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ORAL HEALTH IN CANADA

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COMMENTARY

Summary of a report for Canadian oral health professionals for a safe return to clinical practice during COVID-19

Office of the Chief Dental Officer of Canada[1]

Abstract

Following the onset of the coronavirus disease 2019 (COVID-19) pandemic, Canadian healthcare providers were advised or mandated by their regulatory bodies to cease all routine and elective care and only provide emergent/urgent care in March 2020. Two months later, the provincial/territorial governments initiated plans to "re-open" their jurisdictions; however, oral health practitioners are returning to practice in a very different environment, particularly in the domain of infection control and prevention, to the one they left prior to the onset of the pandemic. During the COVID-19 pandemic, Canadian oral health professional decision-makers at all levels have been making decisions and providing advice and guidance in a highly complex, rapidly evolving environment, often based on imperfect and/or incomplete information. To gather, summarize and present these changes in oral health workplace environments and protocols, the Office of the Chief Dental Officer of Canada has commissioned the development of a multidisciplinary, high-level national expert review document, which resides in the public domain. This document is available for Canada's oral health regulatory authorities, educators, program officials and policy makers.

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Keywords: oral health, clinical practice, post-pandemic, Canada, COVID-19

Introduction

Oral health professional organizational, institutional, clinical and other leaders, as well as frontline dental professionals treating patients, are making decisions each day on how to best manage patients and to guide the professions in the context of the return to clinical practice during the coronavirus disease 2019 (COVID-19) pandemic. These people and organizations are making decisions in a very fast-moving crisis with a changing environment, with multiple, evolving sources of information and in all Canadian jurisdictions. These decisions are made based on instructions and guidelines from governments and other legal entities (such as regulatory authorities), on scientific data and evidence, and on expert opinion and on prioritized needs. They include health care, economic, ethical and other important elements, while also recognizing the information and advice upon which decisions are made is often imperfect, incomplete and/or otherwise limited. In short, oral health professional decision-makers at all levels are making decisions and providing advice and guidance in a highly complex, rapidly evolving environment, based often on imperfect and incomplete information.

A second contextual observation is that oral health practitioners (dentists, dental hygienists, dental assistants, denturists, dental technicians and dental therapists) across all jurisdictions in Canada, the vast majority of whom practice in private offices rather than in public facilities, were advised or mandated by their regulatory bodies to cease all routine and elective care and only provide emergent/urgent care in March 2020. As of May 4th 2020, a first provincial/territorial government activated a plan to "re-open" its jurisdiction, and other jurisdictions soon followed. However, oral health practitioners are returning to practice in a very different environment, particularly in the domain of infection control and prevention, to the one they left prior to the onset of the pandemic. To summarize and analyze these differences, the Office of the Chief Dental Officer of Canada (OCDOC) commissioned McGill University to draft a comprehensive document around which OCDOC then convened a representative multidisciplinary knowledge-based group from the national oral health professional and federal government health domains. A single high-level national expert consensus document on current evidence has now been generated, and

resides in the public domain (1). Canada's oral health regulatory authorities may then choose to consult this document in developing consistent guidance for their respective registrants at the provincial/territorial level; educators, program officials and policy makers may also choose to consult this document as they carry out their respective responsibilities. Evidence gaps identified during this process have been submitted to the Canadian Institutes of Health Research by the Chief Dental Officer, with a recommendation for priority research funding consideration in these areas.

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OVERVIEW

Canada's oral health professionals and antimicrobial stewardship

Office of the Chief Dental Officer of Canada[1]

Abstract

Antimicrobial resistance (AMR) is a global concern as it poses a serious threat to our capacity to treat common infectious diseases. Canada has been engaged in actions to address the AMR challenge since 1997, and these actions include a four-pillar national strategy: surveillance; stewardship; infection prevention and control; and research and innovation. Dentists play a significant role in contributing to the efforts around these four-pillars, especially that of stewardship. Studies show that antibiotic prescriptions for oral health reasons, are increasing over time, and 60% to 80% of antibiotics prescribed in a dental setting are not necessarily clinically indicated. The development, promotion and implementation of initiatives to promote optimal use of antimicrobials across Canada will require collaboration among many stakeholders, including the oral health community. Antimicrobial resistance and antimicrobial stewardship are already being discussed within the dental profession in Canada; however, there is still more work to be done in a variety of areas including, but not limited to, dentist's access to and use of current evidence-based guidelines and prescribing protocols enforced by their governing bodies to ensure appropriate prescribing of antibiotics when necessary, and timely and affordable access to oral health care services by Canadians.

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Keywords: AMR, stewardship, antibiotics, prescription, best practices, dentists

Introduction

The discovery and development of antibiotics is considered one of the greatest medical achievements of the 20th century; however, with increased use, bacteria can develop a resistance to antibiotics over time. The World Health Organization (WHO) has made antimicrobial resistance (AMR) a priority. WHO calls for a global coordinated action to minimize the emergence and spread of AMR, and for each country to have a national action plan in place (1). Canada has been engaged in actions to address the challenges of AMR since 1997, and these actions include a four-pillar national strategy: surveillance; stewardship; infection prevention and control; and research and innovation (2–4). As highlighted in the 2019 Chief Public Health Officer of Canada Spotlight Report, Canada has made progress and rates of antibiotic resistance are lower than in many other countries in the world (5). However, there is still work to be done.

As healthcare providers and prescribers, dentists have a significant role to play in contributing to the efforts around the four-pillar national strategy, especially stewardship. Antimicrobial stewardship (AMS) refers to coordinated interventions designed to promote, improve, monitor and evaluate judicious appropriate antimicrobial use to preserve their future effectiveness and to promote and protect human and animal health (2). The following sections will provide a closer look at the prescribing habits in Canadian oral health practice versus that of medical health practitioners and AMS initiatives already underway, and will provide an overview of the AMS work that lies ahead in Canadian dentistry.

Antimicrobial use and prescribing practices

In Canada, approximately 92% of antibiotics are used outside of the acute care hospital setting; 89% are prescribed by physicians, 8% by dentists and 3% by nurses, pharmacists and optometrists (2). In dentistry, there are two uses for antibiotics: prophylactic and therapeutic. Prophylactic antibiotics are used to prevent infection and these types of prescriptions are more prevalent than those for therapeutic antibiotics, which are used to treat an existing infection (5). The Canadian Dental Association supports the American Heart Association's guidelines for antibiotic prophylaxis prior to certain oral health procedures to prevent infective endocarditis on high-risk patients only. These guidelines

state that, due to a growing body of evidence, the risks of taking preventive antibiotics outweigh the benefits for most patients (6). Despite these guidelines, in a retrospective cohort study conducted in the United States (US) looking at data from 2011–2015, dentists in the US were found to often prescribe primary prophylaxis to healthy patients undergoing invasive oral health procedures even though evidence in support of such use is minimal and inconclusive (7). Specifically, the researchers found that more than 80% of antibiotics prescribed for infection prophylaxis before dental visits were unnecessary (7).

Studies in the United Kingdom and US have shown that between 60% and 80% of antibiotics prescribed in a dental setting are not necessarily clinically indicated (7–9). Unfortunately, at this time, there are limited published data on the antibiotic prescribing practices of dentists in Canada. Canadian data that are available show a downward trend in antimicrobial prescribing rate among physicians (10). An increase in prescriptions among dentists (2010–2012) was followed by a generally stable rate from 2012–2015 (10). A study in British Columbia also showed overall antibiotic use and physician-prescribing declined by 18.2% between 1996 and 2013 (11). However, there was a reported 62.2% increase in antibiotic prescribing by dentists in British Columbia over the same time period—at a time when the use of recommendations and guidelines should have resulted in a decline (11).

The Canadian Dental Association (CDA) attempted to document prescribing practices of dentists across Canada in 2017. Results of a web-based survey showed that most dentists in Canada reported prescribing antibiotics according to the best available evidence and clinical guidelines (12). The results also indicated that there were concerns including, but not limited to, overuse of certain types of antibiotics, discrepancies regarding medical conditions and dental procedures requiring antibiotic prophylaxis for the prevention of infective endocarditis and dental conditions requiring therapeutic antibiotics. Another concern was an apparent lack of awareness, among certain dentists, to changes in antibiotic prescribing guidelines (12). While the survey was based on self-reported information and the sample size was small (n=1,035, representing a 16.5% response rate), the results point to the need for more research to better understand the prescribing practices of Canadian dentists.

Numerous factors, over and above evidence and best-practice, contribute to the decision to prescribe an antibiotic. These factors may include recommendations from other health professionals, patient expectations, unclear, outdated or changing guidelines or lack of awareness of recent guidelines, diagnostic uncertainty and time constraints (5). According to a study done by Suda *et al*. (7), reasons for higher antibiotic prescribing rates among dentists included increasing use of dental implants, an aging population, underinsurance driving antibiotics as an oral surgery substitute, slow adoption of new guidelines, lack of awareness of the role of dentists in antimicrobial resistance, and physician and patient pressure. These characteristics are similar to those associated with physician antibiotic overprescribing (7). In addition, a scoping review found that reasons for prescribing therapeutic antibiotics included limited time for emergency appointments, time constraints, and uninsured patients who were unable to afford appropriate treatment (13). Nonetheless, similar to other prescribing healthcare professionals, the challenge for dentists lies in ensuring that they are prescribing antibiotics only when necessary and in strict compliance with the recommended dosage and duration for that antibiotic (aiming for the shortest possible time for the required therapeutic effect).

Contributing to the issues around AMR, some patients see physicians at hospital emergency departments (EDs). Between 2001 and 2010, visits to US EDs by 20–29 year olds accounted for 42% of all ED toothache visits, which ranked as the fifth most common reason for any ED visit and third most common for uninsured ED visits in this age group (14,15). In 2019, another group of researchers conducted a scoping review using Canadian and US data to map out preliminary factors associated with patients' use of EDs for non-traumatic dental problems (15). While the researchers stated several limitations, their preliminary results showed that patients visit EDs due to demographics, accessibility, economic and social influences with income and inability to afford care as the most common factors.

Dental stewardship initiatives on antimicrobial resistance in Canada

Some stewardship initiatives are already underway to raise awareness and educate dental professionals on AMR. For example, AMR and AMS are already being discussed within the dental profession in Canada. The CDA is raising awareness of AMR, encouraging the mobilization of Canadian oral health professionals and publishing articles on AMR in the CDA magazine (16). The CDA has also been a participant in the Public Health Agency of Canada (PHAC)-sponsored national AMR collaborations. Within PHAC, the Office of the Chief Dental Officer of Canada is also working with the PHAC AMR team and with key national oral health stakeholders to enable the profession to align with best prescribing practices in order to mitigate the risks of AMR. The Canadian Association of Hospital Dentists will be participating in the HealthCare*CAN* Action Roundtable to develop a National Antimicrobial Stewardship Action Plan. It is also working with the dentists and infectious disease physicians to communicate the critical importance of responsible antimicrobial use (17).

In terms of resources for clinicians, in the US, the Massachusetts Department of Public Health has developed an *Antibiotic Stewardship Toolkit for Oral Health Clinicians*, which consists of two short YouTube® videos in addition to webinars (18). In Canada, PHAC has contributed to the sponsorship of training modules on AMR, giving Canadian dentists access to focused continuing education through the University of Waterloo Online

training modules (19). Dentists can also guide their patients toward easy-to-read information about AMR within websites from "Do Bugs Need Drugs" (20) and "Choose Wisely Canada/ Antibiotics Wise" (21).

Moving forward, different approaches should be considered by the dental profession to address AMR. The development, promotion and implementation of initiatives to promote optimal use of antimicrobials across Canada will require collaboration among many stakeholders (22). Governments should further explore oral health care access disparities and inequalities faced by segments of the population in order to prevent unnecessary visits to see physicians and other medical providers for oral health issues (14,15). This would reduce the unnecessary prescription of antibiotics as outlined above in, for example, EDs (14). Federal, provincial and territorial governments and their respective regulatory bodies also play a key role in the shared responsibility of monitoring and evaluating guidelines, an essential component of AMS strategies (22). WHO and US Centers for Disease Control and Prevention (CDC) are formulating policies on AMS (23). Examples of CDC's core elements of outpatient AMS are accountability, provision of training, monitoring and reporting on prescribing patterns, and education for both clinicians and patients (23). Governments and dental associations and governing bodies can use these as a starting point.

There is support for AMS initiatives at the government and dental association levels (2,6,22). Continuing education opportunities, professional guidelines, and awareness-raising should be used and promoted among dentists in addition to additional research in Canada to better understand antibiotic prescribing habits of dental clinicians.

Competing interests

None.

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OVERVIEW

Human papillomavirus and oral health

Office of the Chief Dental Officer of Canada[1]

Abstract

Canada is among the world leaders in oral health. Despite this, there are growing concerns about the rising rates of HPV-related mouth and throat cancers. The link between human papillomavirus (HPV) and cervical cancer is well established; fortunately, thanks to detection and vaccination, Canada has one of the lowest incidence rates of cervical cancer in the world. The HPV-related mouth and throat cancers, however, present a different picture. In Canada, about 25% to 35% of mouth and throat cancers are related to oral HPV infection; and in 2012, the incidence rate of HPV-associated oropharyngeal cancer was more than 4.5 times higher in males than females. Furthermore, HPV vaccination uptake in Canada is higher among females than males. Physicians and nurses in public health and clinical settings have a role to play in the fight against HPV transmission, as do oral health professionals. Oral health professionals can play a key role in preventing HPV infection and HPV-related oropharyngeal cancers by raising awareness, educating and offering counselling to their clients, and promoting evidence-based preventive and diagnostic interventions.

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Keywords: HPV, oral cancer, oral sex, awareness, oral health professionals

Introduction

Canada is considered to be among the world leaders in oral health (1). Oral health is defined by the Canadian Dental Association as "a state of the oral and related tissues and structures that contribute positively to physical, mental and social well-being and the enjoyment of life's possibilities, by allowing the individual to speak, eat and socialize unhindered by pain, discomfort or embarrassment" (2). It might come as a surprise to most Canadians that there are growing concerns about the rise in numbers of human papillomavirus (HPV)-related mouth and throat cancers (3). Sexually transmitted infections (STIs) are a significant public health concern in Canada (4). However, when one first thinks about STIs, their impact on oral health is often not top of mind. HPV infection is a good example of such an overlooked connection. HPV is both very common and very contagious; and different types of HPV are transmitted through sexual activities. More than 70% of sexually active Canadian men and women will have a sexually transmitted HPV infection at some point in their lives (5). While most people will contract this virus in their genital area, it can also be contracted in the mouth and throat (3). People are generally unaware of this fact, and of the potential consequences of an oral HPV infection (6). This overview will provide a synopsis of HPV, HPV-related oropharyngeal cancer (OPC), and how oral health professionals can contribute to reducing the burden of OPC on individuals and health care.

Human papillomavirus epidemiology

There are over 100 types of HPV and the virus can infect different parts of the body (5). Low-risk strains cause minor ailments, such as warts, whereas high-risk strains can cause cancer (7). HPV is the most common STI in Canada and around the world, and most sexually active Canadians will eventually become infected with the virus (5). In many cases, the infection will disappear on its own, but in the small portion of cases, where the infection remains, it may lead to the development of cancers of the cervix, vagina, penis, anus, mouth or throat (8). It can take years before an infection by the high-risk persistent form of the virus can develop, in some cases, into cancer. Therefore, preventing transmission and immunizing pre-adolescents, teenagers, young adults and other potentially vulnerable groups is important (9).

The causal relation between HPV and cervical cancer is well established (10). HPV is the cause for nearly all cervical cancer (11). Indeed, according to a recent article, "cervical cancer continues to be a major public health problem affecting middle-aged women, particularly in less-resourced countries" (12). According to the World Health Organization, cervical cancer is the fourth most frequent cancer in women worldwide (13). In Canada however, we have seen a sharp decline in both incidence and mortality over time, with one of the lowest incidence rates of cervical cancer in the world (14). The combination of an early adoption of wide-spread screening tests and the introduction of the HPV vaccine played a key role in that decline (15).

While women have been seeing decreasing rates in cervical cancer, the incidence of other HPV-related infections and cancers, including OPC, specifically in males, is increasing (7). This is consistent with observations in the United States (US) and in some European countries (7). As presented in **Table 1**, OPC represents the highest number of HPV-related cancer cases in Canada (7). HPV-related OPC is mostly caused by the HPV-16 strain. The highest prevalence of HPV is found in adults of 20–24 years of age (16) with 10%–30% of active infections (17). In Canada in 2012, two-thirds of all HPV-associated cancers were diagnosed in females and one-third in males (7). **Table 2** below presents the incidence of OPC linked to HPV amongst men in Canada and the US (17,18). While comparable data for the same time frames are not available, one can see by these numbers that the incidence is rising.

Table 1: Most common human papillomavirus-related cancers in Canada, 2012

Type of HPV-related cancer	Total number of cases
Oropharyngeal	1,335
Cervical	1,300
Anal	475

Abbreviation: HPV, human papillomavirus

Table 2: Incidence of oropharyngeal cancer linked to human papillomavirus in Canada amongst men

Year	Number of cases per 100,000	
	Canada	United States
1997	4.1	N/A
2012	6.4	N/A
2013–2017	N/A	8.7
2017	N/A	8.9

Abbreviation: N/A, not applicable

Without vaccination, it is likely that most sexually active Canadians will have an HPV infection at some point in their lives. Unfortunately, good epidemiological data are lacking because HPV is not a nationally notifiable disease, is usually asymptomatic and diagnostics for HPV are not publicly available or funded (16,19). Transmission of oral HPV usually takes place through oral sex, but further research is still required to better understand if there are other potential modes of oral transmission; and to determine what are the mechanisms through which, in some cases, the virus will contribute to the development of mouth and throat cancers (20). In addition, a person infected by oral-HPV can be asymptomatic for many years, making it quite challenging to detect and to prevent further transmission (20). Oropharyngeal cancer affects the posterior third of the tongue, tonsils and medial wall of the pharynx and is commonly diagnosed at advanced stages (21).

Human papillomavirus vaccination

While males can now receive the HPV vaccine, the focus that was initially put on the prevention of cervical cancer and the introduction of a vaccine solely for females appears to have created a gender bias that led to the misconception that HPV is a "women's issue" (22). All provinces and territories have announced or introduced HPV immunization programs for girls as part of routine immunization schedules (23). However, it was not until 2017 that all Canadian provinces and territories offered free school-based immunization programs for HPV to both boys and girls with varying eligibility criteria (24–27). As a likely result, HPV vaccination uptake in Canada is higher among females than males (28). Unfortunately, detailed data on vaccination uptake in Canada are not consistent throughout the literature. Better research and surveillance is needed in this area (28).

Three American states, Illinois, Minnesota and Oregon, permit flu vaccinations in dental offices (29); however, only Oregon also allows HPV vaccinations in dental offices (29). Canadian dentists do not presently have the regulatory authority to administer HPV vaccinations, and the responsibility rests with physicians and nurses for the time being. HPV vaccinations in dental offices, however, might assist in increasing vaccination rates, particularly in males. Considerations around vaccinations in Canadian dental offices should be assessed and discussed with the appropriate regulatory bodies. Such discussions would include training, determination of whether dentists have sufficient patient medical histories, and estimation of associated costs (29). In the meantime, the administration of vaccinations in US dental offices should be monitored in order to inform any potential initiative of this kind in Canada.

Moving forward

With the rise of HPV-associated OPC, there is a need for more action to reduce this trend. If not addressed, HPV-associated OPC may have a significant impact on the healthcare system and resources (7). The OPCs are a public health problem because they have a substantial impact at individual, societal and health care system levels (21). The participation of more boys in vaccination programs would contribute to ensuring that males are equitably protected from HPV-related diseases (22). Given the long latency between HPV infection and cancer, it may be years before the impact of vaccination can be assessed. Furthermore, there is strong evidence that female vaccination can help prevent infection in males through herd immunity (7). Vaccination of the population prior to them becoming sexually active is key in to reducing this burden (5). There is also a need to add and strengthen messaging around 1) sexual practices and behaviours, 2) the importance of oral health as part of overall health and 3) the role(s) played by oral health professionals in detecting early signs of anomalies in the mouth (6). Public health professionals need to continue monitoring changing and evolving patterns of HPV transmission and vaccination rates, and

ensure the application of a sex and gender-based lens to the observed trends considering that, for example, males are more likely to develop oropharyngeal cancers than females, while being less likely to get vaccinated (14,22).

Oral health professionals can play a key role in the fight against HPV transmission, particularly against oral HPV infection, and in preventing HPV-related oropharyngeal cancers—after all, HPV infection is preventable—by raising awareness, educating and offering counselling to their clients, and promoting evidence-based preventive and diagnostic interventions (6,13). Particular attention is needed in the area of the prevalence of oral HPV infection and its typical pathways of transmission in addition to vaccination trends. Its role in the development of HPV-related oral cancers should be closely monitored with increased surveillance and research, and there should also be continued research to explore poor oral health—including periodontal disease—and poor oral hygiene as independent risk factors for HPV infection and oral cancer (30). A small preliminary study in this area indicated that the capacity of Ontario dentists to detect and prevent oral cancers is limited due to inadequate training (21), while another small study in Florida showed that dentists were in the precontemplation and contemplation stages of readiness to discuss HPV vaccines with patients (31). In light of these studies, oral health professionals should be encouraged to do the following:

- Stay up-to-date on evidence related to HPV infection and oral cancers
- Conduct mouth cancer screening at regular check-ups
- Recognize and detect signs and symptoms at an early stage, and monitor any abnormal or suspicious lesion(s) in the mouth
- Explore the possibility of collecting samples at the dental office (e.g. oral rinses or swabs) for HPV detection
- Explain to clients the links between oral HPV and oral cancer
- Share clear and evidence-based information and discuss with their clients about known risk factors (such as tobacco use) and modes of transmission, including sexual practices and behaviours
- Continue to actively promote the importance of good oral hygiene and oral health as factors in prevention of HPV infection and HPV-related oral cancers
- Promote the HPV vaccine as a safe and effective way to prevent the infection
- Discuss with dentist regulatory bodies the possibility of administering the HPV vaccine in dental offices

Conclusion

The link between HPV and OPC is evident; and with incidence rates rising, more action is required to curb this trend. There are numerous ways in which oral health professionals can contribute to reducing rates of oral HPV infection and in preventing HPV-related OPCs. Oral health professionals are key players in the fight against HPV transmission and OPC prevention and should create and implement plans in support of this for the health and well-being of their patients.

Authors' statement

None.

Competing interests

None.

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OVERVIEW

Canadian Immunization Guide: "Anaphylaxis and other acute reactions following vaccination" chapter update

Natalie Dayneka[1,2], Christina Jensen[3], Kyla Hildebrand[4,5] on behalf of the National Advisory Committee on Immunization (NACI)*

Abstract

Background: The Canadian Immunization Guide (CIG) is a comprehensive resource on immunization for health professionals and vaccine program decision-makers. It is developed based on the evidence-based recommendations of the National Advisory Committee on Immunization (NACI). The NACI Vaccine Safety Working Group (VSWG) is comprised of NACI members, liaison members and external experts. The World Allergy Organization now recommends that antihistamines should not be used in the initial treatment of anaphylaxis. The update of the chapter was also used to provide further information and clarity to several tables in the chapter.

