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ANTIMICROBIAL RESISTANCE IN CANADA

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CANADA COMMUNICABLE DISEASE REPORT

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

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The picture on the cover of this issue shows *Staphylococcus aureus* (MRSA) bacteria, an increasingly serious threat to global public health that requires action across all government sectors and society. (https://www.shutterstock.com/image-illustration/superbug-staphylococcus-aureus-mrsa-bacteria-3d-483409804?src=yYV-guQhAbiTgk1lAVtgCw-1-19)

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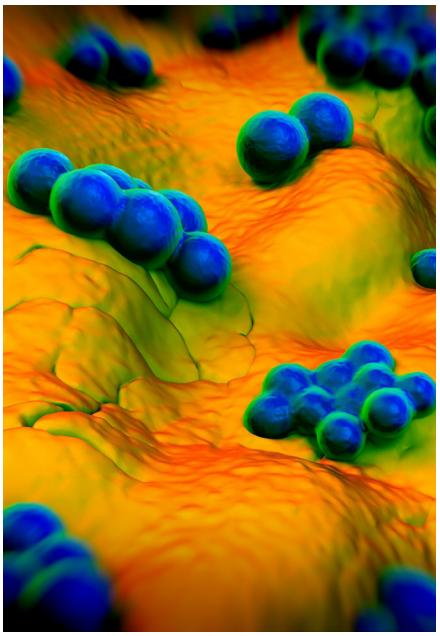

AMR IN CANADA

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Prescriber-led practice changes that can bolster antimicrobial stewardship in community health care settings

Jerome A Leis[1,2,3]*, Karen B Born[3], Olivia Ostrow[4,5], Andrea Moser[6,7], Allan Grill[7,8]

Abstract

Stabilizing the emerging resistance of antibiotics depends on our ability to practise appropriate antimicrobial stewardship (AMS). Over 90% of antibiotics dispensed for human use are prescribed in community health care settings rather than in hospitals, with the main prescribers being family physicians, dentists, pharmacists and nurse practitioners working across a broad range of private offices, family health teams, urgent care clinics, emergency departments and long-term care homes. To improve the reach of AMS in community health care settings, the Public Health Agency of Canada partnered with Choosing Wisely Canada in 2017 to develop a focused campaign titled *Using Antibiotics Wisely*. This campaign is led by the prescribers of antibiotics themselves, who work in community health care settings and are better equipped to identify the specific changes that would support more appropriate use of antibiotics. This article describes these practice changes, the strengths and challenges of *Using Antibiotics Wisely* and future opportunities to further advance AMS across community health care settings.

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Keywords: antimicrobial stewardship, respiratory infection, urinary tract infection, quality improvement, primary care, long-term care

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Introduction

Stabilizing the emerging resistance of antibiotics depends on our ability to practise appropriate antimicrobial stewardship (AMS). In 2015, Canadians filled over 25 million antibiotic prescriptions—or 33% more than other Organization for Economic Cooperation and Development (OECD) countries such as the Netherlands, Sweden and Germany (1). AMS programs have existed in Canadian acute care hospitals for over 10 years and have been an Accreditation Canada Required Organizational Practice since 2013 (2). Yet 92% of antibiotics dispensed for human use are prescribed in community health care settings rather than in hospitals (3), with the main prescribers being family physicians, dentists, pharmacists and nurse practitioners working across a broad range of private offices, family health teams, urgent care clinics, emergency departments and long-term care homes. Coordinating a national effort to promote AMS across these community-based professions and practice settings spanning different provinces and territories is a formidable challenge.

To improve the reach of AMS in community health care settings, the Public Health Agency of Canada partnered with Choosing

Wisely Canada in 2017 to develop a focused campaign titled *Using Antibiotics Wisely*. This campaign has targeted practice change around two clinical syndromes: respiratory tract infection (RTI) in primary care, and urinary tract infection (UTI) in long-term care. The strongest evidence for inappropriate antibiotic prescription is in these practices.

The objective of this article is to describe these practice changes, the strengths and challenges of *Using Antibiotics Wisely* and future opportunities to further advance AMS across outpatient health care settings.

Enabling practice change

Changing antibiotic prescribing in community practices requires stronger engagement of prescribers in the process. This engagement is considered crucial for success; simply being told to change by experts does not result in change (4). Most unnecessary antibiotic use is not related to gaps in knowledge, but rather to other provider-level factors, patient factors and contextual factors (5). For instance, a clinician generally knows that viral rhinosinusitis does not require antibiotics but may decide to prescribe antibiotics if faced with diagnostic uncertainty about whether there is a secondary bacterial infection or if influenced by the perception that a patient is expecting a prescription for antibiotics.

The Theoretical Domains Framework and the behavior change wheel (BCW), a well-recognized model for understanding the determinants of behaviour, has been applied to antibiotic prescribing. Many domains, aside from the knowledge domain, are believed to drive antibiotic prescribing behaviour; these include social influence, environmental context and resources, and beliefs about consequences (6). The challenge has been to identify the specific interventions within these domains that will best target these issues and support practice improvements.

The *Using Antibiotics Wisely* campaign was established to be led by prescribers of antibiotics who work in community health care settings, that is, those who are better equipped to identify the challenges and associated key changes that would support more appropriate use of antibiotics. The College of Family Physicians of Canada (CFPC), with Choosing Wisely Canada, has played an important role in engaging family physicians in discussions to develop "practice change statements" related to the management of RTI and UTI (**Table 1**). In the process, *Using Antibiotics Wisely* uncovered a better understanding of the barriers to AMS and developed clinical approaches that are practical and feasible to implement.

Respiratory infection in primary care

Between 30% and 50% of antibiotic prescriptions for RTI in community practices are unnecessary. This proportion accounts

Table 1: Clinical tools that support practice change in antibiotic prescribing for respiratory tract infection in primary care

Syndrome	When are antibiotics indicated?	Tool or clinical approach to support practice change
Uncomplicated otitis media	For vaccinated individuals ≥6 months, either a perforated tympanic membrane with purulent discharge or a bulging tympanic membrane with one of the following criteria: • Fever (≥39 °C) • Moderately or severely ill • Significant symptoms lasting >48 hours	Patient resources Reassessment as needed or delayed prescription
Uncomplicated pharyngitis	Patient's modified Centor score is ≥2 AND throat swab culture (or rapid antigen test if available) confirms presence of group A streptococcus	Viral prescription Throat swab not indicated if Centor score ≤1
Uncomplicated sinusitis	Symptoms have persisted for >7–10 days without improvement Antibiotics should only be considered if the patient has at least 2 of the PODS symptoms, one of those being O or D, AND the patient meets one of the following criteria: • The symptoms are severe • The symptoms are mild to moderate, with no response after a 72-hour trial with nasal corticosteroids	Viral prescription Reassessment as needed or delayed prescription
Upper respiratory infection (common cold)	No role unless clear evidence of secondary bacterial infection	Viral prescription
Influenza-like illness	No role unless clear evidence of secondary bacterial infection	Viral prescription
Pneumonia	Chest x-ray, where available, showing pneumonia. (Physical examination alone, demonstrating respiratory crackles, is not sufficient to establish a diagnosis)	Chest x-ray only if indicated by physical exam Patients with no vital sign abnormalities and a normal respiratory examination are unlikely to have pneumonia and do not need a chest x-ray
Bronchitis/ asthma/ Bronchiolitis	No role unless clear evidence of secondary bacterial infection	Consider steroids and short-acting bronchodilators
Acute exacerbation of Chronic Obstructive Pulmonary Disease	Clear increase in sputum purulence with either increase in sputum volume and/or increased dyspnea	Consider steroids and short-acting bronchodilators

Abbreviations: PODS, facial Pain/pressure/fullness, nasal Obstruction, purulent/discoloured nasal or postnasal Discharge, hyposmia/anosmia (Smell); >, greater than; ≥, greater than or equal to and older than and equal to; ≤, less than or equal to
Source: Table adapted from Choosing Wisely Canada's The 'Cold' Standard Toolkit (7)

for nearly half of the antibiotics prescribed in family physician offices (8). The first step of the *Using Antibiotics Wisely* campaign used focus groups of family physicians, pharmacists and nurse practitioners in-person and via teleconference to identify specific practices that need to change in the current management of RTI in primary care. These "Practice Change Statements" include specific guidance about how to reduce antibiotic use for eight specific syndromes in primary care practice. The CFPC has disseminated the statements to all family physicians in Canada via their accredited medical journal *Canadian Family Physician* (9). For example, antibiotics for pneumonia should not be prescribed based on physical examination findings alone but be based on a chest radiograph whenever available. Throat swabs should only be performed for those patients who meet criteria based on validated clinical predictive scores, and antibiotics given only to those who test positive for group A streptococcus (10).

A significant focus of the *Using Antibiotics Wisely* campaign has been to identify the key barriers preventing these practice changes. Perceptions about time constraints and patient expectations have been frequently cited reasons for not following best AMS practices (5,11). Building on the work of Meeker et al., the *Using Antibiotics Wisely* campaign has promoted the use of easily visible posters in family physician offices that can act as a behavioral nudge by aligning patient and physician expectations about using antibiotics judiciously (12).

For patients with a viral RTI who have distressing symptoms and are looking for relief, a "viral prescription pad" can be used to outline the diagnosis, symptom management and evidence-based supportive therapies that do not include antibiotics (13). Finally, where there is diagnostic uncertainty about whether the patient has a viral or bacterial RTI, the use of a delayed prescription has been demonstrated to decrease antibiotic use by 55% while still maintaining patient satisfaction (14,15).

Urinary tract infection in long-term care homes

Approximately 50%–70% of long-term care residents in Canada receive at least one antimicrobial agent annually (16). The most common indication is for a UTI (17,18). Overdiagnosis and treatment of UTI in long-term care is well recognized, with at least half of antibiotic prescriptions for this indication considered unnecessary (19).

Antibiotic prescribing for UTI in long-term care is complex and involves interplay between residents, substitute decision-makers and health care providers. Data from Ontario suggest that antibiotic prescribing practices vary widely across long-term care institutions and between providers (20,21). This variability in practice is not explained by differences in patient characteristics; the most significant predictor appears to be the prescriber. One important driver of antibiotic prescribing appears to be the divergent practices in urine culture orders, which are associated with higher antibiotic use and rates of *Clostridium difficile* infection (22).

