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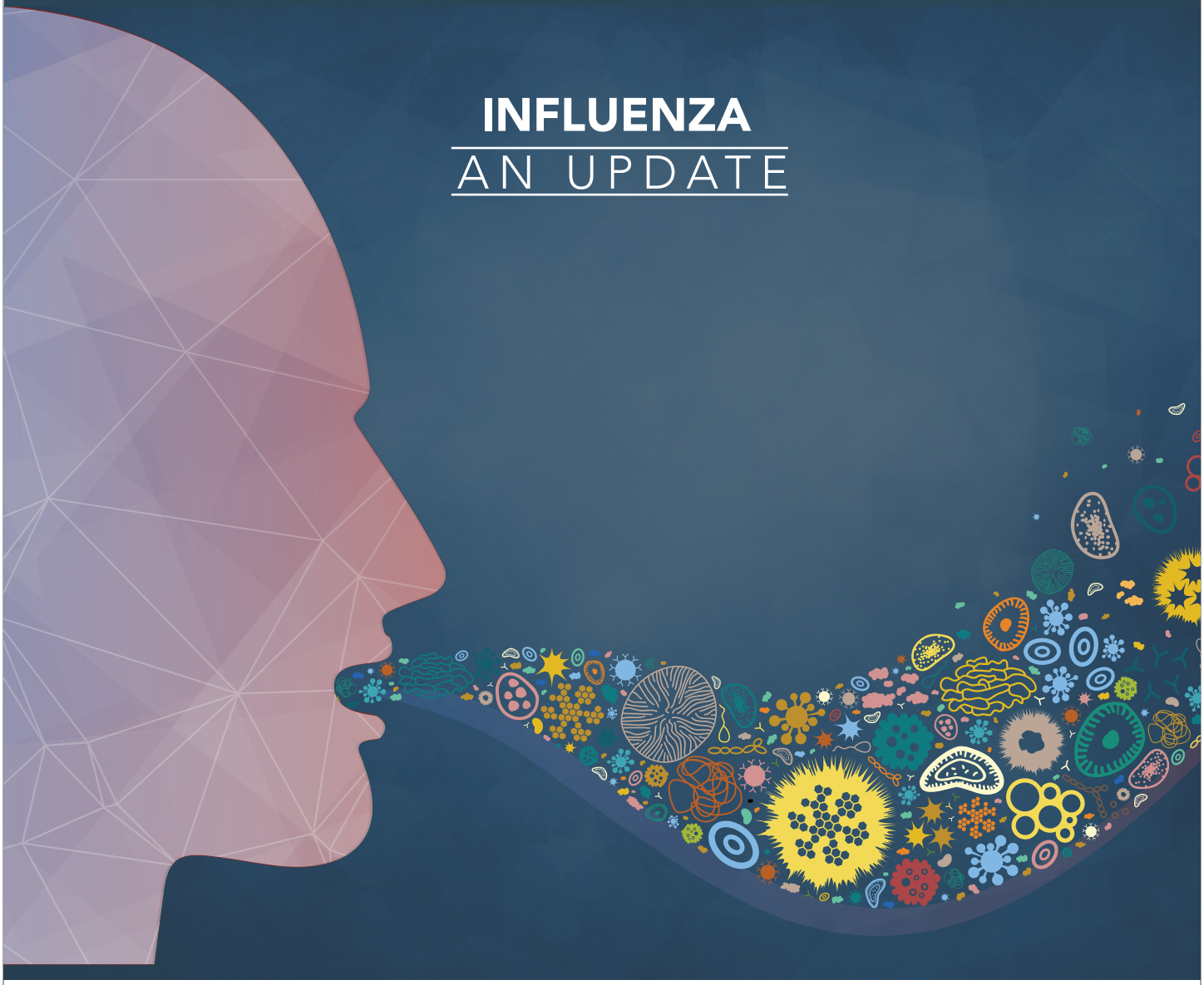
# INFLUENZA
## AN UPDATE