Methods: In updating the CIG anaphylaxis guidance, VSWG conducted an environmental scan, a review of relevant literature and consulted international and Canadian experts and professional societies.

Results: The use of diphenhydramine hydrochloride as adjunctive treatment in the management of anaphylaxis in a community setting is no longer recommended. Other notable changes made to the chapter include the following: 1) retitled: "Anaphylaxis and other acute reactions following vaccination"; 2) inclusion of new tables: "Key distinguishing features of anaphylaxis and vasovagal syncope" and "Signs and symptoms of anaphylaxis"; and 3) updated tables: "Anaphylaxis management kit: recommended items" and "Dosage of intramuscular EPINEPHrine 1:1000 (1 mg/mL) solution, by age or weight".

Conclusion: The updated CIG chapter provides healthcare providers with further clarity in recognizing and managing anaphylaxis in community settings. The updated intramuscular epinephrine dosage table will aid in optimal epinephrine administration, while the revised guidance against the use of diphenhydramine hydrochloride will prevent its unnecessary stockpiling in preparation for potential mass vaccination clinics related to the coronavirus disease 2019 pandemic.

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Keywords: National Advisory Committee on Immunization, NACI, Canadian Immunization Guide, CIG, anaphylaxis, guidance

Introduction

The Canadian Immunization Guide (CIG) is a comprehensive resource on immunization for health professionals and vaccine program decision-makers. It is developed based on the evidence-based recommendations of the National Advisory Committee on Immunization (NACI).

NACI recommendations are developed by topic-specific working groups. The NACI Vaccine Safety Working Group (VSWG) is comprised of NACI members, liaison members and external experts, and is responsible for providing guidance on Part 2

(Vaccine Safety) chapter revisions that pertain to vaccine safety monitoring in Canada, contraindications and precautions, and assessment and management of anaphylaxis.

Since the last chapter update, the World Allergy Organization (WAO) revised its recommendations on anaphylaxis management in the community. WAO now recommends that antihistamines should not be used in the initial treatment of anaphylaxis (1). The update of the chapter was also used to provide further information and clarity to several tables in the chapter.

Methods

In updating the CIG anaphylaxis guidance (2), NACI Secretariat conducted an environmental scan, a review of relevant literature and consulted international and Canadian experts and professional societies. The VSWG reviewed and discussed evidence pertaining to the following:

- The optimal position for individuals experiencing an anaphylactic reaction
- Canadian and international recommendations, guidelines and practices pertaining to the optimal site and dosage of epinephrine administration
- The use of diphenhydramine hydrochloride (Benadryl®) in anaphylaxis management in the community

The updated guidance, including the removal of the adjunctive treatment recommendation and the table on epinephrine dose by age or weight, were presented to NACI for approval.

Results

In the case of anaphylaxis, VSWG clarified its recommendation to place individuals on their back (supine) and elevate their lower extremities. Until the anaphylactic reaction is fully managed, the vaccinee should remain in this recumbent position as fatality can occur quickly due to empty vena cava/empty ventricle syndrome (if the vaccinee stands or sits suddenly).

The VSWG confirmed that there are good data to support the conclusion that neither the deltoid nor the glutinous muscles should be the site for epinephrine administration. Epinephrine should always be provided intramuscularly in the mid-anterolateral aspect of the thigh (*vastus lateralis*) given that it has a large blood supply.

Following the review of evidence from WAO, the VSWG no longer recommends the use of antihistamines as adjunctive treatment in the management of anaphylaxis in a community setting. The use of adjunctive therapy was not considered to be appropriate in the community setting since the role of the vaccine provider in the management of post-immunization anaphylaxis is primarily to manage the patient (by providing epinephrine and monitoring) until emergency care arrives.

The VSWG also provided further guidance for intramuscular epinephrine dosage according to age, since many vaccine providers do not have access to a client's weight (e.g. there may be no scale in a pharmacy, mass immunization clinic, public health clinic, etc.). Although the literature supporting auto-injector administration of epinephrine to infants weighing less than 10 kg was found to be limited, the VSWG took the position that the benefits of epinephrine use in these individuals outweigh the risks, even though this use would be considered off-label in Canada.

The VSWG updated the epinephrine dosage table, which has been in use since June 2013 and was originally developed by the Immunization Action Coalition. The revised epinephrine dosing chart was adapted from the paediatric anaphylaxis algorithm of the Translating Emergency Knowledge for Kids (TREKK) (3,4), which is a Canadian-based program dedicated to improving paediatric emergency care. In addition, age bands for dosing epinephrine were selected from the Australian Immunisation Handbook (5) as they corresponded well with the weight bands of the TREKK chart. This newly adapted table (Table 4: Dosage of intramuscular EPINEPHrine 1:1000 (1 mg/mL) solution, by age or weight) was reviewed and vetted by experts from the Canadian Society of Allergy and Clinical Immunology in August 2020.

Other notable changes made to the chapter include the following:

- New title: previously "Early vaccine reactions including anaphylaxis", now "Anaphylaxis and other acute reactions following vaccination"
- Inclusion of a new table: "Table 1: Key distinguishing features of anaphylaxis and vasovagal syncope"
- Inclusion of a new table: "Table 2: Signs and symptoms of anaphylaxis"
- Updated table: "Table 3: Anaphylaxis management kit: recommended items"

Conclusion

The updated CIG chapter provides healthcare providers with further clarity in recognizing and managing anaphylactic reactions in community settings. The development of the new intramuscular epinephrine dosage table will aid in optimal epinephrine administration, new recommendations on the use of diphenhydramine hydrochloride will prevent its unnecessary stockpiling in preparation for potential mass vaccination clinics related to the coronavirus disease 2019 pandemic.

Authors' statement

CJ — Writing, original draft, review, editing
ND — Review, editing
KH — Review, editing

The Canadian Immunization Guide chapter, "Anaphylaxis and other acute reactions following vaccination" was revised by the National Advisory Committee on Immunization (NACI) Vaccine Safety Working Group and was approved by NACI.

Competing interests

None.

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Device-associated infections in Canadian acute-care hospitals from 2009 to 2018

Canadian Nosocomial Infection Surveillance Program[1]*

Abstract

Background: Healthcare-associated infections (HAIs) pose a serious risk to patient safety and quality of care. The Canadian Nosocomial Infection Surveillance Program (CNISP) conducts national surveillance of HAIs at sentinel acute-care hospitals across Canada. This report provides an overview of 10 years of Canadian data on the epidemiology of select device-associated HAIs.

Methods: Over 40 hospitals submitted data between 2009 and 2018 for hip and knee surgical site infections (SSIs), cerebrospinal fluid shunt SSIs, paediatric cardiac SSIs and/or central line-associated bloodstream infections (CLABSIs). Counts, rates, patient and hospital characteristics, as well as pathogen distributions and antimicrobial susceptibilities are presented.

Results: A total of 4,300 device-associated infections were reported. Central line-associated bloodstream infections were the most common device-associated HAI reported (n=2,973, 69%) and hip and knee arthroplasty infections were the most common SSIs reported (66% of SSIs). Our findings show decreasing CLABSI rates in neonatal intensive care units (4.2 to 1.9 per 1,000 line-days, $p<0.0001$) and decreasing knee SSI rates (0.69 to 0.30 infections per 100 surgeries, $p=0.007$). Rates of device-associated HAIs have remained relatively consistent over the 10-year surveillance period. Overall, 4,599 pathogens were identified from device-associated HAI; 70% of these were related to CLABSIs. Coagulase-negative staphylococci (29%) and *Staphylococcus aureus* (14%) were the most frequently reported pathogens. Gram-positive pathogens represented 68% of identified pathogens, gram-negative pathogens represented 22% and fungi represented 9%.

Conclusion: Understanding the national burden of device-associated HAIs is essential for developing and maintaining benchmark rates for informing infection and prevention control and antimicrobial stewardship policies and programs.

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Keywords: hospital-associated infection, acute-care, surveillance, antimicrobial resistance, device-associated, surgical site infections, Canada

Introduction

Healthcare-associated infections (HAIs) pose a serious risk to patient safety and quality of care and contribute to prolonged hospital stays, increased antimicrobial resistance, costs to the health system and unnecessary deaths (1). Risk factors for HAIs include the use of invasive devices, surgical procedures and inappropriate antibiotic use (2). In Canada, surgical site infections (SSIs) affect an estimated 26,000 to 65,000 patients annually (3). In a 2017 Canadian point prevalence study at sentinel hospitals, device-associated infections accounted for 35.6% of all HAIs reported. Of the device-associated infections, SSIs associated with a prosthetic implant accounted for 19.4% and central line-associated bloodstream infections (CLABSIs) accounted for 21.2% (4).

Device-associated HAI antimicrobial susceptibility information has important implications for antibiotic resistance (5); impacting length of stay and healthcare costs (6). Cumulative antibiograms are a valuable resource for clinical decision-making while sensitivity results are pending (7). The risk of device-associated HAIs varies among patient populations and hospital types; patients admitted to the intensive care unit (ICU) are at higher risk of developing an HAI (8).

Understanding the trends in device-associated HAIs is essential to effective infection prevention and control. Drawing on a decade of HAI data (2009–2018) from over 40 sentinel acute-care hospitals across Canada participating in the Canadian Nosocomial Infection Surveillance Program (CNISP), this report provides an epidemiological overview of select device-associated HAIs.

Methods

Design

Established in 1994, the CNISP, a collaboration between the Public Health Agency of Canada, the Association of Medical Microbiology and Infectious Disease Canada and sentinel hospitals across Canada, conducts national HAI surveillance at sentinel acute-care hospitals across Canada. This report presents data on device-associated HAIs for the following infections: hip and knee SSIs; cerebrospinal fluid shunt SSIs (CSF-shunt-SSIs); paediatric cardiac surgical site infections (paediatric-cardiac-SSIs); and CLABSIs.

Case definitions

Device-associated HAIs were defined according to standardized protocols and expert-reviewed case definitions (**Appendix 1**). Only CLABSIs identified in ICU settings were included in surveillance. Only complex infections, defined as deep incisional and organ space, were included in hip and knee SSI surveillance.

Data source

Participating hospitals submitted epidemiological data on CSF-shunt-SSIs and CLABSIs occurring between January 1, 2009 and December 31, 2018. Paediatric-cardiac-SSI surveillance started in January 2010. Hip and knee SSI surveillance started in January 2011. Data submission and case identification were supported by annual training sessions and continuous evaluations of data quality.

Statistical analysis

CLABSI rates were calculated by dividing the number of cases by line-day denominators. Hip and knee SSI, CSF-shunt-SSI and paediatric-cardiac-SSI rates were calculated by dividing the number of cases by surgery denominators. Proportions of pathogens were calculated by dividing the number of pathogens by the total number of pathogens identified. Missing and incomplete data were excluded from analyses, therefore denominators may vary. Interquartile ranges (IQR) were calculated. The Mann-Kendall test or negative binomial regression was used to test trends over time. Significance testing was two-tailed and differences were considered significant at p-value ≤ 0.05. Analyses were conducted using Excel and SAS 9.4.

Results

Between 2009 and 2018, over 40 hospitals contributed device-associated HAI data to CNISP, most of which were medium (201–499 bed) adult hospitals (**Table 1**). Overall, 4,300 device-associated infections were reported. CLABSIs were the most common device-associated HAI (n=2,973, 69%). Hip and knee SSI were the most common type of SSI reported (66% of SSIs, n=871/1,327).

Table 1: Characteristics of acute-care hospitals participating in device-associated HAI surveillance and frequency of device-associated hospital-acquired infections, 2009–2018

Characteristic of hospitals	CSF shunt SSI	Paediatric cardiac SSI	Hip and knee SSI	CLABSI-adult mixed ICU	CLABSI-adult CVICU	CLABSI-PICU	CLABSI-NICU
Years of surveillance	2009–2018	2010–2018	2011–2018	2009–2018	2009–2018	2009–2018	2009–2018
Number of HAIs reported	266	190	871	1,331	192	348	1,102
Total participating hospitals	8–14	3–4	12–25	22–41	5–8	5–10	9–17
Hospital type							
Adult[a]	2–5	NA	8–16	12–27	3–7	NA	2–3
Mixed	2–4	NA	4–9	4–14	1–2	0–4	1–6
Paediatric	4–7	3–4	NA	NA	NA	4–6	4–8
Hospital size							
Small (1–200 beds)	3–7	2–4	1–2	1–4	0–1	3–5	4–7
Medium (201–499 beds)	4–8	1	7–15	10–27	2–4	1–5	1–7
Large (500+ beds)	0–1	NA	5–8	5–10	2–3	0	1–3
Total beds (2018)	3,558	693	9,973	16,701 ICU beds	3,570 ICU beds	2,209 ICU beds	5,500 ICU beds

Abbreviations: CLABSI, central line-associated bloodstream infection; CSF-shunt SSI, cerebrospinal fluid shunt surgical site infection; CVICU, cardiovascular surgery intensive care unit; HAIs, healthcare-associated infections; ICU, intensive care unit; NA, not applicable; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit; SSI, surgical site infection
[a] Seven hospitals classified as "Adult" also had a NICU

Overall, 4,599 pathogens were identified from device-associated HAI cases between 2014 and 2018; 69.8% of these were related to CLABSIs. Coagulase-negative staphylococci and *Staphylococcus aureus* were the most frequently reported pathogens (**Table 2**). Gram-positive pathogens represented 68.3% of identified pathogens, gram-negative pathogens represented 22.3% and fungi represented 9.4%.

Central line-associated bloodstream infections

Between 2009 and 2018, there were 2,973 reported CLABSIs; the majority of which occurred in adult mixed ICUs (n=1,331, 44.8%) and NICUs (n=1,102, 37.1%). Among CLABSIs identified in adult ICUs, the median age was 63 years (IQR=52–73 years). Males represented 62% of adult CLABSIs. One-third of adult CLABSI patients died within 30 days following the first positive

Table 2: Distribution and rank of the five most frequently reported[a] gram-negative, gram-positive and fungal pathogens, 2009–2018[b]

Category	Rank	Pathogen	N	% of total pathogens identified
Gram-positive	1	Coagulase-negative staphylococci[c]	1,320	28.7
	2	*Staphylococcus aureus*[d]	653	14.2
	3	*Enterococcus* spp.	519	11.3
	4	*Streptococcus*	137	3.0
	5	Methicillin-resistant *S. aureus*	120	2.6
	Other gram-positive		392	8.5
Gram-negative	1	*Klebsiella* spp.	226	4.9
	2	*Escherichia coli*	197	4.3
	3	*Enterobacter*	170	3.7
	4	*Pseudomonas aeruginosa*	133	2.9
	5	*Serratia*	87	1.9
	Other gram-negative		214	4.7
Fungi	1	*Candida albicans*	210	4.6
	2	Other *Candida* spp.	199	4.3
	Other fungi		22	0.5
Total			**4,599**	**100.0**[e]

[a] Up to four pathogens per device-associated hospital-acquired infection were included in the analysis
[b] Paediatric-cardiac-surgical site infection surveillance started in 2010. Hip and knee surgical site infection surveillance started in 2011
[c] Coagulase-negative staphylococci include *S. lugdunesis*, *S. haemolyticus*, *S. epidermidis* and *S. capitis*
[d] *Staphylococcus aureus* includes methicillin-susceptible *S. aureus* and unspecified *S. aureus*
[e] Percentage rounded to the nearest whole number

culture (32.3%, n=482/1,492). Among CLABSIs identified in paediatric intensive care units (PICUs), the median age was six months (IQR=2–22 months). Males represented 51% of PICU cases and within 30 days of positive culture, 11% of infected patients had died (n=37/342). Among CLABSIs identified in the neonatal intensive care unit (NICU), the median age at first positive culture was 20 days (IQR=10–45 days). Males represented 57% of NICU cases and within 30 days of positive culture, 8% of infected patients had died (n=88/1,077).

Overall, NICUs had higher rates of CLABSIs (2.7 cases per 1,000 line-days, on average) than PICUs (1.9/1,000 line-days), adult mixed ICUs (1.1/1,000 line-days) and adult cardiovascular surgery ICUs (0.7/1,000 line-days). While rates remained relatively constant for adult ICUs and PICUs, a 54.8% decrease was observed among NICUs (from 4.2 to 1.9/1000 line-days, 2009 to 2018, $p<0.0001$) (**Table 3**).

Hip and knee surgical site infections

Between 2011 and 2018, 871 complex hip and knee SSIs were reported; the majority of which were hip surgeries (n=530, 60.8%). Fifty-two percent (n=455) were organ space infections and 47.8% (n=416) were deep incisional infections (**Table 4**).

Table 3: Rate of central line-associated bloodstream infection per 1,000 line days by intensive care unit type, 2009–2018

Year	CLABSI rate per 1,000 line-days			
	Adult mixed ICU	Adult CV-surgery ICU	NICU	PICU
2009	1.4	0.8	4.2	2.0
2010	1.1	0.9	3.9	1.7
2011	0.9	1.0	4.1	1.6
2012	1.0	1.3	3.5	1.4
2013	1.1	0.5	2.8	1.3
2014	0.9	0.5	2.1	2.0
2015	1.1	0.7	2.3	2.4
2016	1.0	0.5	2.3	1.7
2017	1.2	0.4	1.8	2.0
2018	1.2	0.9	1.9	2.1
Overall	**1.1**	**0.7**	**2.7**	**1.9**

Abbreviations: CLABSI, central line-associated bloodstream infection; CV, cardiovascular; ICU, intensive care unit; NICU, neonatal intensive care unit; PICU, paediatric intensive care unit

Median patient age was 69 and 67 years for hip and knee SSIs, respectively. Median time from procedure to infection was 20 days for hip infections and 22 days for knee infections. Upon collection of additional data beginning in 2018, the median length of stay for hip and knee surgeries was four and three days, respectively. Ninety-one percent of patients with a surgical site infection were readmitted following hip or knee arthroplasty (hip, n=83/91, 91.2%; knee, n=33/37, 89.1%) and 64.8% (n=83/128) required a revision surgery. At 30 days post-surgery, one death was reported in 2018 among the hip-SSI patients.

Table 4: Frequency of hip and knee surgical site infections by type and rate per 100 surgeries, 2011–2018

Year	Deep incisional SSI		Organ/Space SSI		All hip and knee SSI	
	Cases (n)	%	Cases (n)	%	Cases (n)	Rate per 100 surgeries
Hip arthroplasty						
2011	18	43.9	23	56.1	41	0.82
2012	32	66.7	16	33.3	48	0.73
2013	36	57.1	27	42.9	63	0.79
2014	36	50.7	35	49.3	71	0.85
2015	34	51.5	32	48.5	66	0.75
2016	28	41.2	40	58.8	68	0.79
2017	34	41.5	48	58.5	82	0.80
2018	29	31.9	62	68.1	91	0.87
Overall	**247**	**46.6**	**283**	**53.4**	**530**	**0.80**

Table 4: Frequency of hip and knee surgical site infections by type and rate per 100 surgeries, 2011–2018 (*continued*)

Year	Deep incisional SSI		Organ/Space SSI		All hip and knee SSI	
	Cases (n)	%	Cases (n)	%	Cases (n)	Rate per 100 surgeries
Knee arthroplasty						
2011	20	51.3	19	48.7	39	0.69
2012	26	52.0	24	48.0	50	0.65
2013	21	55.3	17	44.7	38	0.41
2014	26	48.1	28	51.9	54	0.56
2015	21	47.7	23	52.3	44	0.43
2016	15	41.7	21	58.3	36	0.35
2017	20	46.5	23	53.5	43	0.36
2018	20	54.1	17	45.9	37	0.30
Overall	**169**	**49.6**	**172**	**50.4**	**341**	**0.47**

Abbreviation: SSI, surgical site infection

From 2011 to 2018, the rate of hip SSI was stable (from 0.82 to 0.87 infections per 100 surgeries, p=0.26), while the rate of knee SSI decreased significantly (from 0.69 to 0.30 infections per 100 surgeries, p=0.007). *S. aureus* and coagulase-negative staphylococci were the most commonly identified pathogens from hip and knee SSI cases (32% and 17% of identified pathogens, respectively).

Cerebrospinal fluid shunt surgical site infections

Between 2009 and 2018, 266 CSF-shunt-SSIs were reported; 143/260 (55%) were identified from new surgeries and 117/260 (45%) were identified from revision surgeries. The median age of cases was 46 years (IQR=29–67 years) for adult patients and 0.6 years (IQR=0.2–6.8 years) for paediatric patients. Females represented 53.4% (n=140/262) of cases. Median days from surgery to infection were 29 days (IQR=14–64 days).

From 2009 to 2018, the overall rate of CSF-shunt-SSI was 3.2/100 surgeries (range: 1.9 to 5.7/100 surgeries, **Table 5**). Infection rates were similar at paediatric hospitals (n=3.3/100 surgeries) and adult/mixed hospitals (n=3.2/100 surgeries). Coagulase-negative staphylococci and *S. aureus* were the most commonly identified pathogens from CSF-shunt-SSIs (41% and 22% of identified pathogens, respectively).

Paediatric cardiac surgical site infections

Between 2010 and 2018, there were 190 paediatric-cardiac-SSIs reported (**Table 6**). Most cases were superficial infections (58.7%) or organ/space infections (32.3%). The average age of patients with a paediatric-cardiac-SSI was 19 days old (IQR=7–213 days). On average, the time from surgery to date of onset of infection was 10 days (IQR=5–19 days). Three deaths were reported within 30 days of onset of infection (1.6% of cases) but all three deaths were unrelated to the paediatric-cardiac-SSI.

Table 5: Cerebrospinal fluid shunt surgical site infection rates per 100 surgeries by hospital type, 2009–2018

Year	Rate/100 surgeries		
	Adult and mixed hospitals	Paediatric hospitals	All hospitals
2009	2.9	2.8	2.9
2010	3.2	3.9	3.5
2011	5.0	6.3	5.7
2012	2.5	3.9	3.2
2013	2.6	2.8	2.7
2014	1.6	2.6	2.0
2015	3.3	2.1	2.7
2016	4.4	2.4	3.3
2017	4.6	3.2	3.9
2018	2.4	2.3	2.4
Overall	**3.2**	**3.3**	**3.2**

Table 6: Paediatric cardiac surgical infection rates by year and infection type, 2010–2018

Year	Superficial		Organ/space		Deep		All paediatric cardiac surgical site infections	
	Cases	% of annual cases	Cases	% of annual cases	Cases	% of annual cases	Cases	Rates/100 surgeries
2010	9	40.9	10	45.5	3	13.6	22	4.1
2011	8	53.3	5	33.3	2	13.3	15	3.1
2012	15	83.3	2	11.1	1	5.6	18	2.9
2013[a]	12	63.2	7	36.8	0	0.0	19	4.6
2014	11	57.9	8	42.1	0	0.0	19	3.5
2015	12	63.2	6	31.6	1	5.3	19	3.5
2016	9	64.3	3	21.4	2	14.3	14	3.0
2017	17	70.8	5	20.8	2	8.3	24	4.4
2018	18	46.2	15	38.5	6	15.4	40	7.5
Overall	**111**	**58.7**	**61**	**32.3**	**17**	**9.0**	**190**	**4.1**

[a] Excludes one site in 2013 with missing denominator data (number of cases=0 in that year). One case missing infection type info

Overall, the average paediatric-cardiac-SSI rate was 4.1/100 surgeries. While rates remained generally consistent (p=0.35), there was a significant increase in 2018 (n=7.5/100 surgeries, p<0.001) compared to the overall rates from 2010 to 2017

(3.6/100 surgeries). *S. aureus* and coagulase-negative staphylococci were the most commonly identified pathogens from paediatric-cardiac-SSIs (43% and 24% of identified pathogens, respectively).