There is a great need to have long-term care providers share practice behaviours to better understand the reasons for this variability in urine culture ordering and antibiotic prescribing. The *Using Antibiotics Wisely* campaign mobilized the CFPC, the Long Term Care Medical Directors Association of Canada and the Canadian Nursing Association (CNA) (23). Following in-person and teleconference focus groups, "practice change statements" for UTI in long-term care were developed to address nine steps that lead to unnecessary antibiotic prescriptions and to identify the role that different health care providers can play to support practice change.

Some of these statements address outdated, institutionally driven policies such as the use of admission order sets that include periodic screening of urine cultures. Other statements relate to assessments for changes in resident health status and the need to consider alternate, more common explanations aside from a UTI. These "practice change statements" also extend beyond long-term care because overdiagnosis of UTI among residents transferred to emergency departments of acute care hospitals can greatly affect resident and substitute decision-makers' expectations. There is also advice on ways to engage substitute decision-makers when they request urine culture tests in situations that do not fit with recommended criteria.

The optimal interventions to support these practice change statements are not yet known. Many organizations across Canada, for example, Alberta Health Services, Public Health Ontario and the Association of Medical Microbiology and Infectious Diseases, have developed tools to reduce overdiagnosis and subsequent overtreatment of UTI (24–26). One common theme is the need for an objective, standardized approach to the diagnosis of UTI in the long-term care resident population using evidence-based criteria so that all health care providers, patients and substitute decision-makers are aligned in their definition of UTI (27).

Challenges and future opportunities

While the *Using Antibiotics Wisely* campaign has helped to engage community-based clinicians in AMS, significant challenges remain. Despite creating practical resources that can be used at the point of care, community-based prescribers still need to be motivated to adopt these practice changes and balance this clinical priority among many others.

One way to incentivize practice change is by providing Continued Medical Education (CME) credits to those who undertake quality improvement projects to improve their antibiotic prescribing. The *Using Antibiotics Wisely* campaign, in partnership with the CFPC, has provided opportunity for

such credits through the development of a toolkit that family physicians can use to implement changes that support better management of RTI (7). This toolkit provides ways of integrating tools like the viral prescription pad into the electronic medical record making it easier to integrate into workflow and measure its use over time.

Provider-level feedback on antibiotic use, especially when paired with peer comparison, can also motivate clinicians to adopt these practices (28). The Ontario Program To Improve AntiMIcrobial USE (OPTIMISE) trial is a promising study combining the use of physician-specific reports on antibiotic prescribing in Ontario paired with the resources from the *Using Antibiotics Wisely* campaign to reduce antibiotic use for management of RTI (29). This randomized controlled trial launched in 2018 and recruited 3,500 of the primary care physicians in Ontario who prescribed the most antibiotics to receive a feedback letter containing different ideas on how to improve their practice. The primary outcome will be the rate of antibiotic prescribing over 12 months following this intervention.

Conclusion

Antibiotics are being overused to treat RTIs and UTIs, and collaborative efforts among community-based health care providers are needed to address this global problem. Building evidence-based, practical tools for patients and clinicians that target the barriers to change has the potential to improve AMS in outpatient and long-term care settings. Further research on the impact of the *Using Antibiotics Wisely* campaign related to health outcomes is underway and will help determine the scalability of such initiatives.

Authors' statement

JAL — Project conception, literature searches, writing, original draft, review, editing
KBB — Literature searches, writing, original draft, review, editing
OO — Review, editing
AM — Review, editing
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Conflict of interest

None.

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Antimicrobial Resistance and Antimicrobial Use in Canada

CARSS CANADIAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

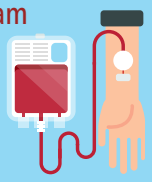
Antibiotic-resistant infections are driving increased mortality and increased costs to the healthcare system.

Healthcare sector

The Canadian Nosocomial Infection Surveillance Program (CNISP) is a collaborative effort of the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada) and the Public Health Agency of Canada. Based on the most recent data available in 2019.

RESISTANT BACTERIA

Rates of resistant bloodstream infections (BSI) associated with high mortality have significantly increased since 2014.

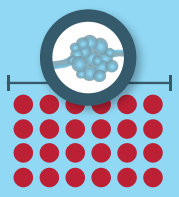


- Methicillin-resistant *Staphylococcus aureus*-BSI increased by ⬆**28%**
- Vancomycin-resistant *Enterococcus*-BSI increased by ⬆**158%**

Medical tourism provides opportunities for resistant organisms to spread.

- In 2019, some Canadians who travelled to other countries for medical procedures were exposed to highly drug-resistant bacteria that cause hard to treat infections.

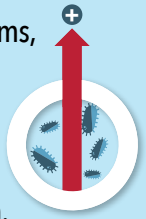
There have been 24 cases of *Candida auris* reported to PHAC since 2014.



- An emerging yeast pathogen associated with invasive infection.

ANTIBIOTIC USAGE

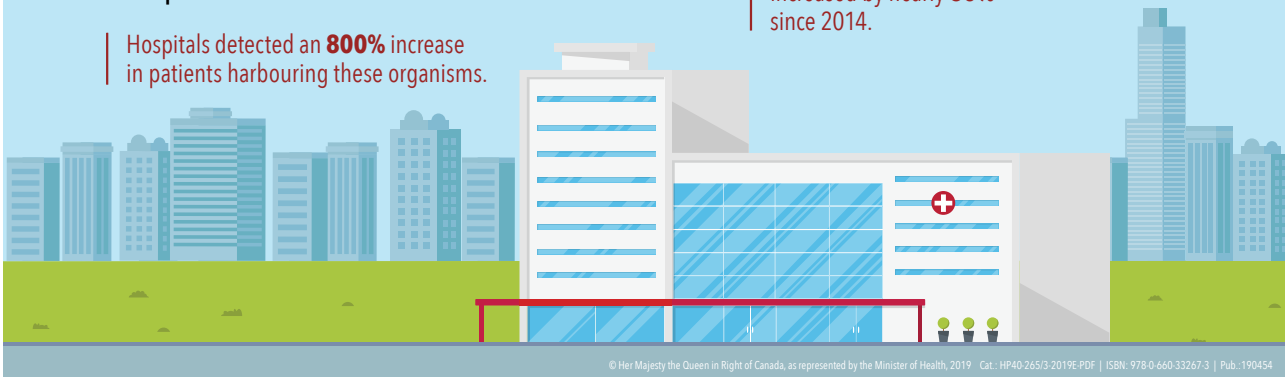
The effectiveness of carbapenems, defined by the World Health Organization as an antibiotic of last resort, is threatened by the emergence of carbapenem-resistant bacteria.



- Hospitals detected an **800%** increase in patients harbouring these organisms.

Drugs previously reserved as last resort are being purchased more frequently by hospitals.

- Daptomycin purchasing increased by nearly **60%** since 2014.



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Canada

Antimicrobial Resistance and Antimicrobial Use in Canada

CARSS CANADIAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

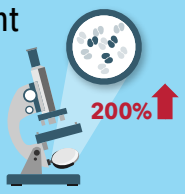
Antibiotic-resistant infections are increasingly common in the community setting.

Community sector

Data are provided by the Canadian Antimicrobial Resistance Surveillance System (CARSS), the Canadian Nosocomial Infection Surveillance Program (CNISP), the Gonococcal Antimicrobial Surveillance Program (GASP), and IQVIA (CSC/CDH). Based on the most recent data available in 2019.

RESISTANT BACTERIA

Cases of multidrug-resistant gonorrhea increased by nearly 200% since 2013.



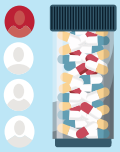
Previously used antibiotics are no longer effective.

Rates of community-acquired methicillin-resistant *Staphylococcus aureus* bloodstream infection have doubled since 2014.

Associated with high mortality.

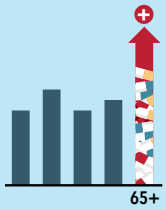
ANTIBIOTIC USAGE

1 in 4 Canadians reported taking antibiotics in the past year.



1 in **10** reported taking more than one antibiotic in the past year.

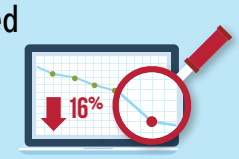
Prescription rates are highest among Canadians aged 65 years and older.



In 2018, there were 24 Million antibiotic prescriptions in Canada, representing $825M in drug costs.

The most frequently prescribed antibiotic was amoxicillin.

Since 2014, the proportion of otitis media diagnoses (middle ear infections) that resulted in an antimicrobial recommendation decreased by 16%.



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Canada

Antimicrobial Resistance and Antimicrobial Use in Canada

CARSS CANADIAN ANTIMICROBIAL RESISTANCE SURVEILLANCE SYSTEM

Food Chain

Antimicrobial-resistant pathogens detected in the Canadian food chain are a potential source for antimicrobial-resistant infections in humans.

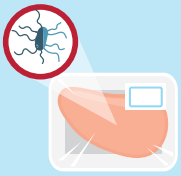
The Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) collects, analyses, and communicates trends in antimicrobial use and in antimicrobial resistance for select bacteria from people, healthy/sick animals, and grocery store meat across Canada. The aim is to preserve the effectiveness of antimicrobials in animals and people. Based on the most recent data available in 2019.

RESISTANT BACTERIA

Increasing numbers of highly drug-resistant *Salmonella* isolates found in the Canadian food chain may represent an emerging public health threat.

Isolates were resistant to at least **6** of **7** antibiotic classes tested.

Nalidixic acid-resistant *S.* Enteritidis isolates were recently identified for the first time since 2010 among retail chicken meat in Canada.



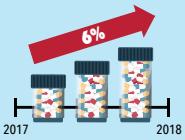
This may represent a step towards fluoroquinolone resistance, an antibiotic considered very important to human medicine.

PHAC is observing increased resistance to 3rd generation cephalosporins among *Salmonella* isolates taken from broiler chickens on-farm and chicken meat purchased at grocery stores.

3rd generation cephalosporins are antibiotics of very high importance to human medicine.

ANTIBIOTIC USAGE

The quantity of antimicrobials distributed for use in animals increased by 6% between 2017 and 2018 when adjusted by animal weight and population size.