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The cover shows an artist's rendition of how influenza viruses can be shared from the mouth along with other microbes. This was based on a Shutterstock photo that was adapted by Lyal Saikaly. (https://www.shutterstock.com/image-vector/vector-illustration-bacteria-viruses-spreading-persons-764666002)

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CCDR
CANADA COMMUNICABLE DISEASE REPORT

# INFLUENZA: AN UPDATE

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# Summary of the NACI Seasonal Influenza Vaccine Statement for 2019–2020

L Zhao[1], K Young[1], I Gemmill[2,3] on behalf of the National Advisory Committee on Immunization (NACI)*

## Abstract

**Background:** Many different influenza vaccines are authorized for use in Canada and new evidence on influenza and vaccines is continually emerging. The National Advisory Committee on Immunization (NACI) provides annual recommendations regarding the use of seasonal influenza vaccines to the Public Health Agency of Canada (PHAC) for the upcoming influenza season.

**Objective:** To summarize NACI recommendations regarding the use of seasonal influenza vaccines for the 2019–2020 influenza season, including conclusions from reviews of evidence on 1) a new split virus quadrivalent inactivated influenza vaccine and 2) the comparative effectiveness and immunogenicity of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older.

**Methods:** For both topics, the NACI Influenza Working Group developed a predefined search strategy to identify all eligible studies, assessed their quality, summarized and analyzed the findings and, according to the NACI evidence-based process, proposed recommendations and identified the grade of evidence that supported them. In light of the evidence, the recommendations were then considered and approved by NACI.

**Results:** NACI concluded that the new split virus quadrivalent inactivated influenza vaccine has a safety and immunogenicity profile comparable to the quadrivalent inactivated influenza vaccines already authorized for adults and children 5 years of age and older (Grade B Evidence). Therefore, NACI recommended that this new vaccine may be considered among the quadrivalent inactivated influenza vaccines offered to adults and children five years of age and older (Discretionary NACI Recommendation). However, NACI concluded that the evidence is not sufficient (Grade I Evidence) to support specific recommendations on the differential use of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older.

**Conclusion:** NACI continues to recommend that an age-appropriate influenza vaccine should be offered annually to anyone six months of age and older who does not have contraindications to the vaccine, with focus on the groups for whom influenza vaccination is particularly recommended. This includes people at high risk of influenza-related complications or hospitalization, people capable of transmitting influenza to those at high risk, people who provide essential community services and people in direct contact with poultry infected with avian influenza during culling operations.

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



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# Introduction

Influenza, together with pneumonia, ranks among the top 10 leading causes of death in Canada (1). Although the burden of influenza can vary from year to year, it is estimated that there are an average of approximately 12,200 hospitalizations (2) and 3,500 deaths (3) related to influenza per year.

The National Advisory Committee on Immunization (NACI) provides annual recommendations regarding seasonal influenza vaccines to the Public Health Agency of Canada (PHAC). For the 2019–2020 influenza season, NACI updated the abbreviations it uses for the different types of influenza vaccines available in Canada. NACI also reviewed evidence from two literature reviews: one on studies relevant to a new split virus quadrivalent inactivated influenza vaccine (Afluria® Tetra, Seqirus) and one on the comparative effectiveness and immunogenicity of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older. Complete details can be found in the *Statement on Seasonal Influenza Vaccine for 2019–2020* (4) and related publications.

The objective of this article is to summarize this annual seasonal influenza statement.

## Updated influenza vaccine abbreviations

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

# Methods

To prepare the *Statement on Seasonal Influenza Vaccine for 2019–2020*, the Influenza Working Group identified two literature reviews and, following review and analysis of the information, proposed recommendations according to the NACI evidence-based process (5). NACI critically appraised the available evidence and approved the specific recommendations brought forward.