Antibiogram

Antimicrobial susceptibility testing results for the most frequently identified gram-positive, gram-negative and fungal pathogens from device-associated HAIs are listed in **Table 7**. Oxacillin/cloxacillin resistance was found in 13% (n=38/288) of all *S. aureus* isolates. Meropenem resistance was low among the gram-negative pathogens with 2/36 *Klebsiella* isolates, 1/33 *E. coli* isolates resistant and 0/33 *Enterobacter* isolates resistant to meropenem. Thirty-two vancomycin-resistant *Enterococci* were identified (n=32/187, 17%, *Enterococcus* spp.).

Discussion

This report describes 4,300 device-associated HAIs reported over ten years of surveillance. With the exception of decreasing CLABSI rates in NICUs and decreasing knee-SSI rates, rates of device-associated HAIs have remained relatively consistent. In general, the most frequently reported pathogens among device-associated HAIs in Canada aligned with results from the United States (US): *S. aureus*, *E. coli* and *Klebsiella* ranked in the top five pathogens in our surveillance and in a 2020 US National Healthcare Surveillance Network (NHSN) report of adult HAIs (including CLABSIs, various SSIs, catheter-associated urinary tract infections and ventilator-associated events) (5).

Table 7: Antibiogram results[a] from pathogens identified from device-associated hospital-associated infections, 2014–2018

Antibiotic	Number of resistant/number tested and %															
	Gram-positive						Gram-negative						Fungi			
	Coagulase-negative staphylococci[b]		*S. aureus*[c]		*Enterococcus* spp.		*Klebsiella* spp.		*E. coli*		*Enterobacter*		*C. albicans*		*Candida* spp. other	
	# of resistant	%	# of resistant	%	# of resistant	%	# of resistant	%	# of resistant	%	# of resistant	%	# of resistant	%	# of resistant	%
Ampicillin	5/8	63	2/10	20	61/235	26	76/78	97	56/86	65	51/55	93	NA	NA	NA	NA
Cefazolin	125/154	81	17/158	11	NA	NA	21/58	36	24/76	32	47/48	98	NA	NA	NA	NA
Ceftriaxone	NA	NA	1/11	9	NA	NA	5/62	8	11/54	20	24/50	48	NA	NA	NA	NA
Clindamycin	109/193	56	47/213	22	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Ciprofloxacin	1/7	14	2/14	14	NA	NA	6/72	8	23/68	34	0/64	0	NA	NA	NA	NA
Cloxacillin/ Oxacillin	241/308	78	38/238	16	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Erythromycin	57/89	64	34/104	33	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Gentamicin	15/31	48	2/27	7	7/58	12	6/84	7	11/81	14	1/14	7	NA	NA	NA	NA
Meropenem	NA	NA	NA	NA	NA	NA	2/36	6	1/33	3	0/36	0	NA	NA	NA	NA
Piperacillin-tazobactam	NA	NA	NA	NA	NA	NA	7/60	12	12/60	20	21/48	44	NA	NA	NA	NA
Penicillin	85/87	98	81/86	94	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Rifampin	1/59	2	0/33	0	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Trimethoprim-sulfamethoxazole	58/147	39	4/177	2	NA	NA	5/56	9	28/59	47	9/53	17	NA	NA	NA	NA
Tobramycin	NA	NA	NA	NA	NA	NA	6/72	8	3/80	4	2/61	3	NA	NA	NA	NA
Vancomycin	3/293	1	1/140	1	32/187	17	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Amphotericin B	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	0/11	0	0/9	0
Caspofungin	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1/40	3	0/11	0
Fluconazole	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	1/55	2	19/59	32

Abbreviation: NA, not available
[a] Antibiotic/organism combinations with fewer than six tests were excluded
[b] Coagulase-negative staphylococci include *S. lugdunesis*, *S. haemolyticus*, *S. epidermidis*, *S. capitis* and *S. warneri*
[c] Includes methicillin-susceptible *S. aureus* and methicillin-resistant *S. aureus*

Surgical site infections

Hip and knee-SSIs were the most common SSI reported in our surveillance. Similar to results from the European Centre for Disease Prevention and Control, a decreasing trend in knee SSI was observed among CNISP hospitals, while hip SSI remained stable (9). In addition, a US point prevalence study observed a significant reduction in the prevalence of complex SSIs between 2011 and 2015 (10). Our findings indicate that the most common pathogens identified among hip and knee-SSIs were *S. aureus* and coagulase-negative staphylococci, consistent with results from other regions (9,11). Frequent identification of *S. aureus* and coagulase-negative staphylococci may be related to the use of implant devices and contamination from the patient's endogenous skin flora (5). Hip and knee-SSIs affect an older population as joint replacements typically occur among older adults (12). As populations age, hip and knee joint replacements are rising and are linked to a rise in surgical complications (i.e. prosthetic joint infections) (12). High observed rates of readmission and revision surgery highlight the financial and resource burden placed on the healthcare system due to hip and knee-SSI (13).

Our overall rate of CSF-shunt-SSIs (n=3.2/100 surgeries) is on the lower end of what is reported internationally; a 2012 review found that reported rates of infection vary from 3% to 12% of shunt operations (14). Stratification of our CSF-shunt-SSI data by paediatric or adult hospital showed little difference in infection rates and in pathogen distributions between paediatric and adult/mixed settings. However, a previous study among CNISP hospitals, conducted between 2000 and 2002, had identified that CSF-shunt-SSIs were more common in children than in adults (15). In this earlier study, the infection rate among paediatric patients was higher than found in this study (4.9% of surgeries in 2000–2002 versus 3.3% 2009–2018) suggesting that SSI rates among paediatric populations have decreased.

Limited literature on paediatric-cardiac-SSI, differences in patient populations and lengths of follow-up makes direct comparisons difficult, but our overall rate of paediatric-cardiac-SSIs (n=4.1/100 surgeries) is similar to the ranges in infection rates reported elsewhere. A 2009–2012 intervention study of neonates undergoing cardiac surgery conducted at a tertiary-care centre in New York found pre and post-intervention paediatric-cardiac-SSI rates of 6.2/100 surgeries and 5.8/100 surgeries, respectively (16). In a 2012–2013 French study of patients younger than one year of age, 19% of patients presented with an SSI (17). A 2010–2012 retrospective study of paediatric patients (younger than 18 years of age) undergoing cardiac surgery at two hospitals in New York found a rate of 1.4 HAIs/100 procedures (18).

There was a significant increase in the rate of paediatric-cardiac-SSI in 2018 to 7.5/100 surgeries. This increase was limited to two hospital sites, where investigations are ongoing. This increase should be interpreted with caution as rates are calculated from a small number of cases and may be sensitive to random fluctuation at individual hospitals.

Central line-associated bloodstream infections

Central line-associated bloodstream infections were the most commonly reported device-associated HAI (69% of included HAIs); however, it is important to note that the number of hospitals participating in the surveillance of each HAI differs and that the surveillance periods for some HAIs were shorter. In a point prevalence study of HAIs, the frequencies of SSIs (19%) and CLABSIs (21%) were very similar (5).

There were no substantive changes in CLABSI rates among surveyed adult ICUs or PICUs; however, there was a 55% decrease in CLABSI rates among NICUs. The methods of measurement differ, but CLABSI rates in NICUs have also decreased in the US; between 2010 and 2016, standardized incidence ratios (defined as the change in relation to the number of CLABSIs per central line days) for CLABSIs in NICUs and rates of central line use in NICUs decreased in the US (19). In addition, CLABSI rates in other ICU types in the US also decreased between 2010 and 2016 (19). Updated NHSN guidelines have been credited for the reduction in rates in the US (20). It is possible that improvements to rates in Canada occurred prior to the study period.

Our overall CLABSI rates in adult ICUs (0.7 and 1.1/1,000 central-line-days for cardiovascular intensive care units and mixed ICUs, respectively) are similar to ranges reported in the US and Australia. In the US, the CLABSI rate in ICUs was estimated to be 0.8/1,000 central-line-days in 2010–2015 (21). In Australia, annual rates of CLABSIs in ICUs ranged between 0.9 and 1.7/1,000 central-line-days in 2010–2013 (22). Higher rates are seen in other regions; a large surveillance study of 703 intensive care units in Latin America, Europe, Eastern Mediterranean, Southeast Asia and Western Pacific reported a CLABSI rate of 4.1/1,000 central-line-days between January 2010 and December 2015 (21).

Antibiogram

The percentage of *S. aureus* isolates that were methicillin-resistant *S. aureus* (MRSA) in this study (13%) is similar to what was reported from a Swiss surveillance network where 8% of *S. aureus* SSI cases were MRSA in 2010–2015 (23). Higher rates of MRSA have been reported elsewhere. In the US, 42% to 48% of *S. aureus* isolates from HAIs (including SSI, CLABSI and others) in NHSN surveillance were MRSA (5). A Japanese study of SSIs at 27 medical centres, found that 72% of *S. aureus* isolates were MRSA in 2010 (24).

Of identified *Enterococcus* spp., 17% were vancomycin-resistant *Enterococci* in our surveillance. In NHSN surveillance in the US, 8.5% of *Enterococcus faecalis* and 84.5% of *Enterococcus faecium* pathogens identified from CLABSIs in ICUs were vancomycin-resistant *Enterococci* in 2015–2017 (5).

Meropenem resistance was low among the gram-negative pathogens with 2/36 (6%) *Klebsiella* isolates and 1/33 (3%) *E. coli* isolates resistant to meropenem. In the US, the percent of carbapenem-resistant *Enterobacteriaceae* among *Klebsiella* spp. ranged from 3.1% (among SSIs) to 6.9% (among expanded list of device-associated infections); the percent of carbapenem-resistant *Enterobacteriaceae* among *E. coli* ranged from 0.6% (among SSIs) to 0.7% (among expanded list of device-associated infections) (5).

Strengths and limitations

The strength of this study lies in the standardized collection of detailed data from a large network of sentinel hospitals over a decade. While the CNISP network extends across Canada, participating hospitals may not be representative of the general Canadian inpatient population; hospitals participating in CNISP tend to be larger, teaching hospitals in urban centres. The CNISP is currently undergoing a recruitment process to increase representativeness and bed coverage, especially in northern, rural and indigenous populations. The CNISP's data, although standardized, may be sensitive to changes in hospital participation, infection prevention and control practices and the application of surveillance definitions. Differences in surveillance protocols and case definitions limit the ability to compare data from other countries. However, the data presented in this report are routinely used by Canadian hospitals for benchmarking.

For CLABSI surveillance, we do not have data on infections occurring outside of ICU settings; however, in the US, CLABSIs outside of the ICU setting represented 55% of all CLABSIs (19)

Conclusion

This report provides an updated summary of rates, pathogen distributions and antimicrobial resistance among select device-associated HAIs and relevant pathogens. Understanding the national burden of device-associated HAIs is essential for developing and maintaining benchmark rates for informing infection and prevention control and antimicrobial stewardship policies and programs.

Authors' statement

Canadian Nosocomial Infection Surveillance Program hospitals provided expertise in the development of protocols in addition to the submission of epidemiological data. Epidemiologists from the Public Health Agency of Canada were responsible for the conception, analysis, interpretation, drafting and revision of this paper.

Competing interests

None.

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Appendix 1: Case definitions

Central line-associated bloodstream infection (CLABSI)

Only central line-associated bloodstream infections (BSIs) related to an intensive care unit (ICU) admission were included in surveillance.

BSI case definition:

BSI is **NOT** related to an infection at another site and it meets one of the following criteria:

Criterion 1: Recognized pathogen cultured from at least one blood culture, unrelated to infection at another site.

OR

Criterion 2: At least one of: fever (>38°C core), chills, hypotension; if aged <1 year: fever (>38°C core), hypothermia (<36°C core), apnea, or bradycardia **AND** common skin contaminant (see list below) cultured from ≥2 blood cultures drawn on separate occasions, or at different sites, unrelated to infection at another site. Different sites may include peripheral veins, CVCs, or separate lumens of a multilumen catheter. Different times include two blood cultures collected on the same or consecutive calendar days via separate venipunctures or catheter entries. The collection date of the first positive blood culture is the date used to identify the date of positive culture. Two positive blood culture bottles filled at the same venipuncture or catheter entry constitute only one positive blood culture.

CLABSI case definition:

A laboratory-confirmed bloodstream infection where a central line catheter (CL) or umbilical catheter (UC) was in place for >2 calendar days on the date of the positive blood culture, with day of device placement being Day 1. If admitted or transferred into a facility with a CL/UC in place (e.g. tunneled or implanted central line), day of first access is considered Day 1.

AND

A CL or UC was in place on the date of the positive blood culture or the day before. If a CL or UC was in place for >2 calendar days and then removed, the BSI criteria **must be fully met** on the day of discontinuation or the next day. If the patient is admitted or transferred into the ICU with a CL in place, the day of first access is considered Day 1. "Access" is defined as line placement, infusion or withdrawal through the line.

ICU-related case definition:

CLABSI onset during ICU stay and the CL has been in place >2 calendar days. The CLABSI would be attributable to the ICU if it occurred on the day of transfer or the next calendar day after transfer out of the ICU.

Common skin contaminants:

Diphtheroids, *Corynebacterium* spp., *Bacillus* spp., *Propionibacterium* spp., coagulase-negative staphylococci (including *S. epidermidis*), viridans group streptococci, *Aerococcus* spp., *Micrococcus* spp. and *Rhodococcus* spp.

Hip and knee surgical site infection (SSI)

Only complex surgical site infections (deep incisional or organ/space) following hip and knee arthroplasty were included in surveillance.

A deep incisional SSI must meet the following criterion:

Infection occurs within 90 days after the operative procedure and the infection appears to be related to the operative procedure and involves deep soft tissues (e.g. facial and muscle layers) of the incision and the patient has at least **ONE** of the following:

1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
2. Deep incision that spontaneously dehisces or is deliberately opened by the surgeon and is culture-positive or not cultured when the patient has at least one of the following signs or symptoms: fever (>38°C), or localized pain or tenderness. A culture-negative finding does not meet this criterion.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

An organ/space SSI must meet the following criterion:

Infection occurs within 90 days after the operative procedure and the infection appears to be related to the operative procedure and infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure and patient has at least **ONE** of the following:

1. Purulent drainage from a drain that is placed through a stab wound into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.

3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

Cerebrospinal fluid shunt surgical site infection

Only patients who underwent a placement or revision of a cerebrospinal fluid (CSF) shunting device and the infection occurred within one year of surgery were included in surveillance.

CSF shunt-associated surgical site infection case definition:

A patient is identified as having CSF shunt SSI if the patient meets the following criteria:
Criterion 1: An internalized CSF shunting device is in place

AND

Criterion 2: A bacterial or fungal pathogen(s) is identified from the cerebrospinal fluid

AND

Criterion 3: The pathogen is associated with at least **ONE** of the following:
1. Fever (temperature ≥38°C)
2. Neurological signs or symptoms
3. Abdominal signs or symptoms
4. Signs or symptoms of shunt malfunction or obstruction

Paediatric cardiac surgery surgical site infection

Only surgical site infections following open-heart surgery with cardiopulmonary bypass among paediatric patients (<18 years of age) were included in surveillance.

A **superficial incisional SSI** must meet the following criterion:

Infection occurs within 30 days after the operative procedure and involves only skin and subcutaneous tissue of the incision and at least **ONE** of the following:
1. Purulent drainage from the superficial incision.
2. Organisms isolated from an aseptically-obtained culture of fluid or tissue from the superficial incision.
3. At least **ONE** of the following signs or symptoms of infection:
    - Pain or tenderness, localized swelling, redness, or heat and the superficial incision is deliberately opened by surgeon, and is culture-positive or not cultured. A culture-negative finding does not meet this criterion
    - Diagnosis of superficial incisional SSI by the surgeon or attending physician

A **deep incisional SSI** must meet the following criterion:

Infection occurs within 90 days after the operative procedure and the infection appears to be related to the operative procedure **AND** involves deep soft tissues (e.g. facial and muscle layers) of the incision **AND** the patient has at least **ONE** of the following:
1. Purulent drainage from the deep incision but not from the organ/space component of the surgical site.
2. Deep incision spontaneously dehisces or is deliberately opened by the surgeon and is culture-positive or not cultured when the patient has at least one of the following signs or symptoms: fever (>38°C), or localized pain or tenderness. A culture-negative finding does not meet this criterion.
3. An abscess or other evidence of infection involving the deep incision is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of a deep incisional SSI by a surgeon or attending physician.

An **organ/space SSI** must meet the following criterion:

Infection occurs within 90 days after the operative procedure and the infection appears to be related to the operative procedure **AND** infection involves any part of the body, excluding the skin incision, fascia, or muscle layers, that is opened or manipulated during the operative procedure **AND** patient has at least **ONE** of the following:
1. Purulent drainage from a drain that is placed through a stab wound into the organ/space.
2. Organisms isolated from an aseptically obtained culture of fluid or tissue in the organ/space.
3. An abscess or other evidence of infection involving the organ/space that is found on direct examination, during reoperation, or by histopathologic or radiologic examination.
4. Diagnosis of an organ/space SSI by a surgeon or attending physician.

OVERVIEW

Translating evidence into practice with the National Advisory Committee on Sexually Transmitted and Blood-Borne Infections

Shamila Shanmugasegaram[1]*, Stephan Gadient[1], Margaret Gale-Rowe[1]

Abstract

For over 30 years, the Government of Canada has developed guidelines on sexually transmitted and blood-borne infections (STBBI) with a group of subject matter experts. This expert group provided advice to the Public Health Agency of Canada (PHAC) from 2004 to 2019; transitioning to the National Advisory Committee on STBBI (NAC-STBBI) in 2019. NAC-STBBI supports PHAC's mandate to prevent and control infectious diseases by providing advice for the development of STBBI guidelines. The methodology for developing the NAC-STBBI recommendations is evolving to a more rigorous, systematic and transparent process that is consistent with current standards in guideline development. It is also informed by—and aligned with—the methods of several other major guideline developers. The methodology incorporates the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach, as appropriate, when conducting evidence reviews and developing recommendations. Recommendations will be published on the canada.ca website with the supporting NAC-STBBI Statement detailing the methodology and evidence used to develop them. This process will ensure that PHAC provides trustworthy evidence-based STBBI recommendations to primary care providers and public health professionals.

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Keywords: evidence-based guidelines, external advisory body, guideline methodology, infection prevention and control, sexually transmitted and blood-borne infections

Introduction

Sexually transmitted and blood-borne infections (STBBI) remain a public health threat to Canadians. Rates of chlamydia, gonorrhea and syphilis have increased steadily in recent years (1), and multiple provinces and territories declared outbreaks of syphilis in 2018 (2) and 2019 (3). The Public Health Agency of Canada (PHAC) provides national leadership for the prevention and control of STBBI through the development of evidence-based public health guidelines. The recommendations in these guidelines are developed—with PHAC support—by the National Advisory Committee on STBBI (NAC-STBBI), an external advisory body of subject matter experts from across Canada. This article describes the new STBBI recommendation development process followed by PHAC and NAC-STBBI.

Background

An expert group has provided advice to the Government of Canada for more than 30 years. The first advisory committee—the Expert Interdisciplinary Advisory Committee on Sexually Transmitted Diseases (STD) in Children and Youth—was established in 1986 by Health and Welfare Canada to provide advice and guidance for the prevention and control of STD. In 1988, this committee published the first *Canadian Guidelines for the Treatment of Sexually Transmitted Diseases in Neonates, Children, Adolescents and Adults* (4). While the Advisory Committee was disbanded in 1991, the Expert Working Group on STD was struck in 1998 under the authority of Health Canada's Laboratory Centre for Disease Control for the purpose of developing guidelines.

Following the creation of PHAC in 2004, the Expert Working Group on STD began providing advice to PHAC, and the name was changed to the Expert Working Group for the Canadian Guidelines on Sexually Transmitted Infections. In 2019, the

Group transitioned to a formal external advisory body that is based on the principles and requirements set out under federal government legislation and policies (5).

Mandate and membership

NAC-STBBI provides PHAC with ongoing, timely advice and recommendations for the development of STBBI guidelines, in support of its mandate to prevent and control infectious diseases in Canada. PHAC retains all decision-making authority and decides how it will use the recommendations and advice of the external advisory body.

NAC-STBBI carries out its mandate as follows: reviewing the epidemiology and scientific literature on STBBI as well as the evidence on specific prevention strategies, diagnosis and treatment; providing advice based on the best available literature evidence or, where there is a paucity of literature evidence, based on expert knowledge and practice; and advising PHAC about current and emerging issues relating to STBBI.

NAC-STBBI consists of 15 voting members with expertise in the areas of healthcare epidemiology, infectious disease, medical microbiology, laboratory diagnostics, pharmacology, obstetrics and gynecology, paediatrics, primary care, psychology, and public health. Recruitment ensures members have a range of knowledge, expertise and experience, as well as varied perspectives. Consideration is also given to geographic representation given that challenges may differ across Canada. PHAC ("the Secretariat") assesses and manages competing interests for NAC-STBBI members who must declare any conflicts upon joining, on an annual basis and prior to each meeting to maintain impartiality of the committee.

Recommendation development process

The methodology for developing the NAC-STBBI recommendations is evolving to a more rigorous, systematic and transparent process to formulate trustworthy recommendations. This new approach was informed by best practice standards in guideline development (6–9) and the methodology of several other major guideline developers (10–16). A manual has been drafted outlining the methodology, which is summarized herein and illustrated in **Figure 1**.