Category 1 antimicrobials, including fluoroquinolones, continue to be used among sick chickens under clinical supervision of a veterinarian.

Since 2015, there has been no reported use of ceftiofur (an antibiotic that is known to trigger resistance to antibiotics critically important to human medicine) among broiler chicken farms that participate in CIPARS.

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Canada

Tuberculosis drug resistance in Canada: 2018

Marie LaFreniere[1], Demy Dam[1,2], Canadian Tuberculosis Laboratory Technical Network[3], Lori Strudwick[4], Sarah McDermott[1]

Abstract

Background: Drug-resistant tuberculosis (TB) is a public health issue of global importance that poses a threat to TB control efforts. Canada conducts nationwide surveillance to monitor emerging drug resistance trends and document progress towards reaching the goal of TB elimination.

Objective: To describe TB drug resistance trends across Canada from 2008–2018, with a focus on 2018, by drug resistance, geographic and demographic patterns.

Methods: TB drug resistance data are captured through two independent surveillance systems managed by the Public Health Agency of Canada: Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) and the Canadian Tuberculosis Reporting System (CTBRS). Data from these systems were analyzed and descriptive statistics were reported by resistance profile, place of residence (province), age groups, sex and country of birth.

Results: In 2018, 1,459 TB isolates underwent drug susceptibility testing, a 4.3% decrease from 2017. Resistance to any first-line drug was reported in 148 isolates (10.1%), compared to 123 (8.1%) in 2017. Of these, 121 were monoresistant, five were polyresistant, 21 were multidrug-resistant tuberculosis (MDR-TB) and one was extensively drug-resistant TB (XDR-TB). Drug resistance was reported in all provinces and territories except Prince Edward Island, Northwest Territories and Yukon. Among individuals younger than 15 years, very little TB drug resistance was detected. Among individuals aged 15 years and older, the distribution of TB drug resistance varied with no discernable trends. The proportion of drug resistance was slightly higher in females than in males. By origin, 10.7% of foreign-born TB cases reported between 2006 and 2016 were drug-resistant. Among the Canadian-born non-Indigenous cases, 9.3% were drug resistant; among Canadian-born Indigenous, 2.4% were drug resistant.

Conclusion: In 2018, the proportion of isolates with TB drug resistance in Canada remained low and below global averages, with stable drug resistance, both geographically and demographically.

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Note: Network members are noted under Contributors at the end of the paper

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Keywords: tuberculosis, surveillance, drug resistance, Canada

Introduction

Tuberculosis (TB), an airborne infectious disease caused by the bacterium *Mycobacterium tuberculosis*, is a major cause of illness globally. The World Health Organization (WHO) estimated that 10 million cases were diagnosed in 2017. Globally, TB is considered to be the number one cause of death due to a single infectious disease (1). While effective treatments exist, control may be hampered by the emergence of drug resistance. TB strains that are resistant to the first-line TB treatment regimens may take much longer to treat, using drugs that have more severe side effects (2). According to WHO, approximately 558,000 cases of TB that were resistant to the first-line anti-TB drug, rifampin, were diagnosed in 2017; of these, 82% were multidrug-resistant TB (MDR-TB). Of the MDR-TB cases diagnosed, about 8.5% were extensively drug-resistant TB (XDR TB) (1).

In September 2018, the United Nations General Assembly gathered for the first high-level meeting on TB. At this meeting, Member States reaffirmed their commitment to end the global TB epidemic by 2030 (3). Created as a result of this meeting, the Political Declaration recognizes that drug-resistant TB has a significant impact on global health and, if this issue is not adequately addressed, any progress made on TB elimination could be reversed (4). While the proportion of TB isolates with drug resistance in Canada has remained low over the preceding decade (5), it is important to maintain the epidemiologic surveillance of drug-resistant TB in order to monitor the evolution of drug-resistant TB in Canada, and inform public health officials on necessary appropriate actions. In addition, the data contribute to monitoring Canada's progress towards eliminating TB and to measuring the global burden of drug-resistant TB.

The Canadian Tuberculosis Standards recommend that all culture-positive TB isolates in Canada undergo drug susceptibility testing to determine the best course of anti-TB drug treatment for that particular case (2). These data can also be used for surveillance of drug-resistant TB. The Canadian Tuberculosis Laboratory Surveillance System (CTBLSS) was implemented in 1998 with the goal of monitoring emerging trends and patterns in TB drug resistance in Canada (6). The Canadian Tuberculosis Reporting System (CTBRS), a case-based surveillance system that maintains nonnominal demographic and clinical data on people diagnosed with active TB disease in Canada.

The objective of this report is to describe drug-resistant TB trend across Canada from 2008–2018, with a focus on 2018, as well as the geographic and demographic patterns.

Methods

Data sources

Data were derived and analyzed from two surveillance systems, the CTBLSS and the CTBRS.

The CTBLSS is an isolate-based laboratory surveillance system used to monitor TB drug resistance across Canada. (For definitions of types of TB drug resistance patterns, see **Table 1**.) Every year, provincial TB laboratories voluntarily submit results of culture-based, phenotypic drug susceptibility testing of isolates from cases with culture-positive TB from the previous calendar year. Basic nonnominal demographic data (sex, age and province/territory of residence) of the cases are also collected. Further details on the CTBLSS methods on data collection, data management and other laboratory processes have been previously described (6). For this report, data were available up to and including 2018.

Table 1: Definitions of tuberculosis drug resistance patterns

Type of resistance	Definition
Monoresistance	Resistance to one first-line anti-TB drug only (isoniazid, rifampin, ethambutol or pyrazinamide)
Polyresistance	Resistance to more than one first-line anti-TB drug, not including the combination of isoniazid and rifampin
Multidrug-resistant tuberculosis (MDR-TB)	Resistance to isoniazid and rifampin with or without resistance to other anti-TB drugs
Extensively drug-resistant tuberculosis (XDR-TB)	Resistance to isoniazid and rifampin AND any fluoroquinolone and at least one of the three injectable second-line drugs (amikacin, capreomycin or kanamycin)

Any TB isolates demonstrating positive cultures of *M. tuberculosis* complex (*M. tuberculosis*, *M. africanum*, *M. canetti*, *M. caprae*, *M. microti*, *M. pinnipedii* or *M. bovis*) were included in the analyses. Isolates positive for *M. bovis* Bacillus Calmette-Guérin (BCG) were excluded as these represent a complication of TB vaccination often found in immunocompromised patients and this strain is not infectious.

While the CTBLSS collects data on *M. tuberculosis* isolates, the CTBRS is a case-based surveillance system with information on active and retreatment TB cases in Canada. The CTBRS collects drug resistance data on TB cases when provincial and territorial health authorities report these cases to the Public Health Agency of Canada.

In this article, the researchers use data from CTBRS to describe TB drug resistance by country of birth, with Canadian-born further stratified by Indigenous and non-Indigenous. Further details on the CTBRS system have been previously described (7). For this report, data were available up to and including 2016.

Data analysis

To the extent possible, potential duplicates were identified using demographic information (sex, date of birth or age, and the province/territory). Potential duplicates, along with any missing data, were subsequently clarified with the submitting laboratories. Following tabulation of the data, isolate counts were sent to provinces and territories for verification to ensure accuracy. Data were cleaned and analyzed using SAS Enterprise Guide 5.1 (Cary, North Carolina, United States (US)) and Microsoft Excel 2010 (Redmond, Washington, US).

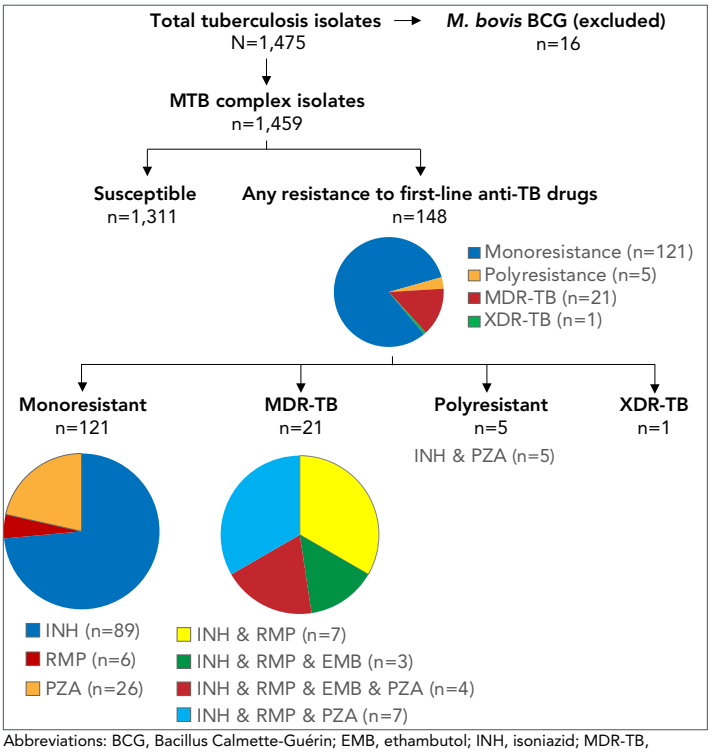
Descriptive statistics of the data, by drug resistance, geographic and demographic patterns, were computed and compared with trends from the previous 10 years. No statistical methods were used for comparative analyses. Supplementary data tables are available upon request (see **Appendix** for the list of tables).

Results

TB drug resistance profiles in 2018

In 2018, 1,475 *M. tuberculosis* isolates were submitted for drug resistance testing. Of these, 16 were determined to be *M. bovis* BCG strain and were excluded from further analysis. The majority of isolates, 1,311 (89.9%), were susceptible to all first-line anti-TB drugs, and the remaining 148 (10.1%) isolates were resistant to one or more drugs. The majority were monoresistant (81.8%, n=121), with isoniazid monoresistance the most commonly reported resistance pattern (n=89), followed by pyrazinamide monoresistance (n=26) and rifampin monoresistance (n=6). Polyresistance was identified in five isolates; these were all resistant to the combination of isoniazid and pyrazinamide. MDR-TB was detected in 21 isolates and XDR-TB in one (**Figure 1**).