## Use of Afluria Tetra influenza vaccine

The Influenza Working Group conducted a systematic review to inform the development of the NACI guidance on the use of Afluria Tetra in Canada. Five electronic databases (MEDLINE, Embase, Scopus, ProQuest Public Health Database and ClinicalTrials.gov) were searched from inception to

**Table 1: New National Advisory Committee on Immunization (NACI) abbreviations for influenza vaccines**

| Influenza vaccine category | Formulation | Type | New NACI abbreviation[a] | Former NACI abbreviation |
|---|---|---|---|---|
| Inactivated influenza vaccine | - | - | IIV | IIV |
| | Trivalent | - | IIV3 | TIV |
| | | Standard dose[b], unadjuvanted, IM administered | IIV3-SD | Standard-dose TIV |
| | | Adjuvanted[c], IM administered | IIV3-Adj | ATIV or adjuvanted TIV |
| | | High dose[d], unadjuvanted, IM administered | IIV3-HD | High-dose TIV |
| | Quadrivalent | - | IIV4 | QIV |
| | | Standard dose[b], unadjuvanted, IM administered | IIV4-SD | Standard-dose QIV |
| Live attenuated influenza vaccine | - | - | LAIV | LAIV |
| | Trivalent | Nasal spray | LAIV3 | Trivalent LAIV |
| | Quadrivalent | Nasal spray | LAIV4 | Quadrivalent LAIV |

Abbreviations: IIV, inactivated influenza vaccine; IIV3, trivalent inactivated influenza vaccine; IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4, quadrivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; IM, intramuscular; LAIV, live attenuated influenza vaccine; LAIV3, trivalent live attenuated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; QIV, quadrivalent inactivated influenza vaccine; TIV, trivalent inactivated influenza vaccine; -, not applicable

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

[b] 15 µg HA per strain

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

[d] 60 µg HA per strain

August 22, 2017 to identify relevant literature on the efficacy, effectiveness, immunogenicity and safety of Afluria Tetra or the trivalent Afluria (1.5% sodium taurodeoxycholate [TDOC]) in adults and children aged six months and older. The use of 1.5% TDOC as a splitting agent was incorporated in the manufacturing process for Afluria and for the new Afluria Tetra after a safety signal in the 2010 Southern Hemisphere influenza season in Australia showed that Afluria made with less than 1.5% of TDOC was associated with an increased rate of fever and febrile seizures in children less than five years of age (6). Two reviewers independently screened the titles and abstracts of records retrieved from the search and eligible full-text articles for inclusion. Two reviewers extracted data from eligible studies and appraised the methodological quality of these studies using the criteria outlined by Harris et al. (7). A narrative synthesis of the extracted data was performed.

### Comparative effectiveness and immunogenicity of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older

A rapid review was performed to inform NACI on potentially important differences between subunit and split virus inactivated influenza vaccines in older adults. Three electronic databases (MEDLINE, Embase and ClinicalTrials.gov) were searched to identify relevant literature published between January 1, 2007 and October 13, 2017 on the effectiveness and immunogenicity of subunit and split virus inactivated influenza vaccines (unadjuvanted, standard dose) in adults 65 years of age and older. A manual search of the reference lists of included articles was performed because of the small number of records retrieved in the initial database search. A single reviewer screened the retrieved records and performed data extraction and quality appraisal of eligible studies. A narrative synthesis of the extracted data was performed.

## Results

### Use of Afluria Tetra influenza vaccine

Based upon a review of two randomized controlled trials of Afluria Tetra and two of Afluria (1.5% TDOC), NACI concluded that Afluria Tetra is safe and has immunogenicity non-inferior to comparable vaccines in adults and children five years of age and older. No direct evidence on the efficacy or effectiveness of Afluria Tetra was available. Furthermore, no evidence for any outcome was available on the use of Afluria Tetra for children less than five years of age, and Afluria Tetra is not authorized for use in this age group in Canada. Fever and febrile seizure were not identified as concerns for both Afluria Tetra and Afluria (1.5% TDOC) in two studies looking at children five years of age and older.