The Secretariat conducts a topic selection and prioritization exercise annually (or on an as-needed basis) to help determine which areas to focus on to update or reaffirm existing recommendations or develop new recommendations during the upcoming fiscal year. **Figure 2** illustrates the topic selection and prioritization exercise. This exercise involves the following:

1. Soliciting topics for development of recommendations

Figure 1: Recommendation development process

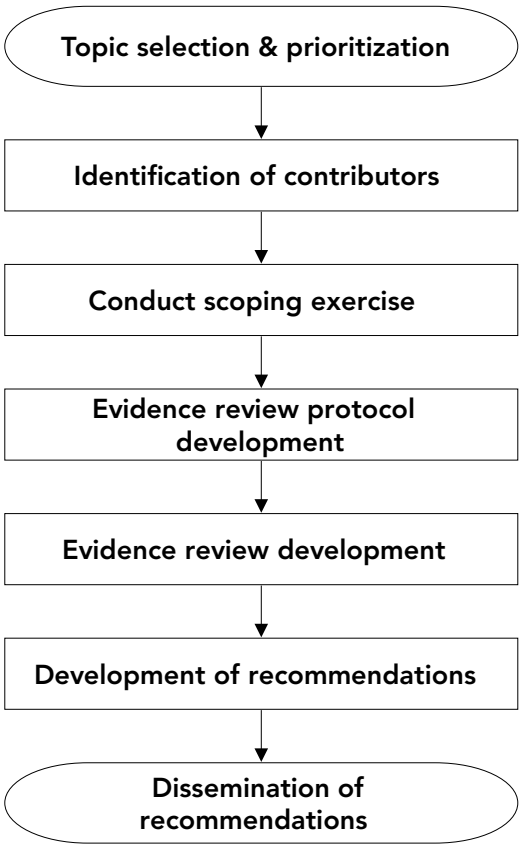
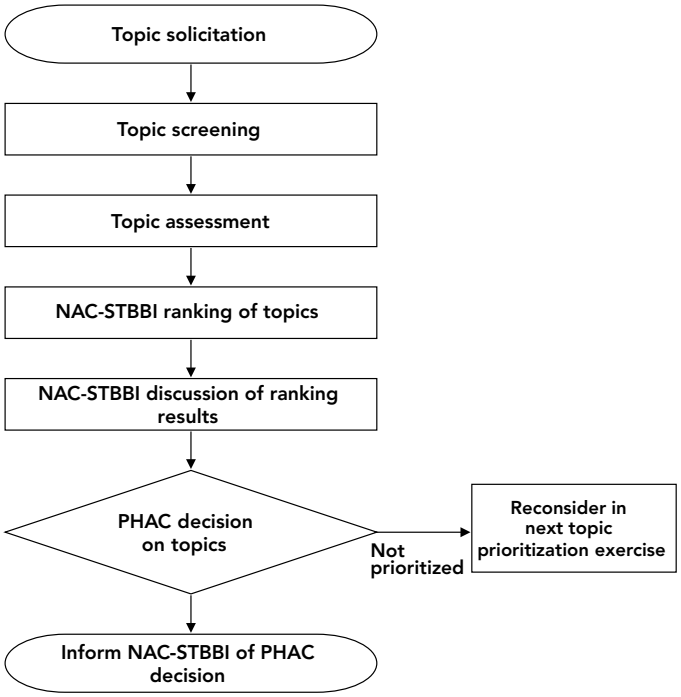


Figure 2: Topic selection and prioritization exercise



Abbreviations: NAC-STBBI, National Advisory Committee on Sexually Transmitted and Blood-Borne Infections; PHAC, Public Health Agency of Canada

2. Screening topics against the scope of the STBBI guidelines and PHAC mandates and priorities
3. Completing an assessment tool which includes questions on the availability of evidence on the topic and epidemiology to help NAC-STBBI rank the topics in order of priority
4. Ranking (repeated, if necessary) topics and discussing the results (NAC-STBBI)
5. Deciding (the Secretariat) on the final list of topics for recommendation development, seeking PHAC approvals and sharing this list with NAC-STBBI. The topics that have not been prioritized for recommendation development will be considered again during the next topic prioritization exercise along with any new suggestions

A working group (WG) composed of experts from NAC-STBBI is formed for each prioritized topic. Other potential contributors include external experts (if necessary) and relevant stakeholders. The WG receives methodological and technical support from the Secretariat. A scoping exercise is conducted to identify relevant systematic reviews, guidelines and any major studies published or in progress since the release of the existing PHAC recommendations (if applicable) to help the WG develop the research (key and contextual) questions, inclusion and exclusion criteria, and analytic framework. The findings from the scoping exercise also help the WG determine the following: whether a systematic review is necessary; whether to use/update an existing systematic review or conduct a new systematic review; and whether to adopt, adapt or develop *de novo* recommendations for the topic under consideration (17,18).

The WG develops the key questions using the population, intervention, comparator and outcomes (PICO) framework and determines the inclusion and exclusion criteria for the evidence review (6). Outcomes (both beneficial and harmful) that are important for decision-making are identified from the scoping exercise and a targeted search of the literature (if necessary) in combination with feedback from the WG members and other contributors. The WG members rate the relative importance of outcomes for decision-making (critical, important or not important) based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach (9). The WG also develops contextual questions and the analytic framework

A systematic review is conducted independently by an external evidence review team. A librarian prepares the search strategy for the systematic review according to protocol parameters (e.g. study designs, time frame and databases) and it is reviewed by a second librarian and the WG. The systematic review protocol is drafted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) (19,20) and includes the research questions, inclusion and exclusion criteria, analytic framework, and search strategy. The final version of the protocol is registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (21).

When conducting a systematic review, the steps undertaken by the external evidence review team will include the following: screening the titles, abstracts and selected full-text articles based on predefined inclusion and exclusion criteria; extracting data; assessing the risk of bias; performing quantitative and/or qualitative synthesis; and preparing the GRADE evidence tables (6,9). The quality/certainty of evidence is graded separately across studies (as high, moderate, low or very low) for each important outcome (9). The systematic review article is prepared based on the PRISMA checklist and the PRISMA flow diagram is used to show the study selection process (22–25). The final version of the article is published in a peer-reviewed journal.

The GRADE Evidence to Decision framework is drafted to help the WG use evidence in a structured and transparent way to develop recommendations (9,26–30). The overall quality of evidence is assessed across outcomes (9,26–30).

Other types of evidence reviews, such as narrative reviews or rapid reviews, may be conducted for certain guidance products. When evidence from the literature is very limited, recommendations are developed based on expert opinion using a systematic and transparent approach.

The WG drafts recommendations using the GRADE wording for direction and strength, as appropriate, (9,14) and presents them to NAC-STBBI for discussion and voting. NAC-STBBI Statement, drafted by the WG, includes the need for the recommendations, the methodology used, the evidence considered, the final recommendations and a summary of the NAC-STBBI deliberations. The Statement is reviewed by NAC-STBBI and published on the canada.ca website after PHAC approvals. The relevant PHAC STBBI guides (formerly the Canadian Guidelines on Sexually Transmitted Infections) are updated with the recommendations.

Conclusion

The methodology for developing the NAC-STBBI recommendations is evolving to meet best practice standards and will continue to be improved and refined as appropriate. The new methodology combined with the ongoing support and expert advice of NAC-STBBI will ensure that PHAC provides trustworthy evidence-based STBBI recommendations to primary care providers and public health professionals.

Authors' statement

SS — Conceptualization, methodology, writing of original draft, review and editing
SG — Conceptualization, writing of original draft, review and editing
MGR — Conceptualization, review and editing

Competing interests

None.

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Health risks of frozen raw breaded chicken products: A local health unit perspective

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Abstract

Raw chicken, including frozen raw breaded chicken products, has been implicated in 18 outbreaks of nontyphoidal salmonellae in Canada since 2017. The Canadian Food and Inspection Agency has since implemented industry requirements, from April 2019, aimed at reducing salmonellosis risks in frozen raw breaded chicken products prior to their distribution in the retail marketplace. This commentary explores key issues identified by a local public health unit during an investigation of two cases of salmonellosis that occurred within the context of a recent Canada-wide outbreak linked to frozen raw breaded chicken products. Consumer handling and preparation practices, product appearance and labelling issues were essential factors in the development of disease. From this front-line perspective, new industry requirements by the Canadian Food and Inspection Agency are analyzed for their potential to reduce salmonellosis risks in such chicken products, while also identifying additional measures that could be implemented to further reduce the risk of product associated outbreaks.

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Introduction

Nontyphoidal salmonellae infection remains a leading cause of foodborne illness in Canada with an annual average of 6,881 reported cases from 2008 to 2017, which represents an average rate of 20 cases per 100,000 people per year (1). In 2018, the national incidence of salmonellae infections was 19 cases per 100,000 people, a significant decrease compared to 2017, while Ontario registered a significant increase from 12 to 18 cases per 100,000 people in the same period. *Salmonella* Enteritidis is the most commonly reported serovar for Canadians, involved in 43% of cases, followed by *Salmonella* Heidelberg (9%) and Typhimurium (6%) (2).

Severity of salmonellae infections (also referred to as salmonellosis) may vary, and while most cases resolve without treatment, others might result in severe dehydration, bacteremia and death, particularly among vulnerable populations such as young children, the elderly, pregnant women, and those who are immunocompromised (3). Salmonellosis' burden includes an estimated $6.43 million annually in healthcare costs and $21.13 million annually in productivity loss (4).

Many commercial food products contaminated with salmonellae have been implicated in outbreaks, including meat, eggs, dairy, fruits and vegetables (3). Of particular interest in recent times are frozen raw breaded chicken products, such as chicken strips and chicken nuggets, which have been linked to salmonellae outbreaks in the United States (5), Australia (6) and Canada since the 1990s (7). Since then, studies have implicated these products as leading risk factors for salmonellosis (7–10), and data from FoodNet, a sentinel site surveillance system led by the Public Health Agency of Canada (PHAC), indicates that in 2018, salmonellae were found in 27% of samples of frozen raw breaded chicken products across its sites (2).

In May 2017, whole genome sequencing was introduced for analysis of all clinical *Salmonella* isolates in Canada, providing increased resolution of genetic relatedness among *Salmonella* isolates and facilitating the identification of clusters and outbreaks of common *Salmonella* serotypes such as Enteritidis (11). The implementation of whole genome sequencing has permitted linking of 18 salmonellosis outbreaks across the country between May 2017 and Mary 2019 to the consumption of chicken products, amounting to 584 laboratory-confirmed cases, 97 hospitalizations. This led to the removal of 14 such products from the marketplace, 13 of which being voluntarily removed by the manufacturers from the marketplace following food recalls issued by the Canadian Food and Inspection Agency (CFIA) (12). Of these, 12 outbreaks and

285 cases were found to be directly associated with exposure to frozen raw breaded chicken products (11). The Region of Peel in Ontario saw similar trends in 2016 and 2017, with annual reports of at least 30 children aged nine or younger developing salmonellosis after consuming these products; a number that likely suffers from some degree of underreporting (13).

In response to these outbreaks, the CFIA announced in July 2018 new requirements for industry to implement manufacturing or processing measures reducing salmonellae to undetectable levels in these products before distribution that took effect on April 1, 2019 (14). This commentary offers a local public health perspective on the risks associated with consumption of raw breaded chicken products by describing contributing factors in two cases of salmonellosis investigated by Peel Public Health and discusses how these might be addressed by the new CFIA requirements.

A local health unit outbreak investigation

In summer 2018, Peel Public Health was notified by local laboratories of two different cases of salmonellosis identified through stool testing, following the usual notification cascade in Ontario. Each case was assigned to a public health inspector in charge of conducting interviews and collecting any necessary samples to help establish the source of infection. Case 1 was a three-year-old female and Case 2 an eleven-year-old male. Each case separately presented at emergency with fever and diarrhea developing over a period of five days and each provided clinical samples for bacterial culture; while both were subsequently discharged, Case 2 was later admitted to hospital for intravenous antibiotic therapy (see **Table 1** for case comparison overview).

Table 1: Comparison overview of confirmed cases investigated by Peel Public Health agents in the context of a salmonellosis outbreak in the summer of 2018

Characteristics investigated	Case 1	Case 2
Sex	Female	Male
Age	3 years	11 years
Hospitalization required	No	Yes
Method of preparation of implicated frozen chicken product	Oven baking	Pan-frying[a]

[a] Does not follow cooking instructions provided by manufacturer

For Case 1, a food diary and investigation revealed the consumption of a nationally distributed brand of frozen raw breaded chicken nuggets and another brand of pre-cooked chicken strips within the illness incubation period. Both food products had been prepared by the case's mother as per the instructions listed on the package (see **Box 1** for chicken nuggets cooking instructions). No one else in the household consumed the food or became ill. Samples from the frozen raw breaded chicken nuggets meal collected from the case home by public health inspectors and submitted to the Ontario Public Health Laboratory for testing and were positive for *Salmonella* Enteritidis; testing of samples from the pre-cooked chicken strips meal were negative. Subsequent whole genome sequencing matched the isolates from the case's stool sample to those from the frozen raw breaded chicken nuggets.

Box 1: Instructions on the inner package of frozen raw breaded chicken nuggets implicated in the outbreak[a]

Do not microwave.

Raw Poultry.

Must be cooked thoroughly.

Conventional Oven:

1. Preheat oven to 425°F (220°C).

2. Place breaded chicken on a non-stick or lightly greased baking sheet.

3. Cook on the middle oven rack according to the times below:

Nuggets: Cook 8 minutes then turn and continue cooking for another 5–7minutes.

Individual appliances vary; these are guidelines only. Cook thoroughly to an internal temperature of 165°F (74°C).

Handling instructions: ensure that raw meat and poultry products are handled and cooked properly. Keep frozen until ready to prepare. Keep cooked/ready-to-eat foods separate from raw foods. Refrigerate leftovers immediately. Thoroughly wash working surfaces, utensils, and hands after touching raw meat and poultry.

[a] Identical instructions in French were printed next to the English ones

For Case 2, a food diary and investigation found that the eleven-year old male consumed the same brand of frozen raw breaded chicken nuggets as Case 1, within the same incubation period. These were not prepared according to the package instructions as they were pan-fried before consumption (see Box 1). No one else in the household consumed the food or became ill. Testing of samples from the frozen raw breaded chicken nuggets meal were positive for *Salmonella* Enteritidis.

On whole genome sequencing, these isolates from the frozen raw breaded chicken nuggets sample matched those found in Case 1. Samples of the same brand of breaded chicken nuggets consumed by confirmed cases in Alberta and British Columbia provided additional genomic sequencing matches of *Salmonella* Enteritidis, and resulted in the product manufacturer issuing a food recall of the implicated food product (15).

Discussion

Key issues identified at the local public health level

Through review of these two cases and other previous investigations, our health unit identified four key issues that likely contributed to salmonellae transmission through frozen breaded chicken products. First, as Case 1 illustrated, was the risk of salmonellae contamination despite product preparation as per the package directions. This could have been due to a breach of food safety practices, such as not handwashing before and after handling the raw breaded chicken products and overlooking the need to sanitize surfaces, dishes and utensils after food preparation and consumption.

Second was the product appearance. These products have been par-fried by the manufacturer, which produces a brown colour on the outside of breaded chicken products. This may lead consumers to believe the food is cooked (16,17) and subsequently undercook it, using alternative preparation methods such as microwaving or pan-frying. These methods may only defrost or unevenly heat the product, without allowing the raw chicken to fully cook to the recommended internal temperature of 74°C (10). The appearance of par-fried products may be particularly misleading to young children, with at least one previous salmonellosis investigation by this local public health unit that arose from a child biting into a frozen chicken product.

Third, inspection by public health investigators revealed the warning labels of the implicated products were small and difficult to read. Fourth, the lot code printed on the inner plastic liner was stamped over the cooking instructions, obscuring both the lot code and the instructions. These aspects of information provided to consumers is particularly relevant in light of previous observations by the health unit that consumers report discarding the box and storing the nuggets in the freezer in the plastic liner only. If the preparation instructions are only printed on the box, they are no longer accessible to the consumer when the box is discarded. Consumers have reported in previous outbreak investigations discarding the box because it is bulky and takes up too much space in the freezer.

Some or all of these four factors may have contributed to Case 2, where the investigation found that the nuggets were prepared incorrectly through pan-frying. While a specific reason for ignoring the instructions was not determined at the time of the investigation, one can hypothesize that clearer instructions, which are not obscured and are printed directly on the inner package, may increase the likelihood that the product will be correctly prepared.

New control measures

Effective April 1, 2019, the CFIA implemented new requirements for manufacturers to control the risk of salmonellae in frozen processed raw chicken products (13). Options for control measures consist of either inclusion of a validated cooking process, implementation of a testing program, a combination of both, or a hold-and-test program for finished products (18). These requirements target specifically non-intact raw, breaded, par-fried chicken products for retail sale, as they are at higher risk for both contamination through processing and undercooking because of their appearance (18). Notably, these requirements do not apply to products for sale to food service processors nor breaded par-fried stuffed chicken products. While the requirements aim to address the root cause of these outbreaks, i.e. exposure to salmonellae in non-stuffed frozen raw breaded chicken products for retail sale, they still leave some residual transmission risk through other products and through the food service industry. Residual risk also remains as the ready-to-eat appearance of par-fried stuffed chicken products might continue to result in unsafe product preparation or handling.

Other key contributing issues identified in our health unit review are related to product labelling and packaging, and fall outside the scope of new CFIA requirements. Mandatory labelling measures put in place in 2004 required manufacturers to put descriptors such as "uncooked" to be placed near the product's name and for cooking instructions to appear on the outer packaging (17). Furthermore, the CFIA, Health Canada and PHAC worked with industry in 2015 to develop voluntary labelling strategies with instructions to ensure consistent messaging, explicit warnings against microwaving the products, and to provide cooking directions on the inner packaging (17). However, our investigation found that the font size used for the "uncooked" label was very small and, in the case of the contaminated uncooked chicken nuggets, was also obscured.

Public awareness campaigns

Although the new requirements are a critical component of a food safety strategy to address the risk of salmonellae infection from inadequately cooked breaded chicken products, consumer awareness is equally vital. Measures to address this are already well underway at the federal level, where CFIA, Health Canada, and PHAC developed large communications campaigns to reach Canadians through social media ads and posts, outreach to

other media and partners, and overarching and outbreak-specific public health notices (17). Additionally, in September 2018, the outbreaks prompted Canada's Council of Chief Medical Officers of Health to issue a statement (see **Box 2**) advising consumers of the importance of following safe food handling and preparation practices when consuming frozen raw breaded chicken products (19).

Local health units have also made efforts to improve consumer awareness of the issue through public communication. For example, in 2018, Peel Public Health ran a local education campaign in Peel Region raising awareness of the outbreaks and the various hazards of consuming undercooked frozen raw breaded chicken products. This campaign consisted of targeted Google ads, editorials in three local newspapers, and web and social media information on safe food preparation practices (see **Figure 1**). The local health unit has also since begun to review evidence to determine effective interventions to encourage safe food handling by consumers at home, with the goal of reducing the risk of foodborne illness arising from risky food handling practices in the home setting.

Future challenges

Much has been done to address the risk of salmonellosis in frozen breaded chicken products that has included industry-level preventive measures and multi-stakeholder efforts to increase public awareness of the issue. However, as was demonstrated by the outbreak linked to frozen raw breaded chicken products that were sold until May 2019 (12) and therefore after the new CFIA requirements came into effect, salmonellosis outbreaks associated with frozen raw breaded chicken products may not yet be a phenomenon of the past. It may well be that this outbreak was a part of a transitional period. Since products produced prior to April 1, 2019 could still be available for up to two years in the marketplace or in consumers' freezers (16), occasional exposure is still possible, but occurrence of new cases should decrease in the coming years. Cases may also emerge in association with products unaffected by the new requirements, such as stuffed chicken products.

Box 2: Excerpt of September 13, 2018 statement: Council of Chief Medical Officers of Health concerned about the risk of salmonellosis from frozen raw breaded chicken products (19)

Most frozen breaded chicken products available for sale in grocery stores in Canada contain raw chicken that can cause Salmonella illness and therefore pose an increased health risk to Canadians who handle, prepare or consume them... Canadians need to be aware that even though these products may appear to be cooked, they are not.

We are very pleased that the Government of Canada is working with the food manufacturing industry and food retailers to reduce Salmonella in frozen raw breaded chicken products produced on or after April 1, 2019, to below detectable amounts…

However, until April 1, 2019, and likely for up to a year after this date, frozen raw breaded chicken products containing Salmonella will continue to be in the marketplace and in freezers across the country. This is why, collectively, we are stressing the importance of handling and preparing frozen raw breaded chicken products with caution.

Always cook your frozen raw breaded chicken products thoroughly according to the package instructions to an internal temperature of at least 74°C (165°F) using a digital food thermometer to ensure that they are safe to eat. Wash your hands before and after handling these products, and wash and sanitize the surfaces, dishes and utensils used to prepare and serve them. Following this advice when handling, cooking or eating these products will help reduce you and your family's chance of becoming infected with Salmonella. For more tips and information on how to properly prepare and cook frozen raw breaded chicken products, visit Canada.ca/foodsafety.

Figure 1: Messaging used in newspaper and digital advertising to highlight the health risks associated with frozen raw breaded chicken products

Indeed, local public health needs to continue surveillance of foodborne illness, remaining alert to whether the measures already taken will ensure the end of these outbreaks or whether further cases will still emerge. Local health units also have a role in conducting detailed case investigations and identifying emerging risk factors, which can in turn be included in future investigation forms and documents, updated regularly where policies change. Peel Public Health is also conducting research on how best to inform consumers about food safety risks in the home, and additional public awareness measures must continue to be taken by local, provincial/territorial and federal health authorities in order to increase the uptake of food safety measures by consumers. Industry-level requirements for easy-to-read labelling and ensuring unobstructed information is provided on both inner and outer packaging could complement public awareness efforts and facilitate appropriate product preparation by consumers. While a combination of modification of labels and public awareness measures alone have reportedly not been sufficient to prevent outbreaks related to frozen breaded chicken products (20), the efficacy of these measures in the presence of CFIA's new industry requirements remains to be seen.

If needed, there is room for additional work to further reduce the risk. While changing the appearance of breaded chicken products so that they are pre-cooked or do not appear to be cooked is one control mechanism, other opportunities for protection that did not emerge through our investigations but have been identified in other Canadian outbreaks involve product packaging and marketing. For example, placement of uncooked products next to fully cooked ones in grocery store freezers and packaging showing the cooked product and raw products being marketed as quick and easy meals may be misleading to consumers (7) and present other potential avenues for risk reduction through regulation by health authorities.

Conclusion

Canada's salmonellosis outbreaks from frozen breaded chicken products are being addressed by new industry-level requirements to reduce the risk of salmonellae contamination of these products for retail purchase as well as public awareness campaigns from the local to federal levels. Local public health units are essential partners and continue to be engaged in this issue from the perspective of local surveillance, investigation, evidence collection and collaboration with other agencies such as Public Health Ontario and the CFIA. Research on how best to inform consumers about food safety risks in the home is also being conducted.

Authors' statement

LCL, JPC and MB jointly conceived the idea for this manuscript. JPC developed the first draft. All authors contributed to the development and revision of this manuscript and approved the final draft for submission.

Competing interests

None.

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Assessing the impact of varying levels of case detection and contact tracing on COVID-19 transmission in Canada during lifting of restrictive closures using a dynamic compartmental model

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic began with a detected cluster of pneumonia cases in Wuhan, China in December 2019. Endemic transmission was recognized in Canada in early February 2020, making it urgent for public health stakeholders to have access to robust and reliable tools to support decision-making for epidemic management. The objectives of this paper are to present one of these tools—an aged-stratified dynamic compartmental model developed by the Public Health Agency of Canada in collaboration with Statistics Canada—and to model the impact of non-pharmaceutical interventions on the attack rate of COVID-19 infection in Canada.

Methods: This model simulates the impact of different levels of non-pharmaceutical interventions, including case detection/isolation, contact tracing/quarantine and changes in the level of physical distancing in Canada, as restrictive closures began to be lifted in May 2020.

Results: This model allows us to highlight the importance of a relatively high level of detection and isolation of cases, as well as tracing and quarantine of individuals in contact with those cases, in order to avoid a resurgence of the epidemic in Canada as restrictive closures are lifted. Some level of physical distancing by the public will also likely need to be maintained.

Conclusion: This study underlines the importance of a cautious approach to lifting restrictive closures in this second phase of the epidemic. This approach includes efforts by public health to identify cases and trace contacts, and to encourage Canadians to get tested if they are at risk of having been infected and to maintain physical distancing in public areas.

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Keywords: COVID-19, case detection, contact tracing, dynamic compartmental model, Canada

Introduction

The coronavirus disease 2019 (COVID-19) pandemic is a global health threat on a scale that was not seen in a century. The first cases of a cluster of pneumonia in Wuhan, China were reported to the World Health Organization (WHO) on December 31, 2019 with the cause of the outbreak identified as a novel coronavirus (now called severe acute respiratory syndrome coronavirus 2; SARS-CoV-2) on January 7, 2020 (1). Cases were soon detected outside China, with the first case of COVID-19 identified in Canada on January 25, 2020 in a resident who had returned from Wuhan, China (2,3). As of September 16, 2020, there have been 28.6 million confirmed cases of COVID-19, and over 900,000 deaths, globally (4); within Canada, there have been 139,747 confirmed cases and 9,193 deaths (3).

A number of researchers have developed dynamic models of COVID-19 transmission to explore the effects of public health interventions for Canadian jurisdictions, including in Ontario (5–7) and British Columbia (similar findings have been

found in *personal communications, Anderson et al. Estimating the impact of COVID-19 control measures using a Bayesian model of physical distancing. medRxiv 2020*), while many provinces and territories have released the results of COVID-19 modelling (8–12). Given the observed variation in the risk of severe outcomes of COVID-19 by age (13,14), and the need to consider differences in contact and transmission rates amongst age groups (15,16), age stratification is an important consideration for dynamic models of COVID-19. As of early July 2020, only a minority of the models for Canada or its provinces presented in the peer-reviewed or pre-print literature are age-structured (similar findings can be found in *personal communications, Tuite et al. Reduced COVID-19-Related Critical Illness and Death, and High Risk of Epidemic Resurgence, After Physical Distancing in Ontario, Canada. medRxiv 2020*).

In Canada, public health intervention strategies including physical (social) distancing, case detection and isolation, contact tracing and quarantine of contacts, among others (16,17) have been implemented with the aim of slowing the spread of the epidemic, reducing peak health care demand, reducing the possibility of infection for those most at risk of severe outcomes of the disease and reducing the overall number of deaths (18). In order to implement and optimize effective interventions, decision-makers in Canada need information on the relative impact of these measures. They also need to assess scenarios for lifting restrictive closures (e.g. stay-at-home orders, workplace, school and university closures, which may have severe economic and non-COVID-19 health impacts), while avoiding resurgence of the epidemic (often termed a "second wave") in a Canadian population that remains largely naïve to this infection.

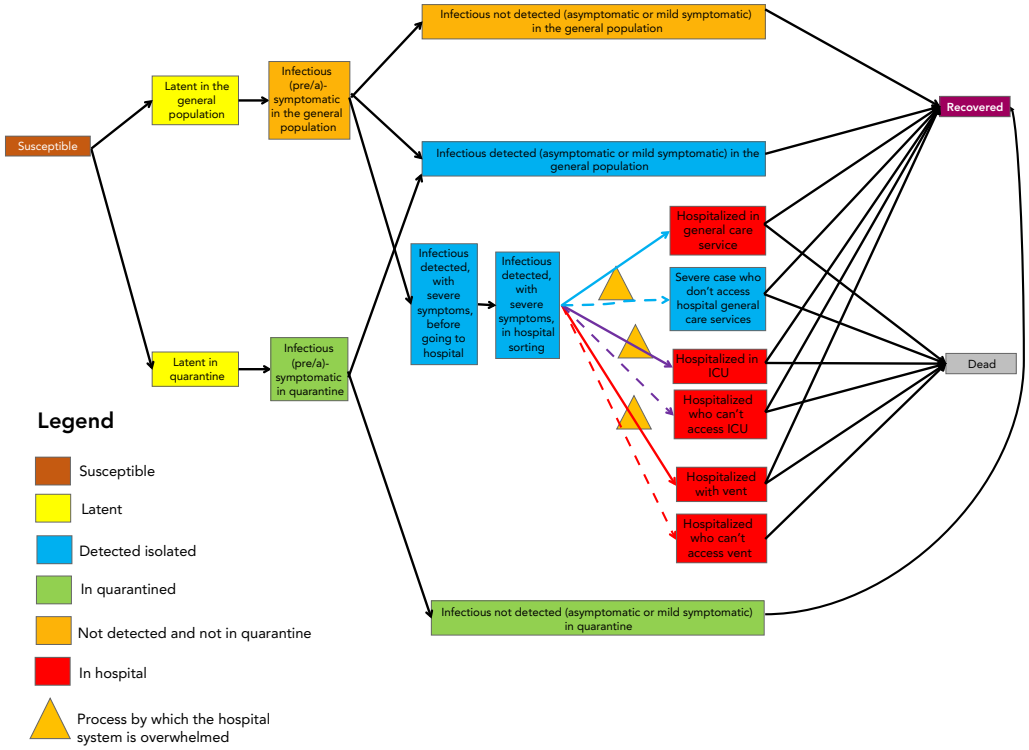
The objectives of this paper are 1) to present an aged-stratified dynamic compartmental model developed by the Public Health Agency of Canada in collaboration with Statistics Canada and 2) to model the impact of non-pharmaceutical interventions (NPIs) including case detection/isolation, contact tracing/quarantine and changes in the level of physical distancing associated with lifting restrictive closures, on the attack rate of COVID-19 infection in Canada.

Simulations of the epidemic

Model presentation

An age-stratified dynamic deterministic compartmental model using the susceptible, exposed, infected, removed framework, was developed and applied to the Canadian population stratified into six age groups. Model states are presented in **Figure 1**. Transmission between individuals can occur within or between age groups at rates influenced by the daily contact number, based on the matrix projected for Canada by Prem *et al*. (19). Individuals in quarantine were assumed to interact with a maximum of one person daily during the course of the quarantine. As the model aimed to explore the epidemic over a short time period (730 days), the model had a closed

Figure 1: Diagram of the states and flows of the model



Abbreviation: ICU, intensive care unit
The susceptible state is the brown box; yellow boxes are latent infection states, blue boxes are detected and isolated case states; green boxes are quarantined contact states; orange boxes are undetected and non-quarantined or isolated case states; red boxes are hospitalized case states, the purple box is the recovered case state, and the grey box indicates deaths. The orange triangles indicate processes by which hospital systems may be overwhelmed if the need for hospital services exceeds available resources

population with no births or non-COVID-19 related deaths, with a population comprising susceptible people at the beginning of the epidemic. Cases who recovered were assumed not to be susceptible to re-infection during the time period of the model (730 days). The model also assumed the infectivity of presymptomatic infectious individuals who become symptomatic was the same as that of symptomatic individuals, as well as individuals who remained asymptomatic throughout the course of infection. Assuming that all detected cases went into isolation, so case detection was a proxy for isolation (see **Table 1**). See **Appendix A** for a description of population flows in the model. While the model includes compartments for hospitalizations, intensive care unit (ICU) admissions, those in ICU on ventilators, and deaths, here are the results of the model for number of cases only. Model equations can be found in **Appendix B**.

Table 1: Variation of the attack rate (at day 730) for different levels of case detection/isolation, contact tracing/quarantining and physical distancing, after day 88, May 4, 2020

Case detection/ isolation	Contact tracing and quarantine					
	0.30	0.40	0.50	0.60	0.70	0.80
Contact rate reduced by 50% after day 88						
0.30	53.57	51.68	49.66	47.49	45.15	42.62
0.40	44.21	41.06	37.61	33.84	29.71	25.24
0.50	31.92	27.10	21.86	16.35	11.09	7.06[a]
0.60	16.46	10.82	6.61[a]	4.34[a]	3.25[a]	2.66[a]
0.70	4.69[a]	3.35[a]	2.68[a]	2.29[a]	2.05[a]	1.88[a]
0.80	2.33[a]	2.06[a]	1.88[a]	1.75[a]	1.65[a]	1.58[a]
Contact rate reduced by 33% after day 88						
0.30	68.68	67.41	66.04	64.56	62.95	61.20
0.40	62.54	60.37	57.95	55.26	52.24	48.84
0.50	54.22	50.68	46.65	42.02	36.70	30.61
0.60	42.70	37.17	30.77	23.49	15.67	8.86[a]
0.70	26.68	18.89	11.18	6.02[a]	3.82[a]	2.88[a]
0.80	8.34[a]	4.69[a]	3.23[a]	2.56[a]	2.19[a]	1.96[a]
Contact rate reduced by 16.7% after day 88						
0.30	76.56	75.65	74.66	73.58	72.41	71.13
0.40	72.20	70.63	68.87	66.89	64.66	62.13
0.50	66.27	63.67	60.67	57.19	53.10	48.29
0.60	57.92	53.73	48.74	42.77	35.59	27.03
0.70	45.80	39.18	31.21	21.85	12.20	6.03[a]
0.80	27.95	18.53	9.65[a]	4.96[a]	3.28[a]	2.57[a]

[a] Scenarios where epidemic control maintained attack rate below 10% (green)

Parameterization and initialization of model

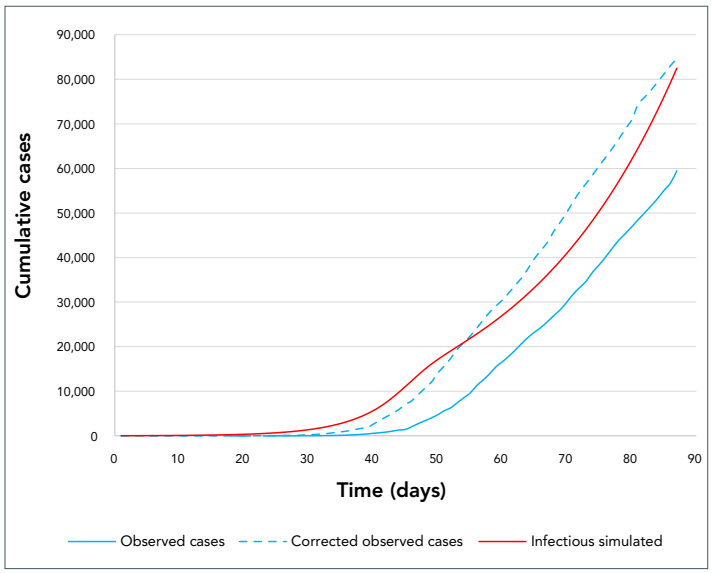
Assuming that the first community transmission of SARS-CoV-2 in Canada was February 8, 2020. The simulations were run for the entire Canadian population (N=37,894,799 inhabitants), stratified in six age groups as shown in Appendix A **Table S1** and **Table S2** (19,20).

Parameter values were set according to observed data for Canada (when available) and values in the literature (see Table S2 in Appendix A), obtained in a scan of the COVID-19 literature (published and pre-published) conducted daily by the Public Health Agency of Canada. Searches to retrieve relevant COVID-19 literature were conducted in Pubmed, Scopus, BioRxiv, MedRxiv, ArXiv, SSRN, Research Square and cross-referenced with the literature on the WHO COVID-19 literature list, and COVID-19 information centers run by Lancet, BMJ, Elsevier and Wiley. Literature with relevant prioritized outcomes were identified from the daily scan and parameter values were recorded in a data-extraction form. Model parameters are reassessed weekly according to new research. The choice of the literature source was made according to the relevance and quality of the publication. Estimates were chosen to reflect the most likely value based on minimum and maximum estimates from studies identified from the literature scanning process, using geography, date of study, sample size and target population as criteria in the choice of the retained literature. Estimates from Canada or similar countries, those with more recent study dates, larger sample sizes and more representative samples were prioritized.

A simple calibration of the probability of successful transmission (beta) of SARS-CoV-2 from an infectious person to an uninfected person when they make contact was obtained (**Figure 2**). This was achieved through iterative trials that compared a target curve based on reported cases from February 8 to May 4, 2020 (21), and simulation results for the same period. The target curve was obtained from increasing the observed count by 25% (assuming later in the epidemic reported cases underestimate the actual number by 25%: *personal communication, Dougherty et al., September 15, 2020*), and moving the entire curve to be one week earlier (assuming each case was reported one week later than symptom onset). The number of reported cases in the target curve and the number of simulated cases were compared visually to ensure that the parameter values for the simulations were reasonable before assessing the impacts of NPIs.

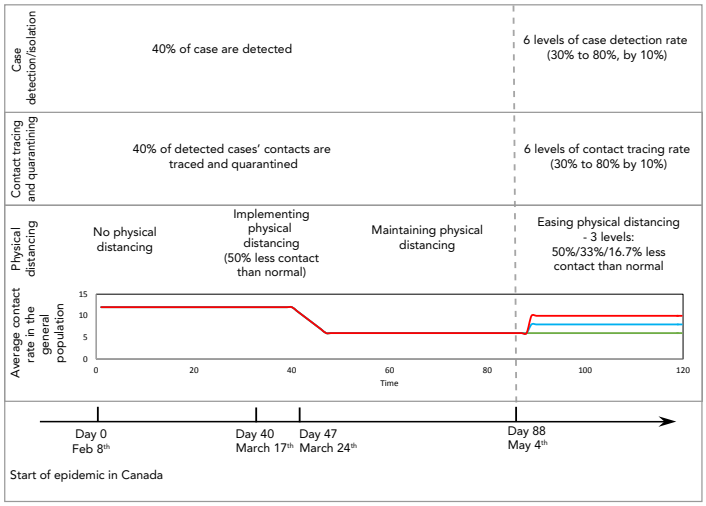
Initial values for each model state were set according to the number of cases reported in Canada at February 8, 2020, which was seven cases. The epidemic was initiated with 10 latent individuals, 20 presymptomatic individuals and two individuals with mild symptoms in the general population. The values were chosen to be higher than the observed number of cases to reflect both likely underdetection of cases, as well as the lag between the moment of exposure and the detection and declaration of cases. All other model state variables were set to zero.

Figure 2: Comparison of observed cases in Canada from February 8 (day 1) to May 4, 2020 (day 88)



Corrected cases (assuming one week of delay between infection end detection, and a level of underreporting of 25%) corresponding to the target curve, and simulated cumulative infectious cases with the age-stratified model

Figure 3: Simulation study design showing initial period of epidemic (before day 88)



During implementation of, and while maintaining physical distancing, along with a consistent level of case detection/isolation and contact tracing/quarantine; and second period of epidemic (after day 88) with varying levels of physical distancing (red at 16.7%, blue at 33% and green at 50% less contact than normal), case detection and contact tracing

The model was implemented in R using RStudio, using the following packages: adaptivetau; deSolve; dplyr; DT; forcats; ggplot2; htmlwidgets; lhs; magrittr; openxlsx; plotly; readxl; scales; tidyr; and triangle. Code is available upon request to the authors.

No ethics approval was required as all data were based on surveillance reports publically available from the Public Health Agency of Canada and published literature sources.

Simulations of non-pharmaceutical interventions

A total of 108 possible epidemics were simulated to assess the impact of different levels of case detection/isolation and contact tracing/quarantine under three scenarios for different levels of contact rates due to changes in physical distancing following de-escalation of restrictive closures as of May 4, 2020 (day 88). The study design is represented in **Figure 3**. From day 0 until day 88, all three scenarios are identical and involved constant levels of case detection/isolation (a conservative 40% of cases detected) and contact tracing/quarantine (40% traced and quarantined) while physical distancing (and thus the contact rates) varied according to the following: 1) an initial period of 40 days during which the level of daily contacts corresponded to what is normally observed in the general population; 2) a seven-day period during which the daily contact rate was gradually reduced by 50% to represent the implementation of physical distancing associated with the start of implementation of restrictive closures in Canada; and 3) a period of 40 days (from day 47 to day 87) over which physical distancing due to the restrictive closures maintained contact rates at 50% below pre-COVID-19 levels.

From day 88 (the date of lifting restrictive closures), there were three scenarios for physical distancing: 1) physical distancing was kept such that contact rates remained 50% less than pre-COVID-19 levels (i.e. restrictive closures are not lifted); while in 2) and 3) restrictive closure were lifted to allow contact rates to increase, respectively, to 33% or 16.7% below pre-COVID-19 levels until the end of the simulation. Six levels of case detection/isolation (from 30% to 80% in 10% increments) and six levels of contact tracing/quarantine (from 30% to 80% by 10% increments) were simulated for each one of the three scenarios of physical distancing, for a total of 108 simulated epidemics.

Outcome measures

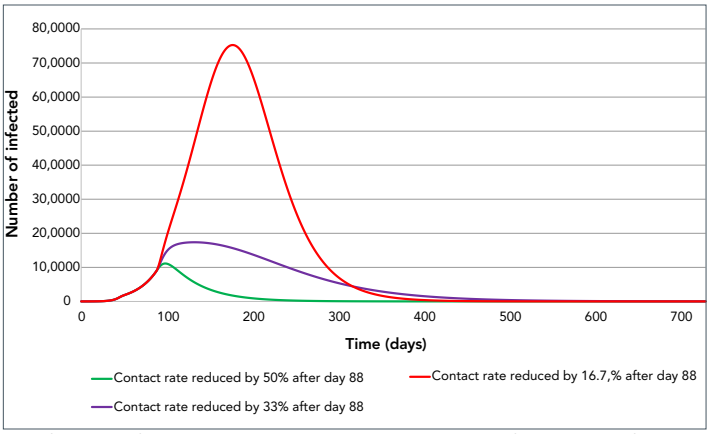
The attack rate was the primary outcome of the simulation experiments, consisting of the cumulative number of infected people over the entire initial population, for the entire 730 days of the epidemic, or at the end of the simulation period if the epidemic was not completed. Simulations longer than two years were considered as unrealistic given the assumption that recovered individuals do not return to the susceptible state during the simulation. Currently, there is not enough scientific evidence to confirm post-infection immunity in all recovered cases, or the duration of immunity any individual may achieve from a COVID-19 infection (22–24). Attack rates below 10% were considered corresponded to a condition of "epidemic control" of COVID-19 in Canada, below which the healthcare system was less likely to be overwhelmed.

A analysis of sensity of the attack rate to an increase or decrease of the transmission coefficient (beta) by 10% (using the formula Sensitivity=((Vi - V0)/V0)/(|(Ti - T0)/T0|) (25) was performed, where V0 is the attack rate without changes to input data [T0] and Vi is the attack rate with a given increase or decrease of input [Ti]).

Outcomes

Attack rates of the 108 simulations are presented in Table 1 and illustrated in **Figure 4**; both table and figure show how the attack rate reduction evolved according to the different levels of NPI. Results showed that relaxing physical distancing at day 88 (40 days after its implementation) had a significant impact on the attack rate in all the simulated epidemics, with the attack rate varying between 1.6% and 76.6%. The extent of the impact of the easing of physical distancing varied according to the values of the other control measures already in place; i.e. the case detection/isolation rate and the contact tracing/quarantine rate. An attack rate below 10%, which was considered here to represent epidemic control, was much more frequent when the contact rate was kept at 50% level below normal after day 88, compared with lower levels of physical distancing.

Figure 4: Simulation of the epidemic for three scenarios after day 88, May 4, 2020



Case detection/isolation at 70%, contact tracing/quarantine at 50% and contact rate reductions of 50%, 33% or 16.7% below pre-pandemic levels. Values for days before 88 are described in Figure 3. The y-axis includes all individuals in the infectious states—presymptomatic, symptomatic (hospitalized or not) and asymptomatic

Additionally, a level of case detection/isolation of 70% or more allowed for control of the simulated epidemics at all levels of contact tracing above 30% when physical distancing is maintained at 50% below normal levels. However, the level of case detection and contact tracing needed to control the epidemic increased markedly if physical distancing was not maintained to reduce contact rates.

The results also suggest that the relative impact of case detection/isolation on the decrease of the attack rate appeared to be higher than that of contact tracing. Even with contact tracing at levels as high as 80%, 50% of cases had to be detected to control the epidemic when physical distancing kept contact rates 50% lower than pre-COVID-19 levels. An even higher level of case detection was required when physical distancing was lifted to allow contact rates to rise to 16.7% or 33% below pre-COVID-19 levels.

The sensitivity analysis for beta showed that the average percent change for the attack rate was lower than 10% in most scenarios, increasing with increasing beta (8.1%; SD=9.2%; data not shown) and decreasing with decreasing beta (4.1%; SD=2.9%). When beta was increased, the number of combinations of case detection and contact tracing rates resulting in an attack rate less than 10% reduced by half (from 32 to 16) while decreasing beta resulted in an increase (from 32 to 43) in the number of combinations resulting in an attack rate less than 10% (see **Appendix C**).

Discussion

Summary of key findings

This work highlights, in order of importance, that ensuring a relatively high level of detection/isolation of cases and tracing/quarantine of potentially infected cases while maintaining some personal physical distancing will all be necessary to avoid a resurgence of the epidemic in Canada.

Comparison with other studies

These results are in accordance with an example presented in Ogden *et al.* (26), based on a deterministic compartmental model that was not age stratified. Additionally, similar studies that assessed the impact of NPIs for Canada as a whole, or for a specific Canadian province, have come to similar conclusions (5,27,28) (similar findings have been found in *personal communication,Tuite et al. Reduced COVID-19-Related Critical Illness and Death, and High Risk of Epidemic Resurgence, After Physical Distancing in Ontario, Canada. medRxiv 2020* and in *Eastman et al. Mathematical modeling of COVID-19 containment strategies with considerations for limited medical resources. medRxiv. 2020*). Even if a direct comparison between results in different studies is difficult because of differences in details of the modelling study design (study region, epidemic start date, inclusion or not of stochasticity and epidemic outbreak metric), they all concluded that control of the epidemic requires a combination of three things: 1) maintenance of some level of physical distancing (for a minimum of 10 months according to Tuite *et al.* (5)); 2) enhanced detection of cases; and 3) tracing and quarantine of contacts, to minimize the attack rate.

Strengths and limitations

A major strength of this study is that it provides a clear signal of the potential impact of lifting restrictive closures (represented in this study by release of physical distancing), which began in many jurisdictions within Canada around mid-May 2020. The results of the simulation experiments presented here demonstrated that during the lifting restrictive closures, public health decision-makers and practitioners will need to maintain continued vigilance to avoid the resurgence of the COVID-19 epidemic (a "second wave"), through the maintenance of a high level of case detection and contact tracing and some level of physical distancing. A further strength of this work is that the

chosen model states are comprehensive and account for the main disease statuses, including latent and presymptomatic states. Additionally, the model accounts for the age structure in the Canadian population, which is an important element of transmission risk heterogeneity (29). Finally, modeling the case detection level instead of the ratio of asymptomatic cases has allowed to circumvent the difficulty of obtaining precise information on the number of asymptomatic cases, which is a still a challenge for COVID-19 modelling.

A limitation of this study, which applies to most mathematical modelling work, is that translating the levels of NPI modelled into the real world is not always easy for the public health stakeholders and can be open to interpretation. In this study, we used our current best estimates for parameter values; however, these values may change as knowledge of COVID-19 increases. The preliminary sensitivity analysis that was conducted shows that the results were relatively robust to changes in beta (the transmission coefficient); therefore, the attack rate values obtained here should be considered as illustrative of the principle that increased case detection and contact tracing, as well as maintenance of some physical distancing, will be needed to control the epidemic as restrictive closures are lifted.

Additionally, the model does not account for delays between onset of symptoms and case detection or between case detection and contact tracing/quarantining. It is recognized that these delays exist and have been reported elsewhere in the world (30). In the United States and the United Kingdom, it has been shown that these delays are subject to significant variation depending on the study population, the strength of symptoms and the vulnerability of the person, though no published estimates of these delays are yet available for Canada (*Personal communication, Lawless et al. Estimation of Symptomatic Case Counts and the COVID-19 Infection Curve Through Reporting Delay Adjustment: An Observational Study of Ontario Surveillance*).

Finally, the contact matrices used are the result of projections for Canada based on data from other countries in Europe and corrected for socio-demographic and health factors (19). Actual contact rate data for Canada would strengthen future versions of this model.

Implications and next steps

his study underlines the importance of a cautious approach to lifting restrictive closures. It appears that maintaining some level of physical distancing (for example, by limitations on the size of gatherings, maintaining a two metre distance, or maintaining a social bubble) or other non-pharmaceutical measures (such as wearing non-medical masks) combined with high levels of case detection and contact tracing are key components of epidemic control. It this context, it seems important to support strategies aimed at encouraging people to get tested when they may have been exposed to suspected or confirmed COVID-19 cases, encouraging people to respect isolation instructions as well as strategies that support personal protection measures, such as mandating the use of non-medical masks in indoor public settings (31), in order to offset the risk of infection from the increase of physical proximity of citizens that comes with re-opening.

Conclusion

This paper presents an aged-stratified dynamic compartmental model for the transmission of COVID-19 in Canada. As well, these results provide estimates of the impact of NPIs, including case detection/isolation, contact tracing/quarantine and changes in the level of physical distancing, on the COVID-19 attack rate, for a period of time after mid-May 2020, when lifting of restrictive closures began at a national level. The model and analyzed scenarios demonstrate that case detection/isolation and contact tracing/quarantine, along with reduced rates of contact through some form of physical distancing, will be essential for future control of the COVID-19 epidemic.

Authors' statement

AL, PB and NO — Conceptualization
AL, PB, AO, HO — Data curation (parameter values)
AL, PB, CN, DH, JB, MD — Analysis
AL, PB, HO — Writing–original draft
AL, PB, NO, AO, HO, CN, DE, JB, MD — Writing–review and editing
NO — Supervision
AL, PB — Contributed equally to this work

Competing interests

None.

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Appendix A: Model flow, compartment definitions, parameter definitions and values

Model flow

Broadly, the naïve individuals (the Susceptible state), enter the latent infection state either in quarantine (state Lq) or while part of the general population (L). After the latent period, the individuals become infectious without developing symptoms—for individuals who will develop symptoms, this corresponds to a presymptomatic state (states Iq_pres or I_pres depending on whether the individual is quarantined or not). For individuals who will remain asymptomatic, the state we call presymptomatic simply corresponds to the first phase of their infectious period, until they may be detected, or not. Individuals are then either detected (a fraction of mild symptomatic individuals, asymptomatic individuals and all with severe symptoms) or not (most of the asymptomatic and a fraction of the mild symptomatic). Detected individual with mild symptoms or who are asymptomatic are isolated at home, while detected individuals with more severe symptoms enter the hospitalization section of the model. Undetected individuals, either with mild symptoms or who are completely asymptomatic are not isolated and are considered to continue to contribute to the epidemic for as long as their infectious period, at which point they recover. Once in the hospital states, depending on severity, individuals move to one of three possible compartments: a general non-emergency ward, an intensive care unit (ICU) if they are a severe case, or an ICU unit with ventilation for the most critical patients. The model accounts for lack of care for severe cases in the situation where hospital capacity is overwhelmed. Each severe case can either die or recover. State definitions can be found in **Table S1**.

Table S1: Model compartment definitions and values

State	Definitions	Initial values
S	Susceptible	Stratification by age group, StatCan Population estimates July 1, 2019 (32) Ages 0–10 estimate of 3,982,527 Ages 10–20 estimate of 4,146,397 Ages 20–40 estimate of 10,286,131 Ages 40–60 estimate of 10,069,708 Ages 60–75 estimate of 6,315,255 Ages 75+ estimate of 2,789,244
Lq	Latent in quarantine	0

Table S1: Model compartment definitions and values

State	Definitions	Initial values
L	Latent in the general population (not in quarantine)	10
I_pres	Infected presymptomatic in the general population (and first infectious period for asymptomatic)	20
Iq_pres	Infected presymptomatic in quarantine (and first infectious period for asymptomatic)	0
Iqnd	Infected in quarantine not detected (asymptomatic or mild symptom)	0
Ind	Infected non-detected (asymptomatic or mild symptom) in the general population	2
Idam	Infectious detected asymptomatic or with mild symptoms in the general population	0
Idss	Infected detected between onset of symptoms, that are severe, and going to the hospital	0
Iss_hosp	Infected with severe symptoms who are in hospital sorting	0
H_g_OK	Infected with severe symptoms who stay at the hospital in the general care service	0
H_ICU_OK	Infected with severe symptoms who stay at the hospital in ICU	0
H_vent_OK	Infected with severe symptoms who stay at the hospital with ventilation	0
H_g_denied	Infected with severe symptoms who are not able to access hospital care because of insufficient/overwhelmed local capacity	0
H_ICU_denied	Infected with severe symptoms who are not able to access ICU because of insufficient/overwhelmed local capacity	0
H_vent_denied	Infected with severe symptoms who are not able to access ventilation because of insufficient/overwhelmed local capacity	0
R	Recovered	0
D	Dead	0

Abbreviation: ICU, intensive care unit

Table S2: Model parameters, definition, values and evidence

<table>
<tr><th>Parameter name</th><th>Definition</th><th>Value</th><th>Evidence</th></tr>
<tr><td>beta</td><td>Probability of transmission when contact made with infectious person</td><td>Ages 0–10 average value of 0.041
Ages 10–20 average value of 0.041
Ages 20–40 average value of 0.041
Ages 40–60 average value of 0.041
Ages 60–75 average value of 0.041
Ages 75+ average value of 0.041</td><td>Based on Stilianakis et al. (33) and adjusted using data from the beginning of the epidemic (Figure 2 in the article)</td></tr>
<tr><td>lambda</td><td>Proportion of exposed to detected infectious who are traced and quarantined (contact tracing/ quarantine)</td><td>Value of 40% until day 87
From day 88 up to the end of the epidemic, the value varied according to control scenarios</td><td>NA</td></tr>
<tr><td>c_{gg}</td><td>Number of daily contacts between two individuals from the general population</td><td>6*6 matrix
Average value of 12.6 from day 0 to day 40 (see below)
<table>
<tr><th>Age group</th><th>0–10</th><th>10–20</th><th>20–40</th><th>40–60</th><th>60–75</th><th>75+</th></tr>
<tr><td>0–10</td><td>4.60</td><td>0.89</td><td>2.59</td><td>1.38</td><td>0.34</td><td>0.04</td></tr>
<tr><td>10–20</td><td>1.03</td><td>0.61</td><td>2.80</td><td>2.45</td><td>0.21</td><td>0.03</td></tr>
<tr><td>20–40</td><td>1.15</td><td>1.67</td><td>8.18</td><td>4.05</td><td>0.35</td><td>0.04</td></tr>
<tr><td>40–60</td><td>1.00</td><td>2.17</td><td>4.89</td><td>5.83</td><td>0.60</td><td>0.07</td></tr>
<tr><td>60–75</td><td>0.63</td><td>0.65</td><td>1.89</td><td>2.06</td><td>1.98</td><td>0.14</td></tr>
<tr><td>75+</td><td>0.45</td><td>0.66</td><td>0.84</td><td>1.42</td><td>0.77</td><td>0.46</td></tr>
</table>
Linear decrease of 50% from days 41 and 47
Value of 50% below normal from day 48 until day 87
From day 88 up to the end of the epidemic, the value varied according to control scenarios</td><td>Based on Prem et al. (19)</td></tr>
<tr><td>c_{gq}</td><td>Number of daily contacts between an individual from the general population and an individual from the quarantined population</td><td>6*6 matrix identical during all the duration of the simulation
<table>
<tr><th>Age group</th><th>0–10</th><th>10–20</th><th>20–40</th><th>40–60</th><th>60–75</th><th>75+</th></tr>
<tr><td>0–10</td><td>0.47</td><td>0.09</td><td>0.26</td><td>0.14</td><td>0.03</td><td>0.00</td></tr>
<tr><td>10–20</td><td>0.06</td><td>0.61</td><td>0.17</td><td>0.15</td><td>0.01</td><td>0.00</td></tr>
<tr><td>20–40</td><td>0.07</td><td>0.11</td><td>0.53</td><td>0.26</td><td>0.02</td><td>0.00</td></tr>
<tr><td>40–60</td><td>0.07</td><td>0.15</td><td>0.34</td><td>0.40</td><td>0.04</td><td>0.00</td></tr>
<tr><td>60–75</td><td>0.09</td><td>0.09</td><td>0.26</td><td>0.28</td><td>0.27</td><td>0.02</td></tr>
<tr><td>75+</td><td>0.10</td><td>0.14</td><td>0.18</td><td>0.31</td><td>0.17</td><td>0.10</td></tr>
</table></td><td>We assumed a person in quarantine is in contact with a maximum of one person each day during his/her quarantine period. The value of one was then standardized according to the total population size in each stratum</td></tr>
<tr><td>20sigma</td><td>Latent period (days)</td><td>4.12 days</td><td>Based on Li et al., 2020 (34)</td></tr>
<tr><td>delta</td><td>Proportion of presymptomatic infectious cases that will be identified (or detected)</td><td>Value of 40% until day 87
From day 88 and to the end of the epidemic, the value varied according to control scenarios</td><td>NA</td></tr>
<tr><td>alpha</td><td>Proportion of cases who develop severe symptoms</td><td>Ages 0–10 average value of 0.02
Ages 10–20 average value of 0.02
Ages 20–40 average value of 0.04
Ages 40–60 average value of 0.10
Ages 60–75 average value of 0.30
Ages 75+ average value of 0.41</td><td>Based on Public Health Agency of Canada (21)</td></tr>
<tr><td>t_{pres}</td><td>Period of time between onset of infectiousness and onset of symptoms in those developing symptoms OR first infectious period for asymptomatic</td><td>2 days</td><td>Based on He et al., 2020 (35)</td></tr>
</table>

Table S2: Model parameters, definition, values and evidence (*continued*)

Parameter name	Definition	Value	Evidence
t_{sm}	Period of time between onset of symptoms and recovery for cases with mild symptoms OR second infectious period for asymptomatic	6 days	Based on Wölfel *et al.*, 2020 (36) and He *et al.*, 2020 (35)
t_{sph}	Period between symptom onset for cases with severe symptoms and being taken care of by the health system	3 days	Based on Khalili *et al.*, 2020 (37)
p_{ICU}	Proportion of hospitalized cases who require/access to ICU in hospital	Ages 0–10 average value of 0.20 Ages 10–20 average value of 0.35 Ages 20–40 average value of 0.36 Ages 40–60 average value of 0.46 Ages 60–75 average value of 0.46 Ages 75+ average value of 0.19	Based on Public Health Agency of Canada (21)
p_{vent}	Proportion of hospitalized cases who require/access to ventilation (Vent)	0	This will be updated in future models once age-specific data become available
$t_{sorting}$	Period of time for sorting severe cases in hospital (before general service, ICU or Vent)	1 day	We assume it takes one day on average between when a severe case arrives in the hospital and when the case is sorted to the appropriate service
m_g	Mortality rate for severe cases in hospital that do not require ICU or Vent (general)	Ages 0–10 average value of 0 Ages 10–20 average value of 0 Ages 20–40 average value of 0 Ages 40–60 average value of 0.02 Ages 60–75 average value of 0.14 Ages 75+ average value of 0.34	Based on Public Health Agency of Canada (34)
m_{ICU}	Mortality rate for severe cases dying in hospital (ICU)	Ages 0–10 average value of 0 Ages 10–20 average value of 0 Ages 20–40 average value of 0.06 Ages 40–60 average value of 0.15 Ages 60–75 average value of 0.32 Ages 75+ average value of 0.57	Based on Public Health Agency of Canada (34)
m_{Vent}	Mortality rate for severe case dying in hospital (Vent)	NA	Not calibrated because this parameter has no impact on the results (e.g. attack rate) presented in this article
t_{hr}	Period of time between first day in hospital after sorting, and recovery or death	12 days	Based on hospitalization and length of stay of COVID-19 cases (38–40)
$m_{g\text{-}}$	Mortality rate for severe cases dying at home because they are not able to access hospital care	NA	Not calibrated because this parameter has no impact on the results (e.g. attack rate) presented in this article
$m_{ICU\text{-}}$	Mortality rate for severe cases dying in hospital because they are not able to access ICU	NA	Not calibrated because this parameter has no impact on the results (e.g. attack rate) presented in this article

Abbreviations: ICU, intensive care unit; NA, not applicable; Vent, ventilator

Appendix B: Equations

$dS / dt = - S * beta * 1/N*[(1-lambda*delta) * (c_{gg} * (I\_pres + Ind) + c_{gq} * (Iq\_pres + Iqnd)) + lambda * delta *(c_{gg} * (I\_pres + Ind) + c_{gq} * (Iq\_pres + Iqnd))]$

$dLq / dt = S * beta *1/N* lambda * delta *(c_{gg} * (I\_pres + Ind) + c_{gq} * (Iq\_pres + Iqnd)) - Lq / sigma$

$dL / dt = S * beta *1/N* (1-lambda *delta) * (c_{gg} * (I\_pres + Ind) + c_{gq} * (Iq\_pres + Iqnd)) - L / sigma$

$dIpres / dt = L / sigma - Ipres / t_{pres}$

$dIq\_pres/ dt = Lq / sigma - Iq\_pres / t_{pres}$

$dIqnd / dt = Iq\_pres *(1-delta) / t_{pres} - Iqnd / t_{sm}$

$dInd / dt = Ipres *(1-delta) / t_{pres} - Ind / t_{sm}$

$dIdam / dt = (Iq\_pres + Ipres)* delta* (1- alpha) / t_{pres} - Idam / t_{sm}$

$dIdss / dt = (Iq\_pres + Ipres)* (delta* alpha) / t_{pres} - Idss / t_{sph}$

$dIss\_hosp / dt = Idss / t_{sph} - Iss\_hosp / t_{sorting}$

$dH\_g\_OK/ dt = Iss\_hosp * (1-p_{ICU}-p_{vent}) / t_{sorting} - H\_g\_OK / t_{hr}$

$dH\_ICU\_OK / dt = Iss\_hosp * p_{ICU} / t_{sorting} - H\_ICU\_OK / t_{hr}$

$dH\_vent\_OK / dt = Iss\_hosp * p_{vent} / t_{sorting} - H\_vent\_OK / t_{hr}$

$dH\_g\_denied / dt = 0 * Iss\_hosp * (1-p_{ICU}-p_{vent}) / t_{sorting} - H\_g\_denied / t_{hr}$ where 0 comes from the assumed infinite capacity.

$dH\_ICU\_denied / dt = 0 * Iss\_hosp * (p_{ICU}) / t_{sorting} - H\_ICU\_denied / t_{hr}$ where 0 comes from the assumed infinite capacity.

$dH\_vent\_denied / dt = 0 * Iss\_hosp * (p_{vent}) / t_{sorting} - H\_vent\_denied / t_{hr}$ where 0 comes from the assumed infinite capacity.

$dR / dt = Idam / t_{sm} + Ind / t_{sm} + Iqnd / t_{sm} + H\_g\_OK * (1- m_{g}) / t_{hr} + H\_g\_denied * (1- m_{g-}) / t_{hr} + H\_ICU\_OK * (1- m_{ICU}) / t_{hr} + H\_ICU\_denied *(1- m_{ICU-}) / t_{hr} + H\_vent\_OK * (1- m_{Vent}) / t_{hr}$

$dD / dt = H\_g\_OK * m_{g} / t_{hr} + H\_g\_denied * m_{g-} / t_{hr} + H\_ICU\_OK * m_{ICU} / t_{hr} + H\_ICU\_denied * m_{ICU-} / t_{hr} + H\_vent\_OK * m_{Vent} / t_{hr} + H\_vent\_denied / t_{hr}$

Appendix C: Sensitivity analysis for beta

Case detection/ isolation	Contact tracing and quarantine					
	0.30	0.40	0.50	0.60	0.70	0.80
Attack rate for a beta 10% higher than expected (beta=0.045)						
Contact rate still reduced by 50% after day 88						
0.30	59.09352	57.4983	55.78916	53.9561	51.98852	49.87534
0.40	51.116	48.47224	45.58901	42.44803	39.03661	35.35465
0.50	40.72402	36.72655	32.39552	27.80149	23.12042	18.6755
0.60	27.68375	22.66857	17.92792	13.9703	11.07788	9.127013[a]
0.70	14.67835	11.41256	9.222685[a]	7.797606[a]	6.846839[a]	6.184861[a]
0.80	7.997407[a]	6.941327[a]	6.220808[a]	5.706796[a]	5.325164[a]	5.032136[a]
Contact rate reduced by 33% after day 88						
0.30	72.12056	71.03947	69.87305	68.6118	67.24506	65.76064
0.40	66.84949	65.00664	62.96262	60.688	58.14878	55.30608
0.50	59.74349	56.76575	53.38173	49.5269	45.13509	40.15337
0.60	49.97753	45.37923	40.1135	34.16619	27.6911	21.21683
0.70	36.56815	30.14937	23.41448	17.23498	12.63568	9.755943[a]
0.80	20.20915	14.69697	10.93404	8.667255[a]	7.296874[a]	6.418942[a]
Contact rate reduced by 16.7% after day 88						
0.30	78.97424	78.18379	77.33041	76.40654	75.40348	74.31118
0.40	75.19535	73.84808	72.34734	70.66763	68.77832	66.64237
0.50	70.09167	67.88819	65.35466	62.42254	59.0075	55.00747
0.60	62.96743	59.44347	55.27892	50.33294	44.45665	37.55202
0.70	52.71792	47.23034	40.70934	33.12933	24.9225	17.4795
0.80	37.83963	30.13374	22.10612	15.33652	11.01025	8.593437[a]
Attack rate for a beta 10% lower than expected (beta=0.037)						
Contact rate still reduced by 50% after day 88						
0.30	46.32687	44.1102	41.73141	39.17554	36.42638	33.46669
0.40	35.37861	31.69369	27.6635	23.2589	18.45491	13.23975
0.50	21.11151	15.51616	9.487262[a]	4.352624[a]	2.026998[a]	1.268084[a]
0.60	4.446911[a]	1.925112[a]	1.178985[a]	0.892557[a]	0.747114[a]	0.659919[a]
0.70	0.917685[a]	0.750175[a]	0.655133[a]	0.594146[a]	0.551763[a]	0.520622[a]
0.80	0.594963[a]	0.550296[a]	0.517993[a]	0.493555[a]	0.474428[a]	0.459053[a]
Contact rate reduced by 33% after day 88						
0.30	64.06551	62.56878	60.95033	59.19649	57.29164	55.21801
0.40	56.83411	54.26817	51.41448	48.22939	44.66162	40.65115
0.50	47.04398	42.87674	38.12076	32.67411	26.42855	19.2982
0.60	33.54144	27.06095	19.59878	11.19984	4.000164[a]	1.648817[a]
0.70	14.97949	6.498159[a]	2.127114[a]	1.165722[a]	0.858549[a]	0.713186[a]
0.80	1.48164[a]	0.962062[a]	0.758895[a]	0.652422[a]	0.587167[a]	0.543146[a]
Contact rate reduced by 16.7% after day 88						
0.30	73.32151	72.24328	71.07465	69.80463	68.42056	66.90782
0.40	68.1969	66.33559	64.25373	61.91416	59.27188	56.27203
0.50	61.2006	58.12787	54.57939	50.45286	45.61944	39.91796
0.60	51.36095	46.40851	40.51931	33.46741	25.00128	14.98944
0.70	37.11735	29.3243	19.98326	9.323668[a]	2.537434[a]	1.234962[a]
0.80	16.33694	6.198483[a]	1.832707[a]	1.050737[a]	0.794449[a]	0.670077[a]

[a] Scenarios where epidemic control maintained attack rate below 10% (green)

Interim guidance on the use of the Abbott ID NOW™ instrument and COVID-19 assay

on behalf of the Canadian Public Health Laboratory Network and the Canadian Society of Clinical Chemists

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Introduction

This document, prepared October 26, 2020, provides interim guidance on the use of the Abbott ID NOW™ instrument and coronavirus disease 2019 (COVID-19) assay in the context of the Canadian public health system.

The Abbott ID NOW COVID-19 assay is an isothermal nucleic acid amplification technology intended for the qualitative detection of nucleic acid from severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) viral ribonucleic acid (RNA) in direct nasal, nasopharyngeal or throat swabs from individuals who are suspected of COVID-19 by their healthcare provider. While already in widespread use globally, there are several reports of a reduced sensitivity associated with the test when compared with other laboratory-developed tests (LDTs) or commercially available nucleic acid amplification tests (NAAT) such as the Cepheid GeneXpert™ based assay (1). The use of a lower sensitivity test, even a real-time transcription polymerase chain reaction (RT-PCR) method, carries risks to decision-making that can only be offset by the magnitude of possible benefits. It must be understood that a significantly greater degree of diagnostic uncertainty will be introduced/remain with use of the Abbott ID NOW assay, relative to the conventional RT-PCR methods commonly used in Canada at the time of writing. These guidelines will be updated periodically as more information is available regarding test sensitivity in different settings (surveillance, screening, diagnosis) and in the overall context of infection with SARS-CoV-2.

Many of these guidelines may also be applied to other less sensitive molecular and rapid antigen-based tests that may be approved for use in the future.