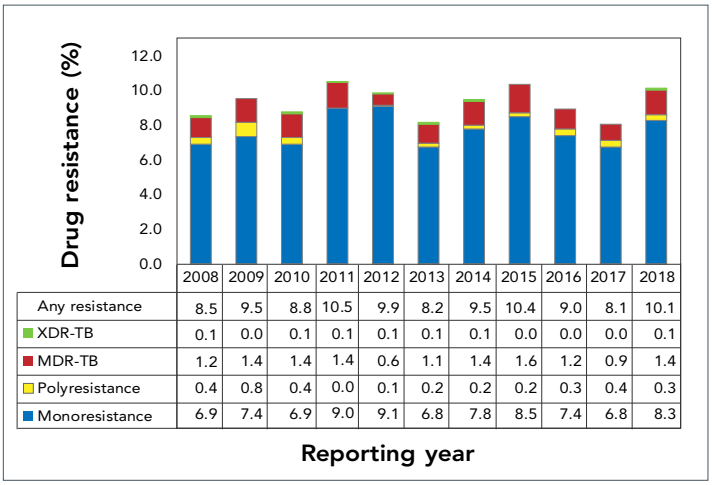
Figure 1: Tuberculosis isolates tested for anti-TB drug susceptibility, Canada, 2018



Abbreviations: BCG, Bacillus Calmette-Guérin; EMB, ethambutol; INH, isoniazid; MDR-TB, multidrug-resistant tuberculosis; MTB, *Mycobacterium tuberculosis*; *M. bovis*, *Mycobacterium bovis*; PZA, pyrazinamide; RMP, rifampin; TB, tuberculosis; XDR-TB, extensively drug-resistant tuberculosis

Between 2008 and 2018, the proportion of TB isolates with drug resistance in Canada changed little (**Figure 2**). The proportion of isolates resistant to anti-TB drugs fluctuated from year to year, but remained within a narrow range of values (8.1%–10.5%). During this time period, proportions of monoresistance ranged from 6.8% to 9.1%, polyresistance from 0.0% to 0.8%, MDR-TB from 0.6% to 1.6% and XDR-TB from 0.0% to 0.1%. A total of seven XDR-TB isolates were detected during this time frame and never were there more than one per year (Figure 2).

Figure 2: Proportion of tuberculosis isolates with reported drug resistance, by drug resistance pattern, Canada, 2008–2018



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Any resistance	8.5	9.5	8.8	10.5	9.9	8.2	9.5	10.4	9.0	8.1	10.1
XDR-TB	0.1	0.0	0.1	0.1	0.1	0.1	0.1	0.0	0.0	0.0	0.1
MDR-TB	1.2	1.4	1.4	1.4	0.6	1.1	1.4	1.6	1.2	0.9	1.4
Polyresistance	0.4	0.8	0.4	0.0	0.1	0.2	0.2	0.2	0.3	0.4	0.3
Monoresistance	6.9	7.4	6.9	9.0	9.1	6.8	7.8	8.5	7.4	6.8	8.3

Abbreviations: MDR-TB, multidrug-resistant tuberculosis; XDR-TB, extensively drug-resistant tuberculosis

Geographic distribution of TB drug-resistant cases

In 2018, the majority of isolates that underwent drug susceptibility testing were from Ontario (n=546; 37.4%), followed by British Columbia (n=255; 17.5%), Quebec (n=213; 14.6%), Alberta (n=161; 11.0%) and Manitoba (n=149; 10.2%). The Atlantic provinces (Newfoundland and Labrador, Prince Edward Island, Nova Scotia and New Brunswick) as well as the territories (Yukon, the Northwest Territories and Nunavut) recorded between zero and two isolates with any anti-TB drug resistance each (**Table 2**).

The highest number of resistant isolates were recorded by Ontario (n=68), Quebec (n=25) and British Columbia (n=23), which together accounted for about 78.4% (n=116) of reported drug-resistant isolates (Table 2). Resistance to any anti-TB drug was slightly higher than the Canadian average (10.1%) in Saskatchewan (13.6%), Ontario (12.5%) and Quebec (11.7%), and lower in British Columbia (9.0%), Manitoba (6.7%), Newfoundland and Labrador (5.6%), Alberta (5.6%) and Nunavut (2.7%). No drug resistance was reported in Prince Edward Island, Northwest Territories and Yukon.

Of all isolates that were MDR-TB in 2018, Ontario reported the most (n=13), followed by Alberta (n=3) and British Columbia (n=2). New Brunswick, Quebec and Manitoba reported one MDR-TB isolate each. The one XDR-TB isolate reported in 2018 was reported in Saskatchewan.

Table 2: Number and proportion of isolates demonstrating anti-TB drug resistance, by province/territory, Canada, 2018

P/T	Total isolates		Any resistance		Monoresistance		Polyresistance		MDR-TB		XDR-TB	
	n	%	n	%	n	%	n	%	n	%	n	%
NL	18	1.2	1	5.6	1	5.6	0	0.0	0	0.0	0	0.0
PE	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NS	8	0.5	2	25.0	2	25.0	0	0.0	0	0.0	0	0.0
NB	6	0.4	1	16.7	0	0.0	0	0.0	1	16.7	0	0.0
QC	213	14.6	25	11.7	23	10.8	1	0.5	1	0.5	0	0.0
ON	546	37.4	68	12.5	54	9.9	1	0.2	13	2.4	0	0.0
MB	149	10.2	10	6.7	9	6.0	0	0.0	1	0.7	0	0.0
SK	59	4.0	8	13.6	6	10.2	1	1.7	0	0.0	1	1.7
AB	161	11.0	9	5.6	5	3.1	1	0.6	3	1.9	0	0.0
BC	255	17.5	23	9.0	20	7.8	1	0.4	2	0.8	0	0.0
YK	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NT	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
NU	36	2.5	1	2.8	1	2.8	0	0.0	0	0.0	0	0.0
Total	1,459	100.0	148	10.1	121	8.3	5	0.3	21	1.4	1	0.1

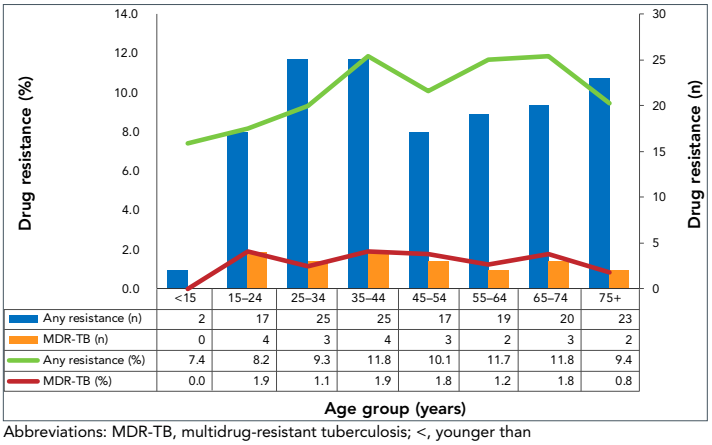
Abbreviations: AB, Alberta; BC, British Columbia; MB, Manitoba; MDR-TB, multidrug-resistant tuberculosis; NB, New Brunswick; NL, Newfoundland and Labrador; NT, Northwest Territories; NS, Nova Scotia; NU, Nunavut; ON, Ontario; PE, Prince Edward Island; P/T, province/territory; QC, Quebec; SK, Saskatchewan; XDR-TB, extensively drug-resistant tuberculosis; YK, Yukon

Tuberculosis drug resistance cases by age group

Of all eligible isolates submitted (n=1,459) for drug susceptibility testing in 2018, only 1.9% (n=27) were from individuals less than 15 years of age. The distribution of isolates across other age groups ranged from 11.2% (n=163) in the 55–64 years old age group to 18.4% (n=268) from individuals in the 25–34 years old age group.

The proportion of isolates with any resistance to anti-TB drugs was 7.4% (n=2) among individuals aged less than 15 years; however, none of these isolates was multidrug resistant (**Figure 3**). Among individuals aged over 14 years, the proportion of isolates with any resistance to anti-TB drugs ranged from 8.2% (15–24 years of age) to 11.8% (35–44 and 65–74 years of age). The proportion identified as MDR-TB (Figure 3) ranged from 0.8% (n=2) in individuals age 75 years and over to 1.9% (n=4) in individuals within the age ranges of 15–24 and 35–44 years.

Figure 3: Number and proportion of tuberculosis isolates with reported drug resistance, by age group and resistance pattern, Canada, 2018



	<15	15–24	25–34	35–44	45–54	55–64	65–74	75+
Any resistance (n)	2	17	25	25	17	19	20	23
MDR-TB (n)	0	4	3	4	3	2	3	2
Any resistance (%)	7.4	8.2	9.3	11.8	10.1	11.7	11.8	9.4
MDR-TB (%)	0.0	1.9	1.1	1.9	1.8	1.2	1.8	0.8

Abbreviations: MDR-TB, multidrug-resistant tuberculosis; <, younger than

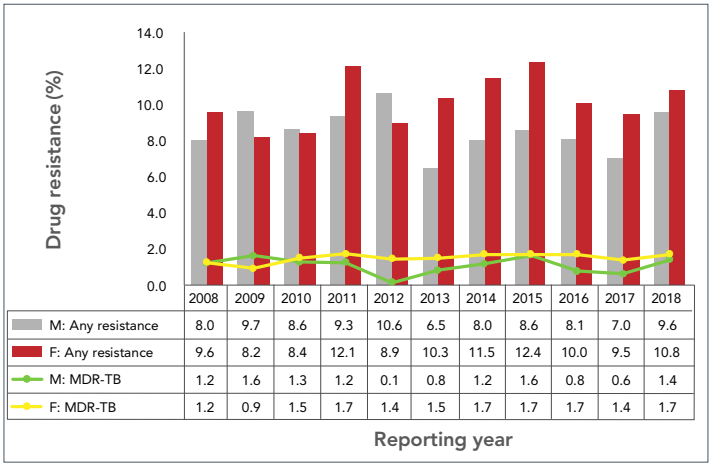
Tuberculosis drug resistance by sex

Of the isolates submitted for drug susceptibility testing in 2018, 54.9% (n=801) were from males and 45.0% (n=657) from females. The sex of the case was not reported for one isolate. The proportions of isolates with drug-resistant TB was similar in both sexes. Among males, 9.6% (n=77) of TB isolates had any resistance to first-line anti-TB drugs and 1.4% (n=11) were MDR-TB. Among females, 10.8% (n=71) had any resistance, and 1.5% (n=10) were MDR-TB. These findings are consistent with the trend from the previous five years (2013–2017), where the proportions of any drug resistance were higher in females than in males (**Figure 4**).