**NACI recommends that Afluria Tetra may be considered among the quadrivalent inactivated influenza vaccines offered to adults and children five years of age and older (Discretionary NACI Recommendation, Grade B Evidence).**

Complete details of the findings of literature review, and rationale and relevant considerations for the recommendation, can be found in the NACI *Supplemental Statement on Afluria Tetra* (6).

### Comparative effectiveness and immunogenicity of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older

Eight studies that assessed either vaccine effectiveness or immunogenicity of subunit compared with split virus inactivated influenza vaccines were identified. These studies did not show statistically significant differences in vaccine effectiveness or immunogenicity. Furthermore, the quality of the included studies was a concern. Based upon a review of these studies, NACI concluded that the evidence is not sufficient (Grade I Evidence) to support specific recommendations on the differential use of subunit and split virus inactivated influenza vaccines in adults 65 years of age and older.

The detailed findings of this review can be found in the *NACI Literature Review on the Comparative Effectiveness and Immunogenicity of Subunit and Split Virus Inactivated Influenza Vaccines in Adults 65 Years of Age and Older* (8).

### Summary of NACI recommendations for the use of influenza vaccines for the 2019–2020 influenza season

NACI continues to recommend influenza vaccination to anyone six months and older who does not have contraindications to the vaccine. Vaccination should be offered as a priority to people at high risk of influenza-related complications or hospitalization, people capable of transmitting influenza to those at high risk of complications, and others as indicated in **Table 2**.

Recommended influenza vaccine options by age group and by dosage and route of administration by age are summarized in **Tables 3** and **4**, respectively.

**Table 2: Groups for whom influenza vaccination is particularly recommended** (4)

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

- All pregnant women[a]
- Adults and children with the following chronic health conditions:
  - cardiac or pulmonary disorders (includes bronchopulmonary dysplasia, cystic fibrosis, and asthma)
  - diabetes mellitus and other metabolic diseases
  - cancer, immune compromising conditions (due to underlying disease, therapy or both)
  - renal disease
  - anemia or hemoglobinopathy
  - neurologic or neurodevelopmental conditions (includes neuromuscular, neurovascular, neurodegenerative and neurodevelopmental conditions and seizure disorders [for children, includes febrile seizures and isolated developmental delay], but excludes migraines and psychiatric conditions without neurological conditions)
  - morbid obesity (body mass index [BMI] of 40 and over)
  - children 6 months to 18 years of age undergoing treatment for long periods with acetylsalicylic acid, because of the potential increase of Reye's syndrome associated with influenza
- People of any age who are residents of nursing homes and other chronic care facilities
- Adults 65 years of age and older
- All children 6–59 months of age
- Indigenous peoples

People capable of transmitting influenza to those at high risk:

- Health care and other care providers in facilities and community settings who, through their activities, are capable of transmitting influenza to those at high risk
- Household contacts, both adults and children, of individuals at high risk, whether or not the individual at high risk has been vaccinated:
  - household contacts of individuals at high risk
  - household contacts of infants less than six months of age, as these infants are at high risk but cannot receive influenza vaccine
  - members of a household expecting a newborn during the influenza season
- Those providing regular child care to children 6–59 months of age, whether in or out of the home
- Those who provide services within closed or relatively closed settings to people at high risk (e.g. crew on a ship)

Others:

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

[a] The risk of influenza-related hospitalization increases with length of gestation (i.e. it is higher in the third than in the second trimester)

**Table 3: Recommendations on choice of influenza vaccine type for individual-level decision making[a] by age group** (4)