Key messages

- Health Canada provided approval for use of the Abbott ID NOW COVID-19 assay (October 2020).
- The intended use for this assay as outlined by Health Canada is as follows:
  - The Abbott ID NOW COVID-19 assay performed on the Abbott ID NOW instrument is a rapid molecular *in vitro* diagnostic test utilizing an isothermal nucleic acid amplification technology intended for the qualitative detection of nucleic acid from the SARS-CoV-2 viral RNA in direct nasal, nasopharyngeal or throat swabs from individuals who are suspected of COVID-19 by their healthcare provider within **the first seven days** of the onset of symptoms.
  - Results are for the identification of SARS-CoV-2 RNA. The SARS-CoV-2 RNA is generally detectable in respiratory samples during the acute phase of infection. Positive results are indicative of the presence of SARS-CoV-2 RNA; clinical correlation with patient history and other diagnostic information is necessary to determine patient infection status. Positive results do not rule out bacterial infection or co-infection with other viruses.
  - Negative results should be treated as preliminary and, if inconsistent with clinical signs and symptoms or necessary for patient management, should be tested with different authorized or cleared molecular tests. Negative results do not preclude SARS-CoV-2 infection and should not be used as the sole basis for patient management decisions. Negative results should be considered in the context of a patient's recent exposures, history and the presence of clinical signs and

symptoms consistent with COVID-19.
    - The Abbott ID NOW COVID-19 test is intended for use by medical professionals or trained operators who are proficient in performing tests using the Abbott ID NOW instrument in laboratory and point-of-care (POC) settings.
- The performance of the assay should be verified in the field before recommending its use. This is critical since data obtained from pre-market evaluations cannot account for the variability in training and quality of sample collection that follows use in a broader population. Therefore, clinical performance must continue to be monitored.
- The "in-field" performance characteristics of the Abbott ID NOW is still under evaluation in Canada; however, data about the nature of the technology from other jurisdictions suggest that the tests have lower sensitivity but comparable specificity to other LDTs and commercial NAAT assays. Although, the rapid nature of the assays makes it suitable for POC applications, these performance characteristics, combined with the incidence of infection within the population being tested, must be considered when interpreting the results.
- In discussion with provincial and territorial laboratory directors, the use of this test must be carefully considered.
    - At this time, until further data is collected, because of the decreased sensitivity, all negatives should be considered preliminary negatives.
    - Owing to an expected higher rate of false negatives, it is recognized that reflexive laboratory-based testing of preliminary negatives from the Abbott ID NOW COVID-19 testing depending on its proposed use) will likely introduce an additional burden to reference laboratories already facing enormous testing volumes.
- This document outlines scenarios where the Abbott ID NOW COVID-19 testing may prove useful, should the expected performance characteristics be confirmed.

Current approach to severe acute respiratory syndrome coronavirus 2 testing in Canada

Since the emergence of SARS-CoV-2, testing has been a key pillar of Canada's response to the pandemic. The broad use of testing, as part of an array of public health measures, led to a flattening of the epidemic curve in the spring of 2020, demonstrating the value of testing as a part of the COVID-19 response. To date, testing has relied on molecular (i.e. RT-PCR) testing performed on a nasopharyngeal sample (NP) or alternate respiratory sample collected by a healthcare professional. **This testing method currently remains the gold standard for diagnosing SARS-CoV-2 infection in Canada.**

Considerations for the use of the Abbott ID NOW COVID-19 assay

It is critically important to understand the timing of specimen collection in relation to symptom onset since the sensitivity of the test is not expected to be uniform over the course of infection. Data suggest that viral shedding may begin 2–3 days before the symptoms peak—around the time of symptom onset—and then gradually declines over time thereafter (2,3).

During the first seven days of infection, viral loads are likely to be above the limit of detection for the Abbott ID NOW assay. Although the time of post-symptom onset still needs to be carefully considered. It is also important to understand test performance in relation to the time since a potential exposure when the test is being used for rapid contact tracing (e.g. how many days after exposure might one expect to have viral loads that can be optimally detected using the Abbott ID NOW?).

Notwithstanding the difference in the performance profile, other features of the Abbott ID NOW (including but not limited to; faster turnaround time, lower per-test cost, ability to do the test in a setting by non-professionals on a more frequent basis) suggest that it could have an important role to play in the next phase of the pandemic response.

It is important for public health, microbiology and infectious diseases experts to identify the scenarios where the use of the Abbott ID NOW may further strengthen the public health response by expanding access to testing beyond existing indications and increasing capacity for molecular detection of SARS-CoV-2. Furthermore, establishing mechanisms to allow a new POC test to report into the public health system efficiently is critical (see "Reporting of results and Quality Control" section below).

Balancing test sensitivity against other considerations

The intrinsic performance characteristics of the Abbott ID NOW are not the only factors determining its utility. **The final interpretation of a test must take into account the performance parameters, the prevalence of infection, predictive values and the intended use of the test result.** Therefore, the tolerance for sensitivity and specificity thresholds will vary based on the reason for testing and the expected action that would follow either a positive or a negative result.

In scenarios where critical decisions and actions rely on a test result (e.g. a symptomatic resident in a long-term care home, a patient in an intensive care unit [ICU] who requires immediate treatment), the recommended test would be the most accurate test. At the time of writing, the indicated (best) test would be RT-PCR performed on a NP sample or on a lower respiratory tract sample in patients with evidence of pneumonia. However, there may be circumstances where a rapid POC test can be permissible and enhance testing capacity to support the public health response, particularly when the demand for RT-PCR testing exceeds laboratory capacity or is otherwise unavailable or in situations where a symptomatic individual may otherwise be lost to follow-up.

Clinical situations where infection is prevalent in the community: When the prevalence of infection is high, and the access to RT-PCR testing is unavailable (i.e. northern, remote and isolated [NRI] communities) or when the results are delayed beyond 48 hours because testing demand is exceeding laboratory capacity issues, a POC test may provide an option that will positively impact public health or clinical management. Here the intended use is for early diagnosis of infection. In this situation, a positive result will allow for early implementation of public health measures and contact tracing or clinical management decision-making. Although there will be a need to further evaluate, preliminary data suggests that performance of the Abbott ID NOW in early infection (1–5 days post-symptom onset) may be similar to RT-PCR in terms of sensitivity and performance. However, negative results should be confirmed using conventional NAAT as soon as possible as clinical decisions cannot be made based solely on the Abbott ID NOW test because of the lowered negative predictive value associate with reduced test sensitivity.

Clinical situations where infection is not prevalent in the community and high sensitivity is not the main consideration: There may be alternative settings where a less sensitive test may be acceptable. Although the Abbott ID NOW is currently approved for testing symptomatic individuals within the first seven days of symptom onset, monitoring of asymptomatic individuals who are at risk of introducing infection into high risk settings (e.g. long-term care, correctional facilities) could be considered. Modelling data suggest that testing protocols that incorporate repeated and frequent re-testing of individuals could be effective (4). Here the intended use of a POC test is for monitoring infection in individuals that may not otherwise be able to be tested with the same frequency due to challenges with testing capacity. Due to the potential reduction in pre-test probability of a positive result, the test would need to be confirmed using a laboratory-based NAAT. The purpose of this requirement for confirmation is to reduce the potential for negative factors associated with a false positive test (unnecessary removal from work, stigma that may be associated with infection, etc.).

Proposed use scenarios

At this time, it is not possible to provide an exhaustive list of all cases where the Abbott ID NOW assay might be of benefit. Several scenarios are given as examples below, but are not meant to be proscriptive.

Scenario 1: Northern, remote and isolated settings

The NRI communities face additional barriers to timely test results due to transportation time required to deliver a specimen to a testing laboratory. Given the importance of accurately identifying new cases in NRI communities to prevent spread of SARS-CoV-2 in the face of limited healthcare resources, RT-PCR testing is the recommended test for these settings. While there have been extraordinary efforts to date to bring high quality POC PCR testing to NRI communities (e.g. Cepheid GeneXpert test), significant challenges remain. First and foremost is the ongoing short supply of the GeneXpert COVID-19 test cartridges. The availability of a relatively low complexity POC solution with an anticipated higher test allocation may be an attractive option as a screen-in test to conserve GeneXpert test cartridges for the testing of symptomatic individuals. In this two-test algorithm, if a sample is shown to be positive using the Abbott ID NOW assay, then appropriate actions can quickly be put in place, while negative results can be confirmed on the highly sensitive Cepheid GeneXpert or in a reference laboratory. This may also be useful in other settings where rapid, accurate results are required (e.g. staging for medical procedures in hospitals involving symptomatic patients). This may have additional benefit in allowing the prioritization of GeneXpert test cartridges for NRI communities.

Scenario 2: Early outbreak identification and investigation

While the use of a less sensitive test would not be recommended for the exclusive management of an outbreak, testing of symptomatic individuals and their direct contacts with the Abbott ID NOW assay can be useful for the early identification of possible outbreaks.

- Testing can be done as part of suspected outbreak identification and investigation where patients can be tested rapidly on site if faster preliminary results will help inform and expedite public health action (triage of patients and contact tracing). This may be particularly relevant in situations where a symptomatic individual may otherwise be lost to follow-up.
    - This would always be followed by confirmatory PCR testing, although this requirement could be revisited to determine if ongoing testing is needed.

Scenario 3: Asymptomatic testing in high risk settings

An additional broad category for use of the Abbott ID NOW includes situations that involve the prospective monitoring of asymptomatic individuals for introduction of SARS-CoV-2 into high risk settings. Note that such a proposed monitoring role for non-PCR testing technologies is referred to as "screening" in some other documents on COVID-19 testing strategies. At this time, the market authorization for the Abbott ID NOW from Health Canada—Medical Devices Bureau is focused on symptomatic testing in the early phase of disease, so the use of this test in a monitoring context will require clinical validation. The frequency of repeat testing is not yet defined (see below).

- Repeated testing of workers in congregated settings to prevent introduction or to minimize the chance of spread within a site, including:
  - Large processing plants
  - Long-term care facilities
  - Homeless shelters
  - Farm/migrant workers
  - Inmates in correctional facilities
- The Abbott ID NOW could be used for prospective testing of low-risk, asymptomatic visitors and staff entering congregated settings.
- Important additional considerations for the use of Abbott ID NOW include the following:
  - Testing would always need to be done in the context of PCR confirmatory testing of all positive cases
  - Reflexive PCR testing of preliminary negative cases needs to be carefully considered and is not being recommended at this time due to the significant impact it would have on current testing capacity in laboratories already facing enormous testing volumes
  - The frequency of repeat testing will need to be carefully examined to ensure the testing strategy can correctly identify individuals during a high viral period early in infection
  - The use of alternative specimen collection (rather than with oral or nasal swabs included with the Abbott ID NOW) may be more acceptable for collecting samples from asymptomatic individuals than NPs

These situations represent scenarios where frequent entries and exits multiply the potential introduction of the virus into high risk settings known to facilitate the rapid spread of infection. It is not yet possible to articulate the implementation approach that best supports the public health goals of testing (case identification, isolation contact tracing, etc.). It is clear that a false negative test can occur early in infection even with the most sensitive RT-PCR methods. As such, repeat testing may be necessary to detect infection in cases with high clinical suspicion of disease. The Abbott ID NOW assay may offer ease of use, the ability to conduct testing outside traditional laboratory settings and rapid time to results to enable frequent testing and offset the reduced sensitivity.

Approach to the potential use of the Abbott ID NOW assay

How the results from the Abbott ID NOW assay are interpreted and how it impacts public health and clinical management of patients need to be considered. To do this, it is critical that end users understand the prevalence of infection in the population they are testing. This necessitates a robust surveillance system that communicates regularly with the end users.

Positive result

Positive results should be considered "preliminary positive" until confirmed using a reference RT-PCR method. While the Abbott ID NOW assay is expected to have high specificity, false positives can be expected, particularly if the prevalence of infection in the population tested is low, thus decreasing the pre-test probability of the assay. All patients with a positive result will require isolation. If the confirmatory RT-PCR is negative, discontinuation of isolation can be considered depending on the clinical context that generated the initial test.

Negative result

In interpretation of a negative Abbott ID NOW result, the clinical context of the test (asymptomatic versus symptomatic) and the pre-test probability of infection must be considered. In patients where the pre-test probability of COVID-19 remains high (e.g. known contact, high community transmission), then the individual should undergo confirmatory testing using RT-PCR to direct further management. If the pre-test probability is low, then the individual can be monitored in the absence of isolation and reference testing.

Frequency of testing

As highlighted above, the Abbott ID NOW assay is ideally used in surveillance/screening programs where individuals get repeat tests to account for a lack in sensitivity. If the Abbott ID NOW is used in a monitoring approach, the ideal frequency of testing remains to be defined. The effectiveness of this strategy is dependent upon several associated factors, including the proportion of asymptomatic infections, the sensitivity of the assay and the time to results (assuming that self-isolation would occur once a positive test is identified).

Reporting of results and quality assurance

The use of the Abbott ID NOW will most likely occur outside of a laboratory environment. The current anticipated market authorizations are expected to require oversight of the testing

procedure by a trained healthcare professional, at least in the short term. It will be essential that a mechanism for reporting of results into the public health system and/or laboratory system be developed to ensure appropriate data capture and quality control, and to support public health action.

It is critical that quality assurance practices be considered when implementing POC testing, regardless of the perceived simplicity of the test. Where POC testing is implemented outside a hospital environment, sites are recommended to partner with local accredited laboratories for ongoing guidance and oversight. The laboratory director and partnering laboratories will guide sites to ensure important quality assurance practices are in-place.

Examples of quality assurance practices that must be considered:

- Training and ongoing authorization of staff who will perform POC testing
- Initial and ongoing reagent validation prior to clinical use
- Quality control practices for regular monitoring of test performance
- Proficiency testing to monitor overall testing practices at a site
- Troubleshooting issues with tests and/or devices
- Reporting of results

Critical scientific questions

The science continues to evolve daily as unprecedented global investment in research and development continues. Despite this, several critical questions remain to inform the use of new tests such as the Abbott ID NOW and sample types.

- How do these tests perform in "real life"?
  - Most submissions for approval have used simulated samples to evaluate the tests. This creates uncertainty about the true performance when applied to patients. There must be a verification of performance by comparing the real-life performance of intended use in the field compared with the traditional nucleic acid amplification methodology.
- How frequently is testing required to close the sensitivity gap?
  - This requires understanding of the dynamics of the test over time. It will be important to determine the frequency of testing to best mitigate the risk of cases being missed due to the lower sensitivity of the Abbott ID NOW.
  - At what threshold of community transmission is repeat testing in specific environments beneficial?
- How do lower sensitivity tests and lower sensitivity sample types interact?
  - If the NP swab is considered the gold standard, then what is the impact on sensitivity of using a less sensitive specimen for testing? How do the assays compare when an oral or nasal swab or alternative sample type such as a saline gargle is used?
  - If oral and/or nasal swabs are used as an alternative to the NP swab, the impact must be evaluated to inform potential for use.

Competing interests

None.

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Mumps outbreaks across Canada, 2016 to 2018

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Abstract

Background: An increase in mumps incidence was observed in late 2016 (365 cases in 2016 compared to 59 cases in 2015). This unusual level of mumps activity prompted the Public Health Network Council and the National Advisory Committee on Immunization to request situation awareness updates from the Centre for Immunization and Respiratory Infectious Diseases (CIRID) at the Public Health Agency of Canada in 2017 and 2018.

Methods: A mumps outbreak survey was developed and administered by epidemiologists within CIRID and sent electronically to provincial and territorial public health officials in charge of mumps surveillance. The survey collected information on mumps outbreaks pertaining to demographics, risk factors, laboratory data and public health interventions. The first survey collected data on outbreaks occurring between January 1, 2016 and February 28, 2017, while the second survey contained outbreak data from January 1, 2017 to July 31, 2018. Duplicate outbreaks entries were removed.

Results: The response rate for the first and second surveys was 61% and 69%, respectively. Twenty-four mumps outbreaks across nine provinces were reported between January 1, 2016 and July 31, 2018, for a cumulative total of 881 mumps cases. Adolescents and adults 15 to 39 years of age accounted for the majority of cases (80.6%). Specifically, adults 20 to 24 years of age represented the largest proportion of cases (24.6%). Community and social gatherings were the most common exposure setting (62.5%). Slightly more than one third of cases were known to have received at least two doses of mumps-containing vaccine (35.6%).

Conclusion: Results from the surveys indicate that the increase in mumps activity was widespread throughout Canada, affecting multiple jurisdictions. Young adults accounted for the largest proportion of cases. These surveys provided evidence to support recommendations on the use of additional mumps vaccination in outbreak settings.

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Keywords: mumps, Canada, outbreak, survey

Introduction

Despite strong vaccination programs in all provinces and territories, mumps remains endemic in Canada, with outbreaks cycles occurring approximately every four to five years (1,2). An increase in incidence beyond the expected trends across Canada was noted in 2016 (1–4). This increased activity resulted in significant public health resources being directed towards prevention and control of various local outbreaks. On February 23, 2017, the Public Health Network Council (PHNC) requested that the Public Health Agency of Canada (PHAC) organise a conference call with their provincial and territorial working level partners to share information regarding the outbreak. In addition, PHNC wanted to get a sense of the pan-Canadian epidemiology regarding the recent resurgence of mumps so that provinces and territories could tailor their approaches to address this situation. The Centre for Immunization and Respiratory Infectious Diseases (CIRID) developed and distributed a survey to the provinces and territories (on February 25, 2020) to gather information on recent mumps outbreaks and public health responses to these outbreaks. On March 2, 2017, CIRID hosted a conference call with provinces and territories to present the results and discuss public health measures that provinces and territories had implemented to address the outbreaks.

In August 2018, during a Canadian Immunization Committee (CIC) teleconference, the National Advisory Committee on Immunization (NACI) requested CIRID of PHAC to conduct a follow-up survey with the provinces and territories. The objective of this survey was to provide an update to the 2016/2017 pan-Canadian epidemiology and to support the work

of the NACI Measles Mumps and Rubella Working Group to investigate the effectiveness of the vaccine and the number of doses required.

This report describes the results of these two surveys, conducted by CIRID within PHAC, to inform PHNC and NACI regarding the pan-Canadian epidemiology of mumps resurgence between 2016 and 2018.

Methods

In February 2017, a survey was developed by CIRID staff to quantify and describe mumps outbreaks activity across Canada. The survey was developed using Microsoft Excel and collected demographic, risk factor, laboratory data and information on public health interventions on temporally defined outbreaks by province and territory. This survey was emailed to the "mumps leads" in all provinces and territories to collects mumps outbreak data between January 1, 2016 and February 28, 2017. A second survey was emailed to mumps leads in all provinces and territories in August 2018, using a slightly revised survey to reflect a new time period (January 2017–August 2018).

Surveys were sent in both English and French. Follow-up emails were conducted to improve response rates. Analyses were conducted using Microsoft Excel. Information on outbreak setting, demographics, vaccination status and genotype were summarized in counts and proportions. Duplicates were assessed by province/territory and removed prior to analysis.

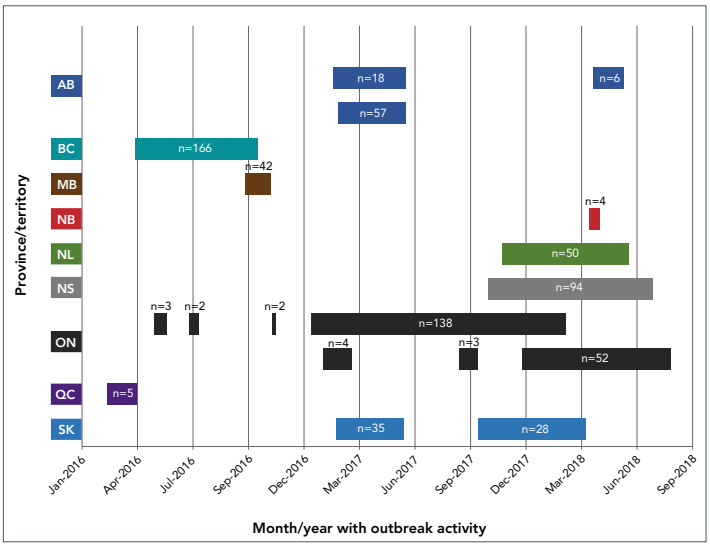
Results presented are for the combined period of January 1, 2016 to July 31, 2018.

Results

The total response rate for these two surveys was 65% (n=17/26); 62% (n=8/13) for the first survey and 69% (n=9/13) for the second survey. Five provinces and territories responded to both surveys; one did not respond to either survey. Nine provinces reported one or more outbreaks during the survey period (British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, Québec, New Brunswick, Nova Scotia and Newfoundland and Labrador) (**Figure 1**). Prince Edward Island, Northwest Territories and Nunavut reported no outbreaks during the survey period.

Among the nine provinces, a total of 24 outbreaks were reported during the survey period, affecting 881 people (**Table 1**). The number of outbreaks reported ranged from one to seven per province and the median number of outbreaks was two per province. For the 18 outbreaks for which the end date was provided at the time of the surveys, the median duration of outbreaks was 7.5 weeks and the median size was 12.5 cases (ranged from two to 166).

Figure 1: Duration and size of outbreaks by province[a]



Abbreviations: AB, Alberta; BC, British Columbia; MB, Manitoba; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; ON, Ontario; QC, Québec; SK, Saskatchewan

[a] Outbreaks with missing end dates are not shown

Table 1: Characteristics of outbreaks reported, January 1, 2016 to July 31, 2018

Indicator	Result
Number of outbreaks	24
Number of cases	881
Median	12.5
Range	2–166
Outbreak duration in weeks[a]	
Median	7.5
Range	1–59
Number of outbreaks reported by province	
Median	2
Range	1–7

[a] Outbreaks for which end dates were provided at the time of the surveys

Community and social gatherings were the most common exposure settings associated with outbreaks (62.5%) (**Table 2**). Of the 814 cases for which age was known, adults 15 to 39 years of age accounted for the majority of reported cases (80.6%) with the highest proportion among those 20 to 24 years of age (25%). Children under the age of four years accounted for less than 2% of all cases (1.2%). For cases where sex was reported, a slight majority of cases were reported in males (55%). Fourteen of 24 outbreaks had genotype information; 11 were identified as being caused by genotype G, one was identified as genotype G and C and two outbreaks were other genotypes. Vaccination status was unknown for approximately one third of cases (29%). Among cases with known vaccination status, nearly half (49%) reported having received two or more doses of the mumps vaccines, 30% had received one dose and 20% reported having never being vaccinated.

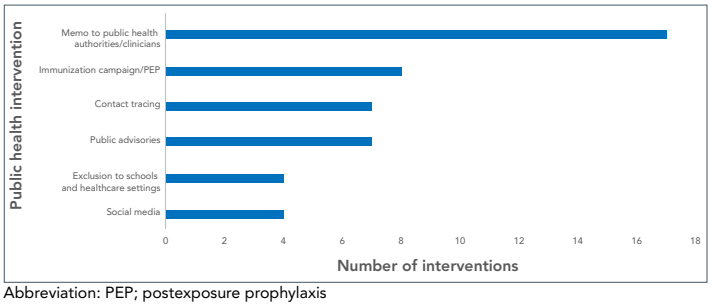
Table 2: Descriptive summary of mumps outbreaks January 1, 2016 to July 31, 2018

Category	Indicator	Number of cases	%
Setting[a] (outbreak)	Community	8	33.3
	Social gathering	7	29.2
	Sports team	5	20.8
	Post-secondary institution	5	20.8
	Bars	4	16.7
	Household/family	4	16.7
	High school	2	8.3
	Workplace	2	8.3
Age (years)	Younger than 1	1	0.1
	1–4	9	1.0
	5–9	24	2.7
	10–14	23	2.6
	15–19	129	14.6
	20–24	217	24.6
	25–29	153	17.4
	30–39	157	17.8
	40–49	65	7.4
	50–59	27	3.1
	Older than or 60	9	1.0
	Unknown age	67	7.6
Sex	Male	487	55.3
	Female	329	37.3
	Unknown sex	65	7.4
Vaccination status	Unvaccinated	127	14.4
	1 dose	187	21.2
	2 doses	307	34.8
	3 doses	7	0.8
	Unknown vaccination status	253	28.7
Genotype (outbreak)	G	11	45.8
	G and C	1	4.2
	Other	2	8.4
	Unknown	10	41.7

[a] Non-mutually exclusive settings

The most common public health intervention reported by provinces was a memo to public health authorities and clinicians and vaccination campaigns (**Figure 2**). Exclusions to schools/healthcare settings and social media were the least frequent interventions reported.