Tuberculosis drug resistance by country of birth

From 2006 through 2016, isolates from Canadians born abroad expressed a higher level of resistance to any anti-TB drugs (n=1,086 of 10,110 isolates; 10.7%) compared to those from Canadians born in Canada (n=211 of 4,373 isolates; 4.8%). The proportions of MDR-TB isolates followed a similar pattern; 1.4% (n=148) of those from Canadians born abroad and 0.2% (n=7) of those from Canadians born in Canada were MDR-TB. Differences in drug resistance proportions were also detected among different subgroups of Canadian-born cases. From 2006

Figure 4: Percentage of tuberculosis isolates with reported drug resistance, by sex and resistance pattern, Canada, 2008–2018



	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
M: Any resistance	8.0	9.7	8.6	9.3	10.6	6.5	8.0	8.6	8.1	7.0	9.6
F: Any resistance	9.6	8.2	8.4	12.1	8.9	10.3	11.5	12.4	10.0	9.5	10.8
M: MDR-TB	1.2	1.6	1.3	1.2	0.1	0.8	1.2	1.6	0.8	0.6	1.4
F: MDR-TB	1.2	0.9	1.5	1.7	1.4	1.5	1.7	1.7	1.7	1.4	1.7

Abbreviations: F, female; M, male; MDR-TB, multidrug-resistant tuberculosis

through 2016, 2.4% (n=68 of 2,822 isolates) of the TB cases among Canadian-born Indigenous people were resistant to any of the first-line anti-TB drugs, and none of these cases were MDR-TB. Among non-Indigenous Canadian-born TB cases, 9.3% (n=145 of 1,551 isolates) were resistant to at least one first-line anti-TB drug; and of these, 4.8% (n=7) were MDR-TB.

Discussion

In 2018, the proportion of drug resistance among culture-positive TB isolates in Canada remained low. Although the percentage of isolates with any reported anti-TB drug resistance increased from 8.1% in 2017 to 10.1% in 2018, the reported proportion was not out of the range observed (8.1%–10.5%) over the last 10 years. No new trends were noted with respect to age, sex or country of birth. Of note, there was one XDR-TB isolate reported in Canada in 2018. While this is the first to be reported since 2014, it is not unusual to see one in a given year, as single XDR-TB isolates were reported in six of the years over the past decade. In 2017, WHO estimated that 3.5% of new TB cases globally had rifampin resistance or were MDR-TB (2). Canadian statistics are significantly below these estimations as can be observed in the 2018 results, which registered only 1.8% of isolates resistant to rifampin or MDR-TB.

Limitations

The CTBLSS is the result of a successful collaboration between federal, provincial and territorial governments and public health laboratories. As the primary source of national data on TB drug resistance in Canada, the data in this report provide information for public health action, as well as policy and program development and assessment. Nonetheless, a few limitations should be considered when interpreting these results.

It is important to note that because the CTBLSS is a laboratory-based surveillance system, limited demographic information is available, and the isolates reported cannot be directly linked to case-based surveillance data from the CTBRS. Drug resistance information reported in CTBRS has been shown to be fairly complete (8) and reasonably comparable to the CTBLSS, although some discrepancies may exist that cannot be resolved. Future efforts to enhance TB surveillance include investigating the possibility of linking these two surveillance systems to provide detailed epidemiologic data on cases of drug-resistant TB, and more in-depth analyses and detailed interpretations.

Even though the overall number of cases of TB globally and in Canada among children under the age of 15 is low (9), the data in this report may still underrepresent the proportion of drug-resistant TB in this age group, as it is difficult to obtain sputum specimens in young children for culture-based drug susceptibility testing.

Conclusion

In 2018, the proportion of isolates with TB drug resistance remained relatively stable and below global averages across Canadian demographics and geographic locations.

Authors' statement

ML — Conceptualization, methodology, software, validation, formal analysis, writing (original draft)
DD — Conceptualization, software, validation, formal analysis, writing (review) and editing, visualization
LS — Validation, writing (review) and editing
SM — Conceptualization, writing (review) and editing, supervision

Conflict of interest

None.

Contributors

The Surveillance and Epidemiology Division, Centre for Communicable Diseases and Infection Control at the Public Health Agency of Canada would like to acknowledge the teams at the Canadian Tuberculosis Laboratory Technical Network for their contribution to and participation in the Canadian Tuberculosis Laboratory Surveillance System (CTBLSS):

Canadian Tuberculosis Laboratory Technical Network members: H Adam, P M Akochy, R Bittner, K Cronin, D Farrell, D Haldane, H Hannah, F Jamieson, H Mackenzie, E Martin, R Needle, K Ray, M Rodrigues, I Sekirov, C Shandro, H Soualhine, R Thomas, G Tyrrell.

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Appendix: List of supplementary tables available upon request

Supplementary Table 1: Total number and percentage of Mycobacterium tuberculosis complex isolates identified with any resistance, as multidrug and extensively drug resistant, by year, 2008–2018, Canada

Supplementary Table 2: Overall pattern of reported tuberculosis drug resistance in Canada, 2008 to 2018

Supplementary Table 3: Results for routine to anti-tuberculosis drug susceptibility testing of Mycobacterium tuberculosis complex isolates originating from Alberta, 2008 to 2018

Supplementary Table 4: Results for routine to anti-tuberculosis drug susceptibility testing of Mycobacterium tuberculosis complex isolates originating from British Columbia, 2008 to 2018

Supplementary Table 5: Results for routine to anti-tuberculosis drug susceptibility testing of Mycobacterium tuberculosis complex isolates originating from Manitoba, 2008 to 2018

Supplementary Table 6: Results for routine to anti-tuberculosis drug susceptibility testing of Mycobacterium tuberculosis complex isolates originating from New Brunswick, 2008 to 2018

Supplementary Table 7: Results for routine to anti-tuberculosis drug susceptibility testing of Mycobacterium tuberculosis complex isolates originating from Newfoundland and Labrador, 2008 to 2018

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A new resource to summarize evidence on immunization from the Canadian Vaccination Evidence Resource and Exchange Centre (CANVax)

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Abstract

Scientific progress around the development, use and best practices for communicating the benefits of vaccines is rapid, and keeping up-to-date with the substantial body of evidence on these topics is challenging. However, the increase in the number of vaccines and decline in vaccine-preventable illnesses has often focused public attention more on the risks of vaccines rather than the risks of the diseases. In Canada and elsewhere, an increasing number of parents are choosing to delay and/or refuse some or all vaccines for their children, leading to declining community protection against vaccine-preventable diseases and an increase in the number of outbreaks of vaccine-preventable diseases. Evidence suggests that the concept of vaccine hesitancy contributes to a deeper understanding of vaccination decisions by moving beyond the traditional binary of pro- or anti-vaccine attitudes to recognize a spectrum of beliefs and associated behaviours that occupies the space between the two poles. At a time of growing antimicrobial resistance to infections, protection conferred by vaccination is more important than ever.

The Canadian Vaccination Evidence Resource and Exchange Centre (CANVax) is an online curated database of resources to support immunization and promotional activities aimed at improving vaccine acceptance and uptake in Canada. It includes both the identification of accurate and reliable resources and the creation of new resources by a group of multidisciplinary professionals.

This issue of the *Canada Communicable Disease Report* (CCDR) includes the first of a series of "CANVax Briefs" that have been developed by experts after conducting scoping reviews and environmental scans and assessing the most rigorous evidence. The aim of the CANVax Briefs is to bring attention to current and emerging issues by providing short summaries of the recent best available evidence to assist frontline public health and clinical care professionals in optimizing the immunization rate in Canada. CANVax Briefs will be published in CCDR throughout 2020.

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Introduction

Scientific progress around the development and use of vaccines has been rapid over the past 40 years (1). In Canada, the number of vaccines included in the publicly funded vaccination program for children from birth to 18 years of age has more than tripled since 1980, from eight to 17 antigens by 2019 (2). Not only has the number of vaccines risen, but the number of immunizations given in a single visit has also increased. For example, up to four different vaccines may be given in a single childhood vaccination visit depending on the provincial and territorial vaccination program (3).

As vaccine schedules grow increasingly complex so do the needs and expectations of patients and health care providers concerning vaccine safety and effectiveness. For some, the increase in the number of vaccines and decline in vaccine-preventable illnesses has focused more attention on the risks of the vaccines rather than the risks of the diseases (4). In Canada and elsewhere, an increasing number of parents are choosing to delay and/or refuse some or all vaccines for their children, leading to declining community protection against vaccine-preventable diseases and major outbreaks of those diseases (5–9). Sadly, reported uptake rates in Canada are falling short of national and international targets (10).

In Canada approximately 15% to 20% of parents are concerned about accepting vaccines for their children, with some deciding to delay, postpone or even refuse some or all vaccines (5,11,12). Given that vaccine-hesitant parents are not uniformly spread across the population but frequently cluster geographically due to common values and lifestyle, we now have fertile grounds for major outbreaks of vaccine-preventable diseases (7–9).

The recent increase in vaccine-preventable outbreaks occurred at the same time as rising rates of antimicrobial resistance. Antimicrobial resistance threatens the effective prevention and treatment of an ever-increasing number of infections (13). In 2019, the World Health Organization identified antimicrobial resistance and vaccine hesitancy as two of the top 10 threats to global health (14), making the optimization of vaccination rates more important than ever.

In this editorial, we identify vaccine hesitancy as including a number of concerns; describe the Canadian Vaccination Evidence Resource and Exchange Centre (CANVax), a new resource that provides curated information on vaccines for frontline public health and clinical care as well as other educational services; and introduce a series of CANVax Briefs that will be published in the *Canada Communicable Disease Report* (CCDR) throughout 2020, starting with this issue.