| Recipient by age group | Vaccine types available for use | Recommendations on choice of influenza vaccine |
|---|---|---|
| 6–23 months | • IIV3-SD<br>• IIV3-Adj<br>• IIV4-SD | • Quadrivalent influenza vaccine should be used, given the burden of influenza B disease in this age group and the potential for lineage mismatch between the predominant circulating strain of influenza B and the strain in a trivalent vaccine<br>• If a quadrivalent vaccine is not available, any of the available trivalent vaccines should be used |
| 2–17 years | • IIV3-SD<br>• IIV4-SD<br>• LAIV4 | • Either IIV4-SD or LAIV4 should be used for children without contraindications, including those with non-immune compromising chronic health conditions, given the burden of influenza B disease in this age group and the potential for lineage mismatch between the predominant circulating strain of influenza B and the strain in a trivalent vaccine<br>• If IIV4-SD or LAIV4 is not available, IIV3-SD should be used<br>• IIV4-SD should be used for children for whom LAIV is contraindicated, such as in children with:<br>- severe asthma<br>- medically attended wheezing in the seven days prior to vaccination<br>- current receipt of Aspirin or Aspirin-containing therapy<br>- immune compromising conditions<br>• LAIV4 may be given to children with:<br>- stable, non-severe asthma<br>- cystic fibrosis who are not being treated with immunosuppressive drugs (e.g. prolonged systemic corticosteroids) |
| 18–59 years | • IIV3-SD<br>• IIV4-SD<br>• LAIV4 | • Any of the available influenza vaccines should be used in adults without contraindications<br>• IIV should be used for adults for whom LAIV is contraindicated, such as in:<br>- pregnant women<br>- adults with any of the chronic health conditions identified in Table 2, including immune compromising conditions<br>- HCWs |
| 60–64 years | • IIV3-SD<br>• IIV4-SD | • Any of the available influenza vaccines should be used |
| 65 years and older[b] | • IIV3-SD<br>• IIV3-Adj<br>• IIV3-HD<br>• IIV4-SD | • When available, IIV3-HD should be used over IIV3-SD, given the burden of influenza A (H3N2) disease and the evidence for better efficacy compared with IIV3-SD in this age group<br>• There is insufficient evidence to make comparative individual-level recommendations on the use of IIV3-Adj or IIV4-SD over IIV3-SD or between IIV3-Adj, IIV3-HD and IIV4-SD |

Abbreviations: HCW, health care worker; IIV, inactivated influenza vaccine; IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine

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

[b] The recommendations on influenza vaccine for individuals 65 years of age and older presented here are for individual-level decision making. For public health program–level decision making (i.e. provinces/territories making decisions for publicly funded immunization programs), NACI recommends that any of the available influenza vaccines be used, as there is insufficient evidence (cost-effectiveness assessments have not been performed) to make comparative public health program–level recommendations on the use of the available vaccines

**Table 4: Recommended dose and route of administration, by age, for influenza vaccine types available for the 2019–2020 influenza season** (4)

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

Abbreviations: IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; - , not applicable

[a] Agriflu (six months and older), Fluviral (six months and older), Influvac (three years and older)

[b] Afluria Tetra (five years and older), Flulaval Tetra (six months and older), Fluzone Quadrivalent (six months and older)

[c] Fluad Pediatric (6–23 months) or Fluad (65 years and older)

[d] Fluzone High-Dose (65 years and older)

[e] FluMist Quadrivalent (2–59 years)

[f] Evidence suggests moderate improvement in antibody response in infants, without an increase in reactogenicity, with the use of full vaccine doses (0.5 mL) for unadjuvanted inactivated influenza vaccines (9,10). This moderate improvement in antibody response without an increase in reactogenicity is the basis for the full dose recommendation for unadjuvanted inactivated vaccine for all ages. For more information, refer to *Statement on Seasonal Influenza Vaccine for 2011–2012* (11)

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

## Conclusion

NACI continues to recommend annual influenza vaccination for all individuals aged six months and older (noting product-specific age indications and contraindications), with particular focus on people at high risk of influenza-related complications or hospitalization. This includes all pregnant women; people capable of transmitting influenza to those at high risk; people who provide essential community services; and people in direct contact during culling operations with poultry infected with avian influenza. For the 2019–2020 influenza season, NACI recommends that the new Afluria Tetra influenza vaccine may be considered among the quadrivalent inactivated influenza vaccines offered to adults and children five years of age and older. NACI concluded that there is insufficient evidence at this time to support specific recommendations on the differential use of subunit and split virus inactivated influenza vaccines in adults 65 years and older.