Figure 2: Public health interventions reported during outbreaks



Abbreviation: PEP; postexposure prophylaxis

Discussion

Data on resurgence of measles in Canada in 2017 and 2018 were gathered from provinces and territories via two surveys that were sent to appropriate public health personnel. These outbreaks largely affected the young adult population (20–39 years of age), who had received at least one mumps-containing vaccine, and were linked to social gatherings and community settings. These results were consistent with those from other studies; young adults, even those who had been vaccinated, accounted for the majority of cases (4–8).

In Canada, the mumps vaccine is available only in combination with 1) the measles and rubella vaccine or 2) the measles, rubella and varicella vaccine. Although immunity to mumps is known to wane at a rate of approximately 10% per year following administration of the mumps vaccine booster, vaccination is still the best prevention strategy (9). Although the survey did not look at date of most recent dose of mumps containing vaccine, the largest proportion of cases with known vaccination status reported having received at least two doses of mumps containing vaccine.

This study did not evaluate the effectiveness of public health intervention strategies used by various provinces; it simply provided an inventory of what intervention strategies were used overall. Although social media campaigns were the least common public health intervention used during this study period, in the course of a recent outbreak in Ontario, social media was deemed highly successful as an intervention during the investigation (6). The efficiency of social media in terms of outreach was echoed in another study (10). Platforms such as Twitter and Facebook can be used as venues to diffuse information rapidly and to cater to a young audience; the population primarily affected in outbreaks.

The impetus of this study was to provide a situational awareness to senior public health officials across Canada through the PHNC. After validating the survey results with provincial and territorial mumps leads during a teleconference call in early March 2017, a briefing note was prepared and distributed to PHNC members

(mid March 2017). Additionally, the combined survey results were presented to the NACI's Mumps Working Group in November 2018 and to NACI in February 2019 for consideration in their deliberations on recommending the use of an additional dose of mumps-containing vaccine during outbreaks.

A large mumps outbreak occurred in the province of Manitoba between September 2016 and November 6, 2018, with more than 2,000 cases (4). These data were not included in the pan-Canadian epidemiology surveys as the Manitoba outbreak had not ended by the time the second survey was distributed. The majority of cases were post-secondary students, between 18 and 29 years of age, living in Winnipeg (11). Exposure settings included university and sports settings. Vaccination status of cases was not reported. Although this outbreak was not reported using the survey tool, and therefore not included in the results of this current study, the epidemiology of the large Manitoba outbreak, in terms of age groups and risk settings, was consistent with what was reported in our survey (4).

Strengths and limitations

The results of these surveys represent a snapshot in time. Although the largest mumps outbreak that occurred in Canada during this time was neither reported nor included in this survey, the survey did provide useful data with respect to epidemiology of mumps outbreaks, specifically the age groups affected, vaccination status and exposure settings.

These surveys provided data that are not currently collected through national routine surveillance of mumps. National surveillance collects data related to age, reporting province/territory but not public health responses. They also provided timely data for public health decision-makers to inform public health actions aimed at reducing the spread and consequently the impacts of the mumps virus within our communities.

The largest mumps outbreak that occurred in Canada during this time was neither reported nor included in this survey. However, the survey did provide useful epidemiological data in terms of age groups affected, vaccination status and exposure settings.

The timing since the last dose of vaccine and the link to the increase in mumps activity has been studied previously and findings have been used to support policy change in vaccination programs (12–14). Neither the routine Canadian national surveillance data nor the enhanced data collected through these surveys were able to address this specific issue. Additionally, information on disease severity of mumps was not explored.

Conclusion

The outbreaks reported between 2016 and 2018 affected most provinces across Canada. Results from the surveys indicated that sustained transmission of mumps occurred, even in populations that received one or more doses of mumps-containing vaccine. This highlights the importance of examining other factors contributing to the sustained high levels of activity, such as the waning of immunity over time, and evaluating various public health strategies aimed at reducing the spread of mumps among populations at risk.

Authors' statement

MS — Formal analysis, writing–original draft, writing–review & editing
SGS — Conception, design, and acquisition of data, drafting and revising of writing, critical review

Competing interests

No potential competing interests were disclosed.

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Fake news and science denier attacks on vaccines. What can you do?

Noni E MacDonald[1]*

Abstract

Misinformation and disinformation ("fake news") about vaccines are contagious—travelling faster and farther than truth. The consequences are serious; leading to negative impacts on health decisions, including vaccine acceptance, and on trust in immunization advice from public health and/or healthcare professional. This article provides a brief overview of evidence-based strategies to address vaccine deniers in public, in clinical practice and in social situations. As well, a strategy to help differentiate between vaccine deniers and simple vaccine refusers in a practice or clinic is provided. Five tactics are widely used by vaccine deniers: conspiracy; fake experts; selectivity; impossible expectations; and misrepresentation and false logic. Recognizing and understanding these tactics can help protect against misinformation and science denialism propaganda. Highlighting the strong medical science consensus on the safety and effectiveness of vaccines also helps. Carefully and wisely choosing what to say and speaking up—whether you are at a dinner party, out with friends or in your medical office or clinic—is crucial. Not speaking up implies you agree with the misinformation. Having healthcare providers recognize and address misinformation using evidence-based strategies is of growing importance as the arrival of the coronavirus disease 2019 (COVID-19) vaccines is expected to further ramp up the vaccine misinformation and disinformation rhetoric. Healthcare providers must prepare themselves and act now to combat the vaccine misinformation tsunami.

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Keywords: science denier, vaccine, misinformation, disinformation

Introduction

Never before has the public been so bombarded by information, nor has it ever been so difficult to know what and whom to believe. The critical importance of this problem is well illustrated by the World Health Organization (WHO) shining a bright light on the coronavirus disease 2019 (COVID-19) pandemic infodemic (1). Infodemic refers to a rapid and far-reaching spread of both accurate and inaccurate information. Misinformation (information that is false but not created with the intention of causing harm) and disinformation (or "fake news"; information that is false and deliberately created to cause harm) travel faster and farther than truth (2,3). Science deniers, including vaccine science deniers, have a strong and very effective platform now—the Web—from which to shill their scientifically-bankrupt wares (4). We, who understand the rigor of science and know the evidence supporting immunization for health and well-being, are often aghast at the falsehoods promulgated and—too often—accepted and acted upon by members of the public. For example, in the United States, the variation in human papillomavirus (HPV) vaccine uptake across the country is better explained by exposure to tweets about HPV than by socioeconomic class data (5).

Why does this happen?

Sadly, we all make most of our decisions based upon our beliefs and not upon carefully weighed scientific evidence (6). We see and hear what we believe, rather than believing what we see and hear (7). We are strongly influenced by what we think others around us (our social networks) are doing or expecting us to do. We see causation in coincidences and we prefer anecdote and stories to data and scientific evidence.

The objective of this article is to draw attention to the importance of fake news and science deniers' attacks on vaccines in the era of social media. It will describe tactics used by science deniers and highlight strategies healthcare providers can use in their office or clinic when they encounter a vaccine refuser or a science denier as well as providing the URL for a WHO website for report concerning misinformation found online.

This is the ninth article produced by the Canadian Vaccination Evidence Resource and Exchange Centre (CANVax) in the CANVax Briefs series. This centre includes a group of multidisciplinary professionals that identify and create useful resources to foster vaccine uptake (8).

What can you do?

What can you do in the face of this tsunami of misinformation and disinformation that is shaping negative beliefs about immunization amongst the general public, patients and even, occasionally, among our professional colleagues? Misinformation is indeed everybody's problem now (9). The consequences are serious, leading to negative impacts on health decisions, including vaccine acceptance, and on trust in immunization advice from public health and/or healthcare professional. This impact of misinformation and disinformation will become even more important when the COVID-19 vaccines arrive, with an expected further ramp up of vaccine disinformation (10). If counteractions are not taken, the antivaccine movement has the potential to overwhelm the pro-vaccine voices online (10). You can and should help combat this vaccine misinformation tsunami.

Prepare yourself: know and recognize tactics used by vaccine deniers

Know the five tactics used widely, often with great vigor, by vocal vaccine deniers on the Web, in mainstream media and in public appearances (11):

- Conspiracies—drug companies, the government, the health system—pick your scapegoat—are out to trick the general public; they withhold information, lie and cover up "the truth"
- Fake experts—quote or use fake experts and vigorously denigrate, even decry, real experts
- Selectivity—refer to obscure and or discredited papers that support their argument but omit the vast science that refute it
- Impossible expectations—vaccine must be 100% safe and effective—and yet no medical intervention is 100% safe and effective
- Misrepresentation and false logic—jump to erroneous conclusion and use false or illogical analogies

Interestingly, once you know these tactics they are easy to recognize, as is evidenced by the fake news complaints and the misinformation and disinformation appearing almost daily in the mainstream and social media.

Teach your patients to recognize tactics of science deniers

There are scientific studies that have shown that one way to protect the public against fake news and science deniers is to teach the public about the tactics used, not just correct the scientific misinformation being presented (12). If an internet site is the misinformation source, consider reporting it via the WHO website "*How to report misinformation online*" (13).

Highlight scientific consensus

Highlighting that there is scientific consensus on the benefits and value of immunization is also helpful (14) when reacting to fake news about vaccines and immunization. Share your sources of accurate and quality vaccine information with your patients. These steps will not convince the vocal vaccine denier but are helpful for those who are vaccine hesitant in your target audience—your patients and the general public.

Addressing vocal vaccine deniers in public

The Regional Office for Europe of WHO has developed effective guidance on how to address vocal vaccine deniers in public (15,16). This is not an easy task but is an important one to undertake if the vocal vaccine science denier is having, or has the potential to have, a significant negative impact on trust in immunization in your community.

The WHO guidance is primarily intended for spokespersons of health authorities who want to prepare themselves for a public event with a vocal vaccine denier, and provides advice on who should be the spokesperson, dos and don'ts of verbal and non-verbal communication, how to behave in a passionate discussion and how to protect yourself. It provides helpful and evidence-supported strategies if you should find yourself asked to speak in public.

An important point—do not participate in a public discussion if you are not media trained.

Strategies to address a vaccine science denier in clinical practice

Differentiating between a science denier and a simple refuser

The first and very important step is to determine if the patient not wanting to take the vaccine is a science denier or a "simple refuser". You may be able to quickly tease this out by asking: "What would it take to move you to a "yes" to accept this vaccine?" The simple refuser may pause, think and name the concern. This is even more likely if you have a good rapport and a trusting relationship with the patient. In contrast, you will get a very different reaction from the vaccine science denier. They most often start with a long list of concerns and want to work hard to persuade you to their viewpoint. Beware.

Strategies to use when addressing vaccine refusers

Vaccine refusers usually have one or possibly two main concerns. When addressing the concern, heed the following advice:

- Do not make the session a "knowledge dump" as overwhelming the refuser with information is rarely helpful and may actually end up raising concerns about which the refuser was not previously worried
- Do not spend time refuting myths, as this does not change attitudes to immunization (17); furthermore, it may be the myths that the refuser remembers and not the correct information
- Mini motivational interviewing is a more helpful strategy to further understand concerns and move the patient towards acceptance (18,19); WHO has a short conversation guide training module on this technique for immunization that you might find helpful (20)

Strategies to use when addressing science deniers

The term "vaccine denier" refers to a member of a subgroup at the extreme end of the hesitancy continuum; one who has a very negative attitude towards vaccination and is not open to a change of mind no matter what the scientific evidence says (11). There are several points to remember when addressing science deniers:

- Do not get into a debate with the denier; it is a time-wasting trap
- State that science is clearly behind immunization. Again, do this without getting into a debate: you are highly unlikely to convince the denier with your arguments and are likely to end up in a unhelpful "yes but" cycle
- You may try mini motivational interviewing as noted above. With strong vaccine science deniers, this is less likely to help than with simple refusers, but it is worth a try

Leave the door open

Regardless of whether the patient is a denier or a refuser, if they chose not to immunize their child or themselves that day, leave the door open for future visits and discussion. Do not dismiss them from your practice—even if that is tempting—as this is not in the best interests of the patient or the community (21). As well, it is clinically important to go over the risks and responsibilities if the patient chooses not to accept the vaccine(s). The Canadian Paediatric Society Caring for Kids website has advice on this that you can then retailor to fit your patient's situation (22).

Do not remain silent

Finally, remember do not remain silent when faced with a vaccine science denier, as your silence may be interpreted by the others around you that you are in agreement with the misinformation. Choose carefully and wisely what to say and speak up—whether it is to a co-worker or a patient or friend. The target audience is not the denier, but those others around you. Remember to educate others about disinformation techniques being used and help to inoculate against fake news and science denial.

Conclusion

In light of fake news about vaccines and science deniers' attacks on vaccines proliferating on both mainstream and social media (10), it is critical to learn how to differentiate the real science deniers from vaccine refusers, and how to identify the simple refusers, who were made unsure in their vaccine acceptance beliefs by the machinations of science deniers. Knowing and using appropriate strategies for both groups empowers healthcare providers to appropriately address situations in professional as well as personal settings.

Author's statement

NEM—Conceptualization, writing of original draft, reviewing and editing.

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How long are people with COVID-19 infectious?

Source: Emerging Sciences Group of the Public Health Agency of Canada. Emerging Evidence on COVID-19: Rapid Review of Infectious Period. September update. Full report available from: phac.emergingsciencesecretariat-secretariatdessciencesemergentes.aspc@canada.ca

Background: COVID-19 cases need to be isolated long enough to prevent further transmission but no longer than needed. Determining the infectious period of COVID-19 is complicated by four factors: 1) people can be diagnosed when they are symptomatic, pre-symptomatic or asymptomatic, 2) the common diagnostic test, RT-PCR, is accurate for diagnosis as it is able to detect viral genetic material, but it cannot document when someone is no longer infectious because it cannot distinguish whether viral particles are still infectious or not, 3) cell culture is the best way to confirm whether infectious virus is present, but it takes time and requires specialized laboratory facilities, and 4) although transmission is primarily respiratory, virus has been found in feces and eye secretions.

Methods: Twenty databases and key websites were searched for relevant reviews, peer-reviewed publications and preprints up to August 31, 2020. Keywords included: "Shedding", "Viral dynamics", "Viral clearance", "Viable", "Culture", "Infectivity", "SARS-CoV-2 detection", "Infectious Period", "Communicability period", "Recurrence", and "Re-positive". Data from studies were extracted into evidence tables on risk of infection, severity of disease and mortality and organized by asymptomatic, pre-symptomatic, symptomatic, recurrent or reinfection, as well as culture versus RT-PCR and sample source (e.g. respiratory, fecal, etc.).

Results: Over 1,000 citations were screened and relevant full texts were reviewed. There were some good quality prospective cohort studies, but the majority of publications were case reports and observational studies of contact tracing; many of these were preprints and are at high risk of bias. Due to their number and preliminary nature, not all case reports were summarized.

Symptomatic infectious period, N=107 studies

CULTURE (that measures viable virus): N=18 studies and two systematic reviews:

- Respiratory
  - Mild illness: Cultures from respiratory samples—taken from the time of self-reported symptom onset—have documented viral shedding for 8–10 days with a peak in viral load ranging from just before to during the first week after onset of illness.
  - Severe illness: Culture from respiratory samples have documented cases of prolonged viable viral shedding (18–32 days). These cases are typically individuals who are either immunocompromised or have multiple chronic underlying health conditions. These studies usually include single cases or small sample sizes and many are still in preprints.
  - Feces: SARS-CoV-2 has been cultured from the fecal/rectal samples of confirmed cases, however the length of viable virus shedding and whether it is a potential transmission route remains unclear.

RT-PCR (that measures viral RNA): N=88 studies and six systematic reviews:

- Nasopharyngeal swabs: Most studies show RT-PCR tests become negative within 14–20 days of self-reported symptom onset.
  - Prolonged viral RNA shedding (up to 83 days) have been reported. Multiple studies have found this is positively associated with severity of COVID-19 and older age. Once these cases have clinically recovered, cultures have not detected viable virus and there has been no evidence of transmission.
- Stool samples: Stool samples can remain positive a few days to four weeks longer than respiratory samples.
- Eye swabs: SARS-CoV-2 RNA has been identified in the eye up to 22 days post onset of self-reported symptoms.

Pre-symptomatic infectious period, N=25 studies

- CULTURE: Viable virus has been cultured from respiratory samples 1–6 days prior to symptom onset and from the rectum as early as three days before symptom onset.
- RT-PCR has detected COVID-19 virus RNA from respiratory samples 1–7 days (2.5 days on average) before symptom onset.

Asymptomatic infectious period, N=25 studies

- CULTURE and RT-PCR: Viable virus and viral RNA was highest during the first week of infection and declined in subsequent weeks. Based on the current evidence, the total infectious period of asymptomatic cases appears to be similar to, or shorter than, mildly symptomatic cases; viral loads have been similar.

Recurrent viral shedding in convalescent period, N=55 studies

- CULTURE and RT-PCR: Only one culture study found viable virus in a recurrent case. Multiple case reports and observational RT-PCR studies have detected recurrent viral RNA shedding in people who were asymptomatic in the convalescent period, typically within seven days of two consecutive negative RT-PCR results. Following recurrence, patients remained viral RNA positive for approximately 1–8 days, but no evidence of transmission was reported.

Reinfection, N=2 studies

- Two studies have been published with compelling evidence that reinfection can occur. In both cases genetic analysis confirmed the virus from the first and second infection were different. This appears to be rare.

Conclusion: Across studies, similar viral loads have been reported for asymptomatic, pre-symptomatic, and symptomatic cases. Mild cases are typically no longer infectious 10 days after diagnosis. More severe cases are generally infectious for at least 20 days; when these cases are no longer infectious can only be confirmed by viral culture.

COVID-19 and Ethnicity: What is the evidence?

Source: Emerging Sciences Group of the Public Health Agency of Canada. Evidence Brief on Ethnicity and COVID-19: Update #1. Full report available from: phac.emergingsciencesecretariat-secretariatdessciencesemergentes.aspc@canada.ca

Background: Multiple studies have found a disproportionate impact of COVID-19 on ethnic minorities, but whether this is due to confounding factors or represents an increased risk is not yet clear. To assess this, a review was done in May 2020 and then updated in September.

Methods: Twenty databases and key websites were searched for relevant reviews, peer-reviewed publications and preprints on COVID-19 where ethnicity was an objective of the study. Ecological studies were excluded except for Canada where all studies were included. Data from relevant studies were extracted into evidence tables on risk of infection, severity of disease and mortality, and the evidence was summarized.

Results: Between May to September 7, 2020, 34 new studies and one new systematic review were identified for a total of 73 studies and two reviews. There were few Canadian studies. A cross-sectional survey reported a higher likelihood of COVID-19 among Black Canadians who also reported a higher frequency of risk factors such as taking public transportation and having a job that required face-to-face interactions. No Canadian data on ethnicity and hospitalizations, severity or mortality were identified. An ecological study found that a 1% increase in the proportion of Black Canadians in a health unit was associated with double the case count and a 2.1-fold increase in COVID-19 death rates. Most of the international studies were from the United States (US) and United Kingdom (UK).

- **Risk of infection:** Twenty US studies found a higher risk of infection among Blacks and Hispanics compared with Whites. Fourteen UK studies also found a higher risk of infection among Black, South Asian and Asian compared with Whites. The systematic review that assessed risk of infection concluded Blacks, Asians and Hispanics were more likely to test positive for COVID-19 compared to Whites.
- **Hospitalization:** In the US studies, Blacks were found to have a higher risk of hospitalization; for Asians and Hispanics there were mixed results. In the UK, Blacks and South Asians had a higher risk of hospitalization compared with Whites; for Asians and those of mixed ethnicity, the findings were inconsistent. One systematic review found increased risk for Blacks (over all countries) and for Asians (UK only), but the adjusted analyses (age, sex and comorbidities) found no statistically significant association.
- **ICU admission:** The more recent US studies had conflicting results regarding the risk of ICU admissions for Blacks and Hispanics compared with Whites. The UK studies showed a higher risk of ICU admission for Blacks and South Asians. The systematic review found Asians were over-represented in the ICU in UK studies but in the meta-analysis of adjusted results for Blacks and Hispanics, there was no significant association.
- **Mechanical ventilation:** A few recent studies examined the risk of ventilation by ethnicity. A US study reported no association for Blacks and Hispanics. A UK study found Blacks and Asians were more likely to need ventilation compared to Whites. The systematic review found no association for Blacks and Hispanics, however a higher risk of ventilation for Asians (four studies) persisted in an age and sex-adjusted analysis.
- **Mortality:** Among hospitalized patients, there were no associations with ethnicity and mortality. However, in studies that looked at the whole population, there was high heterogeneity across studies regarding ethnicity and mortality. The systematic reviews reported no positive association between mortality and being Black or Asian.

There were three studies on ethnicity and Multisystem Inflammatory Syndrome in Children (MIS-C); all found a disproportionate number of MIS-C cases among non-White children.

Conclusion: The more recent large cohort studies have sufficient power to control for many confounding variables. Overall, it appears that Blacks, Asians and Hispanics may be at a higher risk of COVID-19 infection given that the confounding variables measured, such as socio-economic factors and co-morbidities, did not entirely account for this association.

National estimates of Hepatitis C incidence, prevalence and undiagnosed proportion

Source: National estimates of Hepatitis C (HCV) incidence and prevalence in Canada, 2017. People living with Hepatitis C in Canada, 2017. Public Health Agency of Canada. Government of Canada. 2020.

Hepatitis C (HCV) incidence and prevalence in Canada – Globally, viral hepatitis is one of the leading causes of death, accounting for 1.34 million deaths per year—more than HIV/AIDS, tuberculosis or malaria. HCV is not preventable by vaccine and despite the availability of effective treatment for hepatitis C, the healthcare burden in Canada associated with the complications of HCV is not decreasing. This infographic summarizes the estimates of national HCV incidence and prevalence in Canada. A more detailed report will be available in the coming months. Reporting on these measures supports the Government of Canada's commitment to the global goal of ending viral hepatitis, HIV/AIDS and other STBBI as public health threats by 2030.

For more information:

To access the National estimates of people living with hepatitis C Infographic: https://www.canada.ca/en/public-health/services/publications/diseases-conditions/infographic-people-living-with-hepatitis-c-2017.html

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