Vaccine hesitancy

Vaccine hesitancy, or the "delay in acceptance or refusal of vaccine despite the availability of vaccination services" (12), is receiving increasing international attention. The scope of vaccine hesitancy includes instances where "vaccine acceptance in a specific setting is lower than would be expected, given the availability of vaccination services" (12).

The concept of vaccine hesitancy contributes to a deeper understanding of vaccination decisions by moving beyond the traditional binary of pro- or anti-vaccine attitudes to recognize a spectrum of beliefs and associated behaviours that occupies the space between the two poles. A vaccine-hesitant person can delay, be reluctant but still accept, or refuse one, some or all vaccines.

Vaccination decisions are complex and multidimensional, and can be very vaccine-specific.

At the individual level, reviews have focused on factors associated with vaccine acceptance or refusal, identifying determinants such as:

- Fear of side effects
- Perceptions around health and prevention of disease
- A preference for "natural" health
- Low perception of the efficacy and usefulness of vaccines
- Negative past experiences with vaccination services
- A lack of awareness or knowledge about vaccination (4)

The World Health Organization summarizes the diverse factors leading to vaccine hesitancy into three broad categories (12):

- **Complacency:** Perceived risks of vaccine-preventable diseases are low and vaccination is not deemed necessary
- **Convenience:** The real and/or perceived quality of the service and the degree to which vaccination services are delivered at a time and place and in the cultural context that are convenient and comfortable
- **Confidence:** Trust in the effectiveness and safety of vaccines; in the system that delivers them, including the reliability and competence of the health services and health professionals; and in the motivations of the policy-makers who decide which vaccines are needed when and where

The growing interest in vaccine hesitancy—and vaccine acceptance more broadly—has generated an increasing number of publications. Keeping up-to-date with the substantial body of peer-reviewed research and major domestic and international reports relevant to vaccine acceptance and uptake that are being produced can be challenging.

CANVax

CANVax is a new online curated database of resources to support immunization program planning and promotional activities aimed at improving vaccine acceptance and uptake in Canada (15). CANVax has been developed by the Canadian Public Health Association (CPHA) with funding from the Public Health Agency of Canada. It includes curated resources from Canada and around the world, interactive features, educational updates and new resources. CANVax is now a member of Vaccine Safety Net, the World Health Organization global network of vetted websites that provide reliable information on vaccine safety (16).

Curated resources

CANVax houses a collection of selected evidence-based products and resources to make it easier for public health professionals to access and gather resources to inform their planning and activities. It includes a large database that covers five broad areas: vaccine decision making; monitoring and surveillance; vaccine safety and development; program

planning and delivery; and policy. In each area there are multiple topics, and for each topic there are resources on background knowledge, implementation tools and evidence and key influencers or leaders in the field. (**Table 1**).

Table 1: Summary of the subject areas and topics in CANVax's curated database

Subject areas	Topics	Resources
Vaccine decision making	Vaccine hesitancy	Understanding hesitancy and vaccine decision making
		Misconceptions
		Complementary and alternative medicine
	Vaccine acceptance	Understanding vaccine acceptance and uptake
		Counselling and communication
		Anxiety and pain management
Monitoring and surveillance	Vaccine monitoring and surveillance	Vaccination coverage and goals
	Outbreaks and pandemics	Outbreaks
		Influenza pandemics
	Vaccine preventable disease surveillance	Provincial and territorial surveillance
		National surveillance
		Global surveillance
Vaccine safety and development	Vaccine safety	Vaccine safety
		Adverse events following immunization (AEFI)
	Research and development	Vaccine ingredients
		Vaccine development
Program planning and delivery	Promotion and communications	Marketing and campaigns
		Communications
	Program delivery and evaluation	Informed consent
		Clinics
	Vaccine management	Storage and handling
	Outbreak and crisis management	Crisis communications
	Professional development	Education and training
Policy	Immunization policies	Mandatory immunization and activities

Abbreviation: CANVax, Canadian Vaccination Evidence Resource and Exchange Centre

How does it work? CANVax is supported by a multidisciplinary group of experts with skills and knowledge in public health, infectious diseases, medical anthropology, paediatrics, internal medicine, sociology, information technology, social media and library science. This group reviews Canadian and international resources, products and tools prior to their inclusion on the CANVax website.

Interactive features

All users are able to download any resource. In addition, the following interactive features are available when a user registers with CANVax:

- Share – easily share a resource with colleague using social media or email
- Comment – provide feedback on resources you have used
- Save – bookmark the resource you need for easy and convenient access and save your search strategy for future reference

Educational services

In addition to posting curated resources, CANVax's monthly newsletter provides updates on new resources and highlight articles on emerging topics in immunization. CANVax's podcasts and webinars also focus on emerging topics, with experts from across Canada exploring emerging immunization issues and initiatives.

CANVax Briefs

CANVax is developing new resources to provide succinct summaries and highlights of key new research. "CANVax Briefs" are short evidence-based articles that aim to inform, engage and inspire readers by bringing attention to current and emerging issues in immunization, and by profiling initiatives and activities from across Canada that aim to improve vaccine acceptance and uptake.

In this issue, we begin a series of CANVax Briefs by focusing first on how vaccine hesitancy has been increasing with the availability of Web 2.0 and social media, that this hesitancy has been associated with an increase in outbreaks of vaccine-preventable diseases and then identify the best practices to address this (17). More Briefs will be published in subsequent issues of CCDR in 2020.

Topics for the Briefs are identified by the CANVax team. The team consists of CPHA staff and immunization experts, Dr. Noni MacDonald and Dr. Eve Dubé. Experts on the chosen subject are then invited to contribute to the development of the brief. Short scoping reviews of evidence are conducted and reviewed by the CANVax Expert Review Panel, which is made up of external experts in immunization (18).

Conclusion

Enormous evidence-based progress has been made to address the declining community protection against vaccine-preventable diseases that has been seen around the world. CANVax was created to help frontline practitioners remain abreast of these developments in order to promote and maintain higher immunization rates in Canada. One of the strengths of the CANVax website is it is interactive. CANVax welcomes feedback

on its website and its products and is open to suggestions for specific topics to be covered in future CANVax Briefs and webinars. Check out the CANVax website for details.

Authors' statement

NM — Writing – original draft
ED — Writing – review and editing

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Promoting immunization resiliency in the digital information age

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Abstract

The avalanche of online information on immunization is having a major impact on the percentage of the population who choose to get vaccinated. Vaccine misinformation spreads widely with the interactive Web 2.0 and social media; this can bury science-based information. A plethora of immunization misinformation online is affecting trust in health care professionals and in public immunization programs. There are no simple solutions to this, but seven evidence-based strategies can help. First, listen to patients' and parents' concerns, and demonstrate responsiveness by adopting best immunization practices, such as pain mitigation. Second, recognize and alert others to anti-immunization tactics, namely, conspiracy theories, fake experts, selectivity, demands that vaccines be 100% safe and effective, misrepresentation and false logic. Third, avoid unproductive debates with those who have strongly held views, both in person and when using social media. Be respectful, stick to your key message, identify where to find useful information and exit. Fourth, consider establishing an attractive, easily searchable online presence that reflects the complex art of persuasion. Emphasize the benefits of vaccine, use reader-friendly graphics and highlight facts with stories to strengthen your case. Fifth, work with social media platform providers, not to stifle freedom of expression, but to help ensure that misinformation is not favoured in searches. Sixth, promote curriculum development in the schools to improve students' understanding of the benefits and safety of immunization and to foster critical thinking skills. To do this, optimize the use of age-appropriate comics and interactive learning tools such as electronic games. Seventh, to shift the narrative in specific communities with low vaccination rates, work with community leaders to build tailored programs that foster trust and reflect local values.

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Keywords: immunization, vaccine, misinformation, social media, evidence-based strategies, education, vaccine hesitancy, Web 2.0, immunization resiliency, health communication

Introduction

The decision by individuals and parents to accept a vaccine is influenced by many factors. These can vary with time, place, vaccine and context (1). In Canada, as in other countries around the globe, the online immunization information avalanche is having a major impact on uptake. In the early digital age, public health information available online was static "read only" materials; with Web 2.0, online information has evolved into multidirectional, user-generated communication characterized by participation, collaboration and openness. Web 2.0 and social media have become the major modern platform for self-directed learning—a bottom-up approach with users reaching out, rather than a top-down strategy with experts providing information.

Most Canadians seek health information online, including information on immunization. This includes many seniors even though they came of age long before Web 2.0 (2). Unfortunately, only some of the immunization information on Web 2.0 and social media is science or evidence-based. Much online information is opinion or speculation as well as dramatic, often untrue but oft-repeated stories about adverse events presented as "alternative facts." Such vaccine misinformation can spread widely on social media (3), burying science-based information. Exchanges may spread widely, and comments may be vigorous and may become increasingly polarized overtime (4).

Exposure to immunization misinformation and fake news is now very common. A 2018 study from the United Kingdom found that over 40% of parents had been exposed to negative vaccine messages on social media (5). This is not a trivial issue: it poses a risk of confirmation bias (6). Confirmation bias occurs when people seek, select and retain the information that confirms their existing beliefs; it results in a bias in how new information is evaluated. Furthermore, with social media platforms, people are now being exposed to messages that are critical of vaccines even

when they are not seeking this type of information. Negative vaccine information may elicit and/or reinforce vaccine hesitancy. It has been shown that as little as 5 to 10 minutes on an anti-vaccine website can negatively influence decisions to accept a vaccine (7).

A small percentage of people are profoundly anti-vaccine and refuse all vaccines (8). Some are very active online and have very firm opinions that evidence and facts are unlikely to shift. They may see themselves as experts, although this expertise is based upon misinformation gathered online from others holding similar world views. They are often only too willing to share their "knowledge" through YouTube videos, Twitter, Facebook groups and websites that readily pop up on Google searches. Such evergrowing misinformation can negatively influence vaccine decisions (9) and affect reporting of adverse events (10).

The digital information age has also changed the patient–health care professional relationship. Shared decision making is becoming normative and "top-down" paternalism is disappearing. This is not invariably negative; shared decision making is good when supported by sound scientific evidence that is shared and understood, but it is not good when decisions are influenced by misinformation. And the plethora of immunization misinformation online is not only influencing decision making; it is also affecting trust in health care professionals and in public immunization programs. Sadly, trolling for and subsequently online bullying of evidence-based vaccine experts by those with polarized opposite views, is an increasingly recognized problem (11,12).

To address these challenges, "immunization resiliency" needs to be promoted. Immunization resiliency in this context means ensuring that vaccination programs are adapted to the current digital communication environment in order to grow public trust in health care providers and optimize vaccine acceptance over time. The objective of this article is to identify best practices for front line vaccine providers in order to promote vaccine resiliency. This is the first of a series of articles, produced by The Canadian Vaccination Evidence Resource and Exchange Centre (CANVax), which include both the identification of existing resources and the creation of new resources by a group of multidisciplinary professionals (13).

What can health care professionals do to promote immunization resiliency?

There are no simple solutions to addressing the avalanche of digital misinformation about vaccines and the deleterious effects this has caused, but evidence-based strategies can help. We highlight seven key strategies that are based on reviews of psychological research on persuasion, myth debunking, science denialism, communication science and research on impact of social media.

1. Listen to patients and parents

In this postpaternalism world, it is important to learn what the issues of concern are when interacting with people who are contemplating vaccination both at an individual and at a community level. At the clinical level, health care providers need to be prepared to listen and then address concerns as they arise. Using the mini-motivational interviewing tools can be effective in moving the patient towards vaccine acceptance (14). If pain on immunization is a concern—and it is for over 40% of mothers of infants needing immunization—then use best practices for mitigation pain based upon Canada's 2015 guidelines (15).

Frontline health care providers need to be encouraged to report to their local public health unit common concerns they are hearing. Immunization programs can use these concerns as well as those found through analysis of social media to develop targeted communication messages using traditional and social media (16). There is a good rationale for directly countering social media misinformation because of its potential influence. Effective strategies to do this have been proposed (17). Remember: data tells but stories sell—be succinct and straightforward.

2. Recognize and alert others to anti-immunization tactics

Recognize the tactics often used by those opposing immunization: conspiracy theories, fake experts, selectivity, demands that vaccines be 100% safe and effective, misrepresentation and false logic (18). Correcting misinformation and highlighting these techniques being used can help inoculate against misinformation (19). Draw attention to these, especially in a forum where there is a bigger audience, for example, in a Facebook group, etc., and only if your message is not so polarized that it will be buried. Alerting to these tactics and correcting misinformation can be salutary for those without confirmed negative views on immunization (20). Remember your target is not the person promulgating the misinformation but the reader of the misinformation.

3. Avoid unproductive debates and be respectful

Be aware that many online anti-vaccine forums are very polarized; joining in may not be helpful (4). While the evidence is clear that vaccines are safe and effective and that diseases with serious consequences—even death—can occur when immunization is omitted, this will not convince those with strongly held opposing views. Do not fall into the persuasion loop trap. When your efforts to correct repeated examples of selectivity or misrepresentation are met with "yes, but," this can lead to a never-ending dialogue. It is more effective to be respectful, stick to your message, identify where to find more information and exit the conversation, that is, limit direct engagement with those who have strong anti-vaccination views, either online or in person. Repeating their arguments as you attempt to refute them can be counterproductive as the misinformation may stick (21).

When you do engage in social media opportunities, do so wisely. Tailored and targeted messages and information can help shape attitudes and improve uptake (22,23). As noted above, it can be useful to alert others to anti-vaccination tactics in public forums (20,21). Get your point across succinctly—remember that stories are often more powerful than dry facts and numbers—and steer readers to reputable sites for more quality information.

Never be disparaging or demeaning in public or to a patient. The term "vaccine deniers" has been used as convenient shorthand, but a more neutral description, such as "those with strong anti-vaccine opinions," may be better received during discussions.

4. Consider developing an attractive, easily searchable online presence

When health professionals and/or their organizations have a presence on the internet, presenting evidence-based information about immunization online can be helpful. However, avoid "knowledge dumps" or posting large quantities of very technical information to try and counter every new piece of misinformation. Be proactive: promote positive messages about vaccination in a succinct and easy-to-grasp manner.

If you plan to build a pro immunization website, make it appealing, easily searchable and as interactive as possible. Clearly identify your evidence-based key messages, with short reader-friendly text. The complex art of persuasion calls for a blend of different strategies, including the need for a straightforward presentation of the "what", "how", "where", "when" and "who" complemented with stories. Colour and graphics also help to increase the impact of key points (24).

Static websites are dated. If resources permit, include a place where visitors can post questions. Having nowhere to make inquiries can be frustrating. If you do not have the resources for this, consider including a common question-and-answer information sheet or provide a link to a reliable resource with a query service, such as the *Canadian Immunization Guide* (25). If you are able to respond to queries, avoid entering into protracted debates with anyone who has strong anti-vaccination views.

5. Alert social media platform providers to misinformation online

Work with social media platform providers, not to stifle freedom of expression, but to help ensure that searches do not favour misinformation (26). As an example, Facebook has started removing extreme misinformation websites (27). Consider learning from the techniques being used to help control online hate websites and forums (28).

6. Promote immunization and science literacy curriculum development for use in schools

Work with departments of education to help develop curricula that can improve students' understanding of the benefits and safety of immunization and risks of vaccine-preventable disease. Online games, comics, animation and other forms of visual communication may have more appeal than static pages. While many groups in Canada and elsewhere are developing online immunization educational materials for students (29), it is important to ensure that these fit the context of the audience. For example, the British Columbia Centre for Disease Control education website *Kids Boost Immunity* (30), which is formatted as an interactive quiz, is evidence based, educational and well-liked by students. Evaluations and assessments have shown that children learn about immunization from the site.

A vaccine-specific curriculum is not enough to help increase immunization resiliency. Students also need well-developed critical thinking skills and much higher levels of science and digital literacy if they are to see through the misinformation and con-artist techniques in use on the internet. These skills are needed to assess more than just immunization information, but immunization makes an excellent case. There are resources available to help with this, for example, Media Smarts (31).

7. Work with community leaders to build tailored programs in specific communities

Vaccine uptake may be lower in some communities than in others (32). Listen to and work with communities and with community leaders to build trust in immunization through multipronged campaigns (which may involve online media) that explicitly support local values and are respectful of their context (33,34). Tailored programs can help shift the narrative in the community.

Beyond targeting subgroups, pulling together a collaborative network of national/provincial immunization programs, academia, health professional societies, health centres and health authorities, who add their voices to the positive message of the importance of vaccines and safety, can help sway public attitudes. This is known as the "gateway belief" (35). These common messages also save time and support frontline health professionals' positive recommendations for immunization.

Conclusion

Misinformation and polarization of online immunization information is not going to go away. For clinical care and public health, the work to increase immunization resiliency is only going to become even more complex. Health care and public health professionals need to better understand why misinformation is so appealing and why polarization is to be expected. People do need to be listened to. Immunization concerns need to be assuaged. Over time, we must become better at discerning what information is credible, be it about health, climate change, the economy or politics. While teaching critical thinking and digital and science literacy is a major step forward, we also need to focus on how better to connect with communities and how to

reframe the immunization messages so they are more effectively heard and better appreciated. Useful accessible materials can be found are the National Advisory Committee on Immunization summary statements (for example, 36), the *Canadian Immunization Guide* (25), the immunization section on the Caring For Kids Website of the Canadian Paediatric Society (37), Immunize Canada (38) and the CANVax website (13).

Authors' statement

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National Influenza Mid-Season Report, 2019–2020

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Abstract

Canada's national influenza season started in week 47 between November 17 to 23, 2019. Of the 3,762 laboratory-confirmed influenza detections reported from August 25 to December 14, 2019, 61% were influenza A, and of those subtyped, 68% were A(H3N2). Influenza B detections are above average for this time of year. Indicators of influenza activity are within the expected range for this time of year. The majority of hospitalizations reported by provinces and territories have been associated with influenza A(H3N2) (76%), and the greatest proportion have been among adults 65 years and older (40%). Among sentinel pediatric influenza hospitalizations, 55% were associated with influenza B and the majority have been under five years of age (63%). Antigenic and genetic characterization results to date suggest that the majority of circulating A(H3N2) and B viruses are not similar to the virus components recommended for use in the 2019–2020 seasonal influenza vaccines and that the majority of circulating A(H1N1) viruses are similar to the vaccine reference strains.

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Keywords: influenza, surveillance, H1N1, H3N2, outbreaks

Introduction

This is a summary of Canada's influenza season based on data available from August 25 to December 14, 2019 (epidemiologic weeks 35 to 50) in the weekly FluWatch reports prepared by the Public Health Agency of Canada (1). Canada's national influenza season started in week 47 between November 17 to 23, 2019, based on the seasonal thresholds (**Figure 1**) (2). This is similar to the average starting point of influenza seasons in Canada over the past decade.

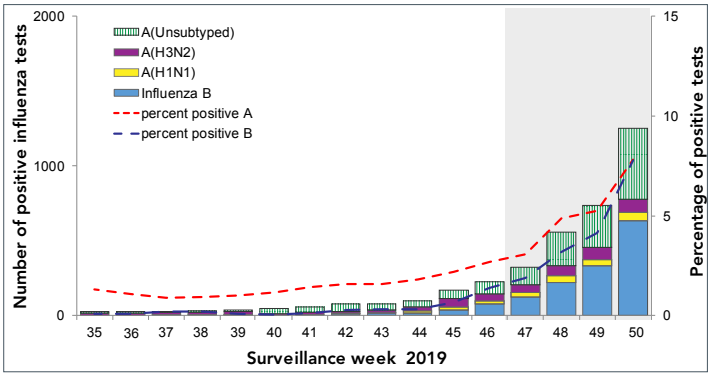
Laboratory-confirmed influenza detections

A total of 3,762 laboratory-confirmed influenza detections have been reported, of which 61% were influenza A. Influenza A(H3N2) accounts for 68% of the 790 influenza A viruses subtyped. The cumulative proportion of detections of influenza B (32%) is higher than the average for this time of year (11%) and the weekly proportion has been increasing since October 27–November 2, 2019 (week 44) to 50% of detections in week 50. The dominance of influenza A is not homogeneous across Canada with influenza B appearing to dominate in certain provinces and territories thus far.