## Authors' statement

LZ — Writing – original draft, writing – review and editing
KY — Writing – original draft, writing – review and editing
IG — Writing – original draft, writing – review and editing

The NACI *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2019–2020* was prepared by L Zhao, K Young, R Stirling and I Gemmill and approved by NACI.

## Conflict of interest

None.

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# Should individuals use influenza vaccine effectiveness studies to inform their decision to get vaccinated?

L Zhao[1], R Stirling[1], K Young[1]*

## Abstract

Studies on the effectiveness of seasonal influenza vaccine can affect an individual's perception of the ability of this vaccine to protect against influenza. However, vaccine effectiveness studies are designed to inform public health decisions rather than for individual decision-making. This overview explains what vaccine effectiveness means and why vaccine effectiveness estimates can vary. Individual variation in the response to seasonal influenza vaccine is based upon risk factors such as age, underlying health conditions, immune status and risk of infection and complications. Therefore, an individual's decision to get vaccinated should be primarily informed by their risk of influenza illness and their risk of transmitting influenza to vulnerable people.

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## Introduction

Influenza is a vaccine-preventable disease that causes significant morbidity and mortality every year. Annual influenza epidemics in Canada result in approximately 12,200 hospitalizations (1) and 3,500 deaths (2). To reduce this burden of illness, Canada's National Advisory Committee on Immunization (NACI) recommends influenza vaccination every year for everyone six months and older who does not have contraindications to the vaccine, especially those at high risk of complications of influenza (3).

Influenza viruses continually undergo genetic changes. Influenza vaccines are reformulated annually, but due to a lag between when the vaccine strains are decided on and when the vaccine becomes available on the market, antigens within the vaccine may no longer provide the desired protection against the viruses circulating in the community. Because these factors can affect the antigenic match between the vaccine and circulating influenza strains, influenza surveillance networks monitor how well the influenza vaccine is working during the current season each year.

In Canada and elsewhere, surveillance networks typically calculate their jurisdiction's estimates of influenza vaccine effectiveness twice in a season – in the middle and again at end of the season. While routine annual estimation of vaccine effectiveness is a valuable public health tool, it does not directly translate into how well the vaccine may protect an individual against influenza. Nevertheless, an individual's awareness of the effectiveness of the influenza vaccine in a given season can affect their perception of the protection offered by the vaccine and their decision to get vaccinated (4).

Therefore, someone considering influenza vaccination may ask, "Will the vaccine protect me from getting influenza?" To help answer this question, this article provides a brief explanation of what vaccine effectiveness means as a measure of influenza vaccine performance and how it relates to individual-level decisions to vaccinate.

## Efficacy versus effectiveness

Two distinct terms describe how well a vaccine performs: vaccine efficacy and vaccine effectiveness. These terms are often used interchangeably although what they each refer to is quite different. Both efficacy and effectiveness describe how well the vaccine works at protecting against influenza infection and resulting complications (e.g. hospitalization). Vaccine efficacy studies are conducted under optimal conditions, such as a highly controlled clinical trial. Vaccine effectiveness studies, the focus of this article, are conducted under "real world" conditions, such as in outpatient settings (e.g. a primary care clinic).

## What does influenza vaccine effectiveness mean?

Influenza vaccine effectiveness is the relative benefit of vaccination in preventing influenza cases compared to no vaccination. In other words, influenza vaccine effectiveness equals the percentage of cases of influenza that could be prevented in a vaccinated group compared with an unvaccinated group. How the vaccine effectiveness estimate was generated, which takes into account the influenza strain and measured clinical outcome, is important in the interpretation of the estimate. When the Canadian Sentinel Practitioner Surveillance Network (SPSN) reported that the influenza vaccine had a vaccine effectiveness of 72% against influenza A(H1N1)pdm09 for the 2018–2019 season among individuals presenting to outpatient clinics with influenza-like illness, it means that the vaccinated individuals in the study were 72% less likely to be infected with medically attended influenza A(H1N1)pdm09 illness than unvaccinated individuals (5).

