HAVE SYMPTOMS

If you have symptoms of COVID-19, you should stay at home and avoid contact with others.

FOR MORE INFORMATION

1-833-784-4375

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- Get the latest guidance and awareness resources
- Some resources are available in multiple languages

Visit www.canada.ca/coronavirus



Modified two-tiered testing algorithm for Lyme disease serology: The Canadian context

Todd Hatchette^{1*}, Robbin Lindsay² on behalf of the Lyme Disease Diagnostics Working Group

Abstract

Background: Lyme disease (LD) is emerging in many parts of central and eastern Canada. Serological testing is most commonly used to support laboratory diagnosis of LD. Standard two-tiered testing (STTT) for LD involves detection of *Borrelia burgdorferi* antibodies using an enzyme immunoassay (EIA) followed by IgM and/or IgG immunoblots. However, improved sensitivity has been demonstrated using a modified two-tiered testing (MTTT) approach, in which a second EIA instead of the traditional immunoblot is used. This article summarises the evidence supporting the MTTT versus STTT for laboratory diagnosis of LD in Canada.

Methods: Peer reviewed literature on the sensitivity and specificity of different EIAs were compared by Canadian experts in LD diagnostic for MTTT vs STTT in patients with clinical history of LD residing in LD endemic areas or in samples from the LD serum repository.

Results: The MTTT approach consistently demonstrated improved sensitivity to detect early infections with *B. burgdorferi* and also maintained high specificity vs STTT.

Conclusion: Diagnostic improvements in sensitivity of LD testing without significant loss of specificity have been consistently reported when MTTT is compared with STTT in studies conducted in highly LD endemic regions. Our working group agrees with the recommendation by the United States Centers for Disease Control that serological testing for LD using MTTT is an acceptable alternative to STTT. This recommendation is contingent on development and implementation of comprehensive validation studies on the performance of MTTT vs STTT within the Canadian context, including evaluation of the test performance in areas of low endemicity for LD.

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Keywords: *Borrelia burgdorferi*, Lyme disease, serology, standard two-tiered testing, enzyme immunoassays, immunoblots, diagnostics

Introduction

Lyme disease (LD) is an emerging tick-borne infection caused by spirochetes belonging to the *Borrelia burgdorferi sensu lato* species complex, which are transmitted to humans by infected ticks (1). The principal tick vectors are the blacklegged tick (*Ixodes scapularis*) and the western blacklegged tick (*Ixodes pacificus*) in eastern/central Canada and British Columbia, respectively (2). In Canada, infected blacklegged tick populations are endemic in parts of British Columbia, Manitoba, Ontario, Quebec, New Brunswick and Nova Scotia (3). The number of Canadians with LD has risen since it became nationally reportable, from 144 cases in 2009 to 2,025 in 2017, which is likely an under-representation of the true numbers (1,2,4). As the geographic range of blacklegged ticks continues to expand, more Canadians will be at risk for acquiring LD (5). It is estimated that more than 300,000 cases of LD occur in the

United States (US) each year (6). The volume of diagnostic tests for LD performed in the US is much greater compared with Canada (7). In part, this has driven efforts to improve testing efficiencies for LD, including the development and approval of the modified two-tiered testing (MTTT) (8). The objective of this document is to summarise the evidence supporting the improved performance of the MTTT approach compared to the currently used diagnostic algorithm for LD.

Intervention

The current reference method most commonly used for laboratory diagnosis of LD is serology, which detects antibodies to *B. burgdorferi* using standard two-tiered testing (STTT), using

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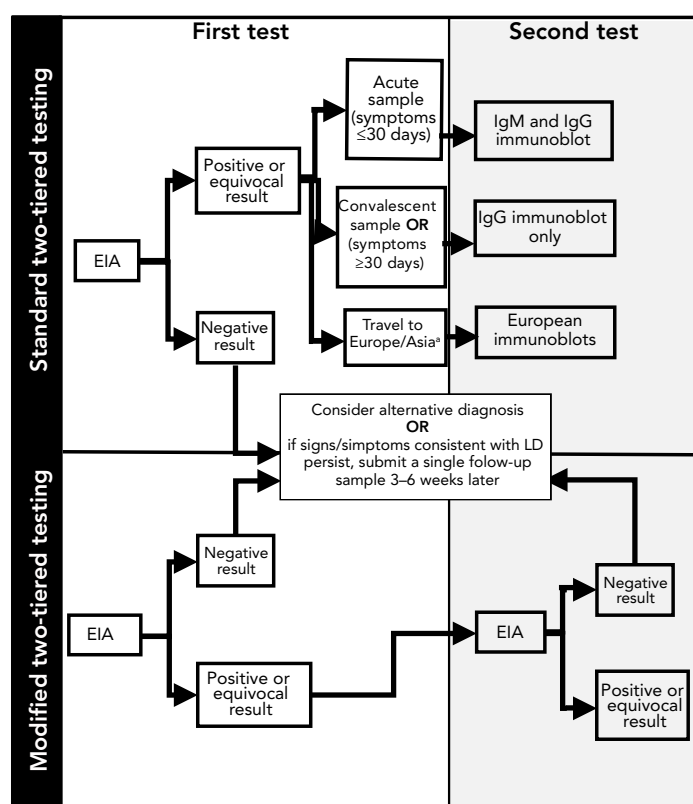
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an enzyme immunoassay (EIA) as the first tier test followed by IgM and/or IgG immunoblots as a supplemental test (**Figure 1**). Most provincial public health or hospital laboratories perform the EIA testing locally while immunoblot testing is performed independently at provincial public health labs in British Columbia, Ontario (and shortly in Quebec) or at the National Microbiology Laboratory (NML). NML performs immunoblot testing for all provinces when LD is suspected in patients who travelled outside of North America (**Figure 1**). Regardless of the type of testing, results are reviewed by laboratory staff and reported to the requesting physician and positive results are also reported to local provincial public health.

Figure 1: Schematic depicting steps in standard two-tiered testing and modified two-tiered testing for Lyme disease^a



Abbreviations: EIA, enzyme immunoassay; IgG, immunoglobulin G; IgM, Immunoglobulin M; LD, Lyme disease

^a Note that suspect LD cases from Europe or Asia would continue to be investigated using the standard two-tiered testing

A number of different EIAs are available for the first tier in the STTT including those composed of whole cell sonicates (WCS) of the laboratory strain of *B. burgdorferi* B31. More recently, EIAs based on synthetic peptides that contain regions conserved among multiple *B. burgdorferi* strains, such as the surface lipoprotein variable major protein-like sequence, expressed (VlsE), C6 (the invariable region 6 of VlsE) or C10 peptide (the conserved amino-terminal portion of outer surface protein C), have been developed (8,9). While the specificity of the newer assays is better than WCS, they are still not sufficiently specific to be used as a standalone assay. As a result, supplemental testing

with immunoblots is recommended (9–12). The STTT does have a number of technical limitations, including that immunoblots are more laborious to perform than EIAs and the scoring of the immunoblots can be subjective, which may lead to inter and intralaboratory variability (11). In addition, immunoblot testing is performed in relatively few reference diagnostic laboratories in the US (7) and Canada so turnaround times are typically longer than for EIAs alone (8,11).

The performance characteristics of the STTT algorithm also depend on the stage of infection. A recent systematic review has shown that the sensitivity of STTT for LD is poor in early localized infection (less than 50%) but in late stages of infection the sensitivity approaches 100% (13). As such, diagnosis and treatment of early localized LD is based on clinical symptoms alone in patients who have exposure history in blacklegged tick endemic areas (10). However, the diagnosis of early LD can be challenging since some patients with early localized *B. burgdorferi* infections do not present with an erythema migrans rash and may have symptoms that overlap with those of other diseases (9,14). Thus, improving the sensitivity of testing in early localized infections is important in identifying patients with LD, allowing for early treatment and potentially preventing infection from disseminating and causing severe disease.

Outcomes

Modified two-tiered testing for serologic diagnosis of Lyme disease

There have been a number of studies evaluating the use of a MTTT approach in which a second EIA is performed instead of the traditional immunoblots (**Figure 1**). A number of different combinations of EIAs have been used in this so-called “two EIA approach” including WCS EIA followed by C6 EIA, VlsE EIA followed by C6 EIA, C6 EIA followed by VlsE and VlsE/C10 followed by WCS (15–20). Samples for these evaluations have been drawn from smaller cohorts of patients with acute LD (15,18) or comparisons were made using well-characterised samples from the Centers for Disease Control (CDC) LD serum repository (16,19,21). Studies were performed on samples from children (17,20) as well as adults (16,19,21). With few exceptions (22), these evaluations have only been performed on patients from the US and the MTTT has not been fully validated for use on patients with exposure in Europe or Asia.

Although different combinations of EIAs were used in the MTTT algorithms, the MTTT was consistently more sensitive in detecting *B. burgdorferi* infections, particularly in early localized LD compared with STTT. Importantly, these MTTT had equivalent sensitivity for detecting late infections and comparable specificities to STTT regardless of the combinations of EIAs used in the MTTT (see summaries in **Tables 1** and **2**). Recently, the US Food and Drug Administration approved a MTTT algorithm for the laboratory confirmation of LD acquired in North America (23).

**Table 1: Sensitivity of modified two-tiered testing and standard two-tiered testing for Lyme disease**

Sample size	Reference	Disease manifestations	EIAs combinations used ^a	MTTT sensitivity % (CI or range)	STTT sensitivity % (CI or range) ^b
140	(15)	EM, ENB, LC	WCS f/b C6	61 (CI 53–69)	48 (CI 40–56)
318	(11)	EM, ENB	WCS f/b C6	60 (CI 55–66)	41 (CI 36–46)
55	(18)	Acute EM	WCS f/b C6; WCS f/b VlsE CLIA; VlsE FLIA f/b C6	42.7 (R 38.0–54.0)	32 (R 25–36)
47	(18)	Convalescent EM	WCS f/b C6; WCS f/b VlsE CLIA; VlsE FLIA f/b C6	70 (R 66–72)	57.3 (R 55.0–60.0)
95	(16)	EM, ENB, LC	Vidas f/b C6 or VlsE ^c	66.8 (R 65.2–68.4)	60.2 (R 56.8–64.2)
114	(17)	All disease stages combined	WCS f/b C6	79.8 (CI 71.1–86.5)	81.6 (CI 73.0–88.0)
40	(19)	Acute EM	VlsE f/b C6; WCS f/b C6; WCS f/b VlsE	54.3 (R 50.0–58.0)	45.3 (R 43.0–50.0)
38	(19)	Convalescent EM	VlsE f/b C6; WCS f/b C6; WCS f/b VlsE	77 (R 76–79)	61; 61; 63
124	(19)	All disease stages combined	VlsE f/b C6; WCS f/b C6; WCS f/b VlsE	76.7 (R 75.0–78.0)	66, 67; 71
30	(25)	Acute EM	VlsE/pepC10 f/b WCS	73.3	50
30	(25)	Convalescent EM	VlsE/pepC10 f/b WCS	83.3	76.7
56	(25)	Early disseminated disease-stage ^a	VlsE/pepC10 f/b WCS	66.1	60.7
29	(15)	LA, LNB	WCS f/b C6	100 (CI 86–100)	100 (CI 86–100)
122	(11)	LA, LNB	WCS f/b C6	98 (CI 93–99)	96 (CI 91–98)
29	(16)	LA	Vidas f/b C6 or VlsE	100	98.9 (R 97–100)
50	(25)	Late disseminated disease-stage ^c	VlsE/pepC10 f/b WCS	100	100

Abbreviations: EIA, enzyme immunoassay; EM, erythema migrans; ENB, early neuroborreliosis; LA, Lyme arthritis; LC, Lyme carditis; LNB, late neuroborreliosis; MTTT, modified two-tiered testing;

STTT, standard two-tiered testing; VlsE, variable major protein-like sequence, expressed; WCS, whole cell sonicates

^a Type of EIA and order that EIAs were performed in; f/b-followed by, see original publications for manufacturer's information

^b See original publications for precisely EIA and immunoblots used in STTT algorithms

^c Data from these two different EIA combinations pooled because no significant difference between them

Table 2: Specificity of modified two-tiered testing and standard two-tiered testing for Lyme disease

Sample size	Reference	Patient cohort ^a	EIAs combinations used ^b	MTTT sensitivity % (CI or range)	STTT sensitivity % (CI or range) ^c
Overall controls					
1,300	(15)	Healthy and symptomatic controls	WCS f/b C6	99.5 (CI 98.9–99.8)	99.5 (CI 98.9–99.8)
2,208	(11)	Healthy controls & patients with other diseases	WCS f/b C6	99.5 (CI 99.1–99.8)	99.5 (CI 99.1–99.7)
347	(16)	Healthy controls & patients with other diseases	Vidas f/b C6 or VlsE ^c	98.3 (CI 96.2–99.3)	98.3 (CI 96.2–99.3)
931	(17)	Healthy and symptomatic controls	WCS f/b C6	96.6 (R 94.6–97.6)	98.7 (R 96.6–100.0)
347	(19)	Healthy controls & patients with other diseases	VlsE f/b C6; WCS f/b C6; WCS f/b VlsE	98.6 (R 97.7–99.4)	98.1 (R 95.7–99.7)
190	(25)	Healthy controls & patients with other diseases	VlsE/pepC10 f/b WCS	98.9 (R 97.8–100.0)	100
Unhealthy controls					
54	(15)	Symptomatic controls	WCS f/b C6	100	100
50	(18)	Patients with other diseases	WCS f/b C6; WCS f/b VlsE CLIA; VlsE CLIA f/b C6	99.3 (R 98.0–100.0)	100
144	(16)	Patients with other diseases	Vidas f/b C6 or VlsE ^d	98.2 (R 96.5–100.0)	97.1 (R 94.4–99.3)
830	(17)	Symptomatic controls	WCS f/b C6	96.5 (R 94.6–97.6)	98.7 (R 96.6–100.0)
144	(19)	Patients with other diseases	VlsE f/b C6; WCS f/b C6; WCS f/b VlsE	98.1 (R 96.5–100.0)	97.4 (R 95.7–99.7)
90	(25)	Patients with other diseases	VlsE /PEPC10 f/b WCS	97.8	100

Abbreviations: EIA, enzyme immunoassay; MTTT, modified two-tiered testing; STTT, standard two-tiered testing; VlsE, variable major protein-like sequence, expressed; WCS, whole cell sonicates

^a Unlike healthy controls, symptomatic controls were subjects with clinical symptoms compatible with Lyme disease (LD) but who did not meet authors LD case definitions; see original publications for list of other diseases but these are look-alike diseases such as syphilis, fibromyalgia and multiple sclerosis

^b Type of EIA and order of EIAs were performed in the MTTT; f/b-followed by; see original publications for manufacturer's information

^c See original publications for precisely EIA and immunoblots used in STTT algorithms

^d Data from these two different EIA combinations were pooled because no significant difference between them



This alternative testing algorithm has been endorsed by the US CDC that states that it is an acceptable alternative to the STTT because “the new Lyme disease assays indicates that test performance has been evaluated and is substantially equivalent to or better than a legally marketed predicate test” (24). It is unknown whether the MTTT approach will be validated in the US for patients who potentially acquired LD outside of North America; however, in Canada the STTT algorithm will be maintained using European-specific assays on Canadians with suspect LD acquired outside of North America (Figure 1).

Benefits and limitations of the modified two-tiered testing

In addition to greater sensitivity for the detection of early *B. burgdorferi* infections, the interpretation of the results of MTTT is less subjective than immunoblot testing (Table 3). The MTTT has also been shown to be more cost-effective than the STTT (26). The tests are also less labour-intensive and can be performed using automated instruments or platforms (8). As such, the MTTT does not require specialized testing (i.e. immunoblots) in a reference laboratory and can be performed by any laboratory that currently does serologic testing. These differences can lead to faster turnaround time for results (8,9).

Table 3: Advantages and disadvantages of the modified two-tiered testing compared to standard two-tiered testing for Lyme disease

Advantages	Disadvantages
<ul style="list-style-type: none"> Improved sensitivity for the detection of early infection (greater than 25% improvement) Less costly than the STTT Less laborious Less subjective Enzyme immunoassay testing performed locally rather than referral to a specialized laboratory, reducing turnaround times Faster turnaround time facilitates acute and convalescent testing for non-erythema migrans early localized LD 	<ul style="list-style-type: none"> Patients presenting with erythema migrans will still require empiric treatment with antibiotics as the test algorithm sensitivity is less than 90% As occurs for the STTT, cannot differentiate between recent and past infections or reinfections Impacts of MTTT on specificity in areas of low prevalence are unclear STTT may be necessary/beneficial in patients with Lyme arthritis, given the potential for reduced specificity of some polyvalent enzyme immunoassays

Abbreviations: LD, Lyme disease; MTTT, modified two-tiered testing; STTT, standard two-tiered testing

The interpretation of the results of the MTTT diagnostic testing is either positive or negative, which is more straightforward than for STTT where IgM and IgG immunoblots can produce different outcomes, which can cause confusion for physicians (11). Although more sensitive than STTT, the sensitivity of the MTTT is still less than 90%, so patients with early localized LD should continue to be treated based on their clinical presentation rather than serologic results. However, the rapid turnaround time for MTTT may be particularly useful in evaluating patients with a clinical suspicion of LD but without an erythema migrans

rash, or in those who present with signs that overlap with other infections (e.g. Bell's palsy or arthritis) where serologic results will help establish the diagnosis (8). The most recent evidence-based guidelines from the United Kingdom suggested that “if LD is still suspected in people with a negative ELISA who were tested within four weeks from symptom onset, repeat the ELISA 4–6 weeks after the first ELISA test” (12). Currently if the convalescent EIA is positive, it would still require further supplemental testing with an immunoblot in the STTT. Given the anticipated faster turnaround time for the MTTT, clinicians may be more inclined to follow the National Institute for Health and Care Excellence recommendation and consider acute and convalescent testing, which increases diagnostic certainty of the testing on patients who do not present with erythema migrans rash. This is a particularly important consideration when the clinical suspicion is not high, such as for patients without known tick exposure in LD risk areas.

Despite the numerous advantages of the MTTT, there are associated limitations. Since antibodies to *B. burgdorferi* can persist for months to years after initial infection (27), the MTTT algorithm (and the STTT) cannot differentiate between active versus past infections, which further confounds serological diagnosis of reinfection with *B. burgdorferi*. In addition, it is possible that the MTTT algorithm may generate false positives based on the IgM component of the polyclonal EIAs used, since false positive IgM immunoblots are known to occur in healthy patients or in those with long-standing symptoms (28–31). The excellent performance characteristics of STTT in late stage LD may be difficult to match in the MTTT format, especially when polyvalent EIAs (containing epitopes for IgM) are used and it is likely that immunoblots will still need to be used in evaluating difficult LD cases (8). As such, the use of immunoblots may still have value in patients with manifestations of late stage LD such as Lyme arthritis or in suspect false positive cases where serologic results do not fit with the clinical presentation. In these circumstances, it is reasonable to consider performing an IgG immunoblot as patients with late stage LD have high IgG antibody responses and the immunoblot may allow for the evaluation of the response to specific Borrelial proteins, which some clinicians may find helpful (32,33). Finally, most of the evaluations of the MTTT algorithm have been conducted in areas of high LD endemicity and testing has been restricted to primarily adult patients. Evaluations of the performance of the MTTT in areas of lower risk of LD and in pediatric populations are knowledge gaps that should be filled over time (20).

Discussion

The Canadian Public Health Laboratory Network agrees with the CDC recommendation (24) that serologic assays for LD that utilize a MTTT approach (i.e. substitute a second EIA for the immunoblot in the second tier of testing) are acceptable alternatives to STTT. This recommendation assumes that the MTTT approach has been validated and shown to have



comparable performance characteristics to the STTT in regions of Canada where incidence of LD is high, as well as in low incidence jurisdictions. At present, only Nova Scotia has data validating the MTTT approach for LD diagnostics. Based on 447 samples from LD patients in that province, a MTTT consisting of an EIA based on a WCS of *B. burgdorferi* followed by a C6 EIA, detected 25% more cases of early localized infection compared to the STTT and had a specificity of 99.5% (34). These results are consistent with previously published data from studies conducted in highly LD endemic areas in the US (11,15) and support the use of the MTTT in this province. However, this validation study was conducted in the province with the highest incidence of LD in Canada (35). Further validation studies of the MTTT will need to be conducted in regions of Canada where LD incidence is lower, as it will be critical to document the performance characteristics of the MTTT in populations with a lower pre-test probability of infection (15,36). Small reductions in specificity can reduce the predictive value of the test (Table 4), which has led to the recommendation that LD testing should not be considered when the pre-test probability is less than 20% (37). Given the strain variation within *B. burgdorferi* populations observed across Canada (38), and the possible impact that this strain variability may have on LD diagnostic assays (39), it seems prudent to verify that the improved sensitivity of MTTT reported in the literature will be maintained when applied within different jurisdictions in Canada that host diverse and varied strains of *B. burgdorferi*.

Table 4: Estimated predictive values of modified two-tier testing depends on the stage of infection and the estimated prevalence of *B. burgdorferi* infection^a

Estimated prevalence (%)	MTTT positive predictive value (%)		MTTT negative predictive value (%)	
	Early localized LD ^b	Late LD ^c	Early localized LD ^a	Late LD ^b
5	84.8	91.3	97.6	100
3	76.6	86.0	98.6	100
1	51.7	66.8	99.5	100
0.1	9.6	16.6	100	100

Abbreviations: LD, Lyme disease; MTTT, modified two-tiered testing

^a Positive and negative predictive values calculated using <http://vassarstats.net/clin2.html>

^b Sensitivity was considered 53% based on data from reference 15; specificity was considered 99.5% based on data from Nova Scotia studies (33)

^c Sensitivity was considered 99.3% based on data from reference 15; specificity was considered 99.5% based on data from Nova Scotia studies (33)

The Lyme Disease Diagnostic Working Group of the Canadian Public Health Laboratory Network is working with provincial laboratories to develop validation plans for the MTTT. The goals of the validation will be to define the performance characteristics of the MTTT in areas with different incidences of LD (and possibly different strains of *B. burgdorferi*) and to evaluate which combination of the different EIAs available in Canada provide the data necessary to ensure that the benefits of the new MTTT algorithms are realized and specificity of LD serological testing is

maintained. A second report will be publicly available once these validation studies are completed.

Conclusion

The US Food and Drug Administration has recently approved a MTTT diagnostic algorithm for LD serology and the US CDC has recommended this new approach as an acceptable alternative to STTT. There are a growing number of scientific publications, using patients from the US, that report improved sensitivity in detection of early localized LD infection, while maintaining high specificity, when MTTT algorithms are compared to STTT. Recent data from Nova Scotia, generated using MTTT, draws similar conclusions. The improved sensitivity of the MTTT and shorter turnaround times associated with this new approach warrant further validation studies and possible rollout of this new diagnostic algorithm for LD in Canada.

Authors' statement

Lyme disease Diagnostics Working Group of the Canadian Public Health Laboratory Network comprises T Hachette (co-chair), LR Lindsay (co-chair), K Bernat, G Desnoyers, A Dibernardo, K Fonseca, G German, A Lang, M Morshed, R Needle, S Patel, K Thivierge and P VanCaeseele.

Conflict of interest

Authors have no conflicts of interest to report.

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Summary of the NACI Seasonal Influenza Vaccine Statement for 2020–2021

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Abstract

Background: Evidence on influenza vaccination is continually evolving. The National Advisory Committee on Immunization (NACI) provides annual recommendations to the Public Health Agency of Canada regarding the use of seasonal influenza vaccines.

Objective: To summarize NACI's recommendations regarding the use of seasonal influenza vaccines for the 2020–2021 influenza season and to highlight new and updated recommendations.

Methods: 1) To update wording on influenza vaccination of health care workers, NACI reassessed the evidence in the context of ethics and acceptability frameworks, in accordance with NACI's recently expanded mandate. 2) To provide recommendations on the use of live attenuated influenza vaccine (LAIV) in HIV-infected individuals, the Influenza Working Group developed a predefined search strategy to identify all eligible studies, then assessed the quality and summarized and analyzed the findings according to the NACI evidence-based process. NACI provided new recommendations based on assessment of the evidence.

Results: 1) NACI continues to recommend that health care workers and other care providers in facilities and community settings should be vaccinated annually against influenza and that this group be included among those particularly recommended to receive the influenza vaccine. 2) NACI concluded that LAIV is immunogenic in children with stable HIV infection; therefore, NACI newly recommends that LAIV may be considered as an option for children 2–17 years of age with stable HIV infection on highly active antiretroviral therapy and with adequate immune function.

Conclusion: NACI continues to recommend that an age-appropriate influenza vaccine should be offered annually to anyone six months of age and older who does not have contraindications to the vaccine, with a focus on the groups for whom influenza vaccination is particularly recommended.

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Keywords: National Advisory Committee on Immunization, NACI, influenza, influenza vaccine, guidance

Introduction

Seasonal influenza epidemics lead to significant morbidity and mortality in the Canadian population (1) and cause significant strain on the health care system during the influenza season each year. Although the epidemiology of influenza varies from year to year, it is estimated that influenza infections cause an average of 12,200 hospitalizations (2) and 3,500 deaths (3) per year.

Given the cyclical nature of seasonal influenza, the frequent changes to the circulating viral strains, and the number of

influenza vaccines authorized for use in Canada, the National Advisory Committee on Immunization (NACI) provides annual recommendations regarding seasonal influenza vaccination to the Public Health Agency of Canada (PHAC). For the 2020–2021 influenza season, NACI has updated the wording used for their recommendation on the vaccination of health care workers (HCW) and has provided a new recommendation on the use of live attenuated influenza vaccine (LAIV) in HIV-infected individuals. Complete details on influenza vaccine can be found



in the NACI *Statement on Seasonal Influenza Vaccine for 2020–2021* (4) and related publications. The objective of this article is to provide a concise summary of the information contained in this annual seasonal influenza statement and to highlight important updates.

Influenza vaccine abbreviations

The abbreviations used by NACI have been recently updated to better describe the defining features of the various types of influenza vaccines. The current abbreviations are listed in **Table 1**.

Table 1: NACI abbreviations for influenza vaccines

Influenza vaccine category	Formulation	Type	Current NACI abbreviation ^a
Inactivated influenza vaccine (IIV)	Trivalent (IIV3)	Standard dose ^b , unadjuvanted, IM administered	IIV3-SD
		Adjuvanted ^c , IM administered	IIV3-Adj
		High dose ^d , unadjuvanted, IM administered	IIV3-HD
	Quadrivalent (IIV4)	Standard dose ^b , unadjuvanted, IM administered	IIV4-SD
Live attenuated influenza vaccine (LAIV)	Quadrivalent (LAIV4)	Unadjuvanted, Nasal spray	LAIV4

Abbreviations: IIV, inactivated influenza vaccine; IIV3, trivalent inactivated influenza vaccine; IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4, quadrivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; IM, intramuscular; LAIV, live attenuated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine

^a The numeric suffix denotes the number of antigens contained in the vaccine ("3" refers to the trivalent formulation and "4" refers to the quadrivalent formulation). The hyphenated suffix "-SD" is used when referring to IIV products that do not have an adjuvant, contain 15 µg hemagglutinin (HA) per strain and are administered as a 0.5 mL dose by intramuscular injection; "-Adj" refers to an IIV with an adjuvant (e.g. IIV3-Adj for Flud® or Flud Pediatric®); and "-HD" refers to an IIV that contains higher antigen content than 15 µg HA per strain (e.g. IIV3-HD for Fluzone® High-Dose)

^b 15 µg HA per strain

^c 7.5 µg (in 0.25 mL) or 15 µg (in 0.5 mL) HA per strain

^d 60 µg HA per strain

Source: Table reproduced from NACI *Seasonal Influenza Vaccine Statement for 2020–2021* (4)

Methods

To prepare the *Statement on Seasonal Influenza Vaccine for 2020–2021*, the Influenza Working Group identified the need for evidence reviews for two topics in particular and, following a review and analysis of the information, proposed new or updated recommendations according to the NACI evidence-based process (5). NACI critically appraised the available evidence and approved the specific recommendations brought forward.

Vaccination of health care workers and other care providers

NACI identified a need to reassess the wording used for the recommendation on the vaccination of HCWs and other care providers with the influenza vaccine. To inform this updated wording, the evidence from four cluster randomized controlled trials (6–9) that assessed the impact of HCW influenza vaccination in geriatric long-term care settings was reassessed and considered in the context of ethics and acceptability. Ethics and acceptability were systematically considered, based on NACI's approved methods for the evaluation of ethics, equity, feasibility and acceptability as part of NACI's recently expanded mandate.

Use of live attenuated influenza vaccine in HIV-infected individuals

The NACI Influenza Working Group oversaw the completion of a systematic review to inform the development of guidance on the use of LAIV in HIV-infected individuals. Six electronic databases (MEDLINE, EMBASE, Scopus, ProQuest Public Health Database, ClinicalTrials.gov and PROSPERO) were searched from inception to April 13, 2018 to identify relevant literature on the efficacy, effectiveness, immunogenicity and safety of LAIV in HIV-infected adults and children aged six months and older. The Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) was also searched to identify any reports received on adverse events following vaccination with LAIV in HIV-infected individuals. Two reviewers independently screened the titles and abstracts of records retrieved from the search and eligible full-text articles for inclusion. One reviewer extracted data from eligible studies and appraised the methodological quality of these studies using the criteria outlined by Harris *et al.* (10). A second reviewer validated the data extraction and quality assessment. A narrative synthesis of the extracted data was performed.

Results

Vaccination of health care workers and other care providers

Based on their reassessment of the evidence in the context of ethics and acceptability, NACI continues to recommend that, in the absence of contraindications, HCWs and other care providers in facilities and community settings should be vaccinated annually against influenza. HCWs and other care providers have the potential to transmit influenza to individuals at high risk and, due to their occupation and close contact with people at high-risk of influenza-related complications, are themselves at increased risk of infection (11). Given the potential to transmit influenza and the increased risk of infection, and knowing that vaccination is the most effective way to prevent influenza, NACI recommends the inclusion of this group among those particularly recommended to receive the influenza vaccine. NACI considers



the receipt of influenza vaccination to be an essential component of the standard of care for all HCWs and other care providers for their own protection and that of their patients. This group should consider annual influenza vaccination as part of their responsibilities to provide the highest standard of care.

Further information on NACI's recommendation for the inclusion of HCWs as a group for whom influenza vaccination is particularly recommended can be found in Section III.2 of the *NACI Seasonal Influenza Vaccine Statement for 2020–2021* (4).

Use of live attenuated influenza vaccine in HIV-infected individuals

The systematic review identified eight articles that reported the findings from five studies investigating the immunogenicity, the safety, or both, of the administration of LAIV in HIV-infected individuals. No studies investigating the efficacy or effectiveness of LAIV in this population were identified. Based on the identified evidence, NACI concluded that LAIV is immunogenic in children with stable HIV infection on highly active antiretroviral therapy (HAART) and with adequate immune function. NACI also concluded that, while there is insufficient direct evidence to detect uncommon or rare adverse events related to the use of LAIV in HIV infected children, LAIV appears to have a similar safety profile to inactivated influenza vaccine (IIV). In addition, some children and their substitute decision-makers may prefer that they receive influenza vaccine through an intranasal spray as opposed to an intramuscular (IM) injection, although preferences will vary. Regarding the use of LAIV in HIV-infected adults, NACI concluded that the quantity of evidence available on the immunogenicity and safety of LAIV in adults with HIV is insufficient to justify a recommendation for the use of LAIV in this age group. Based on their assessment of the evidence, NACI has made the following recommendation:

NACI recommends that LAIV may be considered as an option for children 2–17 years of age with stable HIV infection on HAART and with adequate immune function* (Discretionary NACI recommendation).

*LAIV should only be considered in children with HIV who meet the following criteria:

- receiving HAART for ≥ 4 months
- CD4 count $\geq 500/\mu\text{L}$ if 2–5 years of age, or $\geq 200/\mu\text{L}$ if 6–17 years of age (measured within 100 days before administration of LAIV)
- HIV plasma RNA $< 10,000$ copies/mL (measured within 100 days before administration of LAIV)

While IM influenza vaccination is still considered the standard for children living with HIV by NACI and the Canadian Pediatric and Perinatal HIV/AIDS Research Group, LAIV would be reasonable for children meeting the criteria outlined above, if IM vaccination is not accepted by the patient or substitute decision-maker.

The detailed findings of this review and additional information supporting this recommendation can be found in the *NACI Statement on the Recommendation on the Use of Live-Attenuated Influenza Vaccine (LAIV) in HIV-Infected Individuals* (12).

Summary of NACI recommendations for the use of influenza vaccines for the 2020–2021 influenza season

NACI continues to recommend influenza vaccination to anyone six months of age and older who does not have contraindications to the vaccine. Vaccination should be offered as a priority to people at high risk of influenza-related complications or hospitalization, people capable of transmitting influenza to those at high risk of complications, and others as indicated in the **List 1** below.

List 1: Groups for whom influenza vaccination is particularly recommended

People at high risk of influenza-related complications or hospitalization:

- All pregnant women
- Adults and children with the following chronic health conditions*:
 - Cardiac or pulmonary disorders (includes bronchopulmonary dysplasia, cystic fibrosis and asthma)
 - Diabetes mellitus and other metabolic diseases
 - Cancer, immune compromising conditions (due to underlying disease, therapy or both, such as solid organ transplant or hematopoietic stem cell transplant recipients)
 - Renal disease
 - Anemia or hemoglobinopathy
 - Neurologic or neurodevelopmental conditions (includes neuromuscular, neurovascular, neurodegenerative and neurodevelopmental conditions and seizure disorders [for children, includes febrile seizures and isolated developmental delay], but excludes migraines and psychiatric conditions without neurological conditions)
 - Morbid obesity (body mass index [BMI] of 40 and over)
 - Children six months to 18 years of age undergoing treatment for long periods with acetylsalicylic acid, because of the potential increase of Reye's syndrome associated with influenza
- People of any age who are residents of nursing homes and other chronic care facilities
- Adults 65 years of age and older
- All children 6–59 months of age
- Indigenous people

People capable of transmitting influenza to those at high risk:

- Health care and other care providers in facilities and community settings who, through their activities, are capable of transmitting influenza to those at high risk
- Household contacts, both adults and children, of individuals at high risk, whether or not the individual at high risk has been vaccinated, including:
 - Household contacts of individuals at high risk
 - Household contacts of infants less than six months of age, as these infants are at high risk but cannot receive influenza vaccine
 - Members of a household expecting a newborn during the influenza season
- Those providing regular child care to children 0–59 months of age, whether in or out of the home
- Those who provide services within closed or relatively closed settings to people at high risk (e.g. crew on a ship)

Others:

- People who provide essential community services
- People who are in direct contact with poultry infected with avian influenza during culling operations

* Refer to Immunization of Persons with Chronic Diseases and Immunization of Immunocompromised Persons in Part 3 of the CIG for additional information about vaccination of people with chronic diseases (13)
Source: Table reproduced from *NACI Seasonal Influenza Vaccine Statement for 2020–2021* (4)



Recommended influenza vaccine options by age group and by dosage and route of administration by age are summarized in **Tables 2 and 3**, respectively.

Table 2: Recommendations on the choice of influenza vaccine type for individual-level decision-making^a by age group

Recipient by age group	Vaccine types authorized for use	Recommendations on choice of influenza vaccine
6–23 months	<ul style="list-style-type: none"> • IIV3-SD • IIV3-Adj • IIV4-SD 	<ul style="list-style-type: none"> • Quadrivalent influenza vaccine should be used in infants without contraindications, given the burden of influenza B disease in this age group and the potential for lineage mismatch between the predominant circulating strain of influenza B and the strain in a trivalent vaccine • If a quadrivalent vaccine is not available, any of the available trivalent vaccines should be used
2–17 years ^b	<ul style="list-style-type: none"> • IIV3-SD • IIV4-SD • LAIV4 	<ul style="list-style-type: none"> • Either IIV4-SD or LAIV4 should be used in children without contraindications, including those with non-immune compromising chronic health conditions, given the burden of influenza B disease in this age group and the potential for lineage mismatch between the predominant circulating strain of influenza B and the strain in a trivalent vaccine • If IIV4-SD or LAIV4 is not available, IIV3-SD should be used • IIV4-SD should be used for children for whom LAIV is contraindicated, such as in children with: <ul style="list-style-type: none"> ◦ Severe asthma ◦ Medically attended wheezing in the seven days prior to vaccination ◦ Current receipt of aspirin or aspirin-containing therapy ◦ Immune compromising conditions, with the exception of stable HIV infection, if the child is currently being treated with HAART and has adequate immune function

Table 2: Recommendations on the choice of influenza vaccine type for individual-level decision-making^a by age group (continued)

Recipient by age group	Vaccine types authorized for use	Recommendations on choice of influenza vaccine
2–17 years ^b (continued)	<ul style="list-style-type: none"> • IIV3-SD • IIV4-SD • LAIV4 (continued) 	<ul style="list-style-type: none"> • LAIV4 may be given to children with: <ul style="list-style-type: none"> ◦ Stable, non-severe asthma ◦ Cystic fibrosis who are not being treated with immunosuppressive drugs (e.g. prolonged systemic corticosteroids) ◦ Stable HIV infection, if the child is currently being treated with HAART and has adequate immune function
18–59 years	<ul style="list-style-type: none"> • IIV3-SD • IIV4-SD • LAIV4 	<ul style="list-style-type: none"> • Any of the available influenza vaccines should be used in adults without contraindications • IIV should be used for adults for whom LAIV is contraindicated or not recommended, such as in: <ul style="list-style-type: none"> ◦ Pregnant women ◦ Adults with any of the chronic health conditions identified in Table 2, including immune compromising conditions ◦ HCWs
60–64 years	<ul style="list-style-type: none"> • IIV3-SD • IIV4-SD 	<ul style="list-style-type: none"> • Any of the available influenza vaccines should be used in those without contraindications
65 years and older ^c	<ul style="list-style-type: none"> • IIV3-SD • IIV3-Adj • IIV3-HD • IIV4-SD 	<ul style="list-style-type: none"> • IIV3-HD should be used over IIV3-SD, given the burden of influenza A(H3N2) disease and the good evidence of better protection compared to IIV3-SD in adults 65 years of age and older <ul style="list-style-type: none"> ◦ NACI does not make comparative individual-level recommendations on the use of IIV3-Adj or IIV4-SD over IIV3-SD, or among IIV3-Adj, IIV3-HD, and IIV4-SD ◦ In the absence of any specific product, any of the available influenza vaccines should be used

Abbreviations: HAART, highly active antiretroviral therapy; HCW, health care worker; IIV, inactivated influenza vaccine; IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; LAIV, live attenuated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; NACI, National Advisory Committee on Immunization

^a Recommendations for individual-level decision making are intended for individuals wishing to protect themselves from influenza, or vaccine providers wishing to advise individual patients about preventing influenza

^b Refer to Table 4 of the NACI Seasonal Influenza Vaccine Statement for 2020–2021 for a summary of vaccine characteristics of LAIV compared with IIV in children 2–17 years of age (4)

^c Refer to Table 5 NACI Seasonal Influenza Vaccine Statement for 2020–2021 for a comparison of the vaccine characteristics of influenza vaccine types available for use in adults 65 years of age and older (4)

Source: Table adapted from NACI Seasonal Influenza Vaccine Statement for 2020–2021 (4)



Table 3: Recommended dose and route of administration, by age, for influenza vaccine types authorized for the 2020–2021 influenza season

Age group	Influenza vaccine type (route of administration)				Number of doses required
	IIV3-SD ^a or IIV4-SD ^b (Intramuscular)	IIV3-Adj ^c (Intramuscular)	IIV3-HD ^d (Intramuscular)	LAIV4 ^e (Intranasal)	
6–23 months	0.5 mL ^f	0.25 mL	-	-	1–2 ^g
2–8 years	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1–2 ^g
9–17 years	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1
18–59 years	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1
60–64 years	0.5 mL	-	-	-	1
65 years and older	0.5 mL	0.5 mL	0.5 mL	-	1

Abbreviations: IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; -, no data

^a Afluria® (six months and older), Fluvir® (six months and older), Influvac® (three years and older), Vaxigrip® six months and older). Influvac and Vaxigrip are authorized, but not currently available for sale in Canada

^b Afluria® Tetra (five years and older), Flulaval® Tetra (six months and older), Fluzone® Quadrivalent (six months and older), Influvac® Tetra (18 years and older). Influvac Tetra is authorized for use in Canada in adults 18 years and older; however, NACI has not specifically reviewed this product

^c Flud Pediatric® (6–23 months) or Flud® (65 years and older)

^d Fluzone® High-Dose (65 years and older)

^e FluMist® Quadrivalent (2–59 years)

^f Evidence suggests moderate improvement in antibody response in infants, without an increase in reactogenicity, with the use of full vaccine doses (0.5 mL) for unadjuvanted inactivated influenza vaccines (14,15). This moderate improvement in antibody response without an increase in reactogenicity is the basis for the full dose recommendation for unadjuvanted inactivated vaccine for all ages. For more information, refer to *Statement on Seasonal Influenza Vaccine for 2011–2012* (16)

^g Children six months to less than nine years of age receiving seasonal influenza vaccine for the first time in their life should be given two doses of influenza vaccine, with a minimum interval of four weeks between doses. Children six months to less than nine years of age who have been properly vaccinated with one or more doses of seasonal influenza vaccine in the past should receive one dose of influenza vaccine per season thereafter

Source: Table reproduced from NACI Seasonal Influenza Vaccine Statement for 2020–2021 (4)

Conclusion

NACI continues to recommend annual influenza vaccination for all individuals aged six months and older (noting product-specific age indications and contraindications), with particular focus on people at high risk of influenza-related complications or hospitalization. In addition, people capable of transmitting to high risk individuals, people who provide essential community services and people in direct contact during culling operations with poultry infected with avian influenza are particularly recommended to receive the influenza vaccine. For the 2020–2021 influenza season, NACI continues to recommend that, in the absence of contraindications, HCWs and other care providers in facilities and community settings should be vaccinated annually against influenza, and continues to recommend the inclusion of this group among those particularly recommended to receive the influenza vaccine. NACI also newly recommends that LAIV may be considered as an option for children 2–17 years of age with stable HIV infection HAART and with adequate immune function.

Authors' statement

KY — Writing, original draft, review, editing

IG — Review, editing

RH — Review, editing

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Conflict of interest

None.

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National findings from the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019

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Abstract

Background: The Tracks survey of people who inject drugs (PWID) collected data in 14 sentinel sites across Canada (2017–2019).

Objective: To describe the prevalence of human immunodeficiency virus (HIV) and hepatitis C and associated risk behaviours and to examine trends over time.

Methods: Information regarding socio-demographics, social determinants of health, use of prevention services and testing, drug use, risk behaviours, and HIV and hepatitis C testing, care and treatment was collected through interviewer-administered questionnaires. Biological samples were tested for HIV, hepatitis C antibodies and hepatitis C ribonucleic acid (RNA). Descriptive statistics were calculated and trends over time were assessed.

Results: Of the 2,383 participants, 65.6% were cisgender male, 42.2% were Indigenous, 48.0% completed some high school or less, 62.6% lived in unstable housing and 75.7% had ever been incarcerated. Average age was 40.1 years. The majority experienced stigma and discrimination (88.7%) and physical, sexual and/or emotional abuse in childhood (85.0%) or with a sexual partner (75.9%). The majority reported use of a needle/syringe distribution program (90.1%) and tested for HIV (90.5%) and hepatitis C (90.9%).

Among participants who had ever had sex, the majority (59.2%) reported inconsistent condom use during vaginal and/or anal sex with a casual sex partner. Prevalence of HIV was 10.3% (82.9% were aware of infection status) and many (36.9%) were hepatitis C RNA-positive (50.1% were aware of infection status).

Most surveillance indicators remained relatively stable from Phase 1 to Phase 4. Changes were found in substances used, and improvements were noted related to HIV and hepatitis C prevalence and care cascade indicators.

Conclusion: Many PWID in Canada were living in unstable housing and experienced high levels of stigma and discrimination. Prevalence of HIV and hepatitis C was high in some areas. These findings contribute to the evidence base used to inform targeted prevention and control measures.

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Introduction

People who inject drugs (PWID) represent an important group at risk for human immunodeficiency virus (HIV) and hepatitis C in Canada. It has been estimated that, of the 2,165 new HIV infections in 2016, the proportion attributed to injection drug use was 11.3%. This value had not decreased since the 2014 estimate of 11.2% (1). In North America, the burden of disease of hepatitis C attributable to injecting drug use is greater than for HIV, and was estimated to be 81% in 2013 (2). In Canada, HIV and hepatitis C antibody prevalence was high among PWID surveyed in 2010–2012 (11.2% and 68%, respectively) (3). These findings underscore the need for prevention and treatment efforts to mitigate HIV and hepatitis C morbidity and mortality in this population. Integrated bio-behavioural surveillance, an established World Health Organization (WHO)/Joint United Nations Programme on HIV/AIDS (UNAIDS) globally-endorsed approach (4), is critical to informing response and to guiding public health interventions. This surveillance provides information about risk practices and health-seeking behaviours among the populations most at risk for HIV and is necessary to better understand the factors driving transmission.

The Public Health Agency of Canada (PHAC), in conjunction with provinces and territories including regional and/or local public health partners, monitors trends in the prevalence of HIV and hepatitis C and associated risk factors in key populations, such as PWID, through the Tracks Surveillance Systems. The Tracks survey of PWID (formerly I-Track) involves repeated cross-sectional surveys at selected sites across Canada. It was first implemented in 2003–2005 (Phase 1) in seven sentinel sites. This was followed by three subsequent data collection periods, including the most recent survey, Phase 4 (2017–2019), in 14 sentinel sites (**Appendix 1**).

The objective of this report is to present national surveillance findings from Phase 4 of the Tracks survey of PWID in Canada, conducted between January 1, 2017 and May 9, 2019, at participating sentinel sites in Canada. Findings include socio-demographic characteristics, social determinants of health, use of prevention services and testing, drug use and experiences with overdoses, sexual risk behaviours and HIV and hepatitis C care cascade, prevalence and awareness of infection status. Selected indicators from Phase 1 to Phase 4 of the Tracks survey of PWID are also presented to describe trends over time.

Methods

Data source and sampling methods

The data presented in this report are from the Tracks survey of PWID in Canada. The Tracks survey of PWID makes use of venue-based sampling, in which participants are recruited from settings in which they are likely to gather, most often, but not limited to, needle and syringe distribution programs. Individuals

who had injected drugs six months prior to recruitment and who met the minimum age to provide consent, which was determined at each site according to local research ethics requirements, were eligible to participate in the survey. Eligible and consenting participants completed an interviewer-administered questionnaire and provided a biological sample in the form of a dried blood spot (DBS) specimen (or oral fluid exudate in the SurvUDI network sites).

The surveillance protocol and questionnaire were approved by the Health Canada/PHAC Research Ethics Board, and by local research ethics boards at each sentinel site where required. The same sampling and recruitment strategies and core questionnaire, with minor revisions, were used across all four phases to ensure comparability over time. Survey methods are described in more detail elsewhere (3).

Sentinel site selection

Sentinel sites were selected based on consultations with provincial/territorial representatives, who considered the epidemiology of HIV, hepatitis C and drug use and associated harms. Given this assessment, participating sentinel sites varied by phase of the Tracks Survey of PWID (**Appendix 1**). Data collection in Ottawa (Ontario) and in the province of Quebec was coordinated by the SurvUDI network (5). The SurvUDI network sites were divided into four geographical zones for the Phase 4-specific analyses (see **Appendix 1**).

Interviewer-administered questionnaire

The Tracks PWID questionnaire collects information about socio-demographic characteristics, social determinants of health, use of health and prevention services (including testing), drug use and injecting behaviours, sexual behaviours and care and treatment for HIV and hepatitis C. The questionnaire was first developed for a pilot phase by an expert working group to establish face validity. To ensure comparability, each subsequent phase retained most national-level questions to monitor change over time.

The Phase 4 questionnaire included a limited number of revisions, including new national-level questions that addressed gender identity, financial strain, mental health status, experiences of stigma and discrimination, physical, sexual and/or emotional abuse, borrowing used non-injection drug paraphernalia, overdose-related experiences, use of harm reduction services, condomless sex at last paid sex, substance use before or during sex, adherence to antiretroviral treatment and viral load status.

Biological sample

Dried blood spot samples were tested for HIV (antibody and antigen) and hepatitis C (antibody and RNA). Participants were not informed of their laboratory test results because no identifying information was collected to ensure participant anonymity. Sentinel sites were asked to provide on-site testing (e.g. point of care testing, full phlebotomy) during recruitment



times so that participants who were not aware of their status could get tested, should they wish. Where on-site testing was not feasible, participants were referred to local testing sites and/or health care services. Updated laboratory testing algorithms for DBS were introduced in Phase 4 (see **Appendix 2**). Testing algorithms for SurvUDI samples are found in **Appendix 2**.

Analysis

Descriptive statistics for selected indicators were computed with SAS Enterprise Guide 7.1. Selected indicators from Phase 1 to Phase 4 were compared to examine trends over time. Small cell counts were assessed to determine the risk of identifying individual participants, and were left in when it was determined that there was no risk of reidentification, as per PHAC's *Directive for the collection, use and dissemination of information relating to public health* (PHAC, 2013, unpublished document). Participants who responded as "not stated", "don't know" or "refused" were excluded from each individual analysis.

Results

Sample sizes for Phase 1, Phase 2 and Phase 3 were 2,986, 2,982 and 2,687, respectively. A total of 2,383 individuals were eligible and consented to participate in the Phase 4 survey, among whom 2,379 (99.8%) completed a questionnaire and 2,162 (90.7%) provided a biological sample. Findings for selected indicators by socio-demographic characteristic and social determinants of health of participants are provided in **Supplemental tables A** (prevention and testing indicators), **B** (injecting behaviours and drug use), **C** (sexual risk behaviours) and **D** (selected indicators by Phase).

Socio-demographic characteristics

In Phase 4, 65.6% identified their gender as cisgender male, 32.7% as cisgender female and 1.0% as transfeminine (i.e. those assigned male at birth who identified with either female or a non-binary gender) and 0.7% transmasculine (i.e. those assigned female at birth who identified with either male or a non-binary gender) (**Table 1**). The average age was 40.1 years (**Supplemental table D**).

Of all participants, 42.2% identified as Indigenous, of whom 82.9% identified as First Nations, 14.9% Métis or 2.2% Inuit. Among all Indigenous participants, 13.8% reported living in a First Nations, Métis or Inuit community at the time of the interview. The proportion of participants who identified as other ethnicities was 57.8% of whom the majority (96.3%) identified as White. Most demographics stayed relatively stable over the four phases, while the average age increased slightly, as did the proportion who self-identified as Indigenous (**Supplemental table D**).

Social determinants of health

Among Phase 4 participants, just under half (48.0%) had completed some high school or less and a large proportion

Table 1: Socio-demographic characteristics of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Socio-demographic characteristics		n	Total ^a	%
Gender identity	Cisgender female	775	2,372	32.7
	Cisgender male	1,556	2,372	65.6
	Transfeminine ^b	24	2,372	1.0
	Transmasculine ^c	17	2,372	0.7
Age group	Younger than 25 years	161	2,378	6.8
	25 to 39 years	1,058	2,378	44.5
	40 to 54 years	895	2,378	37.6
	55 years or older	264	2,378	11.1
Sentinel site	Whitehorse, YK	49	2,383	2.1
	Central and Northern Vancouver Island, BC	179	2,383	7.5
	Prince Albert, SK	184	2,383	7.7
	Regina, SK	205	2,383	8.6
	Winnipeg, MB	181	2,383	7.6
	Thunder Bay, ON	200	2,383	8.4
	London, ON	206	2,383	8.6
	Hamilton, ON	157	2,383	6.6
	Ottawa, ON and the region of Outaouais, QC	200	2,383	8.4
	Montréal, QC	200	2,383	8.4
	Québec, QC	125	2,383	5.3
	Other urban sites in Quebec ^d	167	2,383	7.0
	New Brunswick	200	2,383	8.4
	Newfoundland	130	2,383	5.5
Indigenous status	First Nations, Métis, or Inuit	997	2,360	42.2
	Other ethnicity	1,363	2,360	57.8
Living in a FN, Métis or Inuit community ^e	No	802	930	86.2
	Yes	128	930	13.8

Abbreviations: BC, British Columbia; FN, First Nations; MB, Manitoba; ON, Ontario; QC, Québec; SK, Saskatchewan; YK, Yukon

^a Total represents total counts for the corresponding indicator excluding "don't know", "refused" and "not stated" values

^b Transfeminine included those assigned male at birth who identified with either female or a non-binary gender

^c Transmasculine included those assigned female at birth who identified with either male or a non-binary gender

^d Other urban sites in the province of Quebec included Abitibi-Témiscamingue, Montérégie, Saguenay-Lac Saint-Jean, Eastern Townships and Mauricie-Central Québec

^e This question was asked among Indigenous participants only



(86.0%) experienced financial strain (i.e. difficulty making ends meet) in the 12 months prior to the interview (**Table 2**). Overall, 62.6% of participants lived in unstable housing in the six months prior to the interview and 75.7% reported having ever been incarcerated. A large proportion (84.0%) reported their mental health as “fair to excellent” and 16.0% reported poor mental health status. Among Indigenous participants, 83.1% had attended a residential school themselves or had a family member who had attended a residential school.

Table 2: Social determinants of health of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Social determinants of health		n	Total ^a	%
Education, highest level	Less than high school	1,139	2,373	48.0
	Finished high school	621	2,373	26.2
	More than high school	613	2,373	25.8
Experienced financial strain ^b , past 12 months	No	207	1,479	14.0
	Yes	1,272	1,479	86.0
Housing status, past six months	Unstable housing ^c	1,486	2,374	62.6
	Stable housing	888	2,374	37.4
Ever incarcerated ^d	No	422	1,736	24.3
	Yes	1,314	1,736	75.7
Mental health	Fair to excellent	1,401	1,668	84.0
	Poor	267	1,668	16.0
Experience of stigma and discrimination ^e , ever	No	166	1,464	11.3
	Yes	1,298	1,464	88.7
Experience of childhood physical, sexual, and/or emotional abuse	No	220	1,463	15.0
	Yes	1,243	1,463	85.0
Experience of sexual partner physical, sexual, and/or emotional abuse	No	351	1,458	24.1
	Yes	1,107	1,458	75.9

^a Total represents total counts for the corresponding indicator excluding “don’t know”, “refused” and “not stated” values

^b Defined as ever having difficulty making ends meet in the year prior to the interview

^c Unstable housing included living in a hotel or motel room, rooming or boarding house, shelter or hostel, transition or halfway house, psychiatric institution or drug treatment facility, public place or correctional facility

^d Only partial data available at the SurvUDI network sites

^e Defined as ever experienced any stigma or discrimination (e.g. avoidance, pity, blame, shame, rejection, verbal abuse or bullying) based on racial or cultural background, hepatitis C status, HIV status, sexual orientation, use of drugs or alcohol or sex work

Experiences of stigma and discrimination (related to racial or cultural background, hepatitis C status, HIV status, sexual orientation, use of drugs or alcohol or sex work) were reported

by the majority of participants (88.7%). Large proportions of participants had experienced physical, sexual and/or emotional abuse in childhood (85.0%) or with a sexual partner (75.9%).

Over the past four phases, the social determinant indicators stayed relatively stable with the exception of an increase in the proportion reporting living in unstable housing in the six months prior to the interview (51.1%–62.6%) (Supplemental table D).

Use of prevention services and testing

In Phase 4, the majority of participants (90.1%) reported using a needle and syringe distribution program in the 12 months prior to the interview, with lower proportions reporting use of methadone, suboxone or other opioid substitution therapy (47.3%) and use of a supervised injection or consumption site (13.5%). The majority of participants reported ever testing for HIV (90.5%) and hepatitis C (90.9%) (**Table 3**). Some (14.3%) of the participants had heard about preexposure prophylaxis (PrEP). Among participants who did not report an HIV diagnosis, 0.3% had used PrEP in the 12 months prior to the interview to reduce the risk of contracting HIV. The proportion of participants who had ever tested for HIV (90.0%–92.9%) and hepatitis C (87.5%–91.3%) was high and varied slightly across all phases (Supplemental table D).

Table 3: Use of prevention services and testing for HIV and hepatitis C of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Use of prevention services and testing	n	Total ^a	%
Use of a needle and syringe distribution program, past 12 months ^b	1,490	1,653	90.1
Use of a supervised injection or consumption site, past 12 months ^b	223	1,652	13.5
Use of methadone, suboxone or other opioid substitution therapy, past 12 months ^b	780	1,650	47.3
Tested for HIV, ever	2,080	2,299	90.5
Tested for HCV, ever	2,086	2,296	90.9

Abbreviations: HCV, hepatitis C virus; HIV, human immunodeficiency virus

^a Total represents total counts for the corresponding indicator excluding “don’t know”, “refused”, and “not stated” values

^b This question was not asked at the SurvUDI network sites

Injecting behaviours

In Phase 4, over one-third of participants (38.1%) reported injecting daily in the month prior to the interview and over half (52.7%) reported injecting in a public space in the six months prior to the interview. Overall, 11.6% of participants injected with used needles and/or syringes in the six months prior to the interview, of whom the majority (85.2%) borrowed needles and/or syringes from people who they knew well (i.e. family, friends or sex partners). Over one-third (38.0%) injected with other used injection equipment such as water, filters, cookers, tourniquets, swabs or acidifiers in the six months prior to the interview. Among those who borrowed used equipment, the majority (82.9%) reported borrowing from people they knew well. More than half of participants (56.0%) borrowed used non-injection



drug paraphernalia such as straws, dollar bills, or pipes in the six months prior to the interview (Table 4).

Table 4: Injecting behaviours of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Injecting behaviours	n	Total ^a	%
Injected daily in the past month ^b	822	2,155	38.1
Injected drugs in a public space, past six months	1,243	2,357	52.7
Borrowed used needles and/or syringes, past six months	271	2,339	11.6
Borrowed used needles and/or syringes from people known well ^c , past six months	224	263	85.2
Borrowed used other injecting equipment (i.e. water, filters, cookers, tourniquets, swabs, acidifiers), past six months	882	2,324	38.0
Borrowed used other injecting equipment from people known well ^c , past six months	710	856	82.9
Borrowed used non-injection drug paraphernalia (i.e. straws, dollar bills and pipes), past six months ^b	1,153	2,059	56.0

^a Total represents total counts for the corresponding indicator excluding "don't know", "refused", and "not stated" values

^b This question was not asked at the London site

^c People known well was defined as family, friends or sex partners

The proportion of participants who reported borrowing used needles and/or syringes decreased by almost half from 20.2% in Phase 1 and 21.8% in Phase 2 to 11.6% in Phase 4. In contrast, the proportion who reported borrowing other used injection equipment (such as water, filter, cooker, spoons, tourniquets, ties, swabs and acidifiers) increased by almost a third from Phase 1 (29.8%) to Phase 4 (38.0%) (Supplemental table D).

Drug use and overdose experiences

In Phase 4, cocaine was the most commonly injected drug in the six months prior to the interview (60.0%), followed by hydromorphone (50.1%), methamphetamine (43.5%), morphine (41.6%) and heroin (32.4%). Participants consumed a wide range of non-injection drugs over the same period, most frequently cannabis (72.1%), alcohol (62.5%), crack (47.8%), cocaine (46.6%) and methamphetamine (43.0%). Opioid analgesic consumption (non-injection routes) was also reported specifically for methadone (35.0%), hydromorphone (28.2%), codeine (27.5%), morphine (24.7%), fentanyl (19.8%), heroin (19.7%) and oxycodone (15.6%) (Table 5).

Among Phase 4 participants, the majority had heard of overdose kits (87.5%) and reported that kits were available in their community (91.5%); a lower proportion had ever used one on someone else (32.0%). Nearly one-quarter (22.6%) had overdosed in the six months prior to the interview and the drugs most commonly reported at last overdose were fentanyl (43.0%), heroin (38.3%), methamphetamine (28.4%), cocaine (23.1%) and alcohol (15.9%) (Table 5).

Table 5: Drug use and experiences with overdoses of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Drug use and experiences with overdoses	n	Total ^a	%
Types of injection drugs used, past six months ^b			
Cocaine	1,419	2,364	60.0
Hydromorphone	1,184	2,363	50.1
Methamphetamine	1,027	2,360	43.5
Morphine	982	2,362	41.6
Heroin	764	2,357	32.4
Fentanyl	572	2,350	24.3
Amphetamines	506	2,358	21.5
Crack	473	2,362	20.0
Ritalin alone	466	2,361	19.7
Oxycodone	400	2,365	16.9
Heroin and cocaine	330	2,359	14.0
Benzodiazepines	173	2,361	7.3
Talwin and Ritalin	166	2,359	7.0
Methadone	145	2,366	6.1
Other drugs ^c	237	1,751	13.5
Types of non-injection drugs used, past six months ^b			
Cannabis	1,698	2,356	72.1
Alcohol	1,472	2,355	62.5
Crack	1,125	2,352	47.8
Cocaine	1,097	2,354	46.6
Methamphetamine	1,010	2,349	43.0
Amphetamines	836	2,348	35.6
Methadone	824	2,357	35.0
Benzodiazepines	705	2,349	30.0
Hydromorphone	662	2,351	28.2
Codeine	645	2,350	27.5
Morphine	582	2,354	24.7
Fentanyl	462	2,337	19.8
Heroin	462	2,345	19.7
Oxycontin or Oxycodone	367	2,347	15.6
Ecstasy	223	2,351	9.5
Mushrooms	214	2,350	9.1
Talwin and Ritalin	213	2,352	9.1
Barbiturates	200	2,345	8.5
Other drugs ^c	363	1,809	20.1
Awareness, access and use of an overdose kit ^d			
Heard of overdose kits	1,276	1,458	87.5
Ever used an overdose kit	408	1,274	32.0
Overdose kits are available in participants' community			
Yes	1,168	1,212	91.5
No	44	1,276	3.5
Don't know	64	1,276	5.0
Overdose experiences			
Overdosed in the past six months ^e	374	1,652	22.6



Table 5: Drug use and experiences with overdoses of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383) (continued)

Drug use and experiences with overdoses	n	Total ^a	%
Drugs or substances used at last overdose ^{b,d,f}			
Fentanyl	128	298	43.0
Heroin	116	303	38.3
Methamphetamine	87	306	28.4
Cocaine	71	308	23.1
Alcohol	49	309	15.9
Cannabis	40	307	13.0
Benzodiazepines	35	305	11.5
Crack	30	305	9.8
Morphine	25	308	8.1
Methadone	23	308	7.5
Hydromorphone	20	308	6.5
Other drugs ^c	85	310	27.4

^a Total represents total counts for the corresponding indicator excluding “don’t know”, “refused”, and “not stated” values

^b Participants recorded all drugs (that they had injected, consumed or used at last overdose) for non-medical purposes in the six months prior to interview. The most commonly reported drugs among all participants are presented. Responses are non-mutually exclusive

^c Other includes drugs with frequencies of less than 5%

^d This question was not asked at the SurvUDI network and London sites

^e This question was not asked at the SurvUDI network sites

^f Among participants who overdosed in the past six months and who provided a response

The drug most commonly injected across all phases was cocaine (60.0%–81.6%). Between Phase 1 and 4, there was an increasing trend in injecting hydromorphone (29.9%–50.1%), methamphetamine (6.8%–43.5%), fentanyl (1.7%–24.3%) and amphetamines (7.9%–21.5%). Across all phases, non-injection use of cannabis and alcohol stayed at high levels (Supplemental table D).

Sexual risk behaviours

In Phase 4, in the six months prior to the interview, among participants who had ever had sex, 35.2% had two or more sexual partners, 59.2% had inconsistent condom use during vaginal and/or anal sex with a casual sex partner, 84.9% had inconsistent condom use during vaginal and/or anal sex with a regular sex partner and 15.7% had engaged in transactional sex at least once (Table 6). Among those that engaged in transactional sex, 30.7% did not use condoms at last transactional sex. The majority of participants (84.2%) reported substance use before or during sex (Table 6).

Across all phases, of participants who had ever had sex in the six months prior to the interview, the proportion who had two or more sex partners and who had engaged in transactional sex stayed relatively stable (Supplemental table D).

Table 6: Sexual risk behaviours of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Sexual risk behaviours	n	Total ^a	%
Two or more sex partners, past six months ^b	798	2,270	35.2
Inconsistent condom use during vaginal and/or anal sex with a casual sex partner, past six months ^c	413	698	59.2
Inconsistent condom use during vaginal and/or anal sex with a regular sex partner, past six months ^c	1,086	1,279	84.9
Engaged in transactional sex, past six months	280	1,786	15.7
Condomless sex at last transactional sex ^d	66	215	30.7
Substance use before or during sex, past six months ^d	1,088	1,292	84.2

^a Total represents total counts for the corresponding indicator excluding “don’t know”, “refused”, and “not stated” values

^b The denominator excludes participants who never had sex

^c Inconsistent condom use defined as not always using a condom (i.e. never, sometimes, or frequently). This question was not asked at the London site

^d This question was not asked at the SurvUDI network sites

HIV and hepatitis C prevalence and awareness

Based on the laboratory testing, HIV prevalence was 10.3% and of those who were HIV-positive, 82.9% were aware of their HIV-positive status (Table 7). The proportion who tested positive for hepatitis C antibodies was 64.2%, which is a measure of lifetime exposure to hepatitis C infection. Many (36.9%) were hepatitis C RNA-positive—an indicator of current hepatitis C infection—of whom, 50.1% were aware of their hepatitis C RNA positive status. Among participants who provided a biological sample of sufficient quantity for testing for both HIV antibodies and HCV RNA, 4.7% were HIV-positive and hepatitis C RNA positive; 4.3% were HIV-positive and hepatitis C RNA negative; 32.3% were HIV-negative and hepatitis C RNA positive; and 58.7% were HIV-negative and hepatitis C RNA negative.

Over the 15-year period from Phase 1 to Phase 4, HIV prevalence decreased from 14.9% to 10.3%. Among HIV-positive participants, the proportion of participants who were aware of their HIV-positive status increased slightly (77.8%–82.9%). Across all phases, the proportion who tested positive for hepatitis C antibodies was relatively stable with about two-thirds HCV antibody positive (64.2%–69.0%) (Supplemental table D).

HIV and hepatitis C care cascade

Indicators measuring the HIV care cascade were examined among participants aware of their HIV-positive status (Table 7). The majority were under the care of a doctor or health care provider for HIV-related services at the time of the interview (95.0%). The majority had also taken antiretroviral therapy (ART) (97.2%) and were currently taking ART at the time of the interview (87.7%). Adherence to ART, measured as no missed doses in the month prior to the interview, was 42.5%. Among participants currently taking ART at the time of the interview, 62.8% reported an undetectable HIV viral load. Nearly half of all



Table 7: HIV and hepatitis C prevalence, awareness of infection status, and care cascade of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

HIV and hepatitis C prevalence	n	Total ^a	%
HIV prevalence and awareness of infection status			
HIV prevalence ^{b,c}	222	2,162	10.3
Awareness of HIV-positive status ^d	179	216	82.9
HIV care cascade (among participants aware of their HIV-positive status, n=179)			
Linkage to care for HIV-related services ^e	170	179	95.0
Ever taken ART treatment	174	179	97.2
Currently taking ART treatment	157	179	87.7
Adherence to ART, no missed doses in last month ^f	34	80	42.5
Self-reported undetectable HIV viral load ^g	59	94	62.8
Avoidance of HIV services because of stigma and discrimination, past 12 months ^f	43	95	45.3
Hepatitis C prevalence and awareness of infection status			
HCV antibody prevalence ^{c,h}	1,375	2,141	64.2
HCV RNA prevalence ^{c,i}	486	1,316	36.9
Awareness of hepatitis C RNA positive status ^j	238	475	50.1
Hepatitis C care cascade (among participants aware of their hepatitis C RNA-positive status, n=238)			
Linkage to care for hepatitis C ^k	115	237	48.5
Ever taken hepatitis C treatment ^l	25	236	10.6
Currently taking hepatitis C treatment ^l	9	236	3.8
HIV and hepatitis C coinfection ^m			
HIV-positive and hepatitis C RNA positive	62	1,314	4.7
HIV-positive and hepatitis C RNA negative	57	1,314	4.3
HIV-negative and hepatitis C RNA positive	424	1,314	32.3
HIV-negative and hepatitis C RNA negative	771	1,314	58.7

Abbreviations: ART, anti-retroviral therapy; HCV, hepatitis C virus; HIV, human immunodeficiency virus; RNA, ribonucleic acid

^a Total represents total counts for the corresponding indicator, excluding "don't know", "refused", and "not stated" values

^b Among participants who provided a biological sample of sufficient quantity for HIV testing

^c HIV and hepatitis C testing algorithms are provided in Appendix 2

^d Among participants who tested positive for HIV antibodies and who reported their HIV diagnosis. Participants who reported that their last HIV test result was positive and who were found to be HIV positive based on testing of the biological specimen provided at the time of interview were classified as being aware of their HIV positive status

^e Defined as under the care of a doctor or health care provider for HIV-related services at the time of the interview (in the six months prior to the interview in the SurVUDI network and London sites)

^f This question was not asked at the SurVUDI network (n=65) and London sites (n=17). The denominator also excludes participants with missing data

^g Among participants currently on ART treatment at the time of the interview. This question was not asked at the SurVUDI network sites (n=62). The denominator also excludes participants with missing data

^h Among participants who provided a biological sample of sufficient quantity for HCV antibody testing

ⁱ Among participants who provided a biological sample of sufficient quantity for HCV antibody and RNA testing. HCV RNA testing was not conducted at the SurVUDI network sites

^j Among participants who tested HCV RNA positive and who reported their current hepatitis C status. Participants who reported being currently infected with hepatitis C and who were hepatitis C RNA positive based on testing of the biological specimen provided at the time of interview were classified as being aware of their hepatitis C RNA positive status

^k Defined as under the care of a health care provider for hepatitis C-related services at the time of the interview. The denominator excludes participants with missing data

^l The denominator excludes participants with missing data

^m Among participants who provided a biological sample of sufficient quantity for testing for both HIV antibodies and HCV RNA testing. HCV RNA testing was not conducted at the SurVUDI network sites

participants who were aware of their HIV-positive status reported avoiding HIV services because of stigma and discrimination in the 12 months prior to the interview (45.3%).

Indicators measuring the hepatitis C care cascade were examined among participants who were aware of their current hepatitis C infection (Table 7). Nearly half (48.5%) reported being linked to care for hepatitis C; a smaller proportion (10.6%) had ever taken hepatitis C treatment; and an even smaller proportion (3.8%) were currently taking hepatitis C treatment.

From Phase 1 to Phase 4, among participants aware of their HIV-positive status, linkage to care for HIV-related services increased (88.1%–95.0%) as did the proportion of those currently taking ART treatment (52.0%–87.7%). Across all phases, only about half of the participants who were aware of their hepatitis C infection status were under the care of a doctor for their hepatitis C infection and the proportion currently taking hepatitis C treatment was very low (Supplemental table D).

Discussion

People who inject drugs represent an important risk group in Canada's HIV and hepatitis C epidemics (1). Information gathered from the Tracks survey of PWID in Canada help contextualize the epidemiology of HIV, hepatitis C and associated risk behaviours among this population, providing comparisons over time and new baseline data on key emerging indicators, such as experiences of stigma and discrimination, overdoses and the use of PrEP. Factors associated with increased vulnerability to HIV and hepatitis C in previous studies were also identified among this survey sample of PWID. Markers of poverty and marginalization, including high numbers living in unstable housing and/or ever incarcerated, were common. Lived experience of stigma and discrimination, as well as physical, sexual and/or emotional abuse (in childhood or with a sexual partner), were also identified by the majority of participants.

High rates of testing for HIV and hepatitis C and the use of needle and syringe distribution programs were noted. However, access to other key harm reduction services was lower, with less than half of the participants reporting the use of opioid-substitution therapy or the use of a supervised injection or consumption site in the previous year. Drug use and injecting behaviours reported in Phase 4 signalled important proportions of participants who borrow needles and/or syringes and other used injecting equipment. The majority of participants (59.2%) reported inconsistent condom use with a casual sex partner and 84.2% reported substance use before or during sex, both of which are associated with the transmission of STBBI including syphilis. Preexposure prophylaxis awareness was low among participants (14.3%), and the use of PrEP was only 0.3% among those who did not report an HIV-positive diagnosis.



Many of the national surveillance findings are consistent with the findings from other integrated bio-behavioural surveillance systems with comparable HIV and hepatitis C epidemics. Specifically, among PWID surveyed in the United States, Australia and the United Kingdom, similar levels of prevention and testing indicators (i.e. testing for HIV and hepatitis C, use of opioid substitution therapy), injecting behaviours (i.e. borrowing used needles and/or syringes, borrowing used other injection equipment) and sexual practices (i.e. transactional sex, condomless sex) were found (6–8). Previous regional studies among PWID in Canada have also found similar levels of unstable housing (9,10), and high proportions who have experienced violence (10), and abuse (9,10).

The ongoing opioid crisis and other drug-related overdose deaths have greatly affected the population of PWID in Canada. Increased use of methamphetamine, fentanyl and opioid analgesics found among Phase 4 participants echo this alarming trend. Phase 4 surveillance findings provided information regarding new overdose-related indicators. While awareness and access of overdose kits was high, 22.6% had overdosed in the six months prior to the interview with fentanyl and heroin the most commonly reported drugs used at last overdose.

While HIV prevalence among Phase 4 participants (10.3%) had decreased since Phase 1 (conducted in 2003–2005) it was nevertheless high—nearly 10-fold higher compared with rates among PWID in Australia and the United Kingdom (7,8). A slightly higher proportion of participants were aware of their HIV-positive status in Phase 4 (82.9%) compared with the previous phases. For the first time, hepatitis C RNA prevalence was measured in the Tracks survey of PWID and found to be high (36.9%). In addition, only 50.1% of participants were aware of their hepatitis C RNA-positive status (i.e. current hepatitis C infection).

Nearly all participants who were aware of their HIV-positive status were linked to care for HIV-related services and were currently taking ART; however, less than two-thirds (62.8%) reported an undetectable viral load and 45.3% reported avoiding HIV services because of experienced stigma and discrimination. Much lower rates for linkage to care (48.5%) and current treatment use (3.8%) were found among participants who self-reported current infection with hepatitis C. Low numbers of PWID who are linked to hepatitis care and treatment have been observed in other regional studies in Canada (11).

The results from the Phase 4 Tracks survey of PWID can inform evidence-based strategies to address gaps in prevention, testing and linkage to care approaches. This can include better linkage to opioid substitution therapy and supervised injection or consumption sites, and improve access to health and social services for mental health and addictions (12). The confluence of high rates of hepatitis C combined poor awareness, continued but reduced needle sharing and inconsistent condom use despite increased rates of program uptake highlights the need

harm reduction programs to continue to evolve to meet these challenges.

Strengths and limitations

The Tracks survey of PWID is a rich source of information on HIV and hepatitis C among PWID from sites across the country, and provides trends on key indicators since 2003. Notably, it is the only national source of such information, and has been used at the local, provincial and federal levels to inform and guide public health interventions in this population. However, it is important to note that the Tracks survey uses non-probability-based sampling; therefore, findings may not be representative of all PWID at any given site or in Canada. With the exception of the laboratory results, these findings were based on interviewer-administered questionnaires and self-reported data and it is possible that certain risk behaviours were over- or underrepresented.

Conclusion

High levels of unstable housing, experienced stigma and discrimination, borrowing of used injection equipment and inconsistent condom use were found. Both HIV prevalence and hepatitis C RNA-positive prevalence is high among PWID in some areas of Canada. Important gaps related to linkage to care and treatment for hepatitis C were identified. These findings highlight the need for: continued access to testing and prevention services, targeted strategies to address barriers to accessing HIV and hepatitis C treatment and care and improvements in ongoing supports for housing, mental health and addictions.

Authors' statement

JT — Conceptualization, formal analysis, methodology, project administration, writing (original draft and review and editing)

JZ — Conceptualization, data curation, formal analysis, writing (original draft and review and editing)

AL — Conceptualization, formal analysis, writing (review and editing)

FC — Conceptualization, methodology, writing (review and editing)

MB — Conceptualization, methodology, project administration, writing (review and editing)

DP — Conceptualization, funding acquisition, methodology, writing (review and editing)

Conflict of interest

None.

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Appendices

Appendix 1: Tracks survey of people who inject drugs in Canada – total number of participants and sentinel site participation, Phase 1 to Phase 4

Appendix 2: HIV and hepatitis C testing algorithms

Supplementary tables

Table A: Prevention and testing indicators by socio-demographic characteristics and social determinants of health of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Table B: Injecting behaviours and drug use indicators by socio-demographic characteristics and social determinants of health of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Table C: Sexual risk behaviour indicators by socio-demographic characteristics and social determinants of health of participants in the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019 (n=2,383)

Table D: Selected indicators by phase of the Tracks survey of people who inject drugs in Canada, Phase 1 to 4, 2003–2019

Appendix 1: Tracks survey of people who inject drugs in Canada – total number of participants and sentinel site participation, Phase 1 to Phase 4

Phase details	Phase 1 2003–2005	Phase 2 2005–2008	Phase 3 2010–2012	Phase 4 2017–2019
Total number of participants	2,986	2,982	2,687	2,383
Number of sentinel sites	7	10	11	14
Sentinel site				
Whitehorse, YK	-	-	55	49
Central and Northern Vancouver Island, BC	-	220	-	179
Victoria, BC	253	249	-	-
Prince George, BC	-	156	150	-
Edmonton, AB	272	248	183	-
Prince Albert, SK	-	-	-	184
Regina, SK	250	250	251	205
Winnipeg, MB	245	-	-	181
Thunder Bay, ON	-	149	138	200
Sudbury, ON	150	147	148	-
London, ON	-	-	204	206
Hamilton, ON	-	-	-	157
Toronto, ON	257	255	260	-
Kingston, ON	-	224	200	-
SurvUDI network, QC ^a	1,559	1,084	937	692 ^b
New Brunswick	-	-	-	200
Halifax, NS	-	-	161	-
Newfoundland	-	-	-	130

Abbreviations: AB, Alberta; BC, British Columbia; MB, Manitoba; NS, Nova Scotia; ON, Ontario; QC, Quebec; SK, Saskatchewan; YK, Yukon; -, did not participate in this Phase

^a The SurvUDI network includes eight sites in QC (Outaouais, Montréal, Montérégie, Québec, Mauricie-Central Québec, Saguenay-Lac Saint-Jean, Eastern Townships, Abitibi-Témiscamingue) and Ottawa, ON

^b SurvUDI network sites were classified into four geographical zones in Phase 4: Ottawa, ON and the region of Outaouais, QC; Montréal, QC; Québec, QC; and other urban sites in the province of Quebec (Abitibi-Témiscamingue, Montérégie, Saguenay-Lac Saint-Jean, Eastern Townships, Mauricie and Central-Québec)



Appendix 2: HIV and hepatitis C testing algorithms

HIV testing algorithms

For non-SurvUDI sites, HIV status was initially determined by screening dried blood spot specimens using the Bio-Rad GS HIV Combo Ag/Ab assay followed by confirmatory testing using the Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Quant v2.0 assay (London) or the Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Qualitative Test v2.0 (New Brunswick, Newfoundland and Regina). For the remaining non-SurvUDI sites (i.e. Vancouver Island, Thunder Bay, Whitehorse, Winnipeg, Prince Albert and Hamilton), due to recurrent low volume specimens, HIV status was determined by performing screening and confirmatory testing using two separate enzyme immunoassays (EIAs). As a result, specimen volume was sufficient for HIV and hepatitis C testing in most cases. The change in algorithms is not expected to have an impact on the results. Algorithms are described in more detail below.

London: HIV screening was performed using the Bio-Rad GS HIV Combo Ag/Ab assay. A non-reactive result indicated no HIV infection. Confirmatory testing was performed on screened reactive results using the Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Quant v2.0 assay. A detected result indicated a HIV infection. In instances where the Bio-Rad GS HIV Combo Ag/Ab assay was positive, and the Roche COBAS AmpliPrep/COBAS Taqman HIV-1 v2.0 assay result was not detected, a second EIA (AVIOQ HIV-1 Microelisa System) was conducted. A reactive result on both the Bio-Rad GS HIV Combo Ag/Ab assay and the AVIOQ HIV-1 Microelisa System indicated an HIV infection.

New Brunswick, Newfoundland and Regina: HIV screening was performed using the Bio-Rad GS HIV Combo Ag/Ab assay (Bio-Rad). A non-reactive result indicated no HIV infection. Confirmatory testing was performed on screened reactive results using the Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Qualitative Test v2.0 (Roche). A detected result indicated an HIV infection. In instances where the Bio-Rad was reactive, and the Roche result was not detected, a second EIA, the AVIOQ HIV-1 Microelisa System (Avioq), was conducted as a tie-breaker. A reactive result on both the Bio-Rad and the Avioq indicated an HIV infection. A reactive result on the Bio-Rad, not detected result on the Roche, and a non-reactive or an indeterminate (i.e. absorbance results that were near, but did not overlap, the cut-off value for a reactive/non-reactive result) result on the Avioq, was interpreted as an overall indeterminate result.

Vancouver Island, Thunder Bay, Whitehorse, Winnipeg, Prince Albert, and Hamilton: HIV screening was performed using the Bio-Rad GS HIV Combo Ag/Ab assay (Bio-Rad). A non-reactive result indicated no HIV infection. Confirmatory testing was performed on screened reactive results using a second EIA, the AVIOQ HIV-1 Microelisa System (Avioq). A reactive result indicated an HIV infection. In instances where the Bio-Rad was reactive, and the Avioq was non-reactive or indeterminate (i.e. absorbance results that were near, but did not overlap, the cut-off value for a reactive/non-reactive result), the Roche COBAS AmpliPrep/COBAS Taqman HIV-1 Qualitative Test v2.0 (Roche) was used as a tie-breaker. A reactive

result on the Bio-Rad and a detected result on the Roche indicated an HIV infection. A reactive result on the Bio-Rad, non-reactive or indeterminate result on the Avioq, and a not detected result on the Roche, was interpreted as an overall indeterminate result.

For SurvUDI network sites, oral fluid specimens were screened for HIV at the Laboratoire de santé publique du Québec, Institut national de santé publique du Québec, using the Bio-Rad GS HIV1/HIV2 PLUS O EIA, a diagnostic assay approved by Health Canada and validated in the SurvUDI study for use with oral fluid. Confirmatory testing was not performed for samples that tested repeatedly reactive. A positive result indicated an HIV infection.

Hepatitis C testing algorithms

For all non-SurvUDI network sites: hepatitis C screening testing was performed using the Ortho® HCV version 3.0 EIA (Ortho). A non-reactive result indicated never having been infected with hepatitis C. A reactive result indicated lifetime exposure to hepatitis C. Confirmatory testing was performed on screened reactive and indeterminate results (i.e. absorbance results that were near, but did not overlap, the cut-off value for a reactive/non-reactive result) using the Roche COBAS AmpliPrep/COBAS Taqman HCV Quantitative test v2.0 (Roche). A detected result indicated a current hepatitis C infection and a not detected result indicated a lifetime exposure to hepatitis C. For those that screened indeterminate on the Ortho, a detected result on the Roche indicated a current hepatitis C infection and a not detected result on the Roche was interpreted as an indeterminate result.

SurvUDI network sites: hepatitis C antibody testing for oral fluid specimens was performed using the Ortho® hepatitis C version 3.0 EIA at the Institut national de santé publique du Québec laboratories. Confirmatory testing was not performed for samples that tested positive. A positive result indicated past or present hepatitis C infection and did not discriminate acute from chronic or resolved infections. Validation of this test for use with oral fluid was performed in the SurvUDI study.

Sensitivity and specificity of laboratory tests

The specificity of the Bio-Rad GS HIV Combo Ag/Ab EIA, Avioq HIV-1 Microelisa System, and Roche COBAS AmpliPrep/COBAS TaqMan HIV-1 Qualitative Test v2.0 is ≥99.9% on DBS according to kit inserts or internal validation data. Similarly, the sensitivity of each assay is 100% except for the Bio-Rad GS HIV Combo Ag/Ab EIA which is 96.6%. The limit of quantification for the Roche COBAS/AmpliPrep TaqMan HIV-1 Quantitative Test v2.0 on DBS is 616 copies/mL.

The specificity and sensitivity of the ORTHO HCV v3.0 ELISA Test System is 100% according to internal validation data. The limit of quantification for the Roche COBAS AmpliPrep/COBAS TaqMan HCV Test v2.0 is 355 IU/mL.

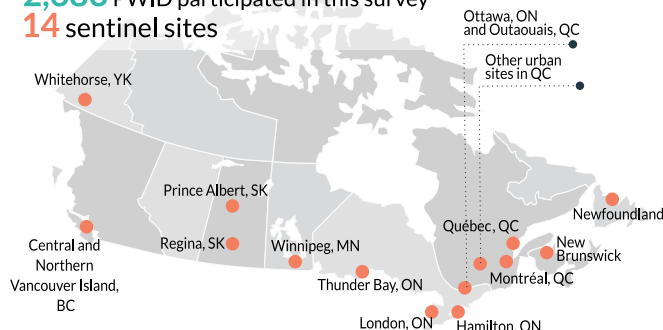


Determinants of HIV and Hepatitis C among people who inject drugs in Canada, 2017–2019

The Tracks survey of people who inject drugs was conducted between January 2017 and May 2019 in 14 sentinel sites in Canada. People who had injected drugs (PWID) in the 6 months prior to the recruitment were invited to complete an interviewer-administered questionnaire and asked to provide a biological sample that was tested for HIV antibodies and hepatitis C antibodies and RNA.

WHO PARTICIPATED?

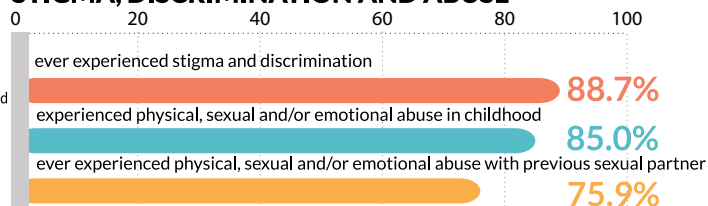
2,383 PWID participated in this survey
14 sentinel sites



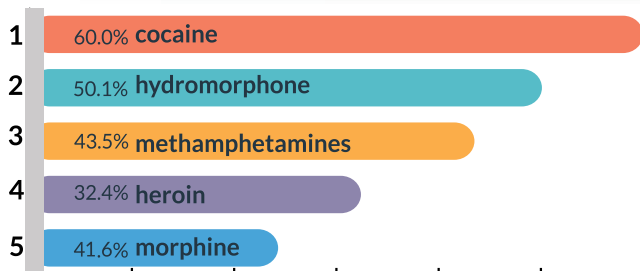
- 65.6% cisgender male
- 42.2% Indigenous
- 48.0% completed some high school or less
- 62.6% living in unstable housing
- 75.7% ever incarcerated
- 84.0% fair to excellent mental health



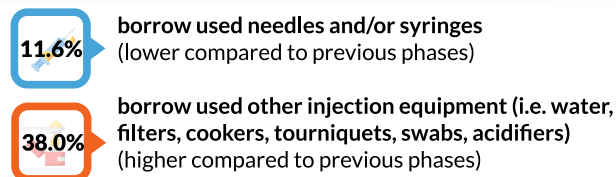
EXPERIENCED STIGMA, DISCRIMINATION AND ABUSE



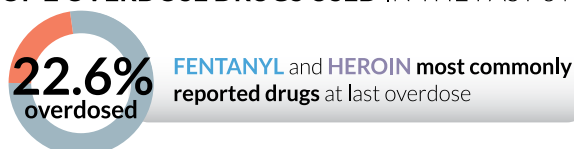
TOP 5 INJECTION DRUGS USED IN THE PAST 6 MONTHS



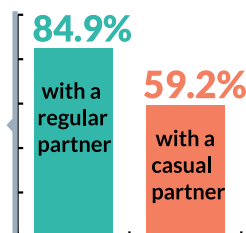
INJECTING BEHAVIOUR IN THE PAST 6 MONTHS



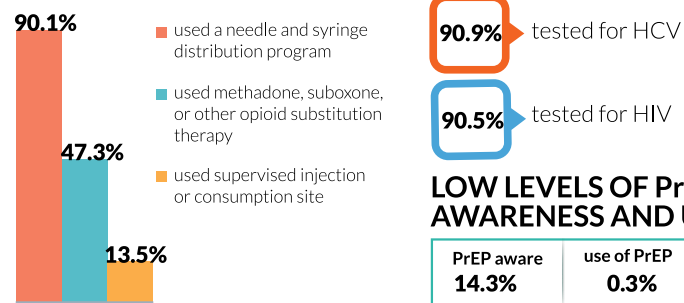
TOP 2 OVERDOSE DRUGS USED IN THE PAST 6 MONTHS



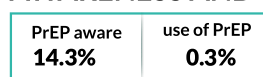
INCONSISTENT CONDOM USE DURING VAGINAL AND/OR ANAL SEX IN THE PAST SIX MONTHS



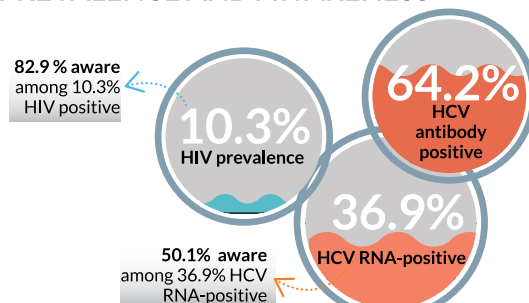
PREVENTION SERVICES AND TESTING



LOW LEVELS OF PrEP AWARENESS AND USE



HIV AND HEPATITIS C (HCV) PREVALENCE AND AWARENESS



Acknowledgements: This survey is possible because of the successful collaboration between the Public Health Agency of Canada (including the National Microbiology Laboratory), and provincial, regional and local health authorities, researchers, and community-based organizations. Special thanks to all participants and sentinel site teams for their contribution. For more information, look for our full length report in CDR titled: *National findings from the Tracks survey of people who inject drugs in Canada, Phase 4, 2017–2019*.



Public Health
Agency of Canada

Agence de la santé
publique du Canada

Canada



Surveillance of persons who tested negative for COVID-19 in Ontario, January 22–February 22, 2020

Michelle Murti^{1,2*}, Michael Whelan¹, Andrea Saunders¹, Karin Hohenadel¹, Jonathan Gubbay^{1,3}, Sarah Buchan^{1,2}

Abstract

As of January 22, 2020, “disease caused by a novel coronavirus” became a reportable disease of public health significance in Ontario. Public health units were provided with guidance on the entry of patients tested for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the virus causing 2019 coronavirus disease (COVID-19), into the provincial public health information system. Between January 22 and February 22, 2020, there were 359 individuals who had a negative test result was recorded and three confirmed cases of COVID-19. Of those who tested negative, 51% were female and 71% were under 50 years of age. The most common symptoms reported were cough (55%), fever (37%) and sore throat (35%). The majority were tested within three days of symptom onset, but over one-quarter tested more than seven days after symptom onset. Over the first month of reportability, reported travel history shifted from China to an increasing proportion with travel outside of China.

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Keywords: coronavirus, COVID-19, surveillance, Ontario, testing

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Introduction

In December 2019, the clinical syndrome caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, (2019 coronavirus disease, COVID-19), was identified following an outbreak of pneumonia-like illness in Wuhan, China (1). Rapid identification of the virus causing the outbreak and development of diagnostic testing methods enabled countries around the world to test and identify cases within their borders (2). At the onset of the epidemic in China, Ontario alerted health care providers to the outbreak and recommended testing those with a travel history to Wuhan, China. As of January 22, 2020, “disease caused by a novel coronavirus” became reportable as a disease of public health significance in Ontario, and included case definitions for persons under investigation (PUI) and for probable, presumptive confirmed and confirmed cases (3,4). In Ontario, local public health units are responsible for receiving notification of PUIs undergoing testing for COVID-19, and for providing guidance on the public health management of individuals undergoing testing (5). On January 28, 2020, Public Health Ontario issued guidance to health units on the use of the integrated public health information system (iPHIS) for capturing information on PUIs as well as cases. Subsequently, there has been global spread of COVID-19 and multiple introductions

into Ontario and other parts of Canada (6), with the first case in Ontario reported on January 25.

Our goal is to describe public health surveillance data on individuals who were reported to public health, and who subsequently tested negative for COVID-19, in the first month after reportability was initiated in Ontario (January 22 to February 22, 2020).

Situation: January–February, 2020

Due to the rapidly evolving global epidemiology and understanding of COVID-19, there were several updates to the PUI case definition (**Table 1**), with expansion of affected areas to include all of mainland China and relaxation of symptom requirements. Clinical guidance on indications for testing also evolved and, as of February 22, all initial laboratory testing was conducted at Public Health Ontario (5,7). Over this time period, both positive and negative test results for SARS-CoV-2 were being reported to the local Medical Officer of Health.

We examined COVID-19 records reported in iPHIS between January 22 and February 22, 2020. We excluded those meeting

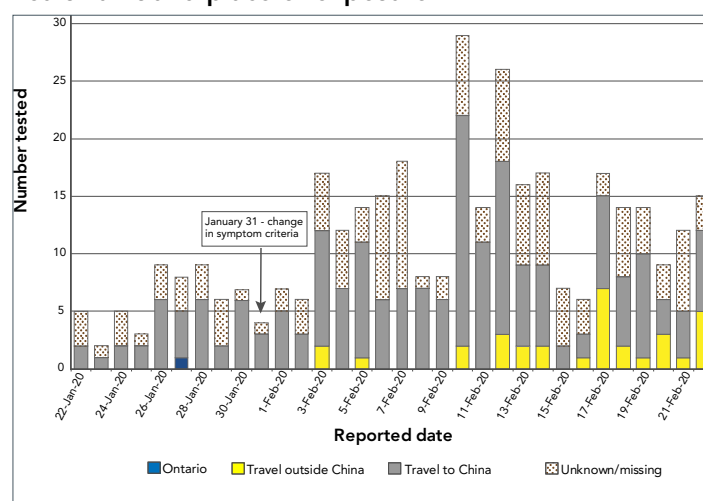
**Table 1: Case definitions for persons under investigation in Ontario, January 22–February 22, 2020**

Date applicable	Case definition version
January 22–27, 2020	<p>A person with fever and acute respiratory illness, or pneumonia AND any of the following:</p> <ul style="list-style-type: none"> Travel to Wuhan, China in the 14 days before onset of illness OR Close contact^a with a confirmed or probable case of COVID-19 OR Close contact with a person with acute respiratory illness who has been to Wuhan, China within 14 days prior to their illness onset
January 28–30, 2020	<p>A person with fever and acute respiratory illness, or pneumonia AND any of the following:</p> <ul style="list-style-type: none"> Travel to Hubei Province, China in the 14 days before onset of illness OR Close contact with a confirmed or probable case of COVID-19 OR Close contact with a person with acute respiratory illness who has been to Hubei Province within 14 days prior to their illness onset
January 31–February 7, 2020	<p>A person with fever and/or cough or difficulty breathing AND any of the following:</p> <ul style="list-style-type: none"> Travel to Hubei Province, China in the 14 days before onset of illness OR Close contact with a confirmed or probable case of COVID-19 OR Close contact with a person with acute respiratory illness who has been to Hubei Province within 14 days prior to their illness onset
February 8–26, 2020	<p>A person with fever and/or cough or difficulty breathing, AND any of the following:</p> <ul style="list-style-type: none"> Travel to mainland China in the 14 days before onset of illness OR Close contact with a confirmed or probable case of COVID-19 OR Close contact with a person with acute respiratory illness who has been to mainland China within 14 days prior to their illness onset

^a A close contact is defined as a person who provided care for the patient, including healthcare workers, family members or other caregivers, or who had other similar close physical contact OR who lived with or otherwise had close prolonged contact with a probable or confirmed case while the case was ill

the confirmed, presumptive confirmed or probable provincial case definition. These records included persons meeting the provincial case definition of a PUI at the time of report, persons with whom the local public health unit was following-up and persons for whom testing for COVID-19 had been performed and reported to the local public health unit (n=466). Records without laboratory data in IPHIS were excluded from the analyses, leaving 359 records in our dataset. We evaluated the exposures, characteristics, symptoms and time between symptom onset and testing of these individuals. Exposures were assigned in a hierarchy of travel to China, travel outside of China and exposure in Ontario. All analyses were conducted using SAS Enterprise Guide v.7.1 (SAS Institute Inc., Cary, North Carolina).

The number of individuals with a negative test result peaked in mid-February with 29 individuals reported on February 10, 2020 (**Figure 1**). Travel to China was reported by the greatest number of patients (n=196, 54.6%) throughout the study period. After February 2, 2020, 32 patients reported travel outside of China.

Figure 1: Number of individuals who tested negative for COVID-19 (N=359), by date reported to the public health unit and place of exposure

Just over half (51.8%) of these patients were female. The majority (71.3%) of the patients were younger than 50 years of age. The greatest number of the patients tested (n=97, 27.0%) were between the ages of 20 and 29 years. Among those younger than 10 years of age, 70.5% were male (**Table 2**). The most commonly reported symptoms among those with symptom data recorded (n=314) were cough, fever and sore throat (**Table 3**).

Among patients with specimen collection date within 30 days of symptom onset (n=291/359, 81.1%), 177 (60.8%) and 210 (72.2%) were sampled within three and seven days of symptom onset, respectively. However, 81 (27.8%) were sampled at least seven days after symptom onset and 23 (7.9%) were collected between 14 and 30 days after symptom onset (**Figure 2**).



Table 2: Age and gender of individuals who tested negative for COVID-19 (N=359)

Age group	Females (n=186)	Males (n=168)	Unspecified gender tested ^a (n=5)	Age group total (N=359)
Younger than 10 years	13	31	0	44
10–19 years	6	8	1	15
20–29 years	56	40	1	97
30–39 years	32	23	2	57
40–49 years	25	18	0	43
50–59 years	34	25	0	59
60–69 years	16	16	0	32
70–79 years	1	6	0	7
80–89 years	3	1	1	5

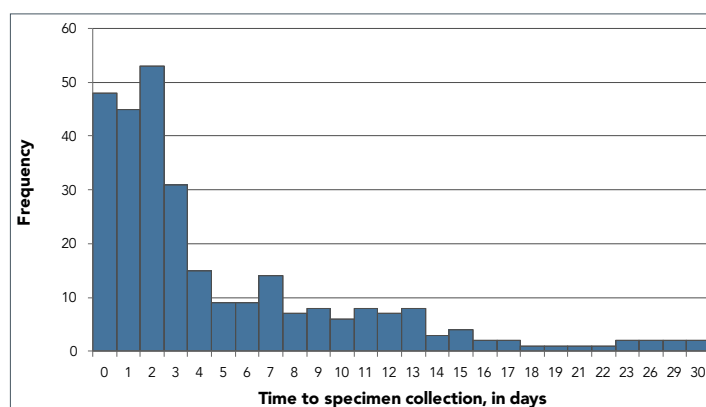
^a "Unspecified gender" includes gender listed as "other" (n=1) or "unknown" (n=4)

Table 3: Symptoms reported by individuals who tested negative for COVID-19 (n=314)

Symptom ^a	Numbers of records	Percentage of patients reporting
Cough	171	54.5%
Fever	115	36.6%
Sore throat	109	34.7%
Pain	58	18.5%
Shortness of breath	47	15.0%
Runny nose	35	11.1%
Chills	21	6.7%
Diarrhea	20	6.4%
Nausea	7	2.2%
Weakness	1	0.3%

^a Did not have symptom information for all cases

Figure 2: Number of days between the episode date and specimen collection (n=291)^a



^a Patients with "time to specimen collection" less than 0 days (n=8) and patients with "time to specimen collection" greater than 30 days (n=14) were excluded. Patients missing specimen date or symptom onset date (n=46) were also excluded

Discussion

In the first month after reportability of COVID-19, there were 359 individuals with negative COVID-19 testing results recorded by public health units in the provincial surveillance system. In comparison, the United States Centers for Disease Control and Prevention reported across the country as of February 23 (8). By February 22, there were only three confirmed cases of COVID-19 in Ontario and all three of these cases had recently travelled to Wuhan, China.

The vast majority of those tested had a travel history to China, as expected, given the initial focus of exportation risk that was centered in Wuhan, China, and the exposure criteria of the PUI case definition. Travel bans were imposed by the city of Wuhan as of January 23, and these bans were extended progressively into other areas in China at the start of Lunar New Year (January 25, 2020) celebrations to slow the spread of the virus to other regions (9). Subsequently, beginning in early February, an increasing proportion of individuals in our analysis reported travel outside of China. By February 1, 2020, there were 7,153 cases in Hubei Province, 11,821 cases in China overall and 132 cases in 23 countries outside of China (10). As of February 26, the case definition had been changed to include additional affected areas, which had further broadened the range of travel exposures reported (data not shown).

In our analysis, the demographics of persons testing negative in Ontario were younger compared with the age distribution of confirmed cases reported in China (11). However, the age groups for those tested in Ontario were similar to those for PUIs assessed in the United States (12). The age structure of PUIs in Ontario may be reflective of younger families and working age adults who had recently arrived from China or who had returned from visiting China, compared with elderly adults who may have been less likely to travel. Information on demographics of all returning travellers from China in this time period would be needed to assess this hypothesis.

As expected from the case definition, most cases reported cough or fever, similar to reports of PUIs and cases in other jurisdictions where these are the two most common symptoms (12,13). The third most common symptom amongst persons testing negative in Ontario was sore throat, with 34.7% of those with symptoms data reporting this symptom. In comparison, only 13.9% of 55,924 laboratory-confirmed cases in China reported a sore throat (13). Over the months of January and February, common seasonal respiratory viruses were circulating in the community, which may account for the higher prevalence of sore throat and may provide an alternative diagnoses of these individuals (14,15). Despite lack of inclusion of gastrointestinal symptoms in the case definition, 6.4% of the individuals in our analysis reported diarrhea. Gastrointestinal symptoms were also reported in a minority of patients with COVID-19 in China (13,16–19).



There appears to be heightened awareness of the necessity for early assessment and testing as the majority of the persons in this study group presented for testing within three days of symptom onset. However, approximately one-quarter of persons tested waited for more than seven days prior to testing. With only three confirmed cases in this time period, we cannot reasonably compare symptom to testing behaviours of those who became positive. However, testing delays have implications for public health follow-up. Late testing may have missed detection of SARS-CoV-2 if individuals were already resolving their infection by the time testing occurred. Delays may be due to mild presentation of illness or heightened concern after symptom onset with increasing global awareness in this time period. This has implications for public health follow-up should these individuals eventually test positive, as there have been reports of transmissions from individuals in the presymptomatic phase of illness (20,21).

With the changing global awareness of COVID-19, reevaluation of the delay from symptom onset to testing over time could inform evaluations of the effectiveness of public health messaging to immediately self-isolate and seek care/testing when symptoms start.

There are several limitations in our findings, which are inherent to public health surveillance data. Firstly, there are incomplete data in iPHIS on persons tested in the province due to individuals not being reported to local public health units, selective entry of individuals tested and incomplete entry of laboratory results into iPHIS. There may also be incomplete capture of symptoms and travel history depending on whether these were collected from the provider or the patient. Finally, there may be differential recall of symptoms and symptom onset among cases with a long time from symptom onset to testing.

Conclusion

Our surveillance findings demonstrate there was substantial testing of individuals identified in the first month after reportability in Ontario compared with other jurisdictions, as well as shifting epidemiology towards non-China travel exposures over time. Further assessment is needed on the relative importance of sore throat as a common symptom of persons tested, when sore throat has been less frequently described among cases in China. As well, further assessment is needed on reasons for extensive delays in testing from symptom onset among some individuals, as these delays may have significant implications for public health follow-up.

Authors' statement

MW and AS analyzed the data. KH oversaw the project. JG provided review of the data. MM and SB drafted the manuscript. All co-authors provided input on the final manuscript.

Conflict of interest

All authors have completed and submitted the International Committee of Medical Journal Editors (ICMJE) form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

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Vaccine acceptance: How to build and maintain trust in immunization

Chandni Sondagar¹, Ruotian Xu^{1*}, Noni E MacDonald², Eve Dubé³

Abstract

In Canada, over 80% of parents choose to vaccinate their children. Although this may appear positive, it is one of the lowest vaccination rates in the western world, and does not meet the 95% coverage rate needed to prevent outbreaks of vaccine-preventable diseases such as measles. A recent national immunization survey showed approximately 50% of parents are concerned about potential side-effects from vaccines, 25% believe that a vaccine can cause the disease it was meant to prevent, and 13% think alternative practices could eliminate the need for vaccines. In addition, vaccine hesitancy—defined by its determinants: confidence, complacency and convenience—is on rise. To address the complacency and trust (confidence) components of vaccine hesitancy, four best practices to optimize trust in vaccines and promote vaccine acceptance are presented. The first best practice is to understand the concerns; this is done at a population level via research and at individual level via motivational interviewing. The second best practice is to address these concerns by effectively presenting science-based information. This is done at a population level by communicating research and at an individual level by applying this research to the specific concerns, values and norms of the individual. Third, present immunization as a social norm, both in educational materials and in conversations. Finally, resilience is fostered by planning ahead (both at a population level and for individual practitioners) to manage events that can undermine trust and drive negative vaccine concerns, such as a new vaccine being added to the routine schedule or the emergence of an unexpected adverse event. Building and maintaining public trust in immunization takes time. Healthcare practitioners must keep in mind that while trust is a key element in vaccine acceptance, it is not the only element; convenience and access can also impact vaccine uptake. Nurturing trust is but one part of increasing vaccine acceptance and this brief will focus on strategies to build and nurture trust.

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Introduction

Over 80% of parents in Canada accept immunization for their infants and children (1). Although this may appear positive, it is one of the lowest vaccination rates in the western world (2). As experience in the United States has recently shown, this rate is not high enough for community protection for vaccine-preventable diseases like measles, where 95% uptake is needed (3).

Studies have shown that many Canadian parents express concerns about vaccinations, and that not all parents are convinced of the accuracy or impartiality of the science (4,5). The results of a survey conducted by the Canadian Immunization Research Network in 2015 found that 70% of respondents believed that, as a parent, it is their role to question vaccines,

and 19% considered themselves to be vaccine-hesitant (4). Surveys conducted in Canada show that a significant portion of Canadians has negative perceptions of vaccines, with approximately 20% still believing that vaccines are linked to autism (6–10).

Vaccine uptake is becoming a growing concern worldwide as we see vaccine-preventable disease outbreaks become more common. Measles, mumps and pertussis, once thought to be under control or near global eradication, are now all on the rise (3,11–14). Despite the tremendous strides made in vaccine development, safety and access, vaccine hesitancy is not uncommon (1) and instead, is increasing. In 2019, it was declared as one of the top ten threats to global health by the



World Health Organization (15). In Canada, vaccine hesitancy exists among those who are concerned about the safety of certain vaccines (especially towards new vaccines), who perceive that vaccines are for “mild” diseases, who question the utility of vaccination and lack trust in the information presented on vaccination (4,6,16,17). While vaccine acceptance is the predominant behaviour (1), we need to aim for higher uptake rates to prevent vaccine-preventable diseases.

To improve vaccine uptake, we need to address the factors that drive negative vaccine concerns and to understand what fosters vaccine acceptance, or the intention to vaccinate (4). While it is equally important to understand and examine access or convenience barriers to accepting vaccines, this brief will mainly focus on trust and complacency (18). Both public health and healthcare providers are well positioned to build trust at both the population and individual levels.

The objective of this article is to identify four best practices to foster vaccine acceptance by building and maintaining trust in immunization. This is the fourth in a series of articles, produced by The Canadian Vaccination Evidence Resource and Exchange Centre (CANVax), an online database supporting immunization program planning and delivery through the identification of existing resources and creation of the new resources developed by a multidisciplinary group of professionals (19). This article builds on the previous three articles in the CANVax Briefs series (20–22), and will show how building resiliency, developing a communication strategy, and practicing motivational interviewing can foster vaccine acceptance.

Understand the concerns

For public health programs at a community level, the best way to understand the common concerns and vaccine hesitancy is through research. Research has shed light not only on the concerns of vaccines, but also on how social media can amplify these concerns, leading to vaccine hesitancy. A 2014 study, for example, demonstrated that 40% of mothers hesitated to have their child vaccinated, most frequently citing safety concerns such as 1) fear of adverse effects and 2) concerns that too many vaccines are being given at once, and that this may weaken a child’s immune system (16). In the most recent 2017 Childhood National Immunization Coverage Survey (1), 52% of parents and guardians indicated concerns about potential side effects from vaccines and 25% thought that a vaccine could cause the same disease that it is meant to prevent. In addition, a small number of parents and guardians (13%) believed that complementary and alternative practices such as homeopathy or chiropractic treatments could eliminate the need for vaccines.

Research has also shed light on factors driving vaccine hesitancy. Advances in social media and internet-based communication technologies over the past decade have fostered the rapid and wide dissemination of information to large audiences, connecting individuals and communities well beyond their local geographies (23,24). In addition, it has been found that negative concerns of

vaccines tend to be remembered more easily (25) and to spread farther and faster than positive comments (26). These factors have amplified vaccine hesitancy (27).

While this research is helpful in anticipating a range of possible concerns, it is important to identify the specific concerns of each individual. Motivational interviewing is a helpful client-centred technique for exploring concerns that patients and parents may have towards vaccines (22,28,29). This type of interviewing focuses on working with the patient and parent rather than talking to them. Techniques involved in this approach include the use of 1) open-ended questions (What are your concerns?), 2) affirmation (I understand your concerns), 3) reflective listening (Your concerns are...) and 4) summarizing (To summarize...) (18).

Address the concerns effectively

For public health programs at the community level, communication research has identified four best practices (21). First, messages advocating too strongly for vaccination can be counterproductive, and may have the paradoxical effect of reinforcing reluctance to accept immunization (30). Second, offering too much data should be avoided, as people stop paying attention. Remember that “facts tell but stories sell”. Third, emphasizing scientific consensus on the benefit, safety and importance of vaccines can reduce concerns (31). For example, a healthcare provider can identify the side effects of the HPV vaccine, but then note that these are very rare and, in fact, the HPV vaccine is 99.9% safe. Framing this fact as a positive (99.9% safe versus <0.1% side effects) is also important, as the negatives are disproportionately heard and remembered (32). Fourth, the message should be tailored to key populations in a community in a way that aligns with their core values (18). For example, when discussing the benefits of HPV vaccines with those who belong to certain religious groups, it may be preferable to emphasize how HPV vaccine protects against certain cancers. These tailored narratives have been shown to change people’s attitudes toward vaccines (33,34). Finally, evaluation of any information material to identify areas for improvement is an essential component of any communication program (18). It is important to test messages with the target population to ensure they are working as intended.

At an individual level, front-line healthcare providers continue to be the most trusted source for vaccination information. As such, once trust is established, provider recommendations often lead to vaccine acceptance and uptake (6,35). To establish trust, healthcare providers must elicit, acknowledge and then address people’s concerns. They must provide information in a constructive and reassuring way that is simple, clear and easy to understand (36). Jargon should be avoided; for example, the term “herd immunity” can be off-putting for some people—consider using the term “community immunity” instead. Stories can be used to help clarify messages. Sometimes sharing an experience of treating a child ill with a vaccine-preventable disease can bring the facts to life.



It is important to know that the majority of parents choose to accept routine vaccinations because they want to protect their children (1). Often, once the information is provided, just a gentle nudge to emphasize the protection that vaccines provide is enough to lead to vaccine acceptance.

Present immunization as a social norm

Social norms are powerful drivers of human behaviours (37) and research has shown that presenting vaccinations as a social norm can reinforce and build support for vaccination. Know, however, that abiding by social norms can work the other way too. One study showed that parents who refused vaccination for their child reported that a larger fraction of their social network was opposed to vaccination, and that this social network bias predicted the parents' decisions better than the characteristics of the parents themselves (38). Thus, healthcare workers must support and give value to the decisions of parents, patients and communities who accept vaccines; they must stress that choosing to vaccinate protects not only the individual but also the wider community. This knowledge can foster acceptance, nurture support for immunization and grow resiliency in the face of anti-vaccine rhetoric (33).

Expanding on the idea of vaccine as the norm, research has shown that, at an individual level, introducing immunization in a presumptive manner promotes vaccine acceptance better than in a participatory manner (39). A presumptive approach could be phrased as follows: "Sarah is due for her routine vaccinations today." This is in contrast to a participatory approach: "What would you like to do about Sarah's vaccinations today?"

Foster resilience by planning ahead

To build public support for vaccines, there is a need to foster trust not only in vaccines, but also in the health system in general and in immunization programs in particular (18). Events that can undermine trust and drive negative vaccine concerns (40–42) include the following:

- The addition of a new vaccine, resulting in an increase in the number of vaccines being recommended
- A new emerging side-effect for a particular vaccine
- A lack of consistency in vaccine recommendations (for example, from one province to the next)

Research has identified that it is useful for public health professionals to work through a specific communications approach for each of these situations ahead of time, so that there can be a quick and constructive response that dispels concerns early. For programs at the community level, there are three key areas to consider (33). First, communication strategies need to be tailored to the different communities and to leverage existing information channels. This includes public health communications to frontline healthcare professionals, so they are kept up-to-date on any changes. Second, trust in vaccines must be built through transparency. For example, if there is a vaccine scare, such as a new adverse event following immunization, vaccine recall, media reports, or rumours about a vaccine, it is essential to be

transparent about this in order to maintain vaccine acceptance and uptake. Healthcare workers should present the facts, explain how vaccines are monitored for safety and effectiveness and how risk is being minimized. Third, at both community and individual levels, the people who accept vaccination and demand access to vaccines should be positively valued and acknowledged—by identifying this behaviour as the social norm.

Conclusion

These four best practices to promote vaccine acceptance are 1) to understand the concerns about immunization, 2) to effectively address those concerns, 3) to present immunization as a social norm that provides protection to both individuals and communities and 4) to foster resilience by planning ahead on how to deal with events that may undermine trust in vaccines. Building and maintaining public trust in immunization in the face of anti-vaccine rhetoric, both public and private, will take time. Beyond building trust, healthcare providers need to be aware that convenience and access are also a part of vaccine acceptance, and that those will need to be addressed to improve vaccine uptake. For healthcare providers working at the community level and the individual level, much can be done to foster trust in vaccines, in the health system and in immunization programs.

Authors' statement

CS — Writing original draft, review and editing
RX — Writing, review and editing
NEM — Writing, review and editing
ED — Writing, review & editing

Conflict of interest

C Sondagar worked as a Senior Project Officer on the Canadian Vaccination Evidence Resource and Exchange Centre (CANVax) project at the Canadian Public Health Association at the time this paper was first written.

R Xu works as a Project Officer on the CANVax project at the Canadian Public Health Association.

NE MacDonald received grants from the Public Health Agency of Canada, the World Health Organization, the Nova Scotia Health Research Foundation, the Canadian Institutes of Health Research, the Canadian Immunization Research Network, and the Social Sciences and Humanities Research Council of Canada. She is a member of the CANVax Team.

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