Detailed information on patient age and influenza type/subtype has been received for 3,241 laboratory-confirmed cases. The age distribution of cases varies by type/subtype and follows expected trends. Among cases of influenza A(H3N2), the largest proportion were in adults 65 years and older (45%). Cases of influenza B were primarily in younger age groups; 63% of cases were under 20 years and 30% between 20 and 44 years of age. Among cases of influenza A(H1N1), 35% of cases were in adults between 45 and 64 years, and 23% between 20 and 44 years of age.

The transmissibility of influenza this season was characterized as low in week 50, which is typical for this time of year. Seasonal

Figure 1: Number of positive influenza tests and percentage of tests positive, by type, subtype and report week, Canada, weeks 35–50 (2019)



Note: The shaded area indicates weeks where the positivity rate was at least 5% and a minimum of 15 positive tests were observed, signalling the period of seasonal influenza activity

intensity thresholds are calculated based on the percentage of tests positive during the peak weeks of previous seasons using the Moving Epidemic Method (3–5).

The transmissibility of influenza this season was characterized as low in week 50, which is typical for this time of year. Seasonal intensity thresholds are calculated based on the percentage of tests positive during the peak weeks of previous seasons using the Moving Epidemic Method (3–5).

Outbreaks

A total of 62 laboratory-confirmed influenza outbreaks have been reported, of which 53% were in long-term care facilities, 15% were in acute care facilities, 8% were in schools/daycare, and 24% were reported in facilities categorized as 'other' which includes facilities such as private personal care homes, correctional facilities and college/universities. Of the outbreaks where influenza type was reported (n=58), 85% were due to influenza A. Among outbreaks where subtype information was available (n=26), 25 were associated with influenza A(H3N2) and one was associated with A(H1N1).

Severe outcomes

Based on influenza-associated hospitalizations across all age groups (n=274) reported by participating provinces and territories (Alberta, Manitoba, New Brunswick, Newfoundland and Labrador, Northwest Territories, Nova Scotia, Prince Edward Island and Yukon), the majority of cases requiring hospitalization had influenza type A (68%). Of those with subtype information (n=164), influenza A(H3N2) was the most common subtype (76%). The greatest proportion of hospitalized cases were adults 65 years and older (40%).

Among pediatric hospitalized cases reported by the Canadian Immunization Program Active (IMPACT) (n=69), 55% were influenza B and 45% were influenza A. The largest proportion of pediatric hospitalized cases have been among children under five years of age (63%). The number of cases reported to date is within the expected range for this time of year based on the previous five seasons.

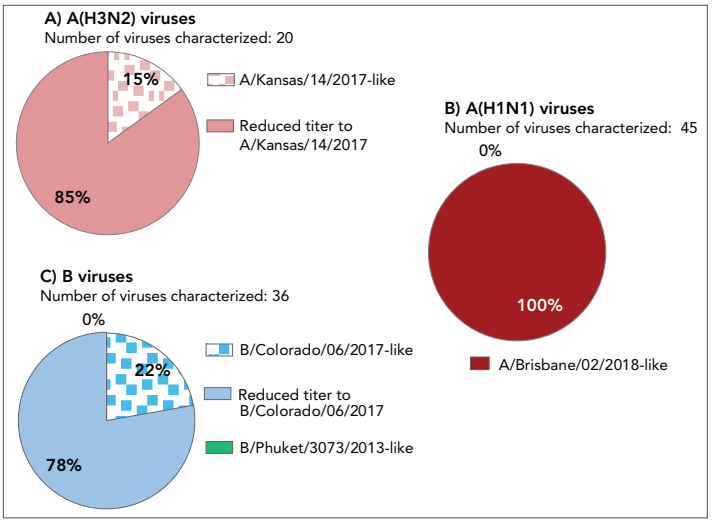
Strain characterization

The National Microbiology Laboratory (NML) has characterized 159 influenza viruses (78 A(H3N2), 45 A(H3N2) and 36 influenza B) that were received from Canadian laboratories.

A total of 65 influenza A viruses have been antigenically characterized (20 A(H3N2) and 45 A(H1N1)); 15% of A(H3N2) viruses and 100% of A(H1N1) viruses were similar to the egg-propagated reference viruses used in the production of the 2018–2019 Northern Hemisphere influenza vaccine (**Figure 2).**

A total of 78 A(H3N2) viruses were genetically characterized and 96% belonged to genetic group 3c.2a1b based on sequence analysis of the hemagglutinin (HA) gene. This is a different genetic group from the HA gene of the A(H3N2) component of the 2019–2020 Northern Hemisphere influenza vaccine (3C.3a).

Figure 2: Distribution of antigenic phenotypes among characterized influenza viruses, Canada, September 1 to December 19, 2019



A total of 36 influenza B viruses have been antigenically characterized; all belonged to the B/Victoria lineage and 22% were similar to the cell culture-propagated reference virus used in the production of the 2018–2019 Northern Hemisphere quadrivalent influenza vaccine. All viruses tested for antiviral resistance by the NML to date were sensitive to oseltamivir and zanamivir and resistant to amantadine.

Discussion

The Canadian influenza season started in mid-November which was within an expected time frame based on previous seasons over the past decade. Viral typing and subtyping data available to date are signaling a mixed season. While A(H3N2) is the predominant strain nationally, A(H1N1) viruses represent one third of subtyped influenza A detections and B detections have been increasing in recent weeks and are above average for this time of year. Moreover, the dominance of influenza A is not homogeneous across all provinces and territories. The percentage of test positives for influenza B to date this season is following a similar trend to the 2017–2018 season when influenza A and B circulated in almost equal proportions. At this time, surveillance data suggest that the transmissibility of influenza during the 2019–2020 season is low compared to the peak of the season which is expected in the early stages of the seasonal influenza epidemic. Given that it is still the early part of the influenza season, increasing activity is expected into the new year. In general, the peak of the season, based on laboratory detections, occurs in the first few weeks of January. High levels of influenza activity usually persist through February and March.

Worldwide, results from World Health Organization's Global Influenza Surveillance Response System laboratories are similar to those reported in Canada (6). Influenza A viruses are predominant, with approximately 70% being A(H3N2) among subtyped detections. Nearly all influenza B viruses circulating belong to the B/Victoria lineage. Among other regions of the Northern Hemisphere, the influenza seasons have also begun in the United States and in the European Region.

Antigenic and genetic characterization results to date suggest that the majority of circulating A(H3N2) and B viruses are not similar to the components recommended for use in the 2019–2020 seasonal influenza vaccines, and that the majority of circulating A(H1N1) viruses are similar to the recommended components (7). This may be indicative of low level protection of the vaccine against the A(H3N2) and B strains. However, it is important to note that the effectiveness of influenza vaccines depend on several factors and cannot be predicted based solely on the similarity of currently circulating viruses relative to the vaccine reference viruses.

The Association of Medical Microbiology and Infectious Disease Canada (AMMI) recently released updated guidelines related to use of influenza antiviral medication for the 2019–2020 influenza season (8). The guidelines underscore that given the potential for suboptimal vaccine effectiveness this season, antiviral therapy may be more important for individuals with suspected influenza illness, notably those in high-risk groups, even with documentation of having received the 2019–2020 influenza vaccine.

Estimates of vaccine effectiveness and coverage for this season are expected in March and will be included in the FluWatch report when available. The weekly FluWatch reports are available on the Weekly Influenza Reports webpage (1).

Authors' statement

The FluWatch team in the Centre for Immunization and Respiratory Infectious Diseases developed the first draft collaboratively; all authors contributed to the conceptualization, writing and revision of the manuscript.

Conflicts of interest

None.

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Benchmarks for Sexually Transmitted Infection (STI) Prevention and Linking to STI Testing Services in Schools

Source: Benchmarks for Sexually Transmitted Infection (STI) Prevention and Linking to STI Testing Services in Schools. Excerpt from: *Canadian Guidelines for Sexual Health Education*. Toronto, ON: Sex Information & Education Council of Canada (SIECCAN). Page 83. SIECCAN. (2019). http://sieccan.org/wp-content/uploads/2019/08/Canadian-Guidelines-for-Sexual-Health-Education.pdf

Sexually transmitted infections (STIs) can negatively impact the health and well-being of young people in Canada, particularly if left untreated. There are a broad range of factors that increase a person's risk for acquiring an STI. These include societal structures and conditions (e.g. socio-economic status, housing status, levels of equality related to gender, sexual orientation, race, and Indigenous identity).

Comprehensive sexual health education should address these factors in seeking to equip youth with the information, motivation, and behavioural skills to reduce their risk of STIs. As a part of this process, it is critical to provide children and youth with timely and age-appropriate information related to personal STI prevention, testing, treatment, and management.

Comprehensive sexual health education can effectively assist youth and young adults in reducing their risk for STI acquisition or transmission and increase their capacity to access STI testing, management, and treatment services.

This section outlines specific benchmarks for the provision of STI prevention information and the linking of youth to STI testing within school-based curricula.

Biggest threats and data

Source: Centres for Disease Control and Prevention. Antibiotic/Antimicrobial Resistance (AR/AMR). Biggest Threats and Data. *2019 AR Threats Report*. https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

CDC's *Antibiotic Resistance Threats in the United States*, 2019 (2019 AR Threats Report) includes the latest national death and infection estimates that underscore the continued threat of antibiotic resistance in the U.S.

According to the report, more than 2.8 million antibiotic-resistant infections occur in the U.S. each year, and more than 35,000 people die as a result. In addition, 223,900 cases of *Clostridioides difficile* occurred in 2017 and at least 12,800 people died.

Dedicated prevention and infection control efforts in the U.S. are working to reduce the number of infections and deaths caused by antibiotic-resistant germs, but the number of people facing antibiotic resistance is still too high. More action is needed to fully protect people.

CDC is concerned about rising resistant infections in the community, which can put more people at risk, make spread more difficult to identify and contain, and threaten the progress made to protect patients in healthcare. The emergence and spread of new forms of resistance remains a concern.

The report lists 18 antibiotic-resistant bacteria and fungi into three categories based on level of concern to human health—urgent, serious, and concerning—and highlights:

- Estimated infections and deaths since the 2013 report
- Aggressive actions taken
- Gaps slowing progress

The report also includes a Watch List with three threats that have not spread resistance widely in the U.S. but could become common without a continued aggressive approach.

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CANADA COMMUNICABLE DISEASE REPORT

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