It is also important to note that a vaccine effectiveness of 72% does not mean that a vaccinated individual has a 72% chance of not getting the clinical outcome measured in the study. Rather, it is the vaccinated group that is 72% less likely to get the outcome. To put this in discrete numbers, one needs to know that about 10% of unvaccinated adults are infected with influenza each season (6). This means that out of a group of 100 unvaccinated adults, 10 would become infected. If an influenza vaccine has a vaccine effectiveness of 72%, out of 100 vaccinated adults only three adults, rather than 10, would become infected. In this scenario, the vaccine would prevent seven out of 10 (or approximately 72%) adults from being infected.

In scientific reporting, vaccine effectiveness estimates are often reported as adjusted values. This means that the estimate accounts for potential confounding factors such as age group, sex, race/ethnicity, study site and time from illness onset to study enrolment. Vaccine effectiveness estimates come with a confidence interval that provides information about the certainty of the estimate. Generally, the narrower the confidence interval, the more likely that the estimate is similar to the true vaccine effectiveness. If the confidence interval includes zero, the vaccine may provide no additional protection compared to no vaccination for that outcome, despite the vaccine effectiveness estimate being greater than zero.

## Why do vaccine effectiveness estimates vary?

No single vaccine effectiveness estimate can sum up how well influenza vaccines work, even within a given influenza season, as each study's vaccine effectiveness estimate is specific to the conditions of that study. The vaccine effectiveness will vary depending on a multitude of factors, including how closely related the vaccine virus strains are to the circulating viruses in a given influenza season, the population studied, when and where the study was conducted and differences in the methodology of studies assessing vaccine effectiveness (e.g. study design, sample size, influenza vaccines used, outcomes measured).

An example of the heterogeneity of vaccine effectiveness estimates is the SPSN's seasonal influenza vaccine effectiveness point estimates from 2004–2005 to 2018–2019. These ranged widely, from 9% to 93%, against any type of influenza. They were similarly wide ranging for specific influenza strains (7).

## Should vaccine effectiveness estimates inform individual decision-making?

Influenza vaccine effectiveness studies are designed to estimate the relative benefits of influenza vaccination at a population level, not at an individual level. Population-level vaccine effectiveness estimates represent the protection offered by the vaccine in a study population of differing ages, underlying health conditions, influenza vaccines used and influenza viruses causing infection.

An individual's risk of influenza depends not only on how well the influenza vaccine works, as estimated by vaccine effectiveness studies, but also by the individual's risk of being exposed to influenza, their susceptibility to infection and their risk of complications from influenza. How well an individual responds to the vaccine depends on their age, underlying health conditions and immune system status. Therefore, the utility of vaccine effectiveness estimates best serves to inform public health policy decisions, such as signalling use of adjunct protective measures including antiviral drugs in a potentially low vaccine effectiveness season (8), and guide vaccine virus strain selection for the future seasons (9).

An individual deciding whether to get vaccinated should consider their risk of influenza-related complications. Pregnant women, children and adults with chronic health conditions, young children 6–59 months old, adults 65 years and older, people residing in nursing homes and other chronic care facilities and Indigenous peoples are at high risk of influenza-related complications and hospitalization. Individuals should also consider their capability of transmitting influenza to those at high risk, for example, care providers of those at high risk of influenza-related complications or hospitalization and their occupation, such as those who provide essential community services or who are in direct contact with poultry infected with avian influenza during culling operations. Further details on groups who are at increased risk of influenza-related complications and groups who can transmit influenza to those at high risk are detailed in the *NACI Statement on Seasonal Influenza Vaccine for 2019–2020* (3).

## Conclusion

Influenza vaccine effectiveness monitoring is an important population-level public health tool, but the findings are not designed to drive an individual's decision whether to get vