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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 illustrate Canada's military public healthcare system in various environments. Illustrations by the Canadian Forces Combat Camera provided by the Directorate of Force Health Protection and adapted by Lyal Saikaly.

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CANADA COMMUNICABLE DISEASE REPORT

FORCE HEALTH PROTECTION

TABLE OF CONTENTS

COMMENTARY

Public health practice within Canada's military healthcare system

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As Canadians, we have so much to be thankful for although we may not always appreciate all the benefits we enjoy just by virtue of living in a country such as Canada. The relative peace, stability and security inherent in living in an Arctic nation bordered on three sides by oceans and on the fourth by a friendly global superpower translate into the requirement for only a modest military—at best—to protect Canada and its interests from foreign aggression. Still, even a modest military needs a healthcare system that can keep its personnel fit for their duties, with the capacity to address any public health issues that might threaten them, whether at home or abroad. What follows is a brief introduction to Canada's military public healthcare system with a focus on the preventive health practice that goes on—often behind the scenes—to maintain operational readiness of Canada's military by optimizing the individual health of its personnel in uniform.

The Canadian Armed Forces (CAF) are the unified armed services of Canada, consisting of sea, land and air elements more commonly known as the Royal Canadian Navy, the Canadian Army and the Royal Canadian Air Force (1). CAF personnel currently number approximately 101,500, including 71,500 full-time members in the Regular Force and 30,000 part-time members in the Reserve Force (1). CAF personnel are supported by an additional 25,000 civilian public service employees of the Department of National Defence (1).

Canada's *Constitution Act, 1867*, established the exclusive authority over matters related to Canada's "militia, military and naval service, and defence" to the federal government (2). This authority extends to healthcare services for CAF personnel who are specifically excluded from the definition of insured persons in the *Canada Health Act* (3). The Canadian Forces Health Services Group (CF H Svcs Gp), led by the Commander CF H Svcs Gp and Surgeon General, exists to fill this gap in the *Canada Health Act* by providing health services to CAF personnel across Canada as well as to those posted or deployed on military operations abroad. Generally speaking, CF H Svcs Gp provides for the comprehensive health care of CAF personnel comparable to that provided to all other Canadians by their provincial healthcare plans (4).

The CF H Svcs Gp is a pan-Canadian healthcare system with significant national and international responsibilities, employing approximately 6,100 health services personnel and with an annual budget of close to $471 M, excluding CAF personnel salaries. It works alongside non-governmental organizations and other health jurisdictions at the provincial and territorial level and other federal departments with health-related interests such as Health Canada and the Public Health Agency of Canada, as well as those with health systems of their own including Indigenous Services Canada and Correctional Services Canada. Finally, it works with its military allies as part of the North American Aerospace Defence Command (NORAD), the North Atlantic Treaty Organization (NATO) and the United Nations.

In terms of operational medicine, the CF H Svcs Gp must be capable of providing the "Canadian standard" of health care—including public health—to CAF members across the full spectrum of military operations; from humanitarian assistance and disaster relief, to peacekeeping, to combat. In a military context, public health is often referred to as "force health protection", which is defined by NATO as: "all medical efforts to promote or conserve physical and mental well-being, reduce or eliminate the incidence and impact of disease, injury and death and enhance operational readiness and combat effectiveness of the forces" (5).

The public health component of CF H Svcs Gp consists of multidisciplinary preventive medicine teams at the tactical (local) and operational (regional) levels supported by subject matter experts within a strategic level headquarters located in Ottawa known as the Directorate of Force Health Protection (DFHP).

The DFHP is made up of approximately 60 personnel in total, including military and civilian subject matter experts and support staff. Its role is to promote the health of CAF members as well as to prevent chronic diseases and injuries, infectious diseases, occupational and environmental diseases, and to prepare for and respond to public health emergencies that affect CAF. These functions form the basis for several national level programs within DFHP including an epidemiology capability, a health promotion program (also known as *Strengthening the Forces*), an occupational and environmental health program, deployable health hazard teams, a medical intelligence capability and, of course, a communicable disease control program—which serves as the main focus for this theme issue of the *Canada Communicable Disease Report*.

The DFHP maintains partnerships with public health organizations within the mainstream civilian Canadian healthcare system, including the Council of Chief Medical Officers of Health (part of the Pan-Canadian Public Health Network) as well as within the global community as part of the NATO Force Health Protection Working Group. Through its communicable disease control program, DFHP collaborates with local public health authorities and also lends its expertise to several highly respected consulting bodies including Canada's National Advisory Committee on Immunization, the Committee to Advise on Tropical Medicine and Travel and the NATO Medical Intelligence Expert Panel.

A robust public health system is as critical for Canada's soldiers, sailors and aviators as it is for all other Canadians. Failure of military leaders to implement appropriate force health protection measures for their troops is known to result in a decrease of operational readiness (6). History has repeatedly shown us that preventing the injuries and illnesses sustained by soldiers outside the heat of battle is critical to preserving military fighting power. Canadian military medical personnel involved in the Great War noted that: "The present war has proved most conclusively that the preventive and hygienic functions of the military medical service are of greater importance than the purely medical functions" (7).

It follows that, to ensure Canada remains strong at home, secure in North America and engaged in the world, it is important for its relatively small military to maintain an effective capability in public health (8). Please read on and enjoy learning more about how public health is currently being practiced within Canada's military healthcare system and contributing to CAF's mission successes at home and globally.

References

1. Government of Canada. National Defence Act (R.S.C. 1985, c. N-5) (modified 2019-10-01; accessed 2019-12-09). https://laws-lois.justice.gc.ca/eng/acts/N-5/FullText.html

2. Government of Canada. Constitution Act of 1867 (modified 2020-04-09; accessed 2019-12-09). https://laws-lois.justice.gc.ca/eng/Const/FullText.html

3. Government of Canada. Canada Health Act (R.S.C. 1985, c. C-6) (modified 2017-12-12; accessed 2019-12-09). https://laws-lois.justice.gc.ca/eng/acts/C-6/FullText.html

4. Government of Canada. About the CAF Spectrum of Care (modified 2019-01-15; accessed 2019-12-09). https://www.canada.ca/en/department-national-defence/services/benefits-military/pay-pension-benefits/benefits/medical-dental/information-management.html

5. North Atlantic Treaty Organization. NATO Standard AJMedP-4, Allied Joint Medical Force Health Protection Doctrine, Ed. A v. 1, July 2018, p 1-1. https://www.coemed.org/files/stanags/02_AJMEDP/AJMedP-4_EDA_V1_E_2561.pdf

6. Canadian Forces Joint Publication JP 4-10, Health Services Doctrine, Final Draft, March 2020, p 5-1. https://www.jcs.mil/Portals/36/Documents/Doctrine/pubs/jp4_10.pdf

7. Adami JG. War Story of the Canadian Army Medical Corps. Vol 1. The First Contingent (to the Autumn of 1915). Published for the Canadian War Records Office (accessed 2019-12-19). https://digital.library.upenn.edu/women/adami/camc/camc.html

8. Government of Canada. National Defence. Strong Secure Engaged: Canada's Defence Policy. DND: 2017 (accessed 2020-01-21). https://www.canada.ca/en/department-national-defence/corporate/reports-publications/canada-defence-policy.html

OUTBREAK REPORT

Three sequential outbreaks of Group A *Streptococcus* over a two-year period at the Canadian Forces Leadership and Recruit School, St. Jean Garrison, Québec

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Abstract

Background: Since December 2016, the basic military training (BMT) facility for the Canadian Armed Forces (CAF) has experienced repeated outbreaks of Group A *Streptococcus* (GAS). In 2018, a voluntary mass antibiotic prophylaxis (MAP) program was implemented to interrupt GAS transmission among recruits. The objective of this study was to describe the epidemiology of three GAS outbreaks and a period of increased pharyngitis infections at the CAF BMT facility in Québec over a two-year span, and to detail the prevention and control measures implemented to mitigate the risk to recruit health.

Methods: Descriptive data were collected on invasive and severe GAS cases along with laboratory data including genotyping of throat swabs from recruits presenting with pharyngitis. A laboratory-based acute respiratory infection surveillance system was used to aid in monitoring and decision-making. Close contacts of recruits were assessed for asymptomatic GAS carriage and MAP adverse events surveillance was conducted.

Results: Three distinct GAS outbreaks occurred at the Canadian Forces Leadership and Recruit School totaling eight invasive (iGAS) and 13 severe (sGAS) cases over two years. All iGAS/sGAS cases, apart from one instructor, were among recruits. The predominant strain in all three outbreaks was type *emm6.4*. A total of 11,293 recruits received MAP (penicillin G benzathine or azithromycin) between March 7, 2018 and November 18, 2019. There were eight reported serious adverse events related to penicillin administration.

Conclusion: The CAF BMT facility experienced three GAS outbreaks over the course of two years, and despite the use of enhanced hygiene measures, only MAP has been effective in quelling these outbreaks.

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Keywords: infectious disease outbreaks, military recruits, Canada, *Streptococcus pyogenes*, mass antibiotic prophylaxis

Background

Streptococcus pyogenes (*S. pyogenes*) or Group A *Streptococcus* (GAS) is a Gram-positive bacterium that manifests in various illnesses ranging from mild non-invasive diseases, such as acute pharyngitis, tonsillitis and impetigo, to severe invasive diseases, such as bacteremia, pneumonia, necrotizing fasciitis and streptococcal toxic shock syndrome. Although mild pharyngeal infections are readily treatable with appropriate antibiotics, invasive disease is associated with substantial morbidity and mortality. Characterization of GAS strains is done through molecular sequencing of the *emm* gene encoding the

M protein; a predominant virulence surface protein. Although there are currently over 240 *emm* types, a relatively small number of types cause the majority of disease (1).

The incidence of invasive Group A *Streptococcus* (iGAS) has been increasing in Canada over the past decade (2) and a number of provinces, including Québec and Ontario, have experienced multiple GAS outbreaks since 2016 (3–5). Long term care facilities, homeless shelters and marginalized persons, such as those who use drugs, have been particularly affected (*emm* types 118, 81, 74 and 9) (3–5).

The United States (US) military experienced recurrent outbreaks of iGAS dating back to the 1940s in their recruit population (6). Despite efforts by the US military to prevent GAS transmission, through hand hygiene, cough etiquette, head-to-toe sleeping arrangements and reduction of crowding when possible, outbreaks continued among recruits (7). It was only through the administration of prophylactic antibiotics first initiated during the mid-1950s that infections and related sequelae were reduced (7). These early studies also found that administration of 1.2 million units of intramuscular penicillin G benzathine (PGB) was more effective than oral penicillin and compliance was considerably higher (8). As well, when mass prophylaxis was discontinued, GAS-related outbreaks recurred among many recruit installations, underscoring the effectiveness of PGB and azithromycin in preventing GAS-related outbreaks in this population (9,10). The Canadian Armed Forces (CAF) experienced their first iGAS outbreak among their recruit population in December 2016. In this article, we describe three successive GAS outbreaks and one notable increase in non-invasive GAS infections at the Canadian Forces Leadership and Recruit School (CFLRS), the basic military training (BMT) facility for the CAF at St. Jean Garrison, Québec (**Appendix A**) and assess the impact of mass antibiotic prophylaxis (MAP).

Methods

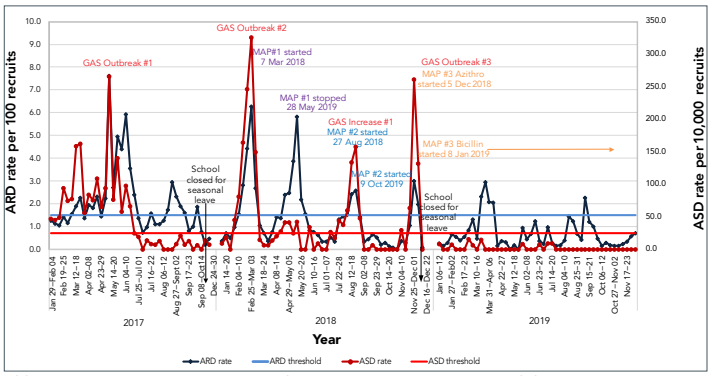
All investigations of GAS infections at CFLRS were approved under the authority of the CAF Surgeon General. Descriptive statistics were used to characterize the outbreaks and national case definitions were used to define confirmed and probable iGAS cases (11). Case definitions for confirmed and probable severe non-invasive GAS cases were also developed (**Appendix B**).

Laboratory data

Throat swabs were taken from symptomatic recruits based on a McIsaac score (12) of at least two, and a subset of positive throat swabs from each outbreak were sent for molecular typing and genomic sequencing. *Emm* typing was performed by polymerase chain reaction and deoxyribonucleic acid sequencing using the Centre for Disease Control *emm* database (13).

Genomic analyses were performed as previously described (14). A laboratory-based acute respiratory infection surveillance program, based on a US military surveillance system (15), was implemented using throat swab results to monitor acute respiratory disease (ARD) trends. The threshold level for action consisted of two metrics: 1) the ARD rate, defined as the weekly number of GAS throat swabs collected divided by the weekly recruit population; and 2) the acute streptococcal disease (ASD) rate, defined as the weekly number of positive GAS throat swabs divided by the weekly recruit population. Thresholds to flag evolving outbreaks were set at an ARD rate of at least 1.5 per 100 recruits or an ASD rate of at least 0.25 per 100 recruits for two consecutive weeks (**Figure 1**) (15).

Figure 1: Weekly acute respiratory disease rate and acute streptococcal disease rate, Canadian Forces Leadership and Recruit School, 2017–2019



Abbreviations: ARD, acute respiratory disease; ASD, acute streptococcal disease; GAS, Group A Streptococcus; MAP, mass antibiotic prophylaxis

Mass antibiotic prophylaxis (penicillin G benzathine and azithromycin)

Numbers and percentages were used to monitor coverage and refusal rates of MAP among recruits and instructors, and any associated adverse events.

Group A *Streptococcus* pharyngeal carriage study

To look for asymptomatic GAS pharyngeal carriers (*emm6.4*), a GAS carriage study among instructors in close contact with recruits was conducted during the first outbreak and in October of 2018 following the second outbreak. For the latter, instructors who had close contact with recruits and were present during both the 2017 and 2018 GAS outbreaks were included. Instructors provided informed consent to a throat swab on a voluntary basis. Close contact was defined according to the iGAS household contact criteria of either spending at least four hours per day on average in a week, or a total of 20 hours per week with recruits.

Results

Outbreak 1

The details of the first GAS outbreak at CFLRS have been previously described (14). Between December 2016 and April 2017, four iGAS cases (three cases [two confirmed and one probable] of pneumonia with empyema and one confirmed case of necrotizing fasciitis) and six non-invasive severe GAS cases (four severe pharyngitis and/or sinusitis and two pneumonias) occurred among recruits and one instructor. Positive GAS throat cultures among recruits had increased substantially beginning in November of 2016. Of the 120 cultures sequenced, 80% were *emm6.4*, which were highly related as per phylogenetic cluster analysis. The majority of GAS-positive cultures were from young (mean age 24 years) male (69.4%) recruits (89.5%), reflecting the population demographics of CFLRS. All 31 instructors (40% of instructors who had contact with a confirmed or probable case) who presented for screening had a negative GAS culture. Standard control measures were implemented during this outbreak and some are still in place (**Table 1**).

Outbreak 2

The second GAS outbreak at CFLRS occurred February 11 to March 11, 2018 with two iGAS cases (one confirmed necrotizing fasciitis, one probable meningitis) and four severe non-invasive cases (one cellulitis, three pneumonias) among recruits. Of the six invasive and severe GAS cases, four were male and two were female (age range 18–45 years). The average number of days from arrival to symptom onset was 38 days (range 14–58 days). During the one month period, 84 (69%) of 122 positive GAS throat swabs were *emm6.4*. The average age of recruits with a positive GAS swab was 24 years (range 18–49 years). Close contacts (all recruits within a platoon) of invasive and severe cases received postexposure prophylaxis according to the Public Health Agency of Canada Guidelines (6).

Given type *emm6.4* persisted, close contacts (mainly instructors) of recruits were asked to undergo voluntary screening by the Base Surgeon (the physician responsible for health care for the St. Jean Garrison) without any reprisal for asymptomatic GAS carriage for the second time. A total of 207 instructors were eligible for screening. At the time of screening, one instructor was symptomatic and 39 others were posted off base, leaving 167 instructors. After seven days of collection, 115 (69%) of 167 throat swabs from instructors were submitted for culture. Seven (6%) of 115 swabs were GAS positive; three of these were type *emm6.4*. Of the three positive *emm6.4* cultures, one instructor refused eradication treatment, another instructor received eradication treatment but had no post-treatment swab to assess carriage status and one instructor was successfully treated as evidenced by a negative GAS throat swab post treatment.

Table 1: Infection control measures implemented during each outbreak at the Canadian Forces Leadership and Recruit School, 2017–2019

Measures implemented	Outbreak 1	Outbreak 2	Outbreak 3
Enhanced hand hygiene and cough etiquette and symptom recognition with augmented prevention signage. Briefing of recruits moved to the first week from week 4	✓	✓	✓
Accessible hand sanitizer at all entrances and throughout the main residence	✓	✓	✓
Prophylaxis of close contacts (platoon members) of invasive cases	✓	✓	✓
Isolation during the first 24 hours of antibiotic treatment	✓	✓	✓
Directly observed hand washing prior to meals	✓	✓	✓
Asymptomatic GAS carriage screening of staff	✓	✓	-
Emphasis placed on reporting to the medical clinic early when symptomatic	✓	✓	✓
Social distancing where possible, maintaining a two-metre distance when speaking in a raised voice	✓	✓	✓
Permission to "break rank" when standing at attention to "cover a cough"	✓	✓	✓
No sharing of personal products (e.g. canteens)	✓	✓	✓
Increase influenza immunizations to prevent future outbreaks	-	-	✓
Reinforcement of need for antibiotic compliance among recruits	✓	✓	✓
Town halls to emphasize control measures needed	-	✓	-
Triaging using a modified McIsaac scoring system with a lower threshold to swab and to treat on spec during an outbreak	-	✓	✓
Enhanced daily cleaning by recruits from once a day to two to three times a day	-	✓	✓
MAP to recruits and instructors (penicillin G benzathine and azithromycin)	-	✓	-
MAP to recruits only (penicillin G benzathine and azithromycin)	-	-	✓

Abbreviations: GAS, Group A *Streptococcus*; MAP, mass antibiotic prophylaxis; ✓,done; -, not done

With a second GAS outbreak occurring in just over a year following the initial outbreak, and with a rising number of pharyngitis cases despite standard control measures, a voluntary MAP program was launched for the first time in CAF in an effort to stop continued GAS transmission. All recruits and instructors received a group briefing from a physician detailing the increased risk of contracting GAS at CFLRS, the modes of transmission and the applicable preventive measures, including MAP. A physician then met with each recruit/instructor individually in a private area to answer questions, review the consent form prior to signing and elicit information about any possible allergies. Refusals remained private between the physician and the recruit/instructor, without reprisal from their chain of command. Current recruits and instructors were offered 1.2 million units of PGB intramuscular. In the case of PGB refusal or penicillin allergic individuals, 500 mg of azithromycin orally once weekly for four consecutive weeks was offered. In addition, given the dynamic rotation of the recruit population, all incoming recruits were offered MAP within two to three days of arrival. From March 7 to May 28, 2018, 2,507 recruits and 200 instructors received MAP (**Table 2**). A precipitous drop in GAS pharyngitis was noted with no new iGAS/severe GAS (sGAS) cases occurring after March 10, 2018 (Figure 1). Six serious adverse events related to MAP administration included the following: one compartment syndrome with rhabdomyolysis and subsequent acute kidney injury; one hematoma at the injection site; one excess vomiting; one cellulitis; and two anaphylactic reactions. Other side effects included vasovagal episodes and pain at the injection site requiring medical attention.

Table 2: Mass antibiotic prophylaxis administration and adverse events by outbreak at the Canadian Forces Leadership and Recruit School, 2018–2019

MAP administration details	Adverse events				
	Outbreak 1	Outbreak 2	Increase in pharyngitis	Outbreak 3	MAP 2019
Outbreak duration	December 2016 to May 2017	February 11 to March 11, 2018	July 29 to August 26, 2018	November 18 to December 9, 2018	N/A
MAP administration period	MAP not used	March 7 to May 28, 2018	August 27 to October 9, 2018	December 5 to 7, 2018	January 8 to November 18, 2019[a]
MAP target	MAP not used	Recruits and instructors	Recruits only	Recruits only	Recruits only
Penicillin G benzathine doses administered					
Recruits (n)	N/A	2,226	1,411	13	5,629
Instructors (n)	N/A	172	N/A	N/A	N/A
Azithromycin prescribed					
Recruits (n)	N/A	281	252	645	836
Instructors (n)	N/A	28	N/A	N/A	N/A
Refusal number					
Recruits (n)	N/A	27	81	46	141
Instructors (n)	N/A	15	N/A	N/A	N/A
Coverage					
Recruits (%)	N/A	99.0	95.4	93.5	96.9
Instructors (%)	N/A	93.0	N/A	N/A	N/A

Abbreviations: MAP, mass antibiotic prophylaxis; N/A, not applicable
[a] MAP is ongoing

Pharyngitis increase of concern

In August 2018, an increase in pharyngitis cases recurred at CFLRS. Despite re-emphasizing previously implemented control measures (Table 1), the ARD and ASD indices continued to rise and the number of GAS-positive swabs increased to 56.7% (n=17/30) from August 12 to 18, 2018. Voluntary MAP was once again offered to all 1,663 current and incoming recruits from August 27 to October 9, 2018. Of the 1,411 recruits that received PGB, 31 (2.2%) recruits experienced lightheadedness, five (0.35%) recruits had a vasovagal response, two (0.14%) recruits had nausea and two (0.14%) recruits reported paresthesia/pain in the lower extremity. The genotyping of GAS isolates from recruits during this period of increased pharyngitis indicated *emm6.4* (52 of 54 isolates).

Outbreak 3

Just short of two months from the last MAP session, the ARD indices increased above set thresholds for two consecutive weeks at the end of November 2018. During a two-week period, 79.7% (n=47/59) of throat swabs were GAS-positive. On December 2, 2018, a recruit was hospitalized for pneumonia and a GAS-positive pulmonary empyema; in addition, three severe non-invasive GAS infections were reported. Genotyping of all recruit throat cultures for the week of December 2 to 8, 2018 (n=13) were *emm6.4*, including the iGAS and sGAS cases. Given the impending closure of the school for holidays from December 12 to January 7, 2019, and the logistics involved in being able to administer PGB, 500 mg azithromycin orally once weekly for two weeks was prescribed to 645 recruits (Table 2).

With three GAS outbreaks within a two-year period among recruits at CFLRS, in addition to the increase in GAS pharyngitis infections in August 2018, a decision was made in consultation with local and provincial public health authorities to administer MAP to recruits on a continuous basis. Adverse/side effects have remained low (**Table 3**) and there have been no prophylaxis failures. All breakthrough GAS pharyngitis cases had either not received MAP (i.e. refused) or had received MAP well beyond the period of effectiveness (more than four weeks). For 2019, there were only 11 GAS-positive throat cultures among recruits for the first half of the year and there have been no GAS-positive throat swabs since the third week of July 2019.

Phylogenetic analysis of Group A *Streptococcus*-positive isolates

A phylogenetic tree of GAS *emm6.4* isolates (**Figure 2**) collected from across Canada from January 2012 to January 2020 (n=403) consists of three major lineages of strains and an overall average

Table 3: Mass antibiotic prophylaxis adverse/side effects in recruits who sought medical attention at the health services clinic, Canadian Forces Leadership and Recruit School, January 8–November 18, 2019

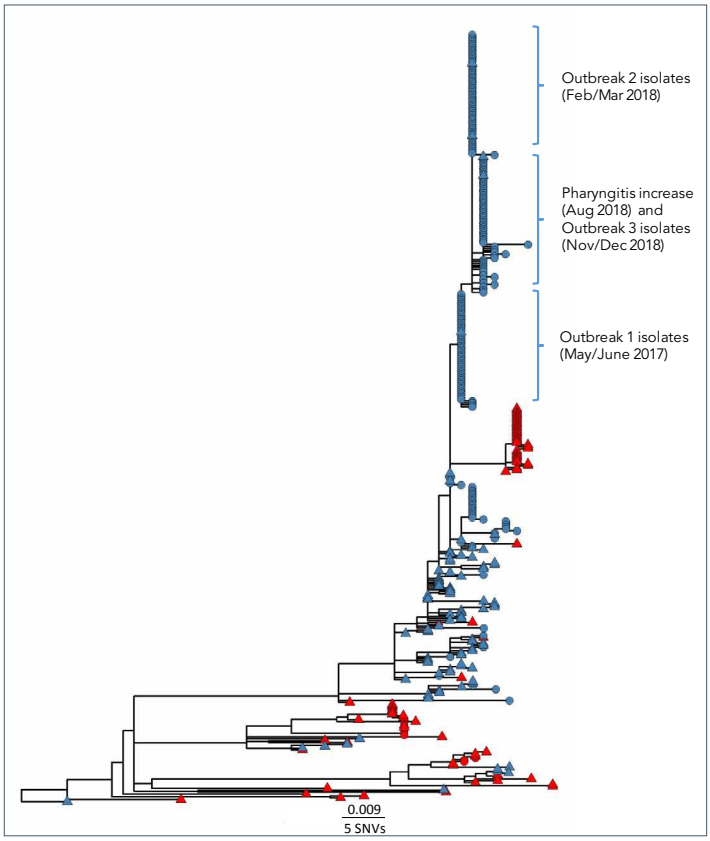
Mass antibiotic prophylaxis adverse/side effects	Total penicillin G benzathine doses N=5,629	
	n	%
Vasovagal response	69	1.2
Lightheadedness	4	<0.01
Rash	4	<0.01
Anaphylaxis-like reaction	2	<0.01
Numbness in leg	2	<0.01
Pain at injection site	2	<0.01
Anxiety	1	<0.01

genetic difference of 18 single nucleotide variations (SNVs) and maximum distance of 71 SNVs. The largest lineage consists predominantly of isolates from these outbreaks in Québec with older sporadic isolates generally located in the lower subclades, while the three more recent outbreak-related clades appear distantly in the upper portion of the tree. Within the major Québec lineage the isolates of the three military outbreak-related clades are closely related to the sporadic background strains; differing by an average of six SNVs (range 1–16 SNVs). Isolates associated with the original outbreak during May to June 2017 differed from isolates of outbreak 2 of February to March 2018 by one SNV; which in turn differed from isolates from the August 2018 pharyngitis increase plus outbreak 3 by 1–2 SNVs. All *emm6.4* isolates were multi-locus sequence type (MLST) ST-382 and possessed a S79A amino acid substitution in *parC* associated with fluoroquinolone resistance, and three isolates from August 2018 also contained *mefAE* associated with macrolide resistance. The superantigen toxin profile of the background sporadic and outbreak 1 strains included SpeA-C-G-H-I-K-SmeZ, whereas the strains of the later outbreaks 2 and 3 lacked the SpeH and SpeI toxins.

Discussion

Between December 2016 and December 2018, CFLRS experienced three consecutive GAS outbreaks and one period of increased pharyngitis infections among recruits; all associated with type *emm6.4*. The outbreaks at CFLRS were unprecedented given no previous documented outbreaks in CAF recruit population. The commonly used non-pharmaceutical interventions were ineffective in preventing GAS transmission among recruits. It was only through implementation of MAP (PGB/azithromycin) with a corresponding high compliance rate that the outbreaks were quickly brought under control.

Figure 2: Maximum likelihood core single nucleotide variant phylogenetic tree of *S. pyogenes emm6.4* isolates[a] collected in Canada, January 2012–January 2020 (n=403)



Abbreviation: SNV, single nucleotide variant

[a] A total of 529 sites were used in the phylogeny using 62% of the core genome. The scale bar represents the estimated evolutionary divergence between isolates based on the average genetic distance between strains (estimated number of sites of the isolate/total number of high quality single nucleotide variants). An internal isolate (sample number SC20-0734-A) was used as the mapping reference and the oldest outlying isolate (SC12-0215-A) was used as a root. Tip node colours represent isolates collected in Québec (blue) or other Canadian provinces (red), and tip node shapes represent non-invasive (circles) or invasive (triangles) Group A streptococcal infections

Elevated rates of streptococcal infections and GAS outbreaks at US military recruit training centres have been documented since the 1940s and continue into the 21st century (15,16). The reason for the first GAS outbreak in CAF in 2016, and the successive outbreaks, is unknown. No factors that would increase the risk of transmission, such as a substantial increase in the recruit population, change in accommodations or training, or standard hygiene measures were observed. As well, the recruit population consists largely of young, healthy individuals. The introduction of a virulent strain as the cause of the outbreaks is possible since *emm6.4* is a relatively rare GAS type in Canada compared with other *emm* types and immunity is likely low. Isolation of streptococcal *emm6* accounted for only 1.9% of all invasive streptococcal *emm* types in Canada in 2017 (2). The introduction of a virulent strain, combined with risk factors favouring respiratory infection transmission (close contact during training, shared living accommodations, limited hours of sleep),

in addition to the physical and psychological impact of basic training and hygiene practices, might have set up the perfect milieu for continued transmission.

Another hypothesis for the introduction of GAS *emm6.4* was the possibility of an asymptomatic carrier. Since there is a constant rotation of new recruits coming into CFLRS and the predominant *emm* type persisted throughout the outbreaks, instructors who had close contact with recruits could be considered as a potential source. The strain of *emm6.4* associated with the military outbreaks, while closely related to other GAS circulating in the local civilian population, was phylogenetically distinct from the sporadic background strains. Isolates of each successive outbreak differed by one SNV for an overall change of about two SNVs over the duration of the three outbreaks from May 2017 to August 2018, consistent with previously reported genetic drift estimates of about 1.7 SNVs per genome per year (17).

Pharyngeal GAS carriage among staff has been known to propagate outbreaks in hospitals and long term care facilities (16,18,19). Instructors were targeted twice, on a voluntary basis, to assess GAS carriage status; however, only 40% of instructors who had contact with one or more invasive cases presented for screening in the first assessment and only two-thirds of all instructors participated after the second outbreak. Although three instructors were positive for *emm6.4* during the second assessment, only one instructor successfully underwent eradication treatment. Without a near census of the carriage status of instructors, the contribution of asymptomatic GAS carriage to the continued transmission of GAS among recruits cannot be ruled out.

Numerous prevention and control measures were implemented and enhanced during each successive outbreak (Table 1). Despite these measures, outbreaks of GAS and increased rates of pharyngitis continued at CFLRS. The reluctance of recruits to seek care early due to the ramifications on course completion was identified during the first outbreak and likely played a role in perpetuating the outbreaks.

In the US military, chemoprophylaxis was trialed during the 1950s and PGB was effective in reducing the incidence of streptococcal disease with only 0.86% of naval recruits having an adverse reaction (20). The PGB has been administered using various schedules (year round, seasonally and single versus tandem dose) depending on the recruit training centre in the US (7). Similarly, it was only through the administration of MAP that there was any precipitous and sustained fall in the ASD rate at CFLRS. The third GAS outbreak prompted the implementation of MAP year round. Although MAP is not without risk of significant adverse events, including anaphylaxis, the benefits were deemed to outweigh the risks. In addition, the development of antibiotic resistance with the use of a macrolide for penicillin allergic recruits was not regarded as a contraindication to its use since the total number of recruits going through basic training and receiving a macrolide for MAP was considered small compared to its use in the general Canadian population. Similar to our US counterparts, MAP has been well tolerated with very few side effects and has had little impact on successfully completing recruit training (*Lu D, Strauss B, Simkus K, Tepper M, Gagnon F, Johnson N; unpublished results*). Webber *et al*. noted in reviewing MAP use in US military training facilities that no case of anaphylaxis had been reported since active surveillance started in 1998 (7).

The ability to administer PGB to a large cohort of recruits had its challenges. Securing the required PGB doses and securing additional qualified healthcare workers to administer PGB took time to coordinate. As well, logistical issues such as space for the recruit briefing, space for the consent process and space for the administration of PGB to maintain privacy, as well as appropriate resuscitation equipment on site, was required. The start-up of each round of MAP was logistically difficult since all recruits (current and incoming) required MAP, compared with routine/ongoing MAP administration for which the necessary preparation was already in place and only incoming recruits required prophylaxis.

Acute Respiratory Infection Surveillance Program

The Acute Respiratory Infection Surveillance Program was implemented after the first outbreak to monitor for future respiratory outbreaks using thresholds defined by the US military. The ARD and ASD thresholds were effective at indicating increased GAS circulation and an impending outbreak; however, we were unable to prevent iGAS and sGAS cases among recruits in two of the outbreaks. Current thresholds should be reevaluated since only recruits who meet the McIsaac score of 2–5 are swabbed for GAS compared to 80% of US recruits (15).

Strengths and limitations

This paper describes the first time administration of MAP in a large cohort of healthy adults that resulted in high compliance, few side effects, and a reduction of GAS pharyngitis.

Recruits represent a unique population and results from the administration of MAP in terms of acceptance and compliance and the logistical capability to administer antibiotics to a large number of individuals may not be generalizable to other populations. Only MAP adverse/side effects that required medical attention were captured; therefore, underreporting of mild side effects is likely. In addition, the contribution of co-infections with other circulating viruses was not evaluated. Furthermore, the low voluntary participation of instructors to determine the GAS carriage rate meant that the contribution of a carrier to these outbreaks could not be ruled out. Lastly, adherence to control measures was not evaluated.

Conclusion

Outbreaks of GAS can have severe consequences—including death. For the first time, CFLRS experienced three outbreaks and one period of elevated numbers of GAS pharyngitis infections in recruits over a two-year period—all linked to type *emm6.4*. Despite enhanced hygiene measures, only MAP was effective in interrupting the transmission of GAS in the recruit population.

Authors' statement

BS, MT, DL, FG, EG and KB were involved in the methodology, outbreak investigation and public health management
MM managed the laboratory collection and reporting at the local level
WD and IM managed the genomic sequencing of the isolates, produced the phylogenetic tree, and related interpretation considering the clinical data
BS summarized the data and wrote the first draft
All authors contributed to the review and revisions of the manuscript

Competing interests

None.

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References

1. Heymann DL. Streptococcal diseases. In Control of Communicable Diseases Manual, 20th ed., pp 581-589. Washington (DC): America Public Health Association, 2015.

2. Public Health Agency of Canada. National Laboratory Surveillance of Invasive Streptococcal Disease in Canada – Annual Summary 2017. Ottawa (ON): PHAC; 2019 (accessed 2020-02-15). https://www.canada.ca/en/public-health/services/publications/drugs-health-products/national-laboratory-surveillance-invasive-streptococcal-disease-annual-summary-2017.html

3. Pilon PA, Savard N, Aho J, Caron J, Urbanek A, Paré R, Le Guerrier P, Savard C, Hammond-Collins K, Tran CD, Allard R, Domingo MC. Invasive group A streptococcal infection outbreaks of typeemm118 in a long-term care facility, and of type emm74 in the homeless population, Montréal, Quebec. Can Commun Dis Rep 2019;45(1):26–31. DOI PubMed

4. Dickson C, Pham MT, Nguyen V, Brubacher C, Silverman MS, Khaled K, Hovhannisyan G. Community outbreak of invasive group A streptococcus infection in Ontario, Canada. Can Commun Dis Rep 2018;44(7/8):182–8. DOI PubMed

5. Teatero S, McGeer A, Tyrrell GJ, Hoang L, Smadi H, Domingo MC, Levett PN, Finkelstein M, Dewar K, Plevneshi A, Athey TB, Gubbay JB, Mulvey MR, Martin I, Demczuk W, Fittipaldi N. Canada-wide epidemic of emm74 Group A Streptococcus invasive disease. Open Forum Infect Dis 2018;5(5):ofy085. DOI PubMed

6. Dingle JH, Theordore J, Badger G, Beard JW, Cresy NL, Feller AE, Gordon I, Langmuir AD, Rammelkamp CH, Strauss E, Talleck H. (Commission on Acute Respiratory Diseases). Acute respiratory disease among new recruits. Am J Public Health Nations Health 1946;36(5):439–50. DOI PubMed

7. Webber BJ, Kieffer JW, White BK, Hawksworth AW, Graf PC, Yun HC. Chemoprophylaxis against group A streptococcus during military training. Prev Med 2019;118:142–9. DOI PubMed

8. Thomas RJ, Conwill DE, Morton DE, Brooks TJ, Holmes CK, Mahaffey WB. Penicillin prophylaxis for streptococcal infections in United States Navy and Marine Corps recruit camps, 1951-1985. Rev Infect Dis 1988;10(1):125–30. DOI PubMed

9. Sanchez JL, Cooper MJ, Myers CA, Cummings JF, Vest KG, Russell KL, Sanchez JL, Hiser MJ, Gaydos CA. Respiratory infections in the U.S. military: recent experience and control. Clin Microbiol Rev 2015;28(3):743–800. DOI PubMed

10. Gray GC, McPhate DC, Leinonen M, Cassell GH, Deperalta EP, Putnam SD, Karcher JA, Sawyer MH, Laurila A, Connor JD. Weekly oral azithromycin as prophylaxis for agents causing acute respiratory disease. Clin Infect Dis 1998;26(1):103–10. DOI PubMed

11. Public Health Agency of Canada. Supplement: Guidelines for the prevention and control of invasive group A streptococcal disease. https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2006-32/canada-communicable-disease-report.html

12. Fine AM, Nizet V, Mandl KD. Large-scale validation of the Centor and McIsaac scores to predict group A streptococcal pharyngitis. Arch Intern Med 2012 Jun;172(11):847–52. DOI PubMed

13. Centers for Disease Control and Prevention. Streptococcus Laboratory: Protocol for emm typing. Atlanta (GA): CDC; 2018 (accessed 2020-03-06). https://www.cdc.gov/streplab/groupa-strep/emm-typing-protocol.html

14. Hammond-Collins K, Strauss B, Barnes K, Demczuk W, Domingo MC, Lamontagne MC, Lu D, Martin I, Tepper M. Group A streptococcus outbreak in a Canadian Armed Forces training facility. Mil Med 2019;184(3-4):e197–204. DOI PubMed

15. Lee SE, Eick A, Ciminera P. Respiratory disease in Army recruits: surveillance program overview, 1995-2006. Am J Prev Med 2008;34(5):389–95. DOI PubMed

16. Smith A, Li A, Tolomeo O, Tyrrell GJ, Jamieson F, Fisman D. Mass antibiotic treatment for group A streptococcus outbreaks in two long-term care facilities. Emerg Infect Dis 2003;9(10):1260–5. DOI PubMed

17. Dickinson H, Reacher M, Nazareth B, Eagle H, Fowler D, Underwood A, Chand M, Chalker V, Coelho J, Daniel R, Kapatai G, Al-Shabib A, Puleston R. Whole-genome sequencing in the investigation of recurrent invasive group A streptococcus outbreaks in a maternity unit. J. Hosp. Infect. 2019;101(3):320–6. DOI

18. Mahida N, Prescott K, Yates C, Spencer F, Weston V, Boswell T. Outbreak of invasive group A streptococcus: investigations using agar settle plates detect perineal shedding from a healthcare worker. J Hosp Infect 2018;100(4):e209–15. DOI PubMed

19. Inkster T, Wright P, Kane H, Paterson E, Dodd S, Slorach J. Successive outbreaks of Group A Streptococcus (GAS) in care of the elderly settings; lessons learned. J Infect Prev 2012;13(2):38–43. DOI

20. Brooks TJ Jr, Moe TI. Use of benzathine penicillin G in carriers of group a beta-hemolytic streptococci. J Am Med Assoc 1956;160(3):162–5. DOI PubMed

Appendix A: Background—Canadian Forces Leadership and Recruit School

The Canadian Forces Leadership and Recruit School (CFLRS), located in St-Jean-Sur-Richelieu, Québec (Canada) is the only facility offering basic military training for all members of the Canadian Armed Forces Regular Force component. More than 5,000 recruits cycle through CFLRS each year. Recruits are housed in a self-contained dormitory style residence within either an individual open cubicle-like space with dividers or in a small single room with shared common spaces for their 10 or 12 week basic training session. The school also has classrooms, a gymnasium and a cafeteria; all housed within the same complex. Recruits are grouped into platoons of approximately 60, and spend the majority of their days in close proximity to one another within their platoon. There is also mixing between platoons in common areas and during certain training sessions. Recruits remain on base at all times for the first five weeks. All primary care is provided by the base medical clinic, which is located in close proximity to the school. When the base medical clinic is closed, civilian health care facilities are used.

Appendix B: Case definition for confirmed and probable severe non-invasive Group A *Streptococcus*

- Confirmed, severe non-invasive Group A *Streptococcus* (GAS) case:
  An individual at the Canadian Forces Leadership and Recruit School (CFLRS) with a laboratory confirmed GAS infection isolated from a non-sterile site requiring an overnight hospitalization since December 2016.

- Probable, severe non-invasive GAS case:
  An individual at CFLRS who had symptoms compatible with a non-invasive GAS infection requiring overnight hospitalization, but lacking laboratory confirmation of GAS infection, since December 2016.

Adverse events following mass antibiotic prophylaxis during a Group A *Streptococcus* outbreak in the Canadian Forces Leadership and Recruit School

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Abstract

Background: Between December 2016 and March 2018, two outbreaks of Group A *Streptococcus* (GAS) infection occurred at the Canadian Forces Leadership and Recruit School. A voluntary mass antibiotic prophylaxis (MAP) program was implemented in March 2018, to interrupt an ongoing GAS outbreak, and to prevent future outbreaks.

Methods: Instructors and recruits were offered a one-time intramuscular injection of 1.2 million units penicillin G benzathine (PGB). Individuals with a penicillin allergy were offered azithromycin; 500 mg orally once weekly for four consecutive weeks. Instructors and recruits were also asked to complete a voluntary and anonymous survey one week after receipt of MAP, to detect MAP-related adverse events.

Results: MAP was offered to 2,749 individuals; 2,707 of whom agreed to receive it (98.5% uptake). The majority of personnel experienced adverse events in the days following MAP; 92.3% of personnel who received PGB reported localized pain at the injection site, and 70.2% of personnel who received azithromycin reported gastrointestinal symptoms. However, only five cases of serious adverse events were reported, and less than 1% of recruits could not complete their basic military training course because of MAP-related adverse events.

Conclusion: The MAP program implemented in March 2018 was the first of its kind in the Canadian Armed Forces, and the largest single use of PGB in a defined group in Canada. It resulted in very few serious adverse events and with minimal impact on military recruits' successful completion of recruit training.

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Introduction

Group A *Streptococcus* (GAS) is a beta-hemolytic Gram-positive bacteria that causes infections that typically present as pharyngitis or tonsillitis (1,2). However, it can cause serious disease in otherwise healthy adults. Outbreaks of invasive GAS (iGAS) in the United States (US) military recruit populations have been documented dating back to the 1940s (3). Risk factors associated with iGAS in military environments include close sleeping quarters, training under stressful conditions and close contact exposure (2–7). Mass antibiotic prophylaxis (MAP) has previously been used to effectively reduce GAS illness in US military training centres (3,8–14). The two antibiotics that are used in MAP are intramuscular penicillin G benzathine (PGB) and oral azithromycin. Commonly reported adverse events in adults for injected PGB include local injection site reactions including pain, rash, joint disorder and dizziness (15). The most commonly reported adverse events in adults following oral

azithromycin administration were diarrhea/loose stools (4%–5%), nausea (3%–4%), abdominal pain (2%–3%) and vomiting (1%) (16). However, the impact of adverse events following MAP administration to US military recruits has not been published.

The Canadian Forces Leadership and Recruit School (CFLRS) is the basic military training (BMT) facility for the Canadian Armed Forces (CAF). Each year, CFLRS provides BMT to approximately 4,400 CAF recruits, in a facility housing up to 1,500 recruits at a time (*Maj E. Girard, personal communication, March 29, 2019*). The training is an intense structured ten to twelve-week program and any lapses in training may contribute to a military recruit failing or having to retake the course. Between December 2016 and March 2018, there were two GAS outbreaks of the laboratory confirmed strain *emm6.4* (17).

Because of these two GAS outbreaks occurring within a ten-month period, Canadian Forces Health Services, in consultation with the regional and provincial civilian public health agencies, decided to implement a voluntary MAP program with the objective of interrupting the outbreak and preventing future spread of GAS among military personnel at CFLRS. This marked the first time a MAP program for a GAS outbreak had ever been implemented in CAF. Given the potential adverse events of the antibiotics used for MAP, a lack of published literature examining its effects on military recruits, and the deleterious impact that this might have on a recruit's ability to successfully complete BMT, the present study examines the short-term adverse outcomes experienced by recruits in CAF and their impact on BMT, as a result of MAP.

Methods

A voluntary MAP program was implemented between March 7, 2018 and May 28, 2018 at the CFLRS, located in Saint-Jean-sur-Richelieu, Québec (Canada). Recruits and instructors were offered a one-time intramuscular injection of 1.2 million units of PGB. PGB was administered intramuscularly into the vastus lateralis for personnel treated March 7–April 22, 2018. Because of a revision of the product monograph, PGB was administered into the dorsogluteal site for personnel treated April 23–May 28, 2018. Individuals reporting a penicillin allergy or refusing PBG were offered azithromycin 500 mg orally once weekly for four consecutive weeks. Recruits and instructors were provided with drug information sheets, available in both official languages (French and English).

A voluntary and anonymous paper-based survey was developed to conduct surveillance of adverse events following MAP. The survey was available in both official languages and consisted of 14 non-demographic questions (**Supplemental 1**). The survey was offered one week after the administration of PGB, or one week after the first oral dose of azithromycin. Survey respondents were asked to self-report the type of antibiotic received, whether they experienced any of the common side effects listed on the antibiotics' respective product monographs, and whether these side effects limited their participation in BMT. Completed surveys were returned to the Directorate Force Health Protection by internal mail. Data were manually entered into an Access database, and a random 10% sample of surveys (n=145) were reentered to ensure accurate data entry by multiple personnel. In addition, passive surveillance using a line listing formatted spreadsheet was developed for local clinicians to provide information on personnel who were assessed for severe or unusual adverse events following MAP.

Results

From March 7 to May 28, 2018, MAP was offered to 2,534 recruits and 215 instructors (**Table 1**). Overall, it was administered to 2,707 CAF personnel (98.5% uptake). Of the 2,707 individuals who were administered MAP, 2,398 (88.6%) received PGB and the other 309 (11.2%) received azithromycin.

Table 1: Frequency of recruits and instructors accepting or refusing mass antibiotic prophylaxis at the Canadian Forces Leadership and Recruit School, March 7–April 30, 2018

Staff administered	PGB		Azithromycin		Refusals		Total
	n	%	n	%	n	%	
Recruit	2,226	87.8	281	11.1	27	1.1	2,534
Instructor	172	80.0	28	13.0	15	7.0	215
Total	2,398	87.2	309	11.2	42	1.5	2,749

Abbreviation: PGB, penicillin G benzathine

Outcomes—adverse events surveillance

During the period of March 14 to May 7, 2018, 2,149 CAF personnel received a MAP adverse events survey. The survey was completed by 1,752 individuals (81.5% response rate), but 41 respondents were excluded from analysis because of missing data (29 did not indicate which antibiotic they received and 12 did not indicate if they were a recruit or instructor). Of the 1,711 individuals, another 41 respondents were excluded because they indicated that they had refused MAP or that MAP had not been offered to them (**Table 2**). The remaining 1,670 respondent were included in the analysis of adverse events.

Of the 1,670 survey respondents, 1,462 (87.5%) received PGB. Among them, 1,358 (92.9%) reported at least one adverse event. The adverse event most commonly reported after PGB injection was localised pain at the injection site (**Table 3**). Twenty recruits and three instructors (i.e. 1.6% of all respondents treated with PGB) sought medical attention for their pain (Table 3). Respondents who received a PGB injection in the vastus lateralis had significantly higher odds of reporting pain than those who received the injection in the gluteal muscle (2.45; 95% CI, 1.76–3.42; p=0.002). Four recruit respondents reported having failed BMT, and another seven reported having to retake the

Table 2: Number of adverse events reported[a] following mass antibiotic prophylaxis antibiotics for recruits and instructors at the Canadian Forces Leadership and Recruit School, March 7–April 30, 2018

Staff administered	PGB		Azithromycin		No MAP[b]		Total
	n	%	n	%	n	%	
Recruit	1,358	86.6	183	11.7	27	1.7	1,568
Instructor	104	72.7	25	17.5	14	9.8	143
Total	1,462	85.4	208	12.2	41	2.4	1,711

Abbreviations: MAP, mass antibiotic prophylaxis; PGB, penicillin G benzathine
[a] Self-reported in adverse events survey one week after treatment
[b] Refused or not offered

course, as a consequence of an adverse event following a PGB injection; together, these 11 respondents represent 0.8% of the 1,358 recruit respondents who reported receiving a PGB injection. Recruits (30.6%; 95% CI, 28.2–33.2) and instructors (27.9%; 95% CI, 20.1–37.3) reported experiencing pain most commonly at the injection site for three days with approximately 50% of recruits and instructors reporting that the most intense day of pain was the first day after the injection.

Of the 1,670 survey respondents, 208 (12.5%) received azithromycin. Among them, 146 (70.2%) reported experiencing at least one gastrointestinal (GI) symptom after their first dose of the antibiotic. Reported GI symptoms included diarrhea, stomach pain and nausea or vomiting (**Table 4**). The GI symptoms were most frequently reported on the first day after receiving the first dose of the oral antibiotic (Table 4). Two recruits respondents reported having failed BMT, and one other reported having to retake the course, as a consequence of an adverse event of azithromycin; together, these three individuals represent 1.6% of the 183 recruits respondents who reported receiving an oral dose of azithromycin.

Of the 2,707 individuals who received MAP, there was a total of five reported cases of serious adverse events requiring hospitalization (four recruits and one instructor), all following PGB injection in March 2018. The five adverse events included one case of each of the following: anaphylaxis, compartment syndrome (rhabdomyolysis with acute renal injury), cellulitis, hematoma at injection site and excessive vomiting. Hospitalization duration ranged from one day (anaphylaxis, hematoma, excessive vomiting) to several days (cellulitis, rhabdomyolysis), with all five individuals recovering fully.

Table 3: Summary of self-reported adverse events and seeking of medical assistance by recruits and instructors at the Canadian Forces Leadership and Recruit School following injection of penicillin G benzathine, March 7–April 30, 2018

Staff self-reporting	Pain at injection site		Headache		Nausea or vomiting		Rash or itchiness		Dizziness or lightheadedness		Joint pain	
	n	(%, 95% CI)	n	(%, 95% CI)	n	(%,95% CI)	n	(%, 95% CI)	n	(%, 95% CI)	n	(%, 95% CI)
Recruits	1,248	(92.2, 90.7–93.5)	225	(17.4, 15.4–19.5)	96	(7.5, 6.2–9.1)	84	(6.6, 5.3–8.1)	223	(17.3, 15.4–19.5)	298	(22.7, 20.5–25.0)
Instructors	98	(94.2, 88.0–97.3)	16	(15.8, 10.0–24.2)	4	(4.0, 1.6–9.9)	4	(4.1, 1.6–10.1)	12	(11.9, 6.9–19.6)	21	(20.6, 13.9–29.4)
Total	1,346	(92.3, 90.8–93.6)	241	(17.3, 15.4–19.3)	100	(7.3, 6.0–8.8)	88	(6.4, 5.2–7.8)	235	(16.9, 15.1–19.0)	319	(22.5, 20.4–24.8)
Number of days experiencing adverse event[a]	3		1		1		1		1		2	
Recruits—Sought medical help as a result of adverse event	20	(1.7, 1.1–2.6)	8	(4.0, 2.0–7.8)	5	(5.7, 2.3–13.1)	6	(9.5, 4.2–20.0)	15	(7.7, 4.7–12.4)	13	(5.1, 2.9–8.5)
Instructors—Sought medical help as a result of adverse event	3	(3.1, 1.0–9.3)	0	(0, 0.0)	0	(0, 0.0)	0	(0, 0.0)	0	(0, 0.0)	1	(5.3, 0.7–30.7)
Recruits reporting receiving sick leave	16 out of 18	(88.9, 61.1–97.6)	2 out of 7	(28.6, 4.2–78.5)	2 out of 3	(66.7, 20.8–93.9)	2 out of 4	(50, 15.0–85.0)	6 out of 11	(54.5, 22.6–83.2)	7 out of 11	(63.6, 28.8–88.3)

[a] Most commonly reported number of days experiencing adverse event following mass antibiotic prophylaxis (recruits and instructors)

Table 4: Summary of self-reported adverse events and seeking of medical assistance following administration of azithromycin[a] for those personnel at the Canadian Forces Leadership and Recruit School, March 7–April 30, 2018

Staff self-reporting	Diarrhea		Stomach pain		Nausea or vomiting	
	n	(%, 95% CI)	n	(%, 95% CI)	n	(%, 95% CI)
Recruits	78	(47.3, 39.8–54.9)	91	(53.2, 45.8–60.5)	57	(35.0, 28.1–42.6)
Instructors	14	(60.9, 40.8–77.8)	15	(65.2, 44.9–81.2)	5	(25.0, 11.2–46.9)
Total	92	(48.9, 41.9–56.0)	106	(54.6, 47.6–61.5)	62	(33.9, 27.4–41.0)
Recruits—Sought medical help as a result of adverse event	1	(1.4, 0.2–7.4)	2	(2.4, 0.7–8.2)	3	(5.3, 1.8–14.4)
Instructors—Sought medical help as a result of adverse event	0		0		0	
Recruits reporting receiving sick leave	None	(0.0)	1 out of 2	(50.0, 9.5–90.6)	2 out of 3	(66.7, 20.8–93.9)

[a] Azithromycin administered as one oral dose—the first of four doses in a full treatment regime

Discussion

Summary of findings

In March 2018, a voluntary MAP program was implemented in CFLRS. Based on self-reported surveys, the majority of personnel experienced adverse events in the first week following MAP; 92.3% of personnel who were injected with PGB reported pain at the injection site, and 70.2% of personnel who were administered azithromycin orally reported GI symptoms after their first dose. However, few of these adverse events appear to have caused significant impact on personnel. Only five serious adverse events were reported in the first month following MAP, and less than 1% of recruits reported being unable to complete BMT as a consequence of MAP.

Comparison to the literature

The reported adverse events from MAP are consistent with those cited in the drug monographs, including the two most commonly reported adverse events: localised pain following PGB injection and GI symptoms following an oral dose of azithromycin (15,16). There were no new unknown adverse events reported by recruits for either antibiotic. Only 0.8% of CAF recruits who received PGB reported an adverse event that resulted in them failing or having to retake BMT.

Surprisingly, the GI symptoms reported by the military recruits who took azithromycin were a magnitude of ten higher than those cited in the monograph (16), which may reflect recall bias especially since the survey was administered one week following MAP. However, the impact on recruit training was minimal since only 1.6% of recruits who received azithromycin reported having failed or having to retake BMT, which is comparable to the reported 1% severe and/or life-threatening adverse events (16).

Rates of serious adverse events were associated with injected PGB administered only during the first month of MAP (March 7–April 22) (0.15%), which is also consistent with previous studies. For example, of the 2,398 personnel injected with PGB, only one had an anaphylactic reaction (n=1/2,398, 0.04%). Similarly, in a US study of 199,862 patients followed for the first 14 days after the administration of penicillin, 0.05% experienced a serious allergic reaction (18). For the past 20 years, there have been no reported cases of anaphylaxis associated with chemoprophylaxis in US military training centres (9).

Strengths and weaknesses

Following the implementation of MAP at CFLRS, there were no new cases of iGAS or severe GAS and there was a precipitous decrease in the number of GAS-positive throat swabs. However, there continued to be adenovirus outbreaks among military recruits. This program is year-round now, which has implications for staffing resources for the administration and timing of mass antibiotic administration, so as to minimize its impact on BMT.

Implications

Although no serious adverse events associated with azithromycin were reported in this intervention, PGB is still the preferred choice of chemoprophylaxis over azithromycin, for several reasons. These reasons include concerns about resistance to azithromycin by GAS (19,20) and other pathogens, such as *Streptococcus pneumoniae* (21), cardiac arrest due to elongation of the QT interval (22) and increased compliance with one time PGB dosing compared to multiple doses required with oral azithromycin (6). Direct observed therapy has been implemented in US military training centres because of non-compliance with this oral antibiotic.

Because of the high prevalence of self-reported pain at the PGB injection site, leadership postponed mandatory fitness testing for the first 24 hours post-injection in order to minimize exacerbation of the localised injection site pain (*Maj E. Girard, personal communication, March 29, 2019*).

Limitations of the survey

It should be noted that, given the urgent need to implement MAP during the GAS outbreak at CFLRS, the adverse event survey could not be validated prior to its administration. Some survey questions may therefore have been unclear to respondents. For example, recruits and instructors reported not having sought medical attention, but having been excused

from duty, because of MAP-related adverse events. This is contradictory, because military personnel can only be excused from duty if they are assessed in clinic. Additionally, information such as gender and age was not obtained in the survey, so we were not able to determine if there were any differences in adverse events because of demographic differences.

Furthermore, survey respondents may have incorrectly recalled the type of antibiotic received. As part of BMT, recruits often receive a number of immunizations, which respondents could have confused for injectable PGB. Because of the anonymous nature of the adverse event survey, it was impossible to confirm the accuracy of self-reported data on the type of antibiotic administered.

Lastly, PGB injections were administered by CAF clinical staff, but azithromycin doses were self-administered over four consecutive weeks. Personnel who were prescribed azithromycin were not observed taking their antibiotic, and compliance is therefore unknown. Furthermore, the adverse event survey was only administered one week after the first azithromycin dose. It is therefore possible that the survey underestimated the true risk of adverse events associated with the use of azithromycin as a prophylaxis to treat GAS.

Conclusion

The intervention described herein corresponds to the first time that MAP had been implemented in CAF, and is the largest single use of PGB in a defined group in Canada. This intervention, which interrupted the ongoing GAS outbreak, was generally well tolerated by both recruits and instructors, with minimal impact on the ability of recruits to complete their BMT. Common adverse events were reported, as expected, with the use of both PGB and azithromycin although serious adverse events were rare. Thus, MAP can be used safely to reduce the spread of GAS among CAF personnel and protect recruits against serious GAS infections.

Authors' statement

DL — Conceptualization of manuscript, original draft, review and editing of manuscript
BS — Data curation, formal analysis, review and editing of manuscript
KS — Conceptualization and drafting of survey, data curation, formal analysis, review and editing of manuscript
MT — Review and editing of manuscript
FG — Formatting and administration of survey, review and editing of manuscript
NJ — Administration of survey, review and editing of manuscript
EG — Review and editing of manuscript
KB — Review and editing of manuscript

Competing interests

Previously presented as a podium presentation at the Canadian Institute for Military and Veteran Health Research (CIMVHR) 2018 Forum, Regina, Saskatchewan, October 15, 2018.

Disclaimer: The views expressed are solely those of the authors and do not reflect the official policy or position of the Canadian Armed Forces or the Government of Canada.

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References

1. Levinson W. Review of Medical Microbiology & Immunology. 12th ed. New York: McGraw-Hill Medical; 2012.

2. Heymann DL. Streptococcal diseases. In: Heymann DL, editor. Control of Communicable Disease Manual. 20th ed. Washington DC: American Public Health Association; 2015. p 581-9

3. Bernstein SH, Feldman HA, Harper OF Jr, Klingensmith WH. Massoral penicillin prophylaxis in control of streptococcal disease. AMA Arch Intern Med 1954;93(6):894–8. DOI PubMed

4. Sanchez JL, Cooper MJ, Myers CA, Cummings JF, Vest KG, Russell KL, Sanchez JL, Hiser MJ, Gaydos CA. Respiratory infections in the U.S. Military: recent experience and control. Clin Microbiol Rev 2015;28(3):743–800. DOI PubMed

5. Lee SE, Eick A, Ciminera P. Respiratory disease in Army recruits: surveillance program overview, 1995-2006. Am J Prev Med 2008;34(5):389–95. DOI PubMed

6. Crum NF, Russell KL, Kaplan EL, Wallace MR, Wu J, Ashtari P, Morris DJ, Hale BR. Pneumonia outbreak associated with group a Streptococcus species at a military training facility. Clin Infect Dis 2005;40(4):511–8. DOI PubMed

7. Gray GC, Callahan JD, Hawksworth AW, Fisher CA, Gaydos JC. Respiratory diseases among U.S. military personnel: countering emerging threats. Emerg Infect Dis 1999;5(3):379–87. DOI PubMed

8. Lazar HP, Maas GI, Harrison W, Hammond JH, Rantz LA. Streptococcal disease and rheumatic fever in Air Force recruits. II. Prophylaxis with tandem oral penicillin. AMA Arch Intern Med 1957;100(4):614–9. DOI PubMed

9. Webber BJ, Kieffer JW, White BK, Hawksworth AW, Graf PC, Yun HC. Chemoprophylaxis against group A streptococcus during military training. Prev Med 2019;118:142–9. DOI PubMed

10. Schreier AJ, Hockett VE, Seal JR. Mass prophylaxis of epidemic streptococcal infections with benzathine penicillin G.I. Experience at a naval training center during the winter of 1955-56. N Engl J Med 1958;258(25):1231–8. DOI PubMed

11. McFarland RB, Colvin VG, Seal JR. Mass prophylaxis of epidemic streptococcal infections with benzathine penicillin G.—Experience at a naval training center during the winter of 1956-57. N Engl J Med 1958 Jun;258(26):1277–84. DOI PubMed

12. Basiliere JL, Bistrong HW, Spence WF. Streptococcal pneumonia. Recent outbreaks in military recruit populations. Am J Med 1968;44(4):580–9. DOI PubMed

13. Thomas RJ, Conwill DE, Morton DE, Brooks TJ, Holmes CK, Mahaffey WB. Penicillin prophylaxis for streptococcal infections in United States Navy and Marine Corps recruit camps, 1951-1985. Rev Infect Dis 1988;10(1):125–30. DOI PubMed

14. Centers for Disease Control (CDC). Group A beta-hemolytic streptococcal pharyngitis among U.S. Air Force trainees-Texas, 1988-89. MMWR Morb Mortal Wkly Rep 1990;39(1):11–3. PubMed

15. Penicillin G benzathine drug monograph (accessed 2019-03-05). https://www.pfizer.ca/sites/g/files/g10050796/f/201710/Bicillin_PM.pdf

16. Azithromycin drug monograph (accessed 2019-03-05). https://www.sandoz.ca/sites/www.sandoz.ca/files/Sandoz%20Azithromycin%20PM_EN.pdf

17. Hammond-Collins K, Strauss B, Barnes K, Demczuk W, Domingo MC, Lamontagne MC, Lu D, Martin I, Tepper M, Group A. Group A Streptococcus Outbreak in a Canadian Armed Forces Training Facility. Mil Med 2019;184(3-4):e197–204. DOI PubMed

18. Johannes CB, Ziyadeh N, Seeger JD, Tucker E, Reiter C, Faich G. Incidence of allergic reactions associated with antibacterial use in a large, managed care organisation. Drug Saf 2007;30(8):705–13. DOI PubMed

19. Barrozo CP, Russell KL, Smith TC, Hawksworth AW, Ryan MA, Gray GC. National Department of Defense surveillance data for antibiotic resistance and emm gene types of clinical group A streptococcal isolates from eight basic training military sites. J Clin Microbiol 2003;41(10):4808–11. DOI PubMed

20. Metzgar D, McDonough EA, Hansen CJ, Blaesing CR, Baynes D, Hawksworth AW, Blair PJ, Faix DJ, Russell KL. Local changes in rates of group A Streptococcus disease and antibiotic resistance are associated with geographically widespread strain turnover events. Virulence 2010;1(4):247–53. DOI PubMed

21. Gray GC, Witucki PJ, Gould MT, Bell SJ, Hiliopoulos KM, McKeehan JA, Fuller JM, Barrozo CP, Hudspeth MK, Smith TC, Ledbetter EK, Wallace MR. Randomized, placebo-controlled clinical trial of oral azithromycin prophylaxis against respiratory infections in a high-risk, young adult population. Clin Infect Dis 2001;33(7):983–9. DOI PubMed

22. Goldstein EJC, Jr Owens RC, Nolin TD. Antimicrobial-associated QT interval prolongation: pointes of interest. Clin Infect Dis 2006;43(12):1603–11. DOI PubMed

Annex: Survey of adverse reactions - antibiotic prophylaxis at Canadian Forces Leadership and Recruit School

Introduction:
Over the past few weeks, you may have been offered one of two medications (antibiotics) to prevent you from becoming ill from an infection called Group A *Streptococcus*. We would like to know your experience with any side effects from these medications by answering a few questions. Please note that this survey is voluntary and anonymous.

Instructions:
Please circle the answer that best applies to you.
When complete, please hand in this form to your Directing Staff.

PART A - ANTIBIOTICS

1. Which antibiotic did you receive?
   a. Bicillin (injection) [Answer only part B]
   b. Azithromycin (pill) [Answer only part C]
   c. Neither (declined antibiotics or was not offered) [STOP survey here]
   d. Unsure [STOP survey here]

PART B – BICILLIN (INJECTION)

Pain at Injection Site

2. For how many days did you experience pain where you received the injection?

No pain	1 day	2 days	3 days	4 days	5 days	6 days or more

3. On which day was the pain the most intense?

No pain	The same day	1 day after	2 days after	3 days after	4 days after	5 days after	6 days or more after

4. Did you seek medical help **due to pain where you received the injection**?

No pain	Yes	No

5. If "Yes" to Question 4, on what day did you seek medical help after the injection?

The same day	1 day after	2 days after	3 days after	4 days after	5 days after	6 days or more after

6. Did you obtain a chit with medical limitations (restricting you from doing activities scheduled in your recruit routine) **due to pain where you received the injection**?

No pain	Yes	No

Other symptoms

7. Did you experience any of the following symptoms after the injection?
   If yes, please indicate for how many days you experienced these other symptoms.

Symptoms	Did not experience	1 day or less	2 days	3 days	4 days	5 days	6 days or more
Headache	O	O	O	O	O	O	O
Nausea or vomiting	O	O	O	O	O	O	O
Skin rash or itchiness	O	O	O	O	O	O	O
Dizziness or lightheadedness	O	O	O	O	O	O	O
Joint and bone pain	O	O	O	O	O	O	O

8. Did you seek medical help **due to any of these other symptoms**?

Symptoms	I did not have this symptom	Yes	No
Headache	O	O	O
Nausea or vomiting	O	O	O
Skin rash or itchiness	O	O	O
Dizziness or lightheadedness	O	O	O
Joint and bone pain	O	O	O

9. Did you obtain a chit with medical limitations (restricting you from doing some of the activities scheduled in your recruit routine) **due to any of these other symptoms**?

Symptoms	I did not have this symptom	Yes	No
Headache	O	O	O
Nausea or vomiting	O	O	O
Skin rash or itchiness	O	O	O
Dizziness or lightheadedness	O	O	O
Joint and bone pain	O	O	O

10. Did you fail recruit training or were you recoursed as a result of side effects from bicillin (injection)?

No	Fail	Recourse

PART C – AZITHROMYCIN (PILL)

11. Did you experience any of the following after taking a dose (pill) of azithromycin?
If yes, please indicate how many days you experienced these symptoms.

Symptoms	I did not have this symptom	1 day or less	2 days	3 days	4 days	5 days	6 days or more
Diarrhea	O	O	O	O	O	O	O
Stomach pain	O	O	O	O	O	O	O
Nausea or vomiting	O	O	O	O	O	O	O

12. Did you seek medical help **due to diarrhea, stomach pain, or nausea/vomiting**?

Symptoms	I did not have this symptom	Yes	No
Diarrhea	O	O	O
Stomach pain	O	O	O
Nausea or vomiting	O	O	O

13. Did you obtain a chit with medical limitations (restricting you from doing some of the activities scheduled in your recruit routine) **due to diarrhea, stomach pain, or nausea/vomiting**?

Symptoms	I did not have this symptom	Yes	No
Diarrhea	O	O	O
Stomach pain	O	O	O
Nausea or vomiting	O	O	O

14. Did you fail recruit training or were you recoursed as a result of side effects from azithromycin (pill)?

No	Fail	Recourse

If you have any health concerns regarding these medications, please seek medical attention. Maj François Gagnon, MD, Base Surgeon 41 CF H Svc C St-Jean-sur-Richelieu, (450) 358-7099 poste 6236

SURVEY REPORT

Trends in pre-military sexually transmitted infections and associated risk behaviours in Canadian Armed Forces recruits

Heather McCuaig Edge[1]*

Abstract

Background: Sexually transmitted infections (STIs) have historically been problematic for militaries. Recent reports indicating that rates of STIs among young male Canadian Armed Forces (CAF) members are higher than civilians prompted a need to better understand CAF members' reported rates of STIs and their behavioural risk factors for STIs. This study examined the prevalence of self-reported pre-military sexual behaviours (i.e. number of sexual partners and frequency of condom use) and history of a STI diagnosis among CAF recruits attending basic military training using data collected from the Recruit Health Questionnaire.

Methods: Data came from 50,603 recruits who participated in the survey between 2003 and 2018 (84.9% male, 78.6% Non-Commissioned Member candidates, 64.9% aged between 17 and 24 years).

Results: Among sexually active recruits, the proportions who had more than one sexual partner in the previous year increased from 30.5% in 2003 (95% CI, 27.8–33.4) to 35.5% in 2018 (95% CI, 34.0–37.0). Of recruits who were not in an exclusive relationship at the time, the proportions who reported always using a condom decreased from 50.8% in 2003 (95% CI, 46.4–55.1) to 40.2% in 2018 (95% CI, 38.3–42.2). Overall, 5.5% (95% CI, 5.3–5.7) reported ever having received a STI diagnosis. Demographic differences by age and sex were also found.

Conclusion: These observations provide an indication of the baseline, pre-enlistment STI risk behaviours, and STI history among CAF recruits, and may provide insight into avenues for targeted interventions and health promotion programming, such as education and screening initiatives.

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Keywords: sexually transmitted infections, Canadian Armed Forces, military recruits, risk behaviours, condom use, number of sexual partners

Introduction

Sexually transmitted infections (STIs) have historically been problematic for militaries (1,2). For example, reported rates of STIs have been much higher in the United States (US) military population compared with the civilian population (3–5). Recent comparisons between the Canadian general population (CGP) and Canadian Armed Forces (CAF) personnel revealed that while rates of STIs were the same as or lower than civilians in most demographic groups, the rates of STIs among young (i.e. younger than 30 years) male CAF members were almost double those of their civilian counterparts (6). A qualitative study revealed that CAF personnel and healthcare providers alike perceived STIs as a problem within CAF, and many indicated that STIs were similarly, or even more, problematic for CAF than for the CGP (7).

The Public Health Agency of Canada has identified behavioural risk factors associated with STIs; including sexual activity in youth younger than 25 years, new or more than two sexual partners in the previous year, unprotected sex, alcohol or substance use and a history of a STI, among others (8). Military members may be at elevated risk for acquiring STIs given the younger age of the majority of personnel, frequent and extended time spent away

from home for training or operations, deployments to areas with higher rates of STIs, or elevated rates of risk-taking attitudes and behaviours associated with STIs (9–11). Self-reported STI risk behaviours among serving CAF members indicated that almost 21% reported having had two or more sexual partners in the previous 12 months, and of those, only 22% reported always using a condom, while approximately 18% reported never using a condom (12).

Determining the baseline prevalence and demographic profiles of STI risk behaviours and STI history among new recruits can inform education, screening and intervention practices at the beginning of the military career. Thus, this study examined the prevalence of STI risk behaviours (i.e. number of sexual partners and frequency of condom use) and self-reported pre-military history of a STI diagnosis among CAF recruits attending basic military training (BMT).

Methods

Data for this study were collected between July 2003 and December 2018 using the Recruit Health Questionnaire (RHQ), administered during the first few weeks of BMT at the Canadian Forces Leadership and Recruit School in St-Jean-sur-Richelieu, Québec. All Regular Force Non-Commissioned Member (NCM) and Officer candidates (hereafter collectively referred to as "recruits") enrolled in BMT were invited to complete the RHQ—a long term, ongoing surveillance study that provides baseline health and lifestyle information about recruits. The RHQ is a voluntary survey that recruits provide written consent to participate in. Participants' data is linked via service number to health data collected later in their career; thus, data are confidential, not anonymous. Approximately 75% of recruits completed the RHQ. The RHQ study protocol was approved by the Defence Research and Development Canada Human Research Ethics Committee.

The RHQ includes items assessing number of sexual partners in the previous year, frequency of condom use and STI history. Number of sexual partners was assessed with the question "How many different sexual partners have you had in the past 12 months?" with response options of "none," "one partner," "two partners," "three partners" or "four or more". Frequency of condom use was assessed with the question, "If you were not in an exclusive relationship at the time, how often did you use a condom in the past 12 months?" with response options of "always," "usually," "occasionally," "never" and "not applicable". The proportion of respondents with a previous STI diagnosis were estimated based on "yes/no" responses to the question, "Have you ever been told by a doctor or nurse that you had a sexually transmitted infection—like chlamydia, gonorrhea, genital herpes, or syphilis?" The procedure of administration and questions related to sexual behaviours and STI history has not changed over the 16-year period.

The data about sexual behaviours and STI history are self-reported and are, thus, subject to recall and social desirability biases, which may result in under or over-reporting (13). As noted elsewhere (14), while the impact of social desirability on self-reports of sexual behaviours is difficult to quantify, studies have confirmed the general reliability of responses.

Descriptive analysis of crude proportions along with 95% CIs was examined for each cohort year. Sequential logistic regressions controlling for age and sex were conducted to identify linear and non-linear (i.e. quadratic or cubic) trends over time, with cohort year (or its squared or cubed value) entered as a continuous variable. A trend was detected if the addition of cohort year (or its squared or cubic values) to the model significantly improved the model fit, as indicated by a significant chi-square. Difference tests between cohort years were conducted using z-tests of proportions, while chi-square analyses were conducted to detect demographic differences.

Results

Data were available for 50,603 cases from recruits who participated in the RHQ between July 2003 and December 2018. Respondents were mostly male (84.9%), NCM candidates (78.6%), primarily English-speaking (72.7%) and between 17 and 24 years old when they completed the RHQ (64.9%; M=24.0; SD=5.9).

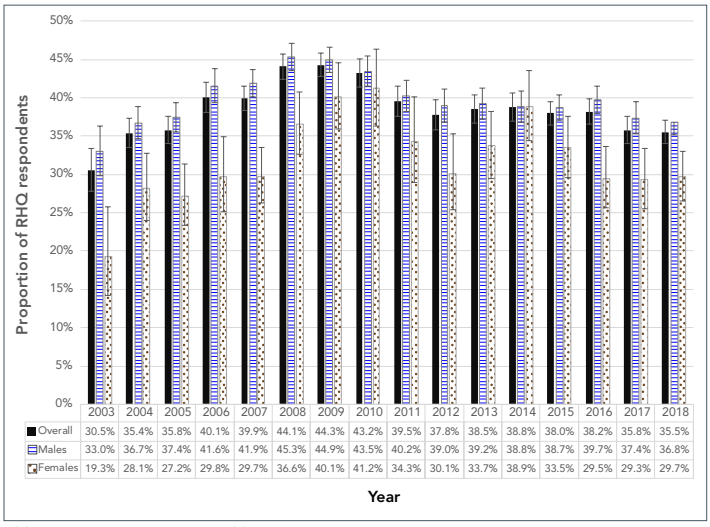
Trends, 2003–2018

Among sexually active recruits, the proportions who had two or more sexual partners in the previous year increased from 30.5% overall in 2003 (95% CI, 27.8–33.4) to 35.5% overall in 2018 (95% CI, 34.0–37.0; p<0.01; **Figure 1**). Significant trends, controlling for age and sex, indicated that the number of sexual partners reported by recruits in the previous year have fluctuated between 2003 and 2018 (χ^2 (5)=1,344.28; p<0.001).

Of recruits who were not in an exclusive relationship at the time, the proportion who reported always using a condom decreased from 50.8% in 2003 (95% CI, 46.4–55.1) to 40.2% in 2018 (95% CI, 38.3–42.2; p<0.001; data not shown). As depicted in **Figure 2**, the proportion who reported never using a condom increased from 16.5% in 2003 (95% CI, 13.5–20.0) to 25.7% in 2018 (95% CI, 24.0–27.5; p<0.001). Respondents who selected "not applicable" were excluded from these analyses, resulting in a reduced n=27,783 for this STI risk behaviour. Significant trends controlling for age and sex were found, indicating that rates of condom use reported by recruits during the previous year have varied significantly over the 16-year period (χ^2 (5)=400.70; p<0.001).

Overall, 5.5% (95% CI, 5.3–5.7) of recruits reported ever having received a STI diagnosis (**Figure 3**). These proportions were not significantly different for the 2003 or 2018 recruit cohorts.

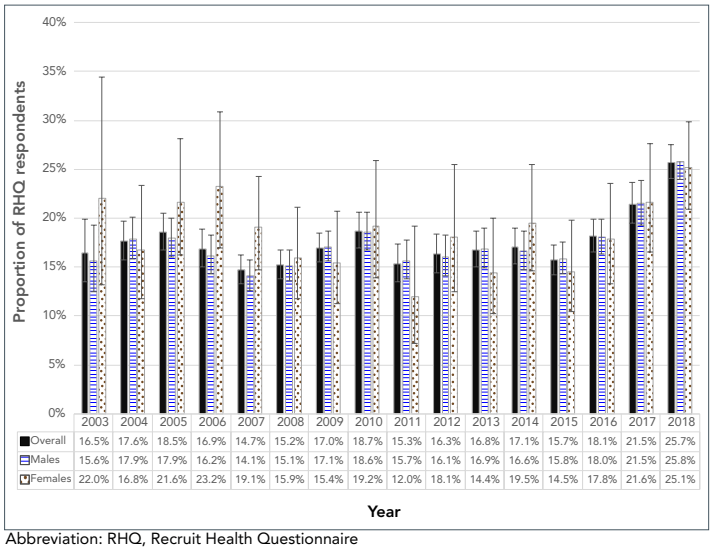
Figure 1: Annual overall and sex-specific rates of self-reported number of sexual partners in Canadian Armed Forces recruits, two or more partners in the previous year, 2003–2018



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Overall	30.5%	35.4%	35.8%	40.1%	39.9%	44.1%	44.3%	43.2%	39.5%	37.8%	38.5%	38.8%	38.0%	38.2%	35.8%	35.5%
Males	33.0%	36.7%	37.4%	41.6%	41.9%	45.3%	44.9%	43.5%	40.2%	39.0%	39.2%	38.8%	38.7%	39.7%	37.4%	36.8%
Females	19.3%	28.1%	27.2%	29.8%	29.7%	36.6%	40.1%	41.2%	34.3%	30.1%	33.7%	38.9%	33.5%	29.5%	29.3%	29.7%

Abbreviation: RHQ, Recruit Health Questionnaire

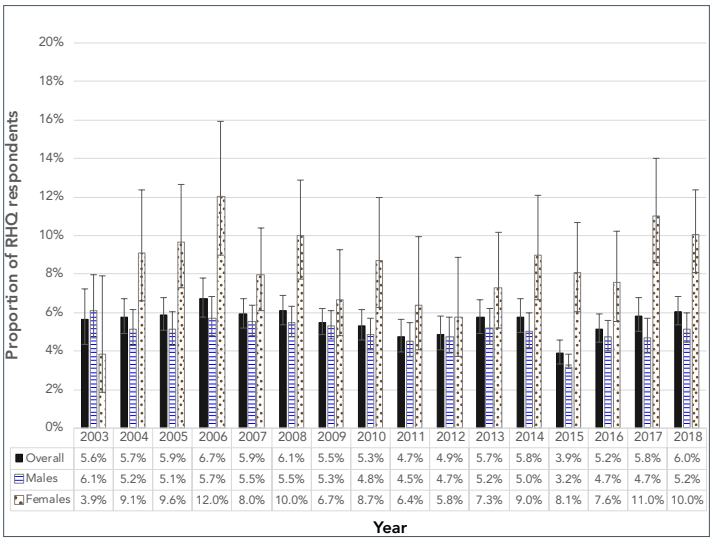
Figure 2: Annual overall and sex-specific rates of self-reported rates of never using a condom in the previous year, for Canadian Armed Forces recruits not in a relationship, 2003–2018



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Overall	16.5%	17.6%	18.5%	16.9%	14.7%	15.2%	17.0%	18.7%	15.3%	16.3%	16.8%	17.1%	15.7%	18.1%	21.5%	25.7%
Males	15.6%	17.9%	17.9%	16.2%	14.1%	15.1%	17.1%	18.6%	15.7%	16.1%	16.9%	16.6%	15.8%	18.0%	21.5%	25.8%
Females	22.0%	16.8%	21.6%	23.2%	19.1%	15.9%	15.4%	19.2%	12.0%	18.1%	14.4%	19.5%	14.5%	17.8%	21.6%	25.1%

Abbreviation: RHQ, Recruit Health Questionnaire

Figure 3: Annual overall and sex-specific rates of self-reported history of sexual transmitted infections diagnosis in Canadian Armed Forces recruits, 2003–2018



	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018
Overall	5.6%	5.7%	5.9%	6.7%	5.9%	6.1%	5.5%	5.3%	4.7%	4.9%	5.7%	5.8%	3.9%	5.2%	5.8%	6.0%
Males	6.1%	5.2%	5.1%	5.7%	5.5%	5.5%	5.3%	4.8%	4.5%	4.7%	5.2%	5.0%	3.2%	4.7%	4.7%	5.2%
Females	3.9%	9.1%	9.6%	12.0%	8.0%	10.0%	6.7%	8.7%	6.4%	5.8%	7.3%	9.0%	8.1%	7.6%	11.0%	10.0%

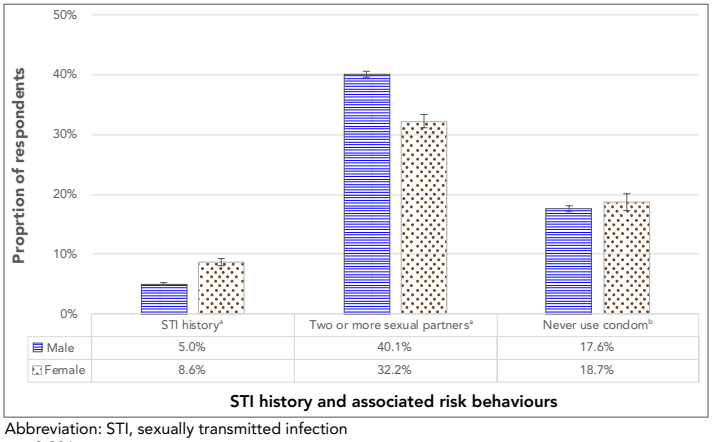
Abbreviation: RHQ, Recruit Health Questionnaire

There was a significant trend found in the rates of recruits having reported ever having had a STI diagnosis (χ^2 (5)=445.18; p<0.001) after controlling for age and sex, indicating that the rates of reported STI diagnoses varied over the 16-year period.

Demographic differences

Pooling responses over the 16-year period, demographic differences by sex and age were also found for number of sexual partners, condom use and STI history. As depicted in **Figure 4**, more male than female recruits reported having two or more sexual partners in the previous year (χ^2 (2)=716.75; p<0.001), while more female than male recruits reported a previous STI diagnosis (χ^2 (1)=43.44; p<0.001). Of recruits who were not in an exclusive relationship at the time, more female than male recruits reported always using a condom (data not shown; χ^2 (2)=84.93; p<0.001); however, there were no differences in the proportions of male and female recruits who reported never using a condom.

Figure 4: Sexually transmitted infections history and associated risk behaviours in Canadian Armed Forces recruits, by sex



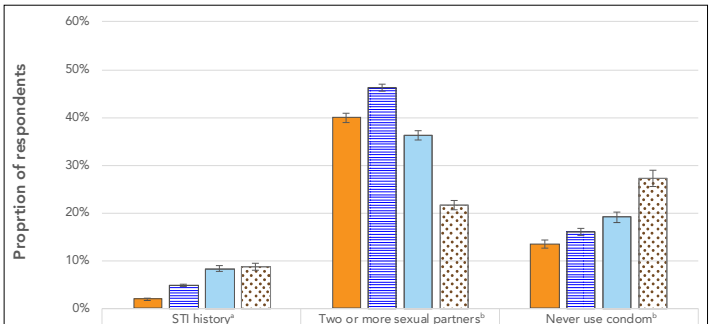
	STI history[a]	Two or more sexual partners[a]	Never use condom[b]
Male	5.0%	40.1%	17.6%
Female	8.6%	32.2%	18.7%

Abbreviation: STI, sexually transmitted infection
[a] p<0.001
[b] not significant

As depicted in **Figure 5**, the proportions of reports of having two or more sexual partners in the previous year significantly differed for each age group (χ^2 (6)=3,183.48; p<0.001), with the highest proportion among recruits aged 20 to 24 years. Recruits aged 30 or older who were not in an exclusive relationship had the highest proportion of reports that they never used a condom,

with the proportions being significantly lower in each descending age group (χ^2 (6)=365.01; p<0.001). There were proportionally more recruits aged 25 or older who reported a history of a STI diagnosis than younger recruits (χ^2 (3)=512.67; p<0.001), with the youngest group of recruits (i.e. those aged 17 to 19 years) reporting the lowest proportion of STI diagnosis history.

Figure 5: Sexually transmitted infections history and associated risk behaviours by age group in Canadian Armed Forces recruits



	STI history[a]	Two or more sexual partners[b]	Never use condom[b]
17–19 years	1.9%	40.0%	13.5%
20–24 years	4.8%	46.3%	16.1%
25–29 years	8.3%	36.2%	19.1%
30+ years	8.7%	21.7%	27.2%

Abbreviation: STI, sexually transmitted infection
[a] The first three columns are p<0.001, the first, second, and fourth columns are p<0.001, and the third and fourth columns are not significant
[b] p<0.001

Discussion

Observations from the RHQ concerning the number of sexual partners, frequency of condom use and STI history, suggest that the majority of recruits were not engaging in risky sexual behaviours. However, at least a third of recruits reported having had two or more sexual partners in the year prior to starting BMT. More recently, among those who were not in an exclusive relationship at the time, a quarter of recruits reported never using a condom. From 2003 to 2018, the proportions of recruits reporting multiple sexual partners and never wearing a condom increased. These patterns in STI risk behaviours mirror the recent increases in rates of STIs reported in the general population in Canada (15–17) and in other high-income countries (18,19), and are also consistent with increased risky sexual behaviours among adolescents and adults in the CGP (14,20,22).

While reports of recruits having had a STI diagnosis prior to BMT have remained relatively low, consistently more female than male recruits reported a history of STI diagnosis. This is unsurprising given that, for certain STIs (e.g. chlamydia), women tend to have higher rates of infection than men (16) and tend to be screened and/or seek health care more regularly, and would, therefore, be more likely to have been diagnosed than men (23–25). Moreover, because of their physiology, women are more susceptible than men to acquire STIs (24).

Differences in the number of sexual partners between men and women were consistent with findings that men tend to report having more sexual partners than women (14,21,22). This difference may be due to socialization, gender roles or sociocultural norms surrounding sexual behaviours and the reporting thereof (26). In line with findings from the CGP (21,22), the proportion of recruits reporting multiple partners was lower in the older age groups, possibly due to increased likelihood of older recruits being in longer term, monogamous relationships. The largest proportion of recruits reporting multiple partners was among the 20 to 24-year old group, which is the age group with the highest rates of gonorrhea (17) and chlamydia (16) and the third highest rates of infectious syphilis in the CGP in 2015 (15).

Consistent with findings from the CGP that have found that regular condom use declines with age (14,20,23), a higher proportion of older recruits who were not in an exclusive relationship at the time reported never using a condom, compared with younger recruits. This could be due to the increased use of other contraceptive methods for preventing pregnancy with increased age (21); however, these methods do not prevent STIs.

Findings from recruits are consistent with the rates and behaviours found in the CGP; this is unsurprising since recruits were drawn from the CGP and had not yet begun their military careers when the RHQ was administered. The importance of this research for CAF in its efforts to prevent STIs are highlighted by the observed increasing rates of STI risk behaviours, the higher STI rates and risk among military members (3–6,9,27) and perceptions of STIs as a problem for CAF (7). These efforts may be especially important for recruits, who have not yet experienced some of the military situations that may place military personnel at increased risk for acquiring STIs, such as deployments (9,11), or having higher levels of risk propensity (28). While the risk for STIs may be elevated for military members, CAF also presents an opportunity for members to more easily access health care for primary and secondary prevention and health promotion programming. Other militaries have implemented programs that have reduced STI rates, such as in US recruit training centers, and have proven effective at increasing STI knowledge and perceived norms for safe sex (29–33). These programs included mass screening and programming that included presentations and activities to educate about the transmission, symptoms and prevention of STIs, or emphasized adaptive decision-making skills and communication strategies. Other programs aimed at the general population using digital interventions, online programs and social media have been effective at increasing condom use, knowledge and perceived norms surrounding safe sex, especially among younger individuals (34–36). Similar programming and interventions could be implemented in CAF's BMT program or in other routine training or health promotion activities throughout the military career.

Strengths and limitations

This surveillance report, based on observational data, presents a baseline indication of pre-enlistment STI risk behaviours and STI history among recruits. It provides trend information for 16 years of recruit cohorts, and describes demographic differences in reports of STI history, number of sexual partners in the previous 12 months and frequency of condom use. These findings underscore the rising trends in risky behaviours associated with acquiring STIs in both the CGP and in CAF recruits, as well as provide insight into demographic information about groups of individuals at particular risk for STIs. These data could inform the development of screening tools to identify segments of the recruit population that might benefit from targeted interventions and health promotion programming.

This study and the RHQ are not without limitations. The RHQ data were self-reported; a technique which is prone to social desirability bias, recall bias and subjectivity (13,37). In addition, there was no way of assessing the accuracy of responses. Further, we had single item measures asking about sensitive topics. As such, some recruits may have been reluctant to disclose personal information about their sexual history and sexual behaviours, which may have resulted in under-reporting. The requirement for an individual to be in an "exclusive relationship" in the question about frequency of condom use may have resulted in the exclusion of individuals who had been in serially monogamous relationships. These individuals may not have responded, as they considered themselves to be in an "exclusive relationship", yet the nature of these relationships may expose them to a significant number of sexual partners in a short period of time. Moreover, the current RHQ does not consider sexual identity or sexual preference, which may impact risk behaviours for STIs and intervention strategies. Future research on STI risk behaviours with CAF members should take sexual preference into consideration. Finally, the RHQ is voluntary, so results are based on the subset of recruits who chose to respond rather than the whole population of recruits who trained during this period. Although the overall response rate was high (75.6%), there may be demographic differences between respondents and non-respondents.

Conclusion

Since 2003, risk behaviours for acquiring STIs have increased among recruits, but these rates are consistent with similar increases observed in CGP. Findings from this study provide baseline information about sexual risk behaviours for STIs among CAF population, and a demographic profile of those at higher risk for STIs. These findings may provide insight, especially for CAF, into avenues for targeted interventions and health promotion programming, such as education, primary and secondary prevention and screening initiatives.

Author's statement

HJME conceived and wrote the article.

Competing interests

None.

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References

1. Gaydos CA, Quinn TC, Gaydos JC. The challenge of sexually transmitted diseases for the military: what has changed? Clin Infect Dis 2000;30(4):719–22. DOI PubMed

2. Rasnake MS, Conger NG, McAllister K, Holmes KK, Tramont EC. History of U.S. military contributions to the study of sexually transmitted diseases. Mil Med 2005;170(4S):61–5. DOI PubMed

3. Aldous WK, Robertson JL, Robinson BJ, Hatcher CL, Hospenthal DR, Conger NG, Murray CK. Rates of gonorrhea and Chlamydia in U.S. military personnel deployed to Iraq and Afghanistan (2004-2009). Mil Med 2011;176(6):705–10. DOI PubMed

4. Jordan NN, Lee SE, Nowak G, Johns NM, Gaydos JC. Chlamydia trachomatis reported among U.S. active duty service members, 2000-2008. Mil Med 2011;176(3):312–9. DOI PubMed

5. Seña AC, Miller WC, Hoffman IF, Chakraborty H, Cohen MS, Jenkins P, McKee KT Jr. Trends of gonorrhea and chlamydial infection during 1985-1996 among active-duty soldiers at a United States Army installation. Clin Infect Dis 2000;30(4):742–8. DOI PubMed

6. Directorate of Force Health Protection. Communicable Disease Database. Ottawa (ON): DND; 2018.

7. Lee JE, Watkins K, Crane F, Schofield S, Tepper M. Perceptions of risk and testing for sexually transmitted infections among military personnel and health care providers in the Canadian Armed Forces: A qualitative study. Mil Behav Health 2015;3(1):37–46. DOI

8. Public Health Agency of Canada. Section 2: Canadian Guidelines on Sexually Transmitted Infections - Primary Care and Sexually Transmitted Infections. Ottawa (ON): PHAC; 2013. https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections/canadian-guidelines-sexually-transmitted-infections-17.html

9. Shafer MA, Boyer CB, Shaffer RA, Schachter J, Ito SI, Brodine SK. Correlates of sexually transmitted diseases in a young male deployed military population. Mil Med 2002;167(6):496–500. DOI PubMed

10. Leigh BC. Peril, chance, adventure: concepts of risk, alcohol use and risky behavior in young adults. Addiction 1999 Mar;94(3):371–83. DOI PubMed

11. Korzeniewski K. Sexually transmitted infections among army personnel in the military environment. In: Malla N, editor. Sexually Transmitted Infections. Rijeka, Croatia: InTech; 2012. p. 165-82.

12. Born JA, Bogaert L, Payne E, Wiens M. Results from Health and Lifestyle Information Survey of Canadian Forces Personnel 2008/2009 – Regular Force Version. Ottawa (ON): DND; 2010. http://publications.gc.ca/site/eng/410267/publication.html

13. Fenton KA, Johnson AM, McManus S, Erens B. Measuring sexual behaviour: methodological challenges in survey research. Sex Transm Infect 2001;77(2):84–92. DOI PubMed

14. Rotermann M. Sexual behaviour and condom use of 15- to 24-year-olds in 2003 and 2009/2010. Health Rep 2012;23(1):41–5. DOI PubMed

15. Choudhri Y, Miller J, Sandhu J, Leon A, Aho J. Infectious and congenital syphilis in Canada, 2010-2015. Can Commun Dis Rep 2018;44(2):43–8. DOI PubMed

16. Choudhri Y, Miller J, Sandhu J, Leon A, Aho J. Chlamydia in Canada, 2010-2015. Can Commun Dis Rep 2018;44(2):49–54. DOI PubMed

17. Choudhri Y, Miller J, Sandhu J, Leon A, Aho J. Gonorrhea in Canada, 2010-2015. Can Commun Dis Rep 2018;44(2):37–42. DOI PubMed

18. Public Health England. Sexually transmitted infections and screening for chlamydia in England, 2018. Health Protection Report. London (UK): Public Health England; 2019. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/806118/hpr1919_stis-ncsp_ann18.pdf

19. The Kirby Institute. HIV, viral hepatitis and sexually transmissible infections in Australia: Annual surveillance report 2017. Sydney (AU): Kirby Institute, University of New South Wales; 2017. https://kirby.unsw.edu.au/sites/default/files/kirby/report/SERP_Annual-Surveillance-Report-2017_compressed.pdf

20. McKay A, Milhausen R, Quinn-Nilas MA. Preliminary report: Sexually transmitted infection (STI) risk among single adults in the Trojan/SIECCAN Sexual Health at Midlife Study. Toronto (ON): SIECCAN; 2016. http://sieccan.org/wp-content/uploads/2018/05/Trojan-SIECCAN-STI-report.pdf

21. Milhausen RR, McKay A, Graham CA, Crosby RA, Yarber WL, Sanders SA. Prevalence and predictors of condom use in a national sample of Canadian university students. Can J Hum Sex 2013;22(3):142–51. DOI

22. Rotermann M, McKay A. Condom use at last sexual intercourse among unmarried, not living common-law 20- to 34-year-old Canadian young adults. Can J Hum Sex 2009;18(3):75–87. https://www.macleans.ca/wp-content/uploads/2009/09/condomusecjhs18309fin.pdf

23. Knight R, Falasinnu T, Oliffe JL, Gilbert M, Small W, Goldenberg S, Shoveller J. Integrating gender and sex to unpack trends in sexually transmitted infection surveillance data in British Columbia, Canada: an ethno-epidemiological study. BMJ Open 2016;6(8 e011209):e011209. DOI PubMed

24. Wong T, Singh A, Mann J, Hansen L, McMahon S. Gender differences in bacterial STIs in Canada. BMC Womens Health 2004;4 Suppl 1:S26. DOI PubMed

25. Thompson AE, Anisimowicz Y, Miedema B, Hogg W, Wodchis WP, Aubrey-Bassler K. The influence of gender and other patient characteristics on health care-seeking behaviour: a QUALICOPC study. BMC Fam Pract 2016;17:38. DOI PubMed

26. Mitchell KR, Mercer CH, Prah P, Clifton S, Tanton C, Wellings K, Copas A. Why do men report more opposite-sex sexual partners than women? Analysis of the gender discrepancy in a British national probability survey. J Sex Res 2019;56(1):1–8. DOI PubMed

27. Russak SM, Ortiz DJ, Galvan FH, Bing EG. Protecting our militaries: a systematic literature review of military human immunodeficiency virus/acquired immunodeficiency syndrome prevention programs worldwide. Mil Med 2005;170(10):886–97. DOI PubMed

28. McCuaig Edge HJ, Beswick-Escanlar V. Risk propensity and risk factors for sexually transmitted infections in Canadian Armed Forces recruits. Mil Behav Health 2020;09. DOI

29. Arcari CM, Gaydos JC, Howell MR, McKee KT, Gaydos CA. Feasibility and short-term impact of linked education and urine screening interventions for Chlamydia and gonorrhea in male army recruits. Sex Transm Dis 2004;31(7):443–7. DOI PubMed

30. Boyer CB, Shafer MA, Shaffer RA, Brodine SK, Ito SI, Yniguez DL, Benas DM, Schachter J. Prevention of sexually transmitted diseases and HIV in young military men: evaluation of a cognitive-behavioral skills-building intervention. Sex Transm Dis 2001;28(6):349–55. DOI PubMed

31. Booth-Kewley S, Minagawa RY, Shaffer RA, Brodine SK. A behavioral intervention to prevent sexually transmitted diseases/human immunodeficiency virus in a Marine Corps sample. Mil Med 2002;167(2):145–50. DOI PubMed

32. Jenkins PR, Jenkins RA, Nannis ED, McKee KT Jr, Temoshok LR. Reducing risk of sexually transmitted disease (STD) and human immunodeficiency virus infection in a military STD clinic: evaluation of a randomized preventive intervention trial. Clin Infect Dis 2000;30(4):730–5. DOI PubMed

33. Sánchez JL, Agan BK, Tsai AY, Macalino GE, Wurapa E, Mbuchi M, Dueger E, Horton KC, Montano-Torres SM, Tilley DH, Saylors KE, Puplampu N, Duplessis CC, Harrison DJ, Putnam SD, Garges EC, Espinosa BJ, Dejli J, Meyers M, Yingst SL, Jerse AE, Maktabi HH, Burke RL, Jordan NN, Nowak G, Hsu K, Soge OO, Holmes KK, McClelland RS, MacDonald MR, Pavlin JA, Gaydos JC, Tramont EC. Expanded sexually transmitted infection surveillance efforts in the United States military: a time for action. Mil Med 2013;178(12):1271–80. DOI PubMed

34. Mevissen FE, Ruiter RA, Meertens RM, Zimbile F, Schaalma HP. Justify your love: testing an online STI-risk communication intervention designed to promote condom use and STI-testing. Psychol Health 2011;26(2):205–21. DOI PubMed

35. Bull SS, Levine DK, Black SR, Schmiege SJ, Santelli J. Social media-delivered sexual health intervention: a cluster randomized controlled trial. Am J Prev Med 2012;43(5):467–74. DOI PubMed

36. Widman L, Nesi J, Kamke K, Choukas-Bradley S, Stewart JL. Technology-based interventions to reduce sexually transmitted infections and unintended pregnancy among youth. J Adolesc Health 2018;62(6):651–60. DOI PubMed

37. Fikretoglu D, D'Agata M, Blackler K, Liu A, McCuaig Edge H, Gottschall S, Blais AR. Social desirability effects in health research with Canadian Armed Forces recruits (DRDC-RDDC-2016-L324). Toronto (ON): Defence Research and Development Canada; 2016.

The role of Force Health Protection in the Canadian Armed Forces' response to the COVID-19 pandemic

Heather McCuaig Edge[1,2]*, Samantha Carlucci[1], Diane Lu[1]

Abstract

Within the Canadian Armed Forces (CAF), public health is managed by the Directorate of Force Health Protection (DFHP), a branch of the Canadian Forces Health Services Group. Since the emergence of the novel coronavirus (SARS-CoV-19), DFHP has become heavily involved in health surveillance, outbreak monitoring, policy development, providing evidence-based guidance and advice, liaising with other national, provincial/territorial, municipal and international public health agencies, and ensuring environmental safety of CAF members. Some specific activities include supporting operations and deployments, amending policies and training and promoting hand hygiene, physical distancing and personal protective equipment use. In addition to taking measures to protect its members, CAF-Department of National Defence has contributed to Canada's national response to coronavirus disease 2019 (COVID-19). The DFHP will be developing training for allied health professionals to assist with contact tracing and follow-up, and will ensure adequate resources are in place to manage surge capacity for COVID-19. With these ongoing efforts, initiatives and lessons learned, DFHP is well placed to carry on with its mandate to protect and promote the health and well-being of CAF members and National Defence civilian employees, assisting Canadians and ensuring that CAF members are ready to serve their missions at home and abroad.

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Keywords: COVID-19, Directorate of Force Health Protection, Department of National Defence, pandemic response, coronavirus, surveillance, Canadian Armed Forces, public health, military

Introduction

In December 2019, a novel coronavirus emerged in Wuhan, China, causing an outbreak of the infectious disease, coronavirus disease 2019 (COVID-19), which has since become a widespread global pandemic (1). Public health agencies around the world and within Canada have been actively monitoring and responding to the needs of their respective jurisdictions. The responsibility of promoting public health within the Canadian Armed Forces (CAF) is managed and maintained by the Directorate of Force Health Protection (DFHP), a branch of the Canadian Forces Health Services Group.

Role of Force Health Protection in the Canadian Armed Forces' response to coronavirus disease 2019

DFHP is responsible for promoting the well-being of military members, and for epidemiological surveillance, communicable disease control and prevention, health promotion and occupational and environmental health. As such, during the COVID-19 outbreak, DFHP became heavily involved in health surveillance, outbreak monitoring, policy development, providing evidence-based guidance and advice, liaising with other national, provincial and territorial, municipal and international public health agencies, and ensuring the environmental safety of CAF members and Department of National Defence (DND) staff members.

CAF is required to maintain operational readiness to respond to emergencies in times of need while protecting the health of its members and taking precautions to prevent the further spread of the virus that causes COVID-19 (2). Like all Canadian government departments, CAF and DND were impacted by the previously unprecedented global and national COVID-19 response enacted in March 2020 following the World Health Organization declaration of a pandemic. Some direct impacts of the COVID-19 pandemic on CAF are outlined as follows:

1. Increasing the monitoring and surveillance of CAF members working abroad, for those deployed on operations, and at home
2. Taking measures to adjust operations, such as delaying deployments, amending the number of personnel who are deployed, and modifying the length of deployments to ensure personnel are protected while continuing to perform critical tasks (3)
3. Promoting good hand hygiene and physical distancing whenever possible, and donning appropriate personal protective equipment (PPE)
4. Reducing contact by imposing a 14-day quarantine before and after deployments on operations, with the Royal Canadian Navy testing sequestered individuals prior to boarding the ship
5. Requiring personnel to disclose their potential exposure to COVID-19 and to seek medical care promptly if they develop flu-like symptoms within 14 days of travel or have come into contact with someone infected with COVID-19 (2)
6. Cancelling annual military exercises and postponing basic military training and educational training across multiple sites, including the Canadian Forces Leadership and Recruit School in St-Jean, Québec and schools at Canadian Forces Base in Borden, Ontario

In addition to taking measures to protect its members, CAF-DND has contributed to Canada's national response to COVID-19, including retrieving and housing repatriated Canadians from travel abroad at Canadian Forces Base Trenton and Operation LASER, which involves assisting with the care of elderly residents in Ontario and Québec long term care facilities, deploying Canadian Rangers to assist northern communities in Québec and Saskatchewan, and contributing to community-level activities to assist municipalities in managing the spread of COVID-19 (4). As part of Operation LASER, Dental Technicians are currently assisting civilian public health authorities with daily follow-up of asymptomatic civilian personnel who are self-monitoring and/or self-isolating following a potential exposure to a COVID-19 positive case.

Many of the decisions, practices, and activities described above were influenced by the advice and direction from DFHP. Each section within DFHP has been heavily involved in and contributed to different aspects of CAF-DND COVID-19 response. The Epidemiology section has provided surveillance and monitoring of Regular and Reserve Force CAF members for COVID-19, especially given deployments to long term care facilities (within Canada) and deployments abroad. This has been achieved with the Canadian Forces Health and Evaluations Reporting Outcomes system and the Disease and Injury Surveillance System. The health promotion branch, *Strengthening the Forces*, has been involved in promoting healthy lifestyle behaviours and providing clinical guidance including smoking cessation and examining the role of vitamin D in preventing COVID-19. The World Health Organization has identified tobacco smoking as a risk factor for COVID-19 (5) and smoking has been presumed to be associated with adverse disease prognosis (6). In response, *Strengthening the Forces* has partnered with dental and pharmacy, among other partners within Canadian Forces Health Services, to actively promote smoking cessation to reduce harm to smokers during the pandemic. *Strengthening the Forces* has also been involved in the implementation of a contact tracing surge capability for CAF members. The Occupational and Environmental Health section has been continuously monitoring the pandemic and adjusting measures to protect CAF members and DND employees accordingly. These control measures consist of providing advice and guidance on feasible and effective engineering controls (i.e. proper operation of building ventilation systems, safeguarding drinking water potability), administrative controls (i.e. personal hygiene measures) and on the use of PPE (i.e. fit testing, medical grade versus industrial respirators, N95 reprocessing and the use of expired respirators). In addition, Occupational and Environmental Health has been providing support to the planning and implementation of Operation GLOBE (repatriation of Canadian citizens from abroad at the start of the pandemic) and Operation LASER, advice for Business Resumption Planning and assistance to the Canadian Forces Intelligence Command to assist their medical intelligence team. The Communicable Disease Control Program has been providing guidance on CAF-specific public health measures and policies to clinicians regarding diagnosis and management of cases including outbreak management. The Communicable Disease Control Program has been involved in infection prevention and control, contact tracing, responding to cluster outbreaks and the development of educational material for healthcare providers and CAF members.

Given that the national response to the pandemic, and CAF members themselves, are dispersed across the country, DFHP has had to work closely with the national, provincial/territorial, and municipal civilian public health sectors to achieve accurate COVID-19 surveillance. Regular Force and Class B and C Reserve Force members typically obtain their health care through base/wing clinics. However, part-time Class A Reserve Force members primarily obtain their health care through the civilian sector and much of the COVID-19 testing for any CAF personnel early during the pandemic was conducted by civilian provincial laboratories. Clinical encounters with Canadian Forces Health Services clinics are captured by DFHP, with initiation of appropriate follow-up and contact tracing. However, surveillance and monitoring for all CAF personnel is complex because testing and contact tracing is intertwined between the military and civilian sectors (local/provincial public health authorities).

Adding to this complexity are the regional differences among the bases/wings across CAF due to provincial/territorial differences in reporting confirmed cases, contact tracing, developing policies around public health measures, and declaring states of emergencies. DFHP has been tasked by the Deputy Surgeon General with developing a training program for allied health professionals to conduct contact tracing to respond to possible surge capacity and cluster outbreaks of COVID-19.

As the situation normalizes and people return to work, a top priority for DND is the health of its CAF personnel. The DFHP is: 1) actively engaged in providing advice to CAF leadership regarding business resumption activities, 2) will continue to follow the epidemiological situation and scientific evidence closely in order to help make evidence-based recommendations on public health preventive measures, and 3) will continue to provide guidance and revise policies as the situation evolves.

Ensuring better emergency preparedness in the future

Throughout this pandemic, DND has been made aware of operational limitations. Some of the ways that DFHP is exploring to ensure better emergency preparedness in the future are described as follows:

1. Increase staffing resources, including ensuring that there is a surplus of readily-deployable trained staff (e.g. Preventive Medicine Technicians)
2. Improve communication, collaboration, and coordination of efforts between the military and civilian sectors
3. Improve surveillance capacity
4. Manage resources (e.g. PPE) as well as expectations of senior leadership/Chain of Command

With adequate support to these ongoing efforts, initiatives, and lessons learned, DFHP is well placed to carry on with its mandate to protect and promote the health and well-being of CAF members, and to ensure that members are ready to serve on their missions, both at home and abroad.

Authors' statement

HJME, SC and DL were all involved in the conceptualization, drafting, and revising of the paper.

Competing interests

None.

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References

1. World Health Organization. Q&A on coronaviruses (COVID-19). Geneva (CH): WHO; 2020 (accessed 2020-05-08). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/question-and-answers-hub/q-a-detail/q-a-coronaviruses

2. Government of Canada. Military response to COVID-19. Government of Canada; 2020 (accessed 2020-05-08). https://www.canada.ca/en/department-national-defence/campaigns/covid-19-military-response.html?utm_source=covid-campaign&utm_medium=heading&utm_campaign=covid19

3. National Defence. Changes to military operations in response to COVID-19. DND; 2020 (accessed 2020-05-08) https://www.canada.ca/en/department-national-defence/services/operations/military-operations/covid-19.html

4. National Defence. Operation LASER. DND; 2020 (accessed 2020-05-08). https://www.canada.ca/en/department-national-defence/services/operations/military-operations/current-operations/laser.html

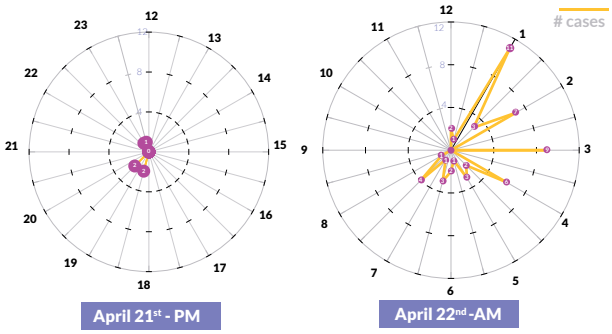
5. World Health Organization (Region Office for the Eastern Mediterranean). Tobacco Free initiative: Tobacco and waterpipe use increases the risk of COVID-19. Cairo (Egypt): WHO (accessed 2020-04). www.emro.who.int/tfi/know-the-truth/tobacco-and-waterpipe-users-are-at-increased-risk-of-covid-19-infection.html

6. Vardavas CI, Nikitara K. COVID-19 and smoking: A systematic review of the evidence. Tob Induc Dis 202018(March):20. DOI PubMed

Foodborne illness outbreak investigation of April 21st 2018

Exercise Maple Resolve 2018

Onset time of cases - MR18 22 Apr 2018 foodborne outbreak



20 Apr
- Pork dish preparation

21 Apr
- **14:30** - Evening meal prepared/reheated
- **16:00** - Meal pickup
- **17:30** - Meal service begins
- **18:30 - 23:59** - **First 8 cases**

22 Apr
- **03:00** - Initial communication with the field clinic (**14 cases total**)
- **04:48** - Coordination of the evacuation (**19 cases total**) to base clinic. Investigation begins
- **07:19** - **21 new cases**, All remaining members in the outpost, transferred to main camp (isolation facility)
- **09:00** - Communication from another outpost, **12 cases** with similar s & s. cases transferred to main camp
- **15:00** - The initial 19 cases were transferred to the main camp
- **16:00** - Arrival of the 19 initial cases, all of the identified cases were housed in the isolation facility (**102 total**, **62 symptomatic**, **40 asymptomatic)**

23 Apr
- **09:00** – Isolated members discharged

24 Apr
- Investigation
- Gathering of the line listing data
- Calculation of the food item attack rate
- Inspection of the food preparation kitchen
- Revision of the operational procedure for food preparation and handling of the thermal containers used for transport of the meals

30 Apr
- **Final investigation report submitted**

Case definition

Status		# of cases
	Members taking part in Exercise (EX) MR18 that ate from hay boxes on the evening of 21 April 2018 [...].	
Confirmed	[...] with symptoms of non-bloody diarrhea with a stool sample confirmed positive for the presence of *C. perfringens*.	6
Probable	[...] who displayed the following symptoms: diarrhea with or without cramping.	55
Possible	[...] who displayed gastro-intestinal symptoms without diarrhea.	1

FOOD ITEM ATTACK RATE

Unit	S&S	Total	Rice	Corn	Pork	Soup	Salad	Dessert	Fruit	Milk	Juice
5 RALC	with	54	49	47	54	20	17	29	6	15	6
	without	29	15	13	12	4	4	10	3	6	1
1 R22R	with	10	10	10	10	7	3	7	2	4	6
	without	9	9	7	9	4	0	6	4	4	6
Total			83	9	85	35	24	52	15	29	19
Attack rate %			71.1	74.0	75.3	77.1	83.3	69.2	53.3	65.5	63.3

Although a higher attack rate was observed with the pasta salad (83.3) and the soup (77.1) their overall consumption by CAF personnel was very low. The pork dish was identified as the most potential causal food item since its overall attack rate was the next highest, every symptomatic individual from both camps ate this food item, and C. perfringens is most often found in meat protein.

(Bennett, S. D., Walsh, K. A., & Gould, L. H. (2013). Foodborne Disease Outbreaks Caused by Bacillus cereus, Clostridium perfringens, and Staphylococcus aureus--United States, 1998-2008. Clinical Infectious Diseases, 57(3), 425-433. https://doi.org/10.1093/cid/cit244

SUSPECTED PATHOGEN

Clostridium perfringens was suspected as the causal food agent in the pork based on clinical presentation (acute onset of non-bloody diarrhea with no emesis). This bacterial agent is present in the environment, which would explain the environmental contamination due to the cow manure present in the nearby field combined with the very windy and dry weather of the season in Alberta. Further proliferation occurred because of the improper use of the thermal containers, which kept the food in the thermal danger zone (4 to 60°C).

SOURCES OF CONTAMINATION AND PROLIFERATION

Initial contamination:

Spores present in the environment contaminated the food prepared in the kitchen tent on a very dry and windy day.

Initial proliferation:

Poor cooling practices from the kitchen staff lead to a prolonged exposure of the pork dish to the thermal danger zone (4 to 60°C).

Secondary proliferation:

Poor practices for the use of the thermal container left the food items in the dangerous temperature zone (4 to 60°C) for a prolonged period of time. By not preheating the container for the prescribed hour before transporting the food pans, and leaving the water in the containers, the water acted as a conductor between the food pans and the containers' walls, thus reducing the temperature of food much faster.

Suspected causes	Improper handling	Risk mitigation
Poor cooling practices prolonged exposure to the thermal danger zone (4 to 60°C).	Cooling of food items at room temperature for four hours without temperature monitoring before refrigeration.	Temperature monitoring of the food item and rapid refrigeration as soon as 60°C is reached.
Poor practices for the preparation of the thermal container allowed for rapid cooling within the thermal danger zone.	Thermal containers were not preheated and hot water was left in them during transport.	The containers should be preheated with boiling water for 1 hour prior to use and the heating water should be discarded before loading the food into them.
Poor practices for the use of the thermal container allowed for rapid cooling and prolonged exposure to the thermal danger zone.	Thermal boxes were left semi open on the service tables for more than 3 hours.	Food items kept in the thermal containers should be discarded within 2 hours after being opened.
Poor maintenance the thermal container prevented optimal insulation.	Most thermal containers had one or multiple broken latch(es), resulting in an incomplete seal of the containers.	Broken containers should not be used; latches should be repaired or the containers replaced.

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Surveillance using outbreak markers for Canadian Armed Forces (CAF) deployed operations, 2017–2019

3 CAF overseas Operations

Canadian Armed Forces (CAF) operations vary by **mission purpose, location, and number of personnel**. To help troops stay healthy on deployments, the **Disease and Injury Surveillance System** is used to meet health surveillance requirements in theatre.

Outbreak markers

	Average CAF denominator per week	GI infections and ARTIs - rates per 100 person-years over a 3 year period	Lost duty days by GI infections and ARTIs over a 3 year period
Op UNIFIER	~201 (99-254)	21.1 65.0	58.6% 41.4%
Op REASSURANCE	~405 (97-540)	13.3 54.6	22.8% 77.2%
Op IMPACT	~277 (190-629)	13.8 42.2	41.8% 58.2%

Outbreak markers
- gastrointestinal (GI) infections
- acute respiratory tract infections (ARTIs)

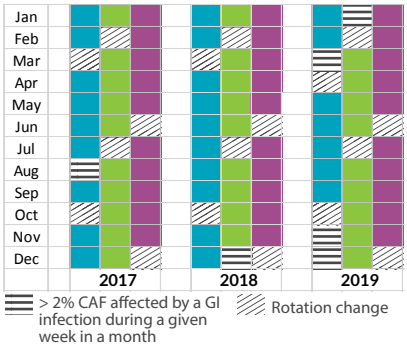
ARTI rates were over three times more common than the rates of GI infections.

Overall ARTIs took a higher toll on lost duty days than GI infections.

3 years of results 2017–2019

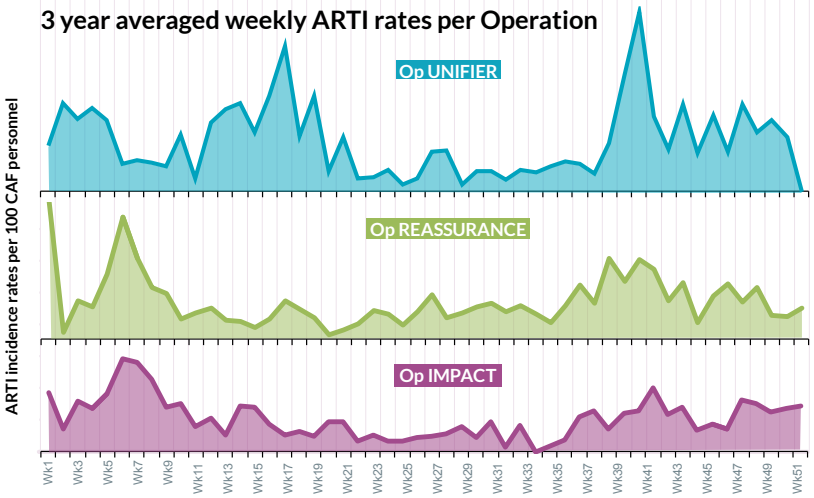
The trend in ARTI rates observed for all three operations are comparable to the influenza seasonal patterns in the northern hemisphere (Sep to Apr).

GI infection outbreaks by year, month and Operation



Less than 2% of CAF personnel were affected by a GI infection during a given week in a month on Op IMPACT.

3 year averaged weekly ARTI rates per Operation



GI infections and to a greater extent ARTIs continue to play an important role in CAF deployed troops in both training and combat settings. Both of these conditions contribute to lost duty days which has the ability to impact operational readiness.

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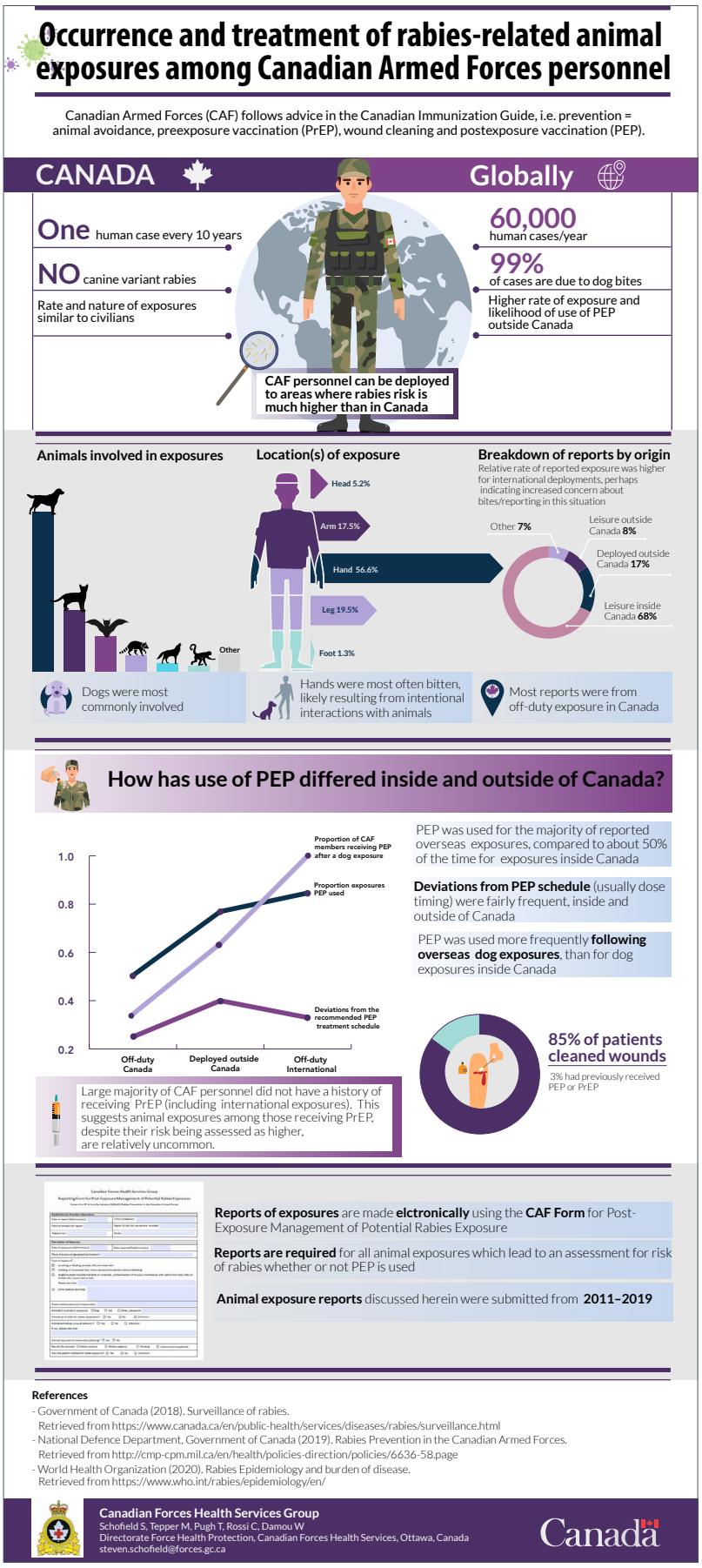

References

- Government of Canada (2018). Surveillance of rabies. Retrieved from https://www.canada.ca/en/public-health/services/diseases/rabies/surveillance.html
- National Defence Department, Government of Canada (2019). Rabies Prevention in the Canadian Armed Forces. Retrieved from http://cmp-cpm.mil.ca/en/health/policies-direction/policies/6636-58.page
- World Health Organization (2020). Rabies Epidemiology and burden of disease. Retrieved from https://www.who.int/rabies/epidemiology/en/

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Extragenital testing increases case detection of gonorrhea and chlamydia: The impact of implementing nucleic acid amplification testing

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Abstract

Background: Nucleic acid amplification testing (NAAT) was validated in Ontario in 2018 to test for chlamydia and gonorrhea at extragenital (pharyngeal, rectal) sites. Prior to this validation, extragenital testing could be done only by culture in Ontario. The objective of this study was to determine the number and proportion of gonorrhea and chlamydia cases that were detected exclusively through extragenital (pharyngeal and/or rectal) testing after the implementation of extragenital NAAT for these two infections at Sexual Health Clinic among gay, bisexual, and other men who have sex with men (gbMSM).

Methods: Case and laboratory data from before and after NAAT implementation were used to compare the rates of diagnosis of gonorrhea and chlamydia among gbMSM who presented at Sexual Health Clinics and the percent increase in diagnoses in gbMSM in the entire population.

Results: Among gbMSM seen at the clinic after implementation of NAAT testing, 70% of gonorrhea cases and 65% of chlamydia cases were detected exclusively at extragenital sites, corresponding to a four and two-fold increase, respectively, in the average annual number of cases diagnosed. As well, although approximately 50% more pharyngeal than rectal testing occurred, a higher proportion of chlamydia cases were detected rectally than would have been expected; this was not the case for gonorrhea, where most infections were pharyngeal.

Conclusion: It is important that clinicians perform extragenital testing among gbMSM who have sexual contact involving extragenital sites with more than one partner.

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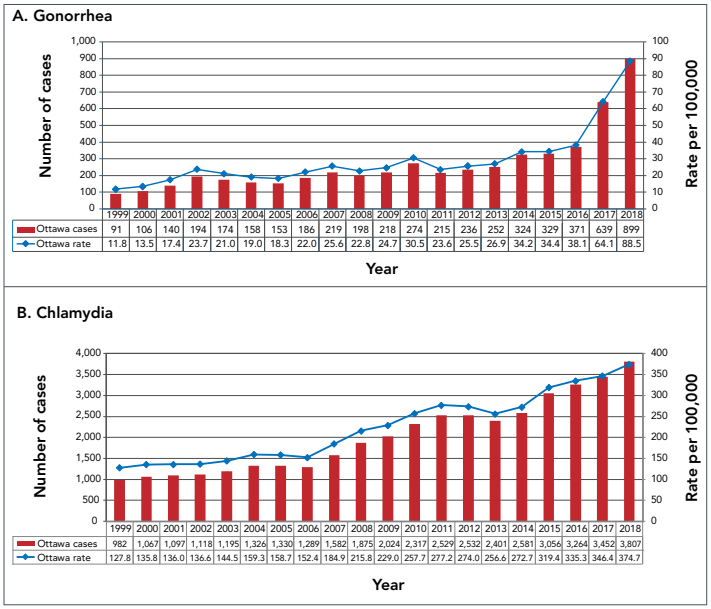
Keywords: gonorrhea, chlamydia, NAAT, extragenital, pharynx, rectum

Introduction

Neisseria gonorrhoea (*N. gonorrhoea*) and *Chlamydia trachomatis* (*C. trachomatis*) are the most commonly reported sexually transmitted infections (STIs) in Canada, and their incidence is increasing (1). In Ottawa (Ontario), the observed incidence rates of gonorrhea and chlamydia have also been increasing over the last 20 years; however, the rate of increase for gonorrhea has been significantly higher since 2016 (**Figure 1**) (2). A total of 90 and 390 cases of gonorrhea and chlamydia, respectively, were diagnosed per 100,000 population in 2018 in Ottawa; up from 38 and 335 cases per 100,000 in 2016 (2). The rates of these infections in Ottawa have increased most markedly among gay, bisexual and men who have sex with men (gbMSM). In 2018, gbMSM comprised 45% of gonorrhea and 10% of chlamydia cases (2).

While gonorrhea and chlamydia are classically considered infections of the genital mucosa, infection of extragenital sites, such as the pharynx and rectum, is common (3). Because these infections are often asymptomatic or clinically non-specific when symptomatic, they are likely a source of ongoing transmission (4). For the same reasons, diagnosis of these infections requires laboratory confirmation (5). Culture was the primary detection method for urogenital, rectal and pharyngeal infections until the availability of more sensitive molecular testing, such as

Figure 1: Number and rate of diagnosis of gonorrhea and chlamydia, Ottawa, 1999–2018



Data notes: Data downloaded from integrated Public Health Information System (iPHIS), November 8, 2019 by Ottawa Public Health (OPH). 2019 count includes reports through September 30, 2019; the 2019 rate is adjusted for partial year

nucleic acid amplification testing (NAAT) (6). Although *Canadian Guidelines on Sexually Transmitted Infections* (5) recommend NAAT, it is not approved by Health Canada for extragenital testing, unless validated by local laboratories.

In Ontario, extragenital NAAT was validated at STI clinics in Ottawa and Toronto among gbMSM, sex trade workers and their clients, and known contacts of persons diagnosed with gonorrhea or chlamydia (7). This validation involved clinicians performing extragenital cultures and NAAT for the foregoing clients when they consented to such testing. All such samples were submitted to the Public Health Ontario Laboratory for testing and comparison. NAAT, compared with culture, had 92.2% sensitivity and 99.9% specificity for pharyngeal testing and 99.4% sensitivity and 99.9% specificity for rectal testing. Gonorrhea NAAT, compared with culture, showed similar results; identifying 100% sensitivity for both pharyngeal and rectal testing and 98.2% and 99.0% specificity for pharyngeal and rectal specificity, respectively (7). Per site, culture, compared with NAAT, had a detection rate of 13% for pharyngeal gonorrhea, 67% for rectal gonorrhea, 17% for pharyngeal chlamydia and 38% for rectal chlamydia. This validation of extragenital NAAT occurred between July and November 2017, followed by full implementation in April 2018. Despite this change in testing methodology, there were no clinical practice changes during this time. National guidelines recommended extragenital testing, and in the Sexual Health Clinic, such testing was routinely performed (using culture) when clinically indicated and was accepted by clients. Extragenital testing was carried out by clinicians who followed established clinical practices for collecting samples from these sites. Samples were then submitted to the Public Health Ontario Laboratory. During the study period, patient-collected extragenital testing was not available.

While the potential impact of changing from culture to NAAT for the detection of extragenital chlamydia and gonorrhea in gbMSM patients has been established (8), the effect on surveillance at the population level has not been described. Furthermore, data on this topic have arisen from studies validating extragenital testing in STI clinics (8) and not from routine clinical practice that incorporates NAAT, such as that which occurs at the Sexual Health Clinic, where there are approximately 20,000 unique patient encounters per year. As such, in this paper, we enumerate extragenital gonorrhea and chlamydia case-finding pre/post-implementation of rectal and pharyngeal NAAT and show the effect of this testing on public health surveillance for these infections in Ottawa. Our analysis shows the proportion of gonorrhea and chlamydia infections that would be missed in an STI clinic if urogenital testing (but not NAAT) was performed.

Methods

Information about individual gonorrhea and chlamydia cases diagnosed among Ottawa residents from 1999 to 2019 was extracted from the integrated Public Health Information System (2) by Ottawa Public Health on November 19, 2019. Date of diagnosis, body site(s) testing positive, testing provider and gbMSM status were extracted and analysed for two time periods relative to validation and implementation of extragenital NAAT: pre-validation/pre-implementation (July 1, 2012–June 30, 2017) and implementation (May 1, 2018–October 31, 2019). Cases diagnosed through extragenital testing were those for whom extragenital testing was positive and genital testing was negative or not performed (**Table 1**). Cases diagnosed through genital testing were those for whom urogenital testing was positive regardless of whether extragenital testing was carried out and irrespective of the results of such extragenital testing.

Table 1: Classification of testing by site of positive test result

Category	Site of positive test result
Extragenital	Pharyngeal only
	Rectal only
	Pharyngeal and rectal
Genital	Urogenital only
	Urogenital and pharyngeal
	Urogenital and rectal
	Urogenital and pharyngeal and rectal

The impact of extragenital testing on case-finding was evaluated in two ways using Stata v.16.0. First, the average annual number of cases of gonorrhea and of chlamydia diagnosed during each time period through extragenital or through genital testing of

gbMSM presenting at the Sexual Health Clinic were calculated and compared using tests of proportion. Second, the percent increase in diagnoses in the entire population due to extragenital testing, as opposed to genital testing, was calculated for each infection and time period. Additionally, we performed a test of proportions to compare the percent positivity of pharyngeal and rectal gonorrhea and chlamydia infections, based on the total volume of such tests that were submitted for testing.

The percent positivity for extragenital NAAT conducted at the Sexual Health Clinic during a subset of the implementation period (April 9–August 8, 2019) was provided by the Public Health Ontario Laboratory, which tests all specimens from the Sexual Health Clinic.

Results

During the five-year period before the validation of extragenital NAAT (July 1, 2012–June 30, 2017), an average of 52 cases of gonorrhea and 83 cases of chlamydia were identified annually among gbMSM attending the Sexual Health Clinic (**Table 2**). In the 18 months (May 1, 2018–October 31, 2019) following implementation of extragenital NAAT at the Sexual Health Clinic, an average annual number of 220 and 210 cases of gonorrhea and chlamydia, respectively, were identified in gbMSM (**Table 3**), and this was despite no increase in testing volume from 2015–2019.

Of the cases identified post-implementation, 70% of gonorrhea cases and 65% of chlamydia infections were identified from extragenital testing only; the remainder was identified from the testing of either exclusively genital or genital and extragenital sites. In contrast, significantly fewer infections (31% of gonorrhea and 41% of chlamydia, $p<0.00001$ for each) identified before validation of extragenital NAAT were detected from extragenital testing only.

Table 2: Detection of gonorrhea or chlamydia by site of infection, gbMSM, Sexual Health Clinic[a], Ottawa, July 1, 2012–June 30, 2017

Cases	Gonorrhea			Chlamydia		
	Number of cases	Average annual number of cases	Percent of all cases	Number of cases	Average annual number of cases	Percent of all cases[b]
All cases	258	51.6	100.0%	414	82.8	100.0%
Total with known site	258	51.6	100.0%	413	82.6	99.8%
Genital only	140	28	54.3%	215	43	51.9%
Genital and extragenital	37	7.4	14.3%	27	5.4	6.5%
Extragenital only	81	16.2	31.4%	171	34.2	41.3%
Pharyngeal	14	2.8	5.4%	18	3.6	4.3%
Rectal	61	12.2	23.6%	142	28.4	34.3%
Pharyngeal and rectal	6	1.2	2.3%	11	2.2	2.7%
Other	0	0	0.0%	1	0.2	0.2%

Abbreviation: gbMSM, gay, bisexual, and other men who have sex with men
[a] Data source: Ministry of Health and Long-term Care, integrated Public Health Information System, extracted by Ottawa Public Health, November 19, 2019
[b] Does not include one case where site was unknown

Table 3: Detection of gonorrhea or chlamydia by site of infection, gbMSM, Sexual Health Clinic[a], Ottawa, May 1, 2018–October 31, 2019

Cases	Gonorrhea			Chlamydia		
	Number of cases	Average annual number of cases	Percent of all cases	Number of cases	Average annual number of cases	Percent of all cases[b]
All cases	348	219.8	100.0%	332	209.7	100.0%
Total with known site	348	219.8	100.0%	330	208.4	99.4%
Genital only	41	25.9	11.8%	75	47.4	22.6%
Genital and extragenital	64	40.4	18.4%	40	25.3	12.0%
Extragenital only	243	153.5	69.8%	215	135.8	64.8%
Pharyngeal	106	66.9	30.5%	19	12.0	5.7%
Rectal	72	45.5	20.7%	152	96.0	45.8%
Pharyngeal and rectal	65	41.1	18.7%	44	27.8	13.3%
Other	0	0.0	0.0%	2	1.3	0.6%

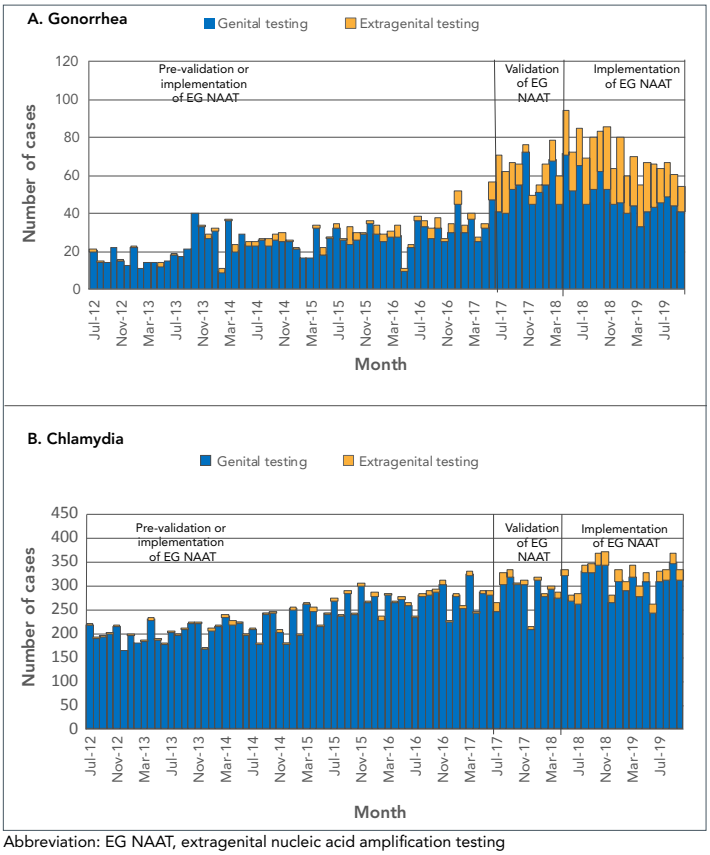
Abbreviation: gbMSM, gay, bisexual, and other men who have sex with men
[a] Data source: Ministry of Health and Long-term Care, integrated Public Health Information System, extracted by Ottawa Public Health, November 19, 2019
[b] Does not include two cases where site was unknown

Gonorrhea and chlamydia were differentially detected in the pharynx and rectum of gbMSM clients at the Sexual Health Clinic. Approximately 50% more pharyngeal than rectal NAATs were carried out, and the percent positivity of pharyngeal and rectal testing was 8.3% and 9.9%, respectively, for gonorrhea, and 1.6% and 11.3%, respectively, for chlamydia (*Personal communication, Public Health Ontario. Impact of pharyngeal and rectal Chlamydia trachomatis and Neisseria gonorrhoeae NAAT, July 2, 2019*). It follows that, for gonorrhea, more cases, in terms of number and proportion of diagnoses, were detected by pharyngeal testing (49%), compared with rectal testing (39%) (Table 3; pharyngeal+pharyngeal/rectal versus rectal+pharyngeal/rectal). In contrast, for chlamydia, while the volume of pharyngeal and of rectal testing would predict the identification of more pharyngeal than rectal cases, a higher proportion of cases were identified through rectal testing (59%) than expected, compared to pharyngeal testing (19%) ($p<0.0001$).

Lastly, the number of cases identified at the population level in Ottawa increased as a result of extragenital NAAT. This increase was most striking for gonorrhea: between 1999 and 2016, the rate of gonorrhea increased an average of 13% each year; between 2016 and 2018, when extragenital NAAT was validated and implemented, the average annual increase was 65%. Before the validation and implementation of extragenital NAAT, infections detected from extragenital sites alone resulted in the identification of 9% and 2% more gonorrhea and

chlamydia cases, respectively, than that identified by genital testing (**Figure 2**). In contrast, 46% and 7% more gonorrhea and chlamydia cases, respectively, were identified in the 18 months following implementation of extragenital NAAT than what was identified using genital testing.

Figure 2: Case-finding by genital or extragenital testing, Ottawa, July 2012–October 2019



Abbreviation: EG NAAT, extragenital nucleic acid amplification testing

Discussion

Our analysis of gonorrhea and chlamydia testing at the Sexual Health Clinic, comparing the period when only culture was available for extragenital testing to the period when this testing was performed by NAAT for gbMSM and other identified groups, showed a significant increase in the proportion of these infections detected exclusively from extragenital sites. These findings indicate that a change in laboratory technology, without a change in clinical practice, resulted in an increase in case finding that had a profound effect on the number of diagnoses across Ottawa. For gonorrhea, the finding of extragenital infections among gbMSM visiting the Sexual Health Clinic increased from accounting for 31% of infections pre-NAAT to 70% post-NAAT; that is, under current practices, for every three cases where gonorrhea caused a genital infection, there were seven cases where this infection was exclusively extragenital. For chlamydia, the finding of extragenital infections increased from 41% pre-NAAT to 65% post-NAAT.

Limitations

These results must be interpreted considering three main limitations. First, the test results that we analyzed were from gbMSM who attended an STI clinic. The gbMSM seen by community providers might have had a lower prevalence of infection at extragenital sites. However, the observation that there were seven cases of extragenital gonorrhea for every three genital infections among this group of STI clinic clients suggests that many infections might be missed in the community, even if the underlying prevalence of infection was lower in the community. Conversely, it is also plausible that gbMSM who visit STI clinics could have a lower burden of STIs, as a result of routine health-seeking practices; meaning that higher rates of extragenital infection could be present among gbMSM who either seek testing less frequently or who do so from community providers. Second, because not all at-risk gbMSM in Ottawa might be receiving extragenital NAAT testing, these results could be an underestimate of its impact. That is, if all community providers performed extragenital NAAT testing on their at-risk gbMSM patients, the impact on detection might be even greater than documented here. Third, the increases seen in our analysis could be due to true increases in incidence, rather than missed infections that were identified by a new testing technology. That is, the increased rates of gonorrhea and chlamydia may have coincidentally corresponded with the change in testing technology. Comparisons with other jurisdictions could be made; however, these would be limited by the fact that currently reported epidemiologic data from these other locations do not differentiate by anatomic site of infection. Another strategy could have been to perform different analyses (e.g. time series approach), although this would require access to data not routinely available to STI clinic or public health unit staff and likely would not have identified markedly different findings, as the overall testing rates between 2015 through 2019 were relatively unchanged in our clinic.

Recommendations

Regarding clinical practice, the main recommendation stemming from our results is that providers should inform patients that they can acquire extragenital gonorrhea and chlamydia infections and should offer extragenital testing to gbMSM who engage in oral and/or anal sex with more than one sexual partner. Such screening should be offered irrespective of reported condom use, as studies (7,9,10) have identified rectal infections despite patients' self-reported safe sexual practices. These results, moreover, support current Public Health Agency of Canada (5) STI screening guidelines to perform extragenital testing on at-risk patients, unless the patient declines testing or denies sexual contact at an extragenital site. These results also align with the United States Centers for Disease Control and Prevention (11) recommendation that extragenital screening should occur "regardless of condom use during exposure". Of issue, however, is that previous research has identified low rates of extragenital testing in many clinical settings (12,13), which could result in many missed diagnoses.

Importantly, our findings also align with Canadian HIV preexposure prophylaxis (PrEP) guidelines (14), which recommend performing STI testing every three months during follow-up. Providers who offer PrEP to gbMSM, but do not perform extragenital testing, may miss a sizeable number of infections. This is problematic from an HIV prevention perspective: because gonorrhea and chlamydia induce inflammation in the rectum, they can increase the risk of HIV acquisition (15). Identifying and treating rectal gonorrhea and chlamydia infections may, therefore, function not only as a control strategy for these two infections, but also as an HIV prevention intervention. Conversely, the detection of these infections is a clinical indication for PrEP, as they provide evidence of condomless receptive anal sex in the context of increased biologic risks for HIV acquisition (16,17). Screening for these infections, therefore, also functions as an HIV prevention strategy, both to reduce biologic susceptibility and to identify persons in need of PrEP.

Because studies have shown that the acceptability of rectal swabs is lower than that of pharyngeal swabs (18,19) providers might consider offering pharyngeal testing with or without rectal testing. While testing at both extragenital sites, when clinically indicated, is ideal, our analysis shows that pharyngeal testing alone would capture 70% and 29%, respectively, of gonorrhea and chlamydia cases among gbMSM that would not be detected with urine testing alone. Testing the pharynx but not the rectum could also be appropriate, as more gbMSM report performing oral sex than receptive anal sex (20); in such cases, the addition of pharyngeal swabs would ensure more comprehensive testing. Offering pharyngeal swabs, irrespective of sexual orientation, may also provide a way for patients to agree to more comprehensive testing without having to disclose the sex of their sexual partners to healthcare providers. This might increase testing among gbMSM in primary care because up to 50% of gbMSM patients report being reluctant to disclose their sexual orientation to healthcare providers (21,22). Offering pharyngeal swabs may also increase detection among other groups, although the proportion of infections at extragenital sites for non-gbMSM groups (e.g. males or females who have opposite sex partners) is unknown and warrants research. One possible downside to this recommendation is that our analysis identified more rectal than pharyngeal chlamydia infections, which aligns with a recent literature review that found rates of rectal chlamydia as 2.1%–23.0% (median 18.9%) compared to 0%–3.6% (median 1.7%) for pharyngeal infections (8). Although cellular tropism for columnar cells (which are found in the rectum but not the pharynx) may explain our findings, further research is required.

Lastly, our findings also yield recommendations for the interpretation of STI epidemiology. Indeed, the availability of a more sensitive laboratory test has changed our understanding of the epidemiology of gonorrhea and highlighted the need to review the site of gonorrhea infection when making conclusions about changes in STI rates. The observed incidence rates of gonorrhea and chlamydia in Ottawa have been increasing over the last 20 years. However, the observed rate of increase in gonorrhea has been significantly higher since validation of extragenital NAAT in 2017. The increase in case-finding due to the use of a new laboratory test suggests that, when this new laboratory method was not available, many existing infections went undiagnosed. Thus, the incidence of gonorrhea in the past might have been higher than previously thought, and the number of diagnoses since 2016 might represent less of an increase than currently believed. Instead, current rates might be a more accurate depiction of the burden of infection. Consideration of this point should guide future analyses of gonorrhea and chlamydia epidemiology.

Conclusion

We reviewed the diagnosis rates and numbers for gonorrhea and chlamydia pre/post-validation and implementation of extragenital NAAT and found that local increases in identified cases of these infections corresponded with the implementation of this new testing technology. Going forward, as extragenital NAAT for gonorrhea is adopted by more healthcare providers, it is possible that the observed rate of gonorrhea may continue to increase. Extragenital testing by NAAT among other non-gbMSM groups may further increase apparent rates—although further research is required to evaluate this. Eventually, with better testing and treatment, we might see a decrease in both the true and observed incidence of gonorrhea and possibly chlamydia as well. In the meantime, offering extragenital NAAT to gbMSM who engage in sexual practices involving extragenital sites with more than one sexual partner is good clinical and public health practice.

Authors' statement

DSF — Writing-original draft & editing, conceptualization, statistical expertise
POB — Writing-original draft & editing, conceptualization, clinical expertise

Competing interests

None.

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References

1. Choudhri Y, Miller J, Sandhu J, Leon A, Aho J. Gonorrhea in Canada, 2010-2015. Can Commun Dis Rep 2018;44(2):37–42. DOI PubMed

2. Ontario Ministry of Health and Long-term Care (MOHLTC). integrated Public Health Information System (iPHIS) (accessed 2019-11-19). https://www.publichealthontario.ca/en/diseases-and-conditions/infectious-diseases/ccm/iphis

3. Dewart CM, Bernstein KT, DeGroote NP, Romaguera R, Turner AN. Prevalence of rectal chlamydia and gonococcal infections: systematic review. Sex Transm Dis 2018;45(5):287–93. DOI PubMed

4. Lusk MJ, Uddin RN, Lahra MM, Garden FL, Kundu RL, Konecny P. Pharyngeal gonorrhea in women: an important reservoir for increasing Neisseria gonorrhoeae prevalence in urban Australian heterosexuals? J Sex Transm Dis 2013;2013:967471. DOI PubMed

5. Public Health Agency of Canada. Canadian Guidelines on Sexually Transmitted Infections. Ottawa (ON): PHAC (updated 2020-05-06). https://www.canada.ca/en/public-health/services/infectious-diseases/sexual-health-sexually-transmitted-infections/canadian-guidelines/sexually-transmitted-infections.html

6. Meyer T. Diagnostic procedures to detect Chlamydia trachomatis infections. Microorganisms 2016;4(3):25. DOI PubMed

7. Public Health Ontario. Chlamydia trachomatis and Neisseria gonorrhoeae – Implementation of Nucleic Acid Amplification Testing (NAAT) for Rectal and Pharyngeal Sites. Toronto (ON): PHO; 2019. https://www.publichealthontario.ca/-/media/documents/lab/lab-sd-005-chlamydia-gonorrhoeae-sensitivity-specificity.pdf?la=en

8. Chan PA, Robinette A, Montgomery M, Almonte A, Cu-Uvin S, Lonks JR, Chapin KC, Kojic EM, Hardy EJ. Extragenital infections caused by Chlamydia trachomatis and Neisseria gonorrhea: A review of the literature. Infect Dis Obstet Gynecol 2016;2016:5758387. DOI PubMed

9. Chamberlain N, Crosby RA, Mena L, Chan PA, Mayer KH. Is patient-reported exposure a reliable indicator of anogenital gonorrhea and chlamydia screening in young Black men who have sex with men (YBMSM)? Sex Transm Dis 2017;44(7):390–2. DOI PubMed

10. Andersson N, Boman J, Nylander E. Rectal chlamydia - should screening be recommended in women? Int J STD AIDS 2017;28(5):476–9. DOI PubMed

11. United States Centers of Disease Control and Prevention. 2015 Sexually Transmitted Diseases Treatment Guidelines – Special Populations: MSM. Atlanta (GA): CDC (updated 2015-06-04; accessed 2020-03-28). https://www.cdc.gov/std/tg2015/specialpops.htm#MSM

12. den Heijer CD, van Liere GA, Hoebe CJ, van Bergen JE, Cals JW, Stals FS, Dukers-Muijrers NH. Who tests whom? A comprehensive overview of Chlamydia trachomatis test practices in a Dutch region among different STI care providers for urogenital, anorectal and oropharyngeal sites in young people: a cross-sectional study. Sex Transm Infect 2016 May;92(3):211–7. DOI PubMed

13. Lutz AR. Screening for asymptomatic extragenital gonorrhea and chlamydia in men who have sex with men: Significance, recommendations and options for overcoming barriers to testing. LGBT Health 2015;2(1):27–34. DOI PubMed

14. Tan DH, Hull MW, Yoong D, Tremblay C, O'Byrne P, Thomas R, Kille J, Baril JG, Cox J, Giguere P, Harris M, Hughes C, MacPherson P, O'Donnell S, Reimer J, Singh A, Barrett L, Bogoch I, Jollimore J, Lambert G, Lebouche B, Metz G, Rogers T, Shafran S; Biomedical HIV Prevention Working Group of the CIHR Canadian HIV Trials Network. Canadian guideline on HIV pre-exposure prophylaxis and nonoccupational postexposure prophylaxis. CMAJ 2017;189(47):E1448–58. DOI PubMed

15. Ward H, Rönn M. Contribution of sexually transmitted infections to the sexual transmission of HIV. Curr Opin HIV AIDS 2010;5(4):305–10. DOI PubMed

16. Barbee LA, Khosropour CM, Dombrowksi JC, Golden MR. New Human Immunodeficiency Virus diagnosis independently associated with rectal gonorrhea and chlamydia in men who have sex with men. Sex Transm Dis 2017;44(7):385–9. DOI PubMed

17. Bernstein KT, Marcus JL, Nieri G, Philip SS, Klausner JD. Rectal gonorrhea and chlamydia reinfection is associated with increased risk of HIV seroconversion. J Acquir Immune Defic Syndr 2010;53(4):537–43. DOI PubMed

18. Rosenberger JG, Dodge B, Van Der Pol B, Reece M, Herbenick D, Fortenberry JD. Reactions to self-sampling for ano-rectal sexually transmitted infections among men who have sex with men: a qualitative study. Arch Sex Behav 2011;40(2):281–8. DOI PubMed

19. Wayal S, Llewellyn C, Smith H, Hankins M, Phillips A, Richardson D, Fisher M; Home Sampling Kit Project Steering Group. Self-sampling for oropharyngeal and rectal specimens to screen for sexually transmitted infections: acceptability among men who have sex with men. Sex Transm Infect 2009;85(1):60–4. DOI PubMed

20. Rosenberger JG, Reece M, Schick V, Herbenick D, Novak DS, Van Der Pol B, Fortenberry JD. Sexual behaviors and situational characteristics of most recent male-partnered sexual event among gay and bisexually identified men in the United States. J Sex Med 2011;8(11):3040–50. DOI PubMed

21. Brooks H, Llewellyn CD, Nadarzynski T, Pelloso FC, De Souza Guilherme F, Pollard A, Jones CJ. Sexual orientation disclosure in health care: a systematic review. Br J Gen Pract 2018;68(668):e187–96. DOI PubMed

22. Coleman TA, Bauer GR, Pugh D, Aykroyd G, Powell L, Newman R. Sexual orientation disclosure in primary care settings by gay, bisexual, and other men who have sex with men. LGBT Health 2017;4(1):42–54. DOI PubMed

The Role of Preventive Medicine Technicians in protecting and promoting health in the Canadian Armed Forces

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Military personnel are deployed to a number of physically challenging/austere locations globally, which presents Canadian Armed Forces (CAF) personnel with some unique health hazards. Keeping CAF personnel healthy—both individually and as a population—are key objectives for the Preventive Medicine Technicians (PMed Tech) in supporting operational readiness (1).

Preventive Medicine Technicians are the strategic and tactical ground battlefield hygiene and sanitation inspectors in CAF. They represent Canadian Forces Health Services in the mitigation of non-battle-related illness, operating within the Directorate of Force Health Protection. The PMed Techs support the CAF healthcare system by performing hygiene, sanitation, environmental and occupational health inspections. They also collect and test water samples for potability and recreational use, manage integrated pest control procedures and provide guidance to deploying CAF members using recognized national and international health recommendations. Senior PMed Techs work collaboratively with the Epidemiology section to monitor and advise on communicable disease surveillance, such as vector, water and foodborne diseases, which can adversely affect CAF personnel and thus impact mission objectives. The PMed Techs routinely deploy internationally and domestically together with other CAF members in quite diverse environments (land, sea and air) to assist with health protection of military personnel. One example of their work is the mentorship training of foreign allies—for example, the Afghanistan Army, Air Force and Police—on the principals of disease and control measures. In summary, PMed Techs play an instrumental public health role in ensuring the health of CAF.

Reference

1. Schofield S, Tepper M, Campbell J. Health Protection of Armed Forces Personnel. In: Dawood R, editor. Travellers' Health: How to stay healthy abroad. 5th ed. Oxford UK: Oxford University Press; 2012, Chapter 11, Section 11.9:pg 419-426.

Canadian Armed Forces Preventive Medicine Technician testing water samples on deployment
Photo credit: Canadian Armed Forces – Combat Camera

Surveillance of laboratory exposures to human pathogens and toxins, Canada 2019

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Abstract

Background: The *Human Pathogens Act* and the *Human Pathogens and Toxins Regulations* mandates laboratory incident reporting to the Public Health Agency of Canada's Laboratory Incident Notification Canada (LINC) surveillance system. The objective of this report is to describe laboratory incidents involving exposures that occurred in Canada during 2019 and individuals affected in these incidents.

Methods: Laboratory incidents occurring in licensed Canadian laboratories in 2019 were analyzed. Exposure incident rate was calculated and descriptive statistics were performed. Exposure incidents were analyzed by sector, root cause, activity, occurrence type, and pathogen/toxin. Affected persons were analyzed by education, route of exposure, sector, role and laboratory experience.

Results: Sixty exposure incidents involving 86 individuals were reported to LINC in 2019. The annual exposure rate was six incidents per 100 active licenses. Most exposure incidents involved microbiology (n=39; 65%) activities and/or were reported by the academic (n=22; 37%) sector. The public health sector had the highest proportion of exposure incidents while the private sector had the lowest. Procedural (n=18, 23%) was the most cited occurrence type. Over a third of exposed individuals had 0–5 years of laboratory experience (n=32; 37%) and were hospital technicians or technologists (n=31; 36%). Inhalation was the most common route of exposure (n=53, 62%). Human interaction (n=35; 24%) was the most cited root cause.

Conclusion: Laboratory incidents were lower in 2019 than in 2018. The most common occurrence type was procedural while issues with human interaction was the most cited root cause. Most exposed individuals were hospital technicians or technologists.

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Keywords: laboratory exposures, laboratory incidents, laboratory-acquired infections, human pathogens and toxins, surveillance, Laboratory Incident Notification Canada, Centre for Biosecurity

Introduction

When working in a laboratory setting with human pathogens and toxins (HPTs), there is an inherent risk of deliberate or accidental exposure. Timely reporting of exposure incidents is essential to mitigate the risk of potential outbreaks and permit a rapid action response. In recent years, this risk to human biosafety and biosecurity to laboratory-acquired infections (LAIs) through exposure has led Canada to establish one of the first comprehensive national surveillance systems for mandatory reporting of laboratory incidents involving HPTs. Throughout the years, the number of reported suspected and confirmed LAIs has varied. In 2016, four incidents led to a suspected or confirmed LAI, and in the following year, of all six reported LAIs, five were suspected and one was confirmed. In 2018, the number of confirmed LAIs remained the same as that of the previous year (1–3). Unlike the mandatory reporting system used in Canada, the majority of reporting concerned with LAIs in other countries, including the United Kingdom and United States, is done so voluntarily or captured through surveys (4–6).

The Public Health Agency of Canada (PHAC) Centre for Biosecurity is mandated to protect the public from the risks posed by HPTs. It oversees activities conducted under the *Human Pathogens and Toxins Act* (HPTA) and the *Human Pathogens and Toxins Regulations* (HPTR). In response to these

requirements, the Laboratory Incident Notification Canada (LINC) surveillance system was established in December 2015. Unless otherwise exempted, facilities handling HPTs require a license to conduct their controlled activities. A single license can cover multiple containment zones, but does not cover multiple risk groups (RGs). When registering for a license, each facility self-identifies as being part of the academic, hospital, private industry/business, public health or other government sector.

Under the HPTA (7,8), HPTs can be categorized into three RGs. The majority of work performed in federally regulated laboratories is with RG2 pathogens that pose a minor risk to public health, but a moderate risk to individuals. The RG3 pathogens pose a high risk to individuals, but a low risk to public health. The RG4 pathogens present the highest risk to both individuals and the community. Security-sensitive biological agents (SSBA) above a trigger quantity can pose a risk to Canada's national security. Outside the scope of the HPTA are RG1 pathogens, which are not regulated in Canada and are of lowest risk. Working with pathogens and toxins in their natural environment may also present risk with incidents involving exposures and LAIs. Though the reporting of incidents involving these pathogens and toxins is not mandatory, PHAC encourages voluntary reporting, and continues to address this source of risk.

In accordance with the HPTA, licenced facilities that work with HPTs of RG2 or higher must report any laboratory incidents to PHAC without delay. The four types of laboratory incidents to be reported to LINC surveillance system are as follows:

- Exposures and LAIs
- Inadvertent possession, production and/or release of an HPT
- Missing, lost, or stolen HPT, including SSBA not being received within 24 hours of expected arrival
- Changes in biocontainment

The initial report from the licence holder to PHAC following an incident provides key dates, cause of exposure, affected persons and HPTs involved. A follow-up report is expected within 15 days after the first notification for SSBA incidents, or within 30 days for other exposures or LAIs. Follow-up reporting allows for identifications of trends and reduces the risk of future incidents by providing information on investigation outcomes, treatment and monitoring of affected persons, root causes and corrective actions following the incident.

The 2019 annual report marks the fourth year of the program. As with previous years, the objective of this report is to describe the distribution of laboratory incidents, focusing on data of exposures and LAIs. Further, it aims to compare exposure incidents with those of previous years, describe laboratory exposures by sector, HPT, occurrence type, activity, number of people exposed (their regular role, education, years of laboratory experience and route of exposure) and root causes.

Methods

Data sources

Notification and follow-up reports of laboratory incidents are submitted through LINC's external Biosecurity Portal interface, and this information is captured by its internal Customer Relationship Management system. For this report, laboratory incidents that took place from January 1, 2019 to December 31, 2019 were extracted from the Customer Relationship Management system. Incidents that did not have a known occurrence date were also included if they were reported during this period. Data of the most recent follow-up reports were used for analysis, while the data of initial reports were used where corresponding follow-up reports and/or data were not present as of the data extraction date, February 11, 2020. Extracted data were cleaned by inspecting for and investigating any outliers and removing duplicate entries.

Within the scope of the HPTA/HPTR, an exposure incident was defined as a laboratory incident that could have resulted in intoxication/infection or had resulted in suspected or confirmed LAI (7,8). A non-exposure incident referred to inadvertent possession, production or release of a pathogen or toxin, a missing, lost or stolen pathogen or toxin or a security-sensitive biological agent not being received within 24 hours of expected arrival. Incidents involving agents in the natural environment were excluded from analysis because reporting of these incidents is voluntary.

Analysis

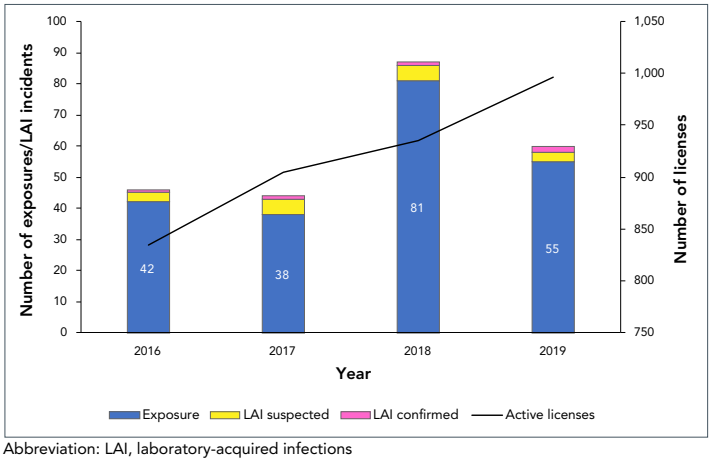
Report data within the LINC surveillance system was extracted to Microsoft Excel 2016 for analysis and R 3.5.1 was used to perform descriptive statistics with cross-validation using SAS EG 7.1. All notified exposure incidents were first subdivided into ruled out incidents and confirmed incidents, with confirmed and suspected LAIs included in the latter. Affected persons in confirmed incidents were also subdivided into confirmed or ruled out individuals. Among confirmed exposure incidents, the numbers of incidents were analyzed against parameters obtained at two levels of reporting. At the level of the active license holder, the distributions of incidents by sector, main activity, root cause, occurrence type, and implicated pathogen/toxin reported were examined. At the level of persons affected in these incidents, the distributions of their highest level of education, years of experience, route of exposure, sector and regular role were examined. A comparison of exposure incidents over time from 2016–2019, and a measure of the exposure incident rate per 100 active licenses in 2019, were also performed. Active licenses were referred to as licenses that were considered active during 2019 and were able to report an incident. The period of surveillance was one year and was defined as January 1, 2019 to December 31, 2019. The calculation for exposure incident rate (R) was derived from well-established epidemiologic principles (9) and was defined as follow:

$$R = \frac{\text{number of exposure incidents reported during period of surveillance}}{\text{total active licenses x period of surveillance}} \times 100 \text{ active licenses}$$

Results

In 2019, there were 996 active licenses held across Canada permitting the use of HPTs. Compared with 2018 (n=89), there were fewer confirmed exposure incidents reported (n=60) but one more confirmed LAI (n=2) (**Figure 1**).

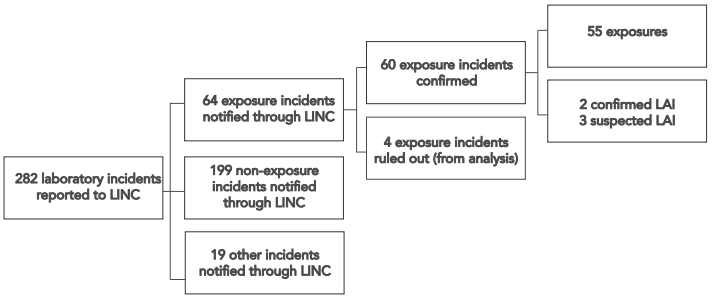
Figure 1: Confirmed exposure incidents, suspected and confirmed laboratory-acquired infections and active licenses, Canada, 2016–2019



Abbreviation: LAI, laboratory-acquired infections

The exposure incident rate was approximately six incidents for every 100 active licenses observed during 2019. From January 1, 2019 to December 31, 2019, 64 exposure incidents, 199 non-exposure incidents and 19 other incidents were reported through LINC (**Figure 2**). Among exposure incidents, four incidents were ruled out from analysis upon further investigation, three incidents resulted in suspected LAI and two incidents resulted in confirmed LAI. In total, 99 people were reportedly exposed in laboratory incidents but 13 of these individuals were ruled out from analysis upon further investigation due to reasons such as reclassification of an exposure incident as a non-exposure incident upon review.

Figure 2: Types of incidents reported to Laboratory Incident Notification Canada and exposure incidents included in analysis, Canada 2019



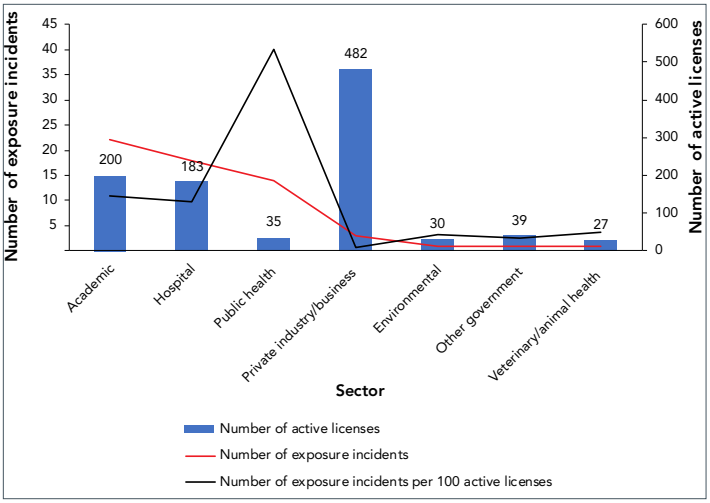
Abbreviations: LAI, laboratory-acquired infections; LINC, Laboratory Incident Notification Canada

Exposure incidents by main activity and sector

Microbiology was the main activity being performed during most exposure incidents (n=39; 65.0%) followed by *in vivo* animal research (n=9; 15.0%). Less frequently cited activities included animal care, autopsy or necropsy, cell culture, education or training, maintenance, molecular investigations, serology or hematology or other (n=12; 20.0%). Definitions of the main activities can be found in **Appendix A**.

Figure 3 compares the number of exposure incidents reported and number of active licenses held by sector. Most exposure incidents reported through LINC occurred in the academic (n=22; 36.7%), hospital (n=18; 30.0%) and public health (n=14; 23.3%) sectors. Furthermore, the public health sector had the greatest number of exposure incidents for every 100 licenses held (40 incidents per 100 active licenses) while the private sector had the lowest (one incident per 100 active licenses) despite having the highest number of active licenses (n=482).

Figure 3: Confirmed exposures incidents and active licenses by sector reported to Laboratory Incident Notification Canada, Canada 2019



Implicated human pathogens and toxins

Salmonella was the agent implicated in both of the confirmed LAIs that occurred in 2019. Table 1 shows the distribution of biological agents involved in exposure incidents reported (bacteria, fungus, parasite, virus, unknown) by security status (non-SSBA, SSBA) and risk group (RG2, RG3, unknown). Among the 71 pathogens and toxins implicated, most exposure incidents involved non-SSBA pathogens and toxins (n=61; 85.9%) and/or occurred in RG2 licensed laboratories (n=44; 62.0%). Bacteria were the most implicated (n=45; 63.4%) agent and parasites were the least implicated (n=1; 1.4%). The most implicated agents among RG2 licensed laboratories were Neisseria meningitidis (N. meningitidis) (n=5; 7.0%), Staphylococcus aureus (S. aureus) (n=4; 5.6%), and Escherichia species (n=3, 4.2%). The most implicated agent in RG3 licensed laboratories was Brucella melitensis (B. melitensis) (n=5; 7.0%).

Table 1: Human pathogens or toxins involved in reported exposure incidents by risk group level and security sensitive status, Canada 2019 (N=71)

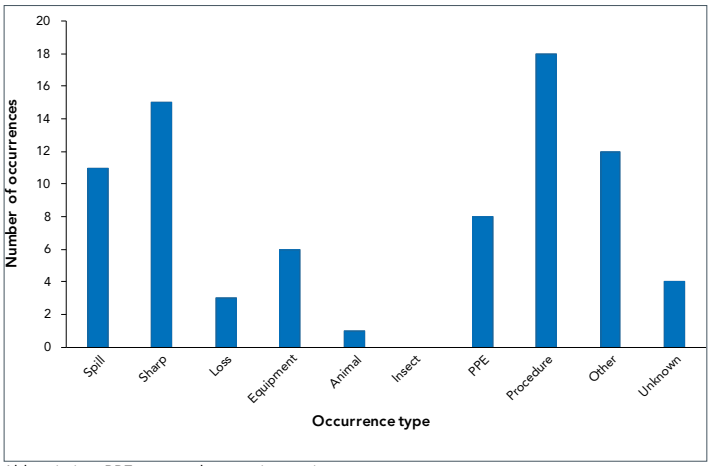
Biological agent type by risk group	Non SSBA		SSBA		Total	
	n	%	n	%	n	%
RG2	44	72	0	0	44	62
Bacteria	32	52	0	0	32	45
Fungus	2	3	0	0	2	3
Parasite	1	2	0	0	1	1
Virus	9	15	0	0	9	13
Unknown	0	0	0	0	0	0
RG3	8	13	10	100	18	25
Bacteria	4	7	9	90	13	18
Fungus	2	3	1	10	3	4
Parasite	0	0	0	0	0	0
Virus	2	3	0	0	2	3
Unknown	0	0	0	0	0	0
Unknown	9	15	0	0	9	13
Bacteria	0	0	0	0	0	0
Fungus	0	0	0	0	0	0
Parasite	0	0	0	0	0	0
Virus	0	0	0	0	0	0
Unknown	9	15	0	0	9	13
Total	61	100	10	100	71	100

Note: Percentages rounded to the nearest whole number

Occurrence types

Figure 4 presents the reported types of occurrence involved in exposure incidents. Procedural (n=18, 23.1%) and sharps-related (n=15; 19.2%) were the most commonly reported types of occurrences.

Figure 4: Reported occurrence types involved in reported exposure incidents, Canada 2019 (N=78)



Abbreviation: PPE, personal protective equipment

Exposed individuals

In total, 86 individuals were exposed through the 60 confirmed exposure incidents reported to LINC. The highest level of education was unknown for seven exposed individuals. Most exposed individuals had a technical/trades diploma (n=48; 55.8%) or Bachelor's degree (n=15; 17.4%). Other highest education levels reported included high school diploma (n=6; 7.0%), Master's degree (n=7; 8.1%) and MD or PhD (n=3; 3.5%).

Table 2 presents the number of exposed individuals by their sector and main role. A majority of individuals exposed belonged to the hospital (n=38; 44.2%), public health (n=22; 25.6%), or academic (n=19; 22.1%) sectors. Notably, most individuals exposed were technicians or technologists (n=64; 74.4%) belonging mainly to the hospital (n=31) or public health (n=21) sectors.

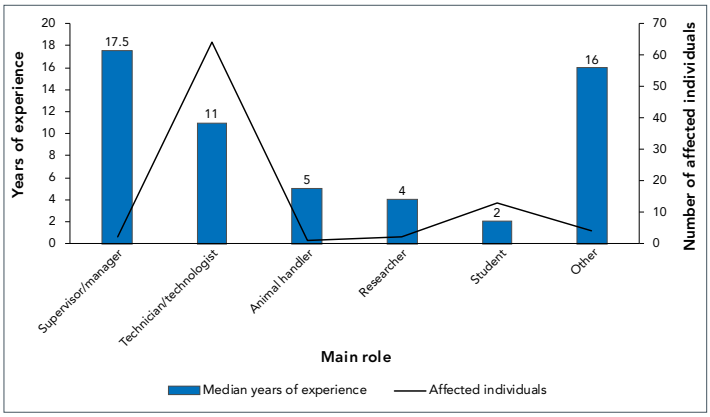
Table 2: Individuals affected in exposure incidents reported by sector and main role, Canada 2019 (N=86)

Sector	Main role													
	Animal handler		Researcher		Student		Supervisor/ manager		Technician/ technologist		Other[a]		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Academic	1	100	2	100	9	69	1	50	5	8	1	25	19	22
Hospital	0	0	0	0	4	31	0	0	31	48	3	75	38	44
Private industry/ business	0	0	0	0	0	0	0	0	5	8	0	0	5	6
Public health	0	0	0	0	0	0	1	50	21	33	0	0	22	26
Veterinary/ animal health	0	0	0	0	0	0	0	0	1	2	0	0	1	1
Other government	0	0	0	0	0	0	0	0	1	2	0	0	1	1
Total	1	100	2	100	13	100	2	100	64	100	4	100	86	100

[a] Other roles included instructor, microbiologist and medical laboratory assistant
Note: Percentages rounded to the nearest whole number

Figure 5 depicts the distribution of exposed individuals by their years of laboratory experience and main role. Nineteen exposed individuals' number of years of laboratory experience was unknown. Supervisors and managers (n=2) had the highest median years of experience ($\tilde{x}$=17.5) while students (n=13) had the lowest ($\tilde{x}$=2). Overall, most exposed individuals had 0–5 years of laboratory experience (n=32; 37.2%).

Figure 5: Individuals affected in exposure incidents reported by number of years of laboratory experience[a] and main role[b], Canada 2019 (N=67)



[a] The highest level of education for 19 of the 86 exposed individuals was not reported
[b] Other roles included instructor, microbiologist, and medical laboratory assistant

Among the 86 exposed individuals, most were exposed to HPTs through inhalation (n=53; 61.6%) or through inoculation or injection by a needle or sharp (n=13; 15.1%). Some other routes of exposure included absorption through contact with mucous membranes or skin, ingestion and inoculation or injection by a bite or scratch.

Root causes and areas for laboratory safety improvement

In total, 144 root causes were identified through follow-up reports for the 60 confirmed exposure incidents reported. **Table 3** describes the root causes and their distribution. Human interaction (n=35; 24.3%) and standard operating procedures (n=27; 18.8%) were the most commonly cited root causes, followed by management (n=20; 13.9%) and equipment (n=20; 13.9%).

Table 3: Root causes reported in follow-up reports of exposure incidents, Canada 2019 (N=144)

Root cause	Examples of areas of concern	Citations	
		n	%
Communication	Communication did not occur but should have	17	12
	Communication was unclear, ambiguous, etc.		
Equipment	Equipment quality control needed improvement	20	14
	Equipment failed		
	Equipment was not fit for purpose		

Table 3: Root causes reported in follow-up reports of exposure incidents, Canada 2019 (N=144) (*continued*)

Root cause	Examples of areas of concern	Citations	
		n	%
Human interaction	A violation (cutting a corner, not follow correct procedure, deviating from standard operating procedure)	35	24
	An error (a mistake, lapse of concentration, or slip of some sort)		
Management and oversight	Supervision needed improvement	20	14
	Lack of auditing of standards, policies, and procedures		
	Risk assessment needed improvement		
Training	Training not in place but should have been in place	17	12
	Training not correct for the task/activity		
	Staff were not qualified or proficient in performing the task		
Standard operating procedure	Documents were followed as written but not correct for activity/task	27	19
	Procedures not in place but should have been in place		
	Documents were not followed correctly		
Other	Not applicable	8	5

Note: Percentages rounded to the nearest whole number

Discussion

In 2019, 60 laboratory exposures to HPTs had been reported to LINC, a decrease from the 89 reported in 2018. Of the 60 laboratory exposures, five led to suspected LAIs and two of them were confirmed. The most common agents involved in exposure incidents were RG2 and/or non-SSBA. Bacteria were the most commonly reported type of agent, with *B. melitensis*, *N. meningitidis* and *S. aureus* being the predominantly reported. The two confirmed LAIs were caused by *Salmonella* species, which was also one of the human pathogens most frequently responsible for LAIs (10–12).

The exposures occurred mostly in the public health, academic and hospital sectors and were commonly due to procedure breaches, sharps or spills and while performing microbiology activities. Eighty-six individuals, mainly technicians or technologists were exposed to a HPT. The leading root causes identified leading to an exposure were human interactions and lack of awareness or compliance with standard operating procedures.

The private sector had the highest number of active licenses but the lowest rate of exposure incidents

The distribution of exposures by sector in 2019 was similar to the previous years' and mostly occurred in the academic, hospital and public health sectors (1–3). However, the exposure incident rate (9) allowed for making an unbiased comparison across

sectors by taking into account the number of licences per sector. Although they held the highest number of licenses, the private sector had the lowest exposure incident rate, whereas the public health sector had the highest exposure incident rate, followed by the academic and hospital sectors. These differences could be explained either by an actual difference in the exposure incident rate across sectors or by a difference in reporting exposures. A truly higher exposure incident rate in the hospital sector could be explained by a greater uncertainty in pathogens that they handle compared with the private sector, wherein most cases the pathogen is already identified (such as in vaccine development) (11). Factors influencing reporting exposure incidents across sectors in Canada are not well established and need to be explored.

The role and the experience of laboratory workers might be important factors to consider for prevention. In 2019, affected people with the lowest median years of laboratory experience were students. The academic sector is expected to be the place where students would be acquiring their first experience in the laboratory setting and represent laboratory staff at the early stages of their career. The high exposure rate in the academic sector may partially be explained by the well-established link between lack of experience and increased risk of errors (13). Another explanation could be the complexity of the organisational structure in academic settings that may perhaps lead to an unawareness of accountability from students, researchers and administrators. Such a situation could potentially result in non-compliance with safety requirements, thereby engendering exposure incidents (14).

Unawareness of the occurrence of an exposure might be an underlying cause of laboratory-acquired infections

As reported in previous reports and concurrent with literature, the most common pathogens involved in exposure incidents in 2019 were bacteria, mainly represented by *B. melitensis*, *N. meningitidis* and *S. aureus*. However, the two confirmed LAIs were caused by *Salmonella* species, which is also one of the human pathogens most frequently responsible for LAIs (10–12). In the case of these two LAIs, no postexposure prophylaxis was given following the exposure incident because the affected persons were not aware of the exposure at the time of occurrence. The exposure was established retrospectively after onset of symptoms and suspicion of a LAI. The absence of postexposure prophylaxis could have been one of the factors that contributed to the exposure becoming a LAI (15). Unawareness of the exposure could have been the result of human interactions and lack of awareness of standard operating procedures. These factors have frequently been identified as the root causes of exposures in past years (1–3).

Strengths and limitations

The main strength of this study was the standardized and mandatory reporting process of laboratory incidents in laboratories across Canada. This provided a near real-time assessment of trends and potential for risk mitigation in prescribing or improving corrective measures at licensed facilities. Regular communication with stakeholders through Eblasts and newsletters allowed for the identification of potential risk factors. For example in 2019, the main activity involved was microbiology. This information could be used by licenced facilities to examine current safety protocols involving this activity to reduce the risk of exposures to laboratory workers in the future.

The current surveillance system of laboratory incidents does not currently capture information such as laboratory workforce size or distribution of roles within laboratories. Therefore, the main limitations of this report were the reduced accuracy inherent to using active licenses as a proxy for workforce size and the inability to report on more comprehensive trend analysis of incidents in 2019 and over time. In addition, all reportable incidents and exposures may not have been reported to LINC. We continue to address this possible issue through various compliance and monitoring activities as well as consistent communications with stakeholders through newsletters and biosafety advisories. We are also updating the notification and reporting guideline to address the process of reporting pathogens not covered by the HPTA/HPTR.

Conclusion

The annual incidence of laboratory exposures in Canada in 2019 was lower compared with 2018 but higher than in 2016 and 2017. It remains unclear if this was a true decrease as the LAI program has only been in place since 2015 and we are still establishing our baseline. Analysis of the reported exposures served to inform guidelines for ongoing improvement of biosafety and biosecurity in Canada.

Authors' statement

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

Competing interests

There are no competing interests to declare.

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References

1. Choucrallah D, Sarmiento L, Ettles S, Tanguay F, Heisz M, Falardeau E. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2018. Can Commun Dis Rep 2019;45(9):244–51. DOI PubMed

2. Bienek A, Heisz M, Su M. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2016. Can Commun Dis Rep 2017;43(11):228–35. DOI PubMed

3. Pomerleau-Normandin D, Heisz M, Tanguay F. Surveillance of laboratory exposures to human pathogens and toxins: Canada 2017. Can Commun Dis Rep 2018;44(11):297–304. DOI PubMed

4. Singh K. Laboratory-acquired infections. Clin Infect Dis 2009;49(1):142–7. DOI PubMed

5. Willemarck N, Van Vaerenbergh B, Descamps E, Brosius B, Dai Do Thi C, Leunda A, Baldo A. Laboratory- Acquired Infections in Belgium (2007-2012)_An Online Survey. Brussels (Belgium): Wetenschappelijk Instituut Volkgezondheid; 2015. https://www.researchgate.net/publication/291331348_Laboratory-Acquired_Infections_in_Belgium_2007-2012_An_online_survey

6. Wurtz N, Papa A, Hukic M, Di Caro A, Leparc-Goffart I, Leroy E, Landini MP, Sekeyova Z, Dumler JS, Bădescu D, Busquets N, Calistri A, Parolin C, Palù G, Christova I, Maurin M, La Scola B, Raoult D. Survey of laboratory-acquired infections around the world in biosafety level 3 and 4 laboratories. Eur J Clin Microbiol Infect Dis 2016;35(8):1247–58. DOI PubMed

7. Government of Canada. Human Pathogens and Toxins Act (HPTA). S.c. 2009, c. 24. Government of Canada; 2015 (modified 2020-04). https://lois-laws.justice.gc.ca/eng/acts/H-5.67/FullText.html

8. Public Health Agency of Canada. Canadian Biosafety Standard Handbook. 2nd Edition. Ottawa (ON): PHAC; 2016 (modified 2018-08). https://www.canada.ca/en/public-health/services/canadian-biosafety-standards-guidelines/second-edition.html

9. Szklo M, Nieto J. Incidence rate based on person time. In: Epidemiology: Beyond the Basics. 2nd ed.: Mississauga, ON: Jones and Bartlett; 2007. p. 57.

10. Peng H, Bilal M, Iqbal HM. Improved Biosafety and Biosecurity Measures and/or Strategies to Tackle Laboratory-Acquired Infections and Related Risks. Int J Environ Res Public Health 2018;15(12):2697. DOI PubMed

11. Coelho AC, García Díez J. Biological Risks and Laboratory-Acquired Infections: A Reality That Cannot be Ignored in Health Biotechnology. Front Bioeng Biotechnol 2015;3:56. DOI PubMed

12. Siengsanan-Lamont J, Blacksell SD. A Review of Laboratory-Acquired Infections in the Asia-Pacific: Understanding Risk and the Need for Improved Biosafety for Veterinary and Zoonotic Diseases. Trop Med Infect Dis 2018;3(2):36. DOI PubMed

13. Plebani M. Exploring the iceberg of errors in laboratory medicine. Clin Chim Acta 2009;404(1):16–23. DOI PubMed

14. Huising R, Silbey SS. Surveillance and Regulation of Laboratory Practices. In: Felt U, Fouche R, Miller CA, Smith-Doerr L, editors. The Handbook of Science and Technology Studies. 4th ed. Cambridge MA: The MIT Press; 2013 P.793-822. https://mitpress.mit.edu/books/handbook-science-and-technology-studies-fourth-edition

15. Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report (MMWR): Recommendations and Reports. 2001. Vol. 50, No RR-11, p-1-54. https://www.cdc.gov/mmwr/PDF/rr/rr5011.pdf

Appendix A

Definitions of main activity

Animal care: Activities such as attending to the daily care of animals and providing animals with treatment
Autopsy or necropsy: Post-mortem surgical examinations for purposes such as determining cause of death or to evaluate disease or injury for research or educational purposes
Cell culture: The process of growing cells under controlled conditions; it can also involve the removal of cells from an animal or plant
Education or training: Education or training of students and/or personnel on laboratory techniques and procedures
***In vivo* animal research:** Experimentation with live, non-human animals
Maintenance: The upkeep, repair, and/or routine and general cleaning of equipment and facilities
Microbiology: Activities involving the manipulation, isolation, or analysis of microorganisms in their viable or infectious state
Molecular investigations: Activities involving the manipulation of genetic material from microorganisms or other infectious material for further analysis
Serology: Diagnostic examination and/or scientific study of immunological reactions and properties of blood serum
Hematology: Scientific study of the physiology of blood

Summary of the NACI systematic review and recommendation on the use of live attenuated influenza vaccine (LAIV) in HIV-infected individuals

Dorothy Moore[1,2], Ian Gemmill[3,4], Robyn Harrison[5,6] on behalf of the National Advisory Committee on Immunization (NACI)*

Abstract

Background: Annual influenza vaccination is recommended for all individuals six months of age and older, including those with HIV infection. Prior to this statement, the National Advisory Committee on Immunization (NACI) stated that live attenuated influenza vaccine (LAIV) was contraindicated for all individuals with HIV infection. The objective of this article is to update NACI's guidance on the use of LAIV for HIV-infected individuals.

Methods: A systematic literature review of the use of LAIV in individuals with HIV was undertaken. The Canadian Adverse Events Following Immunization Surveillance System was searched for reports of adverse events following vaccination with LAIV in HIV-infected individuals. NACI approved the revised recommendations.

Results: NACI concluded that LAIV is immunogenic in children with HIV, and available data suggest that it is safe, although data were insufficient to detect possible uncommon adverse effects. LAIV may be considered as an option for vaccination of children 2–17 years old who meet the following criteria: 1) receiving highly active antiretroviral therapy for at least four months; 2) CD4 count of 500/μL or greater if age 2–5 years, or of 200/μL or greater if age 6–17 years; and 3) HIV plasma RNA less than 10,000 copies/mL. LAIV remains contraindicated for adults with HIV because of insufficient data. Intramuscular influenza vaccination is considered the standard for children living with HIV by NACI and the Canadian Paediatric & Perinatal HIV/AIDS Research Group, particularly for those without HIV viral load suppression (i.e. plasma HIV RNA is 40 copies/mL or greater). However, if intramuscular (IM) vaccination is not accepted by the patient or substitute decision-maker, LAIV would be reasonable for children meeting the criteria listed above.

Conclusion: LAIV may be considered as an option for annual vaccination of selected children with HIV.

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Keywords: National Advisory Committee on Immunization, NACI, HIV, live attenuated influenza vaccine, literature review

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Introduction

Annual vaccination against influenza is recommended for all individuals with HIV infection (1) who are six months of age or older. Live vaccines are generally contraindicated in persons with immunodeficiency. Nevertheless, criteria have been established to permit vaccination with measles-mumps-rubella and varicella vaccines when immune function is not severely impaired. These

vaccines have been shown to be safe and are recommended for persons with HIV if the HIV infection is controlled and immune function is satisfactory. The National Advisory Committee on Immunization's (NACI) previous recommendation against live attenuated influenza vaccine (LAIV) use for individuals with immune compromising conditions including HIV was based on expert opinion and the small number of studies available (NACI Recommendation Grade D) (2). The product monograph states that LAIV administration to immunosuppressed individuals should be based on careful consideration of potential benefits and risks (3).

Immunization protocols state that LAIV is contraindicated for HIV-infected individuals in British Columbia, Alberta, Manitoba, Saskatchewan and New Brunswick, as well as in the United States (4–10). Some jurisdictions, such as Québec, the United Kingdom, and France (11–13) and professional organizations including the Infectious Diseases Society of America and the British Children's HIV Association (14,15) state that LAIV may be given to individuals with HIV who meet specific criteria.

The objective of this advisory committee statement is to review the evidence for efficacy, effectiveness, immunogenicity and safety for LAIV use in HIV-infected individuals and to provide updated guidance on the use of LAIV in this population.

Methods

A systematic review of literature on the use of LAIV in HIV-infected individuals was performed. The systematic review's methodology was specified *a priori* in a written protocol that included review questions, search strategy, inclusion and exclusion criteria and quality assessment. The NACI Influenza Working Group (IWG) reviewed and approved the protocol.

Six electronic databases (EMBASE, MEDLINE, Scopus, ProQuest Public Health, ClinicalTrials.gov and PROSPERO) were searched from inception to April 13, 2018 using search terms for LAIV and HIV. Searches were restricted to articles published in English and French. In addition, hand searching of included studies was performed by checking reference lists to identify additional relevant publications. Hand searching of reference lists was also performed for any relevant retrieved secondary research articles.

Two reviewers independently screened the titles and abstracts and eligible full-text articles.

Studies were included if they met the following criteria:
1. The study population or subpopulation consisted of HIV-infected individuals
2. The study assessed efficacy or effectiveness, immunogenicity, safety (including impact on markers of HIV infection), or vaccine virus shedding

Studies were excluded if they met one or more of the following criteria:
1. The study did not present data on any of: efficacy and effectiveness, immunogenicity, safety or vaccine virus shedding outcomes for LAIV
2. The study was in a language other than English or French
3. The study was a non-human or *in vitro* study
4. The article was an editorial, opinion, or news report
5. The study presented only secondary research (e.g. literature review, systematic review, meta-analysis)
6. The LAIV investigated was not a seasonal LAIV based on the Ann Arbor backbone

Data were extracted into evidence tables. One reviewer extracted data and appraised the methodological quality of the eligible studies. A second reviewer validated the data extraction and quality assessment. The Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) was also searched for reports of adverse events (AE) following immunization (AEFI) with LAIV in HIV-infected individuals. A narrative synthesis of the extracted data was produced and a recommendation for LAIV use developed. NACI critically appraised the available evidence and approved the recommendation.

Results

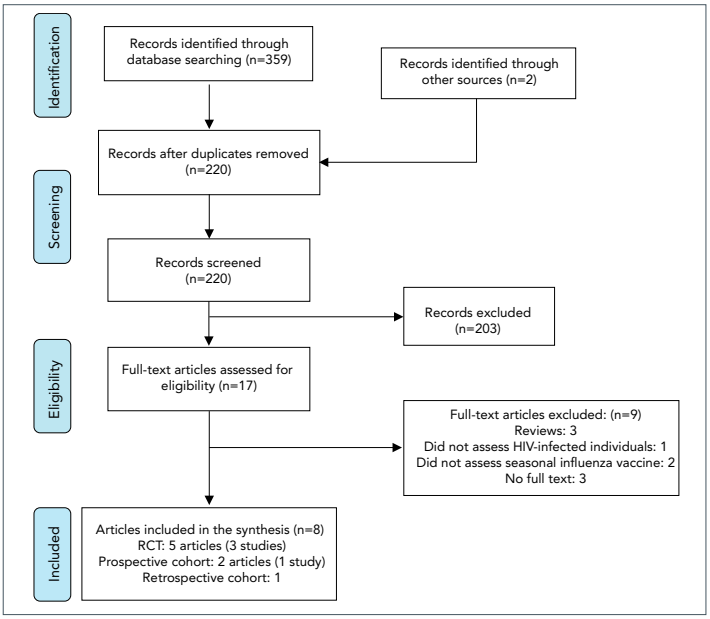
The systematic review retrieved 220 unique articles, of which eight were retained for data extraction and analysis. These eight articles reported findings from five studies investigating the immunogenicity, safety or both of LAIV in HIV-infected individuals. Four studies were of good quality and one was fair according to ratings of Harris *et al.* (16). No studies investigating the efficacy or effectiveness of LAIV in this population were identified. A flow diagram of the study selection process is presented in **Figure 1**. Key study characteristics are summarized in **Table 1**.

Immunogenicity

Three studies investigated the immunogenicity of LAIV in a total of 191 HIV-infected children and young adults, 2–25 years of age (18–23), and one study investigated the immunogenicity in 28 HIV-infected adults 18 years of age and older (17). All four studies were of good quality according to the Harris *et al.* criteria (16). Immunologic correlates of protection against influenza are relatively well established for hemagglutination inhibition (HI) antibodies for adults, but not for microneutralization (MN) antibodies for adults and not for any serological response for children.

There were no major differences in HI antibody responses following receipt of LAIV between individuals with and without HIV (17,18,22). In the study by Curtis *et al.* (22), HI response to influenza B/Yamagata was better in the group with HIV than in the HIV-negative control group (22,23). The proportions of

Figure 1: Flow diagram of the study selection process for the systematic review on the efficacy, effectiveness, immunogenicity and safety of live attenuated influenza vaccine in HIV-infected individuals



Abbreviation: RCT, randomized controlled trial

HIV-infected individuals with HI titres of at least 40 vaccinated with LAIV or inactivated influenza vaccine (IIV) were similar for influenza A(H1N1) and A(H3N2) but higher with IIV for influenza B and antibody titres were statistically significantly higher with IIV for influenza A(H3N2) and B vaccine strains (19) and for mismatched strains (20). A significant increase in MN titres was observed against mismatched, but not the vaccine A(H1N1) strain, in a study of HIV-infected children and young adults (22,23). The proportion of HIV-infected individuals with MN titres greater than or equal to 1:40 was similar post-vaccination for LAIV and IIV, but the magnitude of response was higher for IIV than LAIV (20).

LAIV induces humoral and mucosal antibody responses as well as T and B cell-mediated responses. Correlates of protection have not been established for LAIV or for cell-mediated responses, and HI titre may underestimate protection (25). Two studies looked at mucosal antibody responses. There was no important difference in nasal IgA antibody response to LAIV by HIV status (22,23), or in salivary IgG antibody response to LAIV and IIV in HIV-infected individuals (19,20). One study investigated memory B cell and T cell responses. The IgG memory B cell responses did not differ significantly by HIV status for influenza A(H1N1) or A(H3N2); however, a lower absolute response to B/Yamagata post-vaccination was observed in the HIV-infected group (22,23). The magnitude of the rise in T cell response did not differ by HIV status (22,23).

Safety

Five studies reported AEFI with LAIV: three in a total of 191 HIV-infected children and young adults (18,19,22), one

Table 1: Characteristics of studies included in the systematic review

Author	Study design (vaccine administered)	Study population	Outcomes
King *et al.*, 2000 (17)	RCT (LAIV3 versus placebo)	Adults 18–58 years of age with HIV (n=57 total; 28 received LAIV3) and without HIV (n=54 total; 27 received LAIV3) Eligibility criteria for HIV-infected subject: Immune class A1-2, plasma HIV RNA less than 10,000 copies/mL, and more than 200 CD4 cells/μL; if less than or equal to 500 CD4 cells/μL, on stable antiretroviral regimen) within three months prior to vaccination	HI antibody response AE within 10 days of vaccination Effect on HIV replication and CD4 cell counts Vaccine virus shedding
King *et al.*, 2001 (18)	RCT (LAIV3)	Children younger than 8 years of age with HIV (n=24); without HIV (n=25) Eligibility criteria for HIV-infected subject: Immune class N1-2 or A1-2 and plasma HIV RNA less than 10,000 copies/mL within 100 days prior to enrolment	HI antibody response AE within 10 days of vaccination Effect on HIV replication and CD4 cell counts Vaccine virus shedding
Levin *et al.*, 2008 (19) Weinberg *et al.*, 2010a (20) Weinberg *et al.*, 2010b (21)	RCT (LAIV3 vs. IIV3)	Children 5 to less than 18 years of age with HIV (n=243 total; 122 received LAIV3; 121 received IIV3) Eligibility criteria for HIV-infected subject: Stable HIV on HAART for more than or equal to 16 weeks and with HIV-1 plasma RNA fewer than 60,000 copies/mL within 60 days prior to vaccination. All subjects had received IIV3 in at least one of the prior two years	HI, MN antibody response Salivary mucosal IgA and IgG antibody response T cell response AE within 28 days of vaccination Effect on HIV replication and CD4 cell counts Vaccine virus shedding
Curtis *et al.*, 2015 (22) Weinberg *et al.*, 2016 (23)	Prospective cohort study (LAIV4)	Children and young adults 2–25 years of age with HIV (n=45) and without HIV (n=55)	HI, MN antibody response Nasal mucosal IgA response

Table 1: Characteristics of studies included in the systematic review (*continued*)

Author	Study design (vaccine administered)	Study population	Outcomes
Curtis *et al.*, 2015 (22) Weinberg *et al.*, 2016 (23)	Prospective cohort study (LAIV4) (*continued*)	Eligibility criteria for HIV-infected subject: CD4 greater than 15% or more than 200 cells/μL on cART, or greater than 25% or more than 500 cells/μL if not on cART. All subjects had received influenza vaccine in one or more previous seasons	IgA and IgG memory B cell response; T cell response AE within six weeks of vaccination Vaccine virus shedding
Menegay *et al.*, 2017 (24)	Retrospective cohort study (LAIV vs. IIV)	Adults—all active duty US Air Force members diagnosed with HIV (n=437)	Influenza-like illness within 30 days of vaccination

Abbreviations: AE, adverse event; cART, combination antiretroviral therapy; HAART, highly active antiretroviral therapy; HI, hemagglutination inhibition; IgA, immunoglobulin A; IgG, immunoglobulin G; IIV3, trivalent inactivated influenza vaccine; LAIV, live attenuated influenza vaccine; LAIV3, trivalent live attenuated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; MN, microneutralization; RCT, randomized controlled trial; RNA, ribonucleic acid; US, United States

in 28 adults (17) and one in 437 adults investigated only for vaccine-associated influenza-like illness (ILI) (24). Four of the studies were of good quality and one was rated as fair.

In both children and adults with HIV, rates of AEFI with LAIV were comparable to rates observed in individuals without HIV receiving LAIV except for more muscle aches and decreased energy in those with HIV (17,18,22). Rates of AEFI in individuals with HIV receiving LAIV or IIV were also similar, with the exception of more frequent but expected nasopharyngeal symptoms (runny nose and nasal congestion) after LAIV (19). Reports of ILI after receiving LAIV were rare (24). No serious or severe AEFIs attributable to LAIV were reported in any study. There have been no reports to CAEFISS of AEFI with LAIV in HIV-infected individuals.

Effects of LAIV on HIV infection were assessed in two studies in children (18,19) and one in adults (17). LAIV had no significant effect on HIV RNA viral load or CD4 count.

Four studies reported on the effect of HIV status on LAIV vaccine virus shedding: three in 191 HIV-infected children and young adults (18,19,22) and one in 28 HIV-infected adults (17). Vaccine virus shedding did not differ by HIV infection status (17–19,22).

NACI recommendation for individual level decision-making

Following thorough review of the evidence, NACI 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 highly active antiretroviral therapy (HAART) and with adequate immune function* (Discretionary NACI recommendation).

- NACI concludes that there is fair evidence based on immunogenicity data to recommend the use of LAIV vaccine as an option for children 2–17 years of age with stable HIV infection on HAART and with adequate immune function (Grade B Evidence)
- NACI concludes that, while LAIV appears to have a similar safety profile to IIV, there is insufficient evidence to detect uncommon AE related to the use of LAIV in HIV infected children (Grade Evidence)

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

- Receiving HAART for at least four months
- Have a CD4 count greater than or equal to 500/μL if 2–5 years of age, or greater than or equal to 200/μL if 6–17 years of age (measured within 100 days before administration of LAIV)
- Have a level of HIV plasma RNA fewer than 10,000 copies/mL (measured within 100 days before administration of LAIV)

While intramuscular (IM) influenza vaccination is considered the standard for children living with HIV by NACI and the Canadian Paediatric and Perinatal HIV/AIDS Research Group, particularly for those without HIV viral load suppression (i.e. IM, plasma HIV RNA more than 40 copies/mL), LAIV would be reasonable for children meeting the criteria outlined above, if vaccination is not accepted by the patient or substitute decision-maker.

The decision to use LAIV in children with stable HIV should be made on a case-by-case basis. The evidence is considered Grade B as there is no direct evidence on the efficacy or effectiveness of LAIV in HIV-infected individuals and the sample size for the evidence base is small.

- There is evidence that LAIV is immunogenic in children 2–17 years of age with stable HIV infection on HAART and with adequate immune function
- LAIV appears to have a similar safety profile to IIV; however, the total number of subjects assessed is insufficient to effectively detect uncommon or rare AE

- Children with HIV receive all the routine childhood vaccines and additional parenteral vaccines warranted by their actual or potential immunocompromised state. Offering intranasal LAIV instead of IIV avoids one IM injection annually. A discussion on preference for route of administration should take place prior to vaccination, and may improve acceptance of the seasonal influenza vaccine (26,27)

NACI concluded that the quantity of evidence available on the immunogenicity and safety of LAIV in adults with HIV is insufficient to justify a change in the current recommendation against the use of LAIV in this group. (Grade I Evidence). This recommendation is based on expert opinion.

The detailed findings of the literature review and additional information supporting this recommendation can be found in the NACI advisory committee statement: *Recommendation on the Use of Live Attenuated Influenza Vaccine (LAIV) in HIV-Infected Individuals* (28).

Conclusion

LAIV is immunogenic in children with HIV and appears to have a similar safety profile to IIV, although uncommon or rare AE may not have been detected. NACI 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. Studies with sufficient sample size to detect uncommon or rare AE or to address efficacy or effectiveness of LAIV in children may not be feasible, given the limited numbers of children with HIV in high income countries where LAIV is used.

Authors' statement

DM — Writing, original draft, review, editing
IG — Review, editing
RH — Review, editing
The National Advisory Committee on Immunization (NACI) advisory committee statement: *Recommendation on the Use of Live Attenuated Influenza Vaccine (LAIV) in HIV-Infected Individuals* was prepared by D Moore, N Dayneka, L Zhao, A Sinilaite, K Young and I Gemmill, on behalf of the NACI Influenza Working Group and was approved by NACI.

Competing interests

None.

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References

1. National Advisory Committee on Immunization. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019–2020. Ottawa (ON): NACI; 2019 (accessed 2020-02-17). https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2019-2020.html

2. National Advisory Committee on Immunization. Recommendations on the use of live, attenuated influenza vaccine (FluMist®). Supplemental Statement on Seasonal Influenza Vaccine for 2011-2012. An Advisory Committee Statement (ACS). Can Commun Dis Rep. 2011;37(ACS-7):1–77. DOI

3. AstraZeneca. Product Monograph: FluMist® Quadrivalent. 2018 (accessed 2020-02-17). https://pdf.hres.ca/dpd_pm/00047438.PDF

4. U.S. Department of Health and Human Services. AIDS Info. Guidelines for the Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children (accessed 2020-02-17). https://aidsinfo.nih.gov/guidelines/brief-html/5/pediatric-opportunistic-infection/0

5. BC Centre for Disease Control. Human Immunodeficiency Virus (HIV) Infection. BCCDC; 2018 (accessed 2020-02-17). http://www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Epid/CD%20Manual/Chapter%202%20-%20Imms/Part2/HIV.pdf

6. Alberta Health. Immunization of Specific Populations (Immunosuppressed and Chronic Health Conditions). Government of Alberta; 2019 (accessed 2020-02-17). https://open.alberta.ca/dataset/aip/resource/8a92b77b-351b-4f1e-9d4d-31aaa9effdb3/download/AIP-Specific-Populations-Immunocompromised.pdf

7. Manitoba Health, Seniors and Active Living. Seasonal Influenza Immunization Program: Live Attenuated Influenza Vaccine (LAIV) (FluMist® Quadrivalent): Questions and Answers for Health Care Providers. Government of Manitoba; 2018 (accessed 2018-11-01). https://www.gov.mb.ca/health/flu/docs/flumist_hcp.pdf

8. Government of New Brunswick. 2013-2014 FluMist®, Live Attenuated Influenza Vaccine, Information for Immunization Providers. Government of NB; 2014 (accessed 2020-02-17). https://www2.gnb.ca/content/dam/gnb/Departments/h-s/pdf/en/CDC/vaccines/FLUMISTInformationForImmunizationProviders.pdf

9. Government of Saskatchewan. Saskatchewan Immunization Manual. Chapter 7 – Immunization of Special Populations. Government of SK; 2015 (accessed 2020-02-17). https://www.ehealthsask.ca/services/manuals/Documents/sim-chapter7.pdf

10. Grohskopf LA, Alyanak E, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2019-20 Influenza Season. MMWR Recomm Rep 2019;68(3):1–21. DOI PubMed

11. Ministère de la Santé et des Services sociaux. Vaccinologie pratique: Immunodépression. MSSS; 2019 (accessed 2020-02-17). http://www.msss.gouv.qc.ca/professionnels/vaccination/piq-vaccinologie-pratique/immunodepression/

12. Public Health England. Influenza: the Green Book, Chapter 19. Government UK (updated 2019-04-23; accessed 2020-02-17). https://www.gov.uk/government/publications/influenza-the-green-book-chapter-19

13. Haut Conseil de la santé publique. Vaccination des personnes immunodéprimées ou asplèniques. Recommandations actualisées. HCSP; 2014 (accessed 2020-02-17). https://www.hcsp.fr/explore.cgi/avisrapportsdomaine?clefr=504

14. Rubin LG, Levin MJ, Ljungman P, Davies EG, Avery R, Tomblyn M, Bousvaros A, Dhanireddy S, Sung L, Keyserling H, Kang I; Infectious Diseases Society of America. 2013 IDSA clinical practice guideline for vaccination of the immunocompromised host. Clin Infect Dis 2014;58(3):309–18. DOI PubMed

15. Children's HIV Association (CHIVA). Vaccination of HIV infected children (UK schedule, 2018). CHIVA; 2018 (accessed 2020-02-17). https://www.chiva.org.uk/files/8315/4453/4519/Vaccination_of_HIV_infected_children_2018.pdf

16. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D; Methods Work Group, Third US Preventive Services Task Force. Current methods of the US Preventive Services Task Force: a review of the process. Am J Prev Med 2001;20(3 Suppl):21–35. DOI PubMed

17. King JC Jr, Treanor J, Fast PE, Wolff M, Yan L, Iacuzio D, Readmond B, O'Brien D, Mallon K, Highsmith WE, Lambert JS, Belshe RB. Comparison of the safety, vaccine virus shedding, and immunogenicity of influenza virus vaccine, trivalent, types A and B, live cold-adapted, administered to human immunodeficiency virus (HIV)-infected and non-HIV-infected adults. J Infect Dis 2000;181(2):725–8. DOI PubMed

18. King JC Jr, Fast PE, Zangwill KM, Weinberg GA, Wolff M, Yan L, Newman F, Belshe RB, Kovacs A, Deville JG, Jelonek M; HIV Influenza Study Group. Safety, vaccine virus shedding and immunogenicity of trivalent, cold-adapted, live attenuated influenza vaccine administered to human immunodeficiency virus-infected and noninfected children. Pediatr Infect Dis J 2001;20(12):1124–31. DOI PubMed

19. Levin MJ, Song LY, Fenton T, Nachman S, Patterson J, Walker R, Kemble G, Allende M, Hultquist M, Yi T, Nowak B, Weinberg A. Shedding of live vaccine virus, comparative safety, and influenza-specific antibody responses after administration of live attenuated and inactivated trivalent influenza vaccines to HIV-infected children. Vaccine 2008;26(33):4210–7. DOI PubMed

20. Weinberg A, Song LY, Walker R, Allende M, Fenton T, Patterson-Bartlett J, Nachman S, Kemble G, Yi TT, Defechereux P, Wara D, Read JS, Levin M; IMPAACT P1057 Team. Anti-influenza serum and mucosal antibody responses after administration of live attenuated or inactivated influenza vaccines to HIV-infected children. J Acquir Immune Defic Syndr 2010;55(2):189–96. DOI PubMed

21. Weinberg A, Song LY, Fenton T, Nachman SA, Read JS, Patterson-Bartlett J, Levin MJ. T cell responses of HIV-infected children after administration of inactivated or live attenuated influenza vaccines. AIDS Res Hum Retroviruses 2010;26(1):51–9. DOI PubMed

22. Curtis D, Ning MF, Armon C, Li S, Weinberg A. Safety, immunogenicity and shedding of LAIV4 in HIV-infected and uninfected children. Vaccine 2015;33(38):4790–7. DOI PubMed

23. Weinberg A, Curtis D, Ning MF, Claypool DJ, Jalbert E, Patterson J, Frank DN, Ir D, Armon C. Immune Responses to Circulating and Vaccine Viral Strains in HIV-Infected and Uninfected Children and Youth Who Received the 2013/2014 Quadrivalent Live-Attenuated Influenza Vaccine. Front Immunol 2016;7:142. DOI PubMed

24. Menegay JL, Xu X, Sunil TS, Okulicz JF. Live versus attenuated influenza vaccine uptake and post-vaccination influenza-like illness outcomes in HIV-infected US Air Force members. J Clin Virol. 2017;95:72-5. DOI

25. Mohn KG-I, Smith I, Sjursen H, Cox RJ. Immune responses after live attenuated influenza vaccination. Hum Vaccin Immunother. 2018;14(3):571-8. DOI

26. Marien AG, Hochart A, Lagrée M, Diallo D, Martinot A, Dubos F. Parental acceptance of an intranasal vaccine: example of influenza vaccine. Arch Pediatr 2019 Feb;26(2):71–4. DOI PubMed

27. Santibanez TA, Kahn KE, Bridges CB. Do parents prefer inactivated or live attenuated influenza vaccine for their children? Vaccine 2018 Nov;36(48):7300–5. DOI PubMed

28. National Advisory Committee on Immunization. Recommendation on the Use of Live Attenuated Influenza Vaccine (LAIV) in HIV-Infected Individuals. Ottawa (ON): NACI; 2020. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/live-attenuated-influenza-vaccine-hiv-infected-individuals.html

Vaccine Injury Compensation Programs: Rationale and an overview of the Québec program

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Abstract

Vaccines are among the safest therapeutic agents, and serious adverse events rarely occur. When they do occur, an individual may have to bear some or all of the costs associated with their injuries, seek compensation through litigation or, if available, seek compensation from a publicly-supported Vaccine Injury Compensation Program (VIC Programs). The VIC Programs are "no-fault" compensation schemes in which governments compensate individuals who are harmed by properly manufactured vaccines. There are ethical, legal and practical rationales to support these programs. Worldwide there are 19 countries that have implemented VIC Programs; in the majority of these countries, vaccines are not mandatory. They all have similar processes with respect to process, standard of proof and elements of compensation. In Canada, only the province of Québec has a VIC Program, which has been running successfully since 1985. Concerns with VIC Programs include cost, difficulties assessing causality and concern that such programs may undermine public trust in vaccines; but these concerns can be addressed, especially in high-income countries that can bear the costs and have the capacity to manage the program.

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Introduction

Vaccines are amongst the safest and most effective tools. Yet, vaccines—like any medical intervention—are not without a possibility of harm, albeit small. Most adverse events following immunization (AEFIs) are mild and resolve quickly and completely (e.g. fever, swelling at the injection site, rashes, etc.). In rare instances, however, serious adverse events can occur regardless of proper vaccine design, manufacture and delivery (1). A serious AEFI is defined as one that is life-threatening, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or results in a congenital anomaly/birth defect (2). The absolute risk of serious AEFIs is extremely low (e.g. fewer than one per 10 million doses for tetanus toxoid vaccines; 1–2 per one million doses for the inactivated influenza vaccine) (3). At a population level, these rare serious risks are far outweighed by the benefits of high uptake of vaccination. However, this implies that, in rare instances, an individual will suffer from significant consequences for the benefit of others, and that such an event can be anticipated (expected, even), though not necessarily predicted at the individual level (1).

The above state of affairs begs the question: What are the roles and responsibilities of jurisdictions for those who experience a "vaccine injury" (i.e. a serious AEFI) when given a vaccine recommended by public health? Halabi and Omer (3) identified three types of approaches toward AEFIs. While the acute costs of a serious AEFI are covered through the public healthcare system, for any additional costs, individuals may 1) bear the costs associated with their injuries by themselves, 2) seek compensation through litigation against private-sector actors (i.e. the vaccine manufacturers) or 3) seek compensation from publicly supported systems, or Vaccine Injury Compensation Programs (VIC Programs) (3).

The objective of this article is to provide a rationale and global overview of VIC Programs and to describe the situation in Canada and, specifically, in Québec. This is the seventh in a series of articles produced by the Canadian Vaccination Evidence Resource and Exchange Centre (CANVax). This Centre includes a group of multidisciplinary professionals that identify and create useful resources to foster vaccine uptake.

Rationale for Vaccine Injury Compensation Programs

There are a number of reasons why jurisdictions have implemented VIC Programs. As noted by Looker and Kelly, these programs often arise from political and economic pressures, litigation threats and the imperative to ensure an ongoing vaccine supply (4,5). Generally, there are biological, ethical, legal and practical arguments supporting the implementation of VIC Programs (6).

- Biological: Vaccinations are extremely safe, but the possibility of harm in rare instances exists and has been recognized (e.g. anaphylaxis, intussusception from a rotavirus vaccine no longer used)
- Ethical: Vaccination benefits not only the vaccinated individual, but the whole community through herd immunity. Ethical principles of solidarity, reciprocity, fairness and justice all support the implementation of measures to compensate the few individuals who will be harmed by vaccines. These arguments are stronger in jurisdictions where governments use mandatory policies to ensure widespread vaccination
- Legal: We have developed a rights-based society where everyone's physical integrity is, in some measure, guaranteed, and where incursions against this integrity give rise to justifiable claims for redress
- Practical: Tort litigation relating to AEFIs is costly and uncertain, and exposure to this uncertainty and potential liability can discourage manufacturers from producing vaccines. The VIC Programs remove the uncertainty of litigation for manufacturers and ensure the security of vaccine supply. They also help to forge an environment in which vaccine innovation can occur

Global overview

A recent review has shown that compensation programs have been implemented in 19 jurisdictions worldwide. Interestingly, twelve of the jurisdictions with such programs have no vaccine mandates (**Table 1**) (4).

The VIC Programs are "no-fault" compensation schemes in which federal or provincial governments compensate individuals who are harmed by properly manufactured vaccines (3). There is considerable variability in how these programs are administered, who is eligible and which vaccines are covered, the decision-making process for administration and how funds are sourced and allocated (5). Looker and Kelly (1) have conducted an extensive review of common program elements (**Table 2**).

The Canadian situation

In Canada, with the exception of Québec, any major health care costs from vaccine injury are covered through the public healthcare system. If a disability occurs, support would likely

Table 1: Jurisdictions with Vaccine Injury Compensation Programs (including the year of introduction)

Vaccination is not mandatory	Vaccination is mandatory
Austria (1973)	France (1963)
Denmark (1972)	Hungary (2005)
Finland (1984)	Italy (1992)
Germany (1961)	Republic of Korea (1994)
Iceland (2001)	Slovenia (2004)
Japan (1970)	Taiwan (1988)
New Zealand (1974)	United States (1988)
Norway (1995)	
Québec (1985)	
Sweden (1978)	
Switzerland (1970)	
United Kingdom (1979)	

Sources: Looker and Kelly, 2011 (1); Attwell *et al.*, 2019 (4)

Table 2: Common elements in Vaccine Injury Compensation Programs

Element	Comment
Administration	Most compensation programs are enacted and run by the government at the national or sub-national levels
Funding	National, state or municipal treasuries Manufacturers' levy Vaccine tax
Eligibility	Only mandatory vaccines Only vaccines recommended by public health All licensed vaccines Only vaccines believed to have an associated risk (e.g. Vaccine Injury Table)
Process	The process is similar in most jurisdictions: • Threshold injury or disability criteria to be met before making a claim • Initial revision by an administrative body for initial eligibility and compensation decisions • Revision by external review committee if a claim is deemed complex or contentious • A formalized appeal process for claimants • Prioritization of timely resolution of claims
Standard of proof	"Balance of probabilities" (i.e. more evidence than not that a vaccine caused the injury) Probable cause "Preponderant probability"
Elements of compensation	Lump sum or reimbursement proportional to the severity of vaccine injury, including: • Unreimbursed medical costs • Disability pension • Non-economic loss, including pain and suffering • Death benefits • Compensation to family • Reasonable legal costs (in the United Kingdom, for both successful and unsuccessful claimants)

Table 2: Common elements in Vaccine Injury Compensation Programs (*continued*)

Element	Comment
Litigation right	In most countries, claimants can seek either damage through the courts or compensation through the program, but not both Other countries adjust compensation payments if damage has been received through the courts

Source: Looker and Kelly, 2011 (1)

come from disability incomes for those who are covered. The only means for compensation beyond this is through litigation.

There is a limited understanding of the number and scope of vaccine-injury related lawsuits in Canada (5). We do know that very few cases reach the courts, and these are often in relation to procedural matters, not the merits of the cases (i.e. requests for certification as class actions, requests to have claims struck, etc.) (7). One exception is *Morgan vs. City of Toronto* (8), wherein the plaintiff sued the City of Toronto for damages stemming from chronic fatigue syndrome, which she alleged resulted from the city's negligent administration of hepatitis B vaccine in 1994. In dismissing the claim, the Court held that, while the standard for disclosure of risks is very high, not every suspicion of risk constitutes a "known" or "material" risk, and that the city did not breach the standard in failing to warn the plaintiff about possible effects that were not, at the time of the inoculation, considered material. Note that many more cases are adjudicated through bodies such as Workers' Compensation Tribunals and Workplace Safety and Insurance Appeals Tribunals, but no comprehensive survey of the outcomes of these cases have been conducted.

Québec's Vaccine Injury Compensation Program

The following description comes from the Québec Ministry of Health website (https://www.msss.gouv.qc.ca/en/). In 1979, a five-year-old girl, Nathalie Lapierre, developed viral encephalitis shortly after being vaccinated for measles, and was left severely disabled. Her parents brought an action against the Government of Québec for damages, including those relating to tutoring. In *Québec (Attorney-General) vs. Lapierre* (9), the Québec Court of Appeal held that, while there was a causal link between the vaccination and the injury, there was no fault on the part of the Province (or the administering nurse), and there was no obligation under Québec law to compensate in the absence of fault. In dismissing Lapierre's appeal, both the Court of Appeal and the Supreme Court of Canada observed that "an obligation independent of any fault in circumstances such as those of the case at bar would be an excellent thing, but it does not exist in our law at present". In the result, perhaps for political reasons, or in recognition of the demands of social justice, the Government of Québec provided some support to the family in this case. Subsequently, in 1985, it introduced its VIC Program, which was statutorily grounded in a new division of the *Public Health Protection Act*. A regulation specific to this program was adopted in November 1987, and the first claims for compensation were filed the following year.

The principle of the VIC Program is that the Québec's Minister of Health and Social Services must compensate anyone injured as a result of a voluntary vaccination with a vaccine or immunoglobulins against a disease or infection identified in the regulation, or any compulsory or imposed vaccination. The vaccination must have taken place in Québec, and the claim form must be filed within three years of the injury. The claim is reviewed by an external committee of experts in vaccinology who 1) makes recommendations to the Minister on the existence or lack thereof of a causal link between the injury sustained and the vaccination and 2) assesses, if required, the percentage of permanent impairment to the victim's physical or mental integrity, and other elements required regarding compensation.

The Minister then renders a decision. If the claim is rejected, the claimant is informed and has 60 days to file an appeal. If the claim is accepted, the amount of compensation is determined using earnings and medical costs. The Minister has entered into an agreement with the *Société de l'assurance automobile du Québec* whereby the *Société* calculates and pays the compensation in cases with a favourable decision. Amounts are calculated pursuant to the rules and regulations prescribed in the *Automobile Insurance Act* and are identical to those awarded in case of an automobile accident.

As of April 1, 2018, 228 completed claims have been submitted and 187 met the admissibility criteria and were evaluated. Of these 187 cases, 43 claims were accepted, which resulted in $5.49 million of compensation paid. There is usually between three and five claims per year, but 11, 16, nine and 28 claims were submitted between 2009 and 2012, respectively. In 2009–2010, 5.7 million Quebecers received the influenza A(H1N1) vaccine, and this increased vaccination rate could explain the increase in claims observed in the three years following the mass vaccination campaigns (10).

Concerns with Vaccine Injury Compensation Programs

Arguments against VIC Programs are often grounded on the costs of these programs, the difficulties with causality assessment (i.e. determining whether there is a causal relationship between a vaccine and a specific injury) and the concern that these programs can decrease public trust in vaccines and fuel anti-vaccination movements (4).

Some of these concerns regarding VIC Programs have been addressed. The experience in the 19 jurisdictions where such programs have been implemented indicates that costs are both manageable and predictable (7). One caveat, however, is that 17

of these 19 countries are high-income countries, which means that, on the whole, they can bear the costs and have the capacity to manage the program.

Similarly, the difficulties with causality assessment appear to be resource dependent, as the countries who have adopted VIC Programs have had the expertise to assess vaccine quality and causality of injuries. Finally, to date, there is insufficient evidence to assess the concern regarding the potential to decrease public trust in vaccines. The absence of a VIC Program has not been identified as a major concern amongst those who are hesitant. There is no evidence to show that having VIC Programs support vaccine acceptance; however, when a VIC Program is adopted there could be a communication strategy that reassures the public that, much like accident insurance, if it does occur, they will be covered.

Conclusion

Many affluent countries have VIC Programs; Canada and the United States are the only G7 countries that do not. There is a strong public health justification for the implementation of VIC Programs. Although there is no direct proof that these programs improve vaccine acceptance, they do help to maintain vaccine supply. If and when other provinces and territories in Canada consider such programs, the ethical, legal, and practical considerations as well as the successful 35-year track record in Québec may help to inform this policy decision.

Authors' statement

ED — Writing original draft, review and editing
DG — Writing, review and editing
NEM — Writing, review and editing
SHEH — Writing, review and editing
SH — Writing, review and editing

Competing interests

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References

1. Looker C, Kelly H. No-fault compensation following adverse events attributed to vaccination: a review of international programmes. Bull World Health Organ 2011;89(5):371–8. DOI PubMed

2. World Health Organization. Global Manual on Surveillance of Adverse Events Following Immunization. Geneva (CH): WHO; 2014 (revised 2016; accessed 2019-05-15). https://www.who.int/vaccine_safety/publications/Global_Manual_revised_12102015.pdf?ua=1

3. Halabi SF, Omer SB. A Global Vaccine Injury Compensation System. JAMA 2017;317(5):471–2. DOI PubMed

4. Attwell K, Drislane S, Leask J. Mandatory vaccination and no fault vaccine injury compensation schemes: an identification of country-level policies. Vaccine 2019;37(21):2843–8. DOI PubMed

5. Hapuhennedige S, Nisbet C. A scoping review on vaccine injury compensation. Understanding Canadian Immunization Policy. Background Paper. Simcoe Muskoka District Health Unit. 2017. p. 40.

6. Wilson K, Keelan J. The case for a vaccine injury compensation program for Canada. Can J Public Health 2012 Mar-Apr;103(2):122–4. DOI PubMed

7. Adam, Abudu v. Ledesma-Cadhit et al., 2014 ONSC 5726; Batten v. Boehringer Ingelheim (Canada) Ltd., 2017 ONSC 53; Re Tluchak Estate, 2018 SKQB 311.

8. 2006 CanLII 41574 (ON SC).

9. (1983) 7 DLR (4th) 37 (QC CA), affirmed in Lapierre v. A.G. (Québec), [1985] 1 SCR 241.

10. Government of Québec. Vaccine Injury Compensation Program. Government of Québec (updated 2019; accessed 2019-05-15). https://www.quebec.ca/en/health/advice-and-prevention/vaccination/vaccine-injury-compensation-program/#c3896

Interim guidance: Care of residents in long term care homes during the COVID-19 pandemic

Source: Interim guidance: Care of residents in long term care homes during the COVID-19 pandemic. Government of Canada. 2020. https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/residents-long-term-care-homes-covid-19.html

This document provides care guidance specific to the COVID-19 pandemic in Canadian homes/facilities where older adults require continuous supervised care, including professional health services, personal care and other services such as meals, laundry and housekeeping. These facilities may have different names, including but not limited to care homes/facilities, continuing care homes/facilities, personal care homes/facilities, nursing , centres d'hébergement et de soins de longue durée (CHSLDs), or other long term care homes/facilities, all hereafter referred to as LTCHs. Some of the content may be adapted to other settings as appropriate (i.e. retirement homes).

This guidance provides employed and contracted LTCH staff including physicians (most often family physicians, medical specialist consultants), nurse practitioners, registered nurses, licensed or registered practical nurses, clinical pharmacists, and health care aides/assistants, continuing care/personal care attendants/assistants, resident attendants/care workers, and personal support workers (all hereafter referred to as support workers), and others who provide care for residents in LTCHs, with interim advice on important aspects of care for all LTCH residents during the COVID-19 pandemic, and on the timely and safe supportive management of residents with suspected or confirmed COVID-19. The guidance in this document is also important for medical and nursing administrators/directors and their associates who can play a pivotal role in building infrastructure and collaborating with LTCH care providers to implement recommended measures.

Recommendations for LTCH staff, resident and family/caregiver preparedness, resident assessment, active medical management, palliative care, mental health disorders, delirium and responsive behaviours, and psychosocial aspects of care are included.

International Coalition of Medicines Regulatory Authorities (ICMRA) Statements on Vaccine Confidence

Source: International Coalition of Medicines Regulatory Authorities (ICMRA). Statements on Vaccine Confidence. International Coalition of Medicines Regulatory Authorities (ICMRA). http://www.icmra.info/drupal/en/covid-19

During the COVID-19 pandemic, the International Coalition of Medicines Regulatory Authorities (ICMRA) continues to provide a forum for Heads of Agencies to support strategic coordination and international cooperation among global medicines regulatory authorities, with Health Canada serving as one of its 29 members, and as an executive committee member. On June 17, 2020, ICMRA released two statements, directed to members of the general public and health-care professionals to highlight the safety and effectiveness of vaccines.

West Nile virus and other mosquito-borne diseases surveillance report - Annual edition (2018)

Source: West Nile virus and other mosquito-borne diseases surveillance report - Annual edition (2018). Public Health Agency of Canada. Government of Canada. 2020. https://www.canada.ca/en/public-health/services/publications/diseases-conditions/west-nile-virus-other-mosquito-borne-diseases-surveillance-annual-report-2018.html

Mosquito-borne diseases in Canada - Zoonotic diseases are infectious diseases caused by bacteria, viruses and parasites that spread between animals and humans. West Nile virus (WNV) continues to be the leading cause of domestically acquired mosquito-borne disease in Canada. West Nile virus circulates between avian hosts and competent mosquito vectors. Mosquitoes may then infect a broad-range of dead-end hosts (i.e. not able to transmit the disease further) including humans, horses, other mammals, and amphibians. As a result, surveillance efforts of mosquito-borne diseases require a One Health approach that recognizes the health of humans is interconnected to animals and the environment. In addition to describing the human health burden of WNV, this report will demonstrate the efforts made to strengthen animal health surveillance in collaboration with multi-disciplinary health partners with the goal of achieving optimal human health outcomes.

For more information:

To access the 2018 West Nile Virus and Other Mosquito-borne Diseases Surveillance Report (https://www.canada.ca/en/public-health/services/publications/diseases-conditions/west-nile-virus-other-mosquito-borne-diseases-surveillance-annual-report-2018.html)

To access 2020 weekly West Nile Virus and Other Mosquito-borne Disease Surveillance Report (https://www.canada.ca/en/public-health/services/diseases/west-nile-virus/surveillance-west-nile-virus/west-nile-virus-weekly-surveillance-monitoring.html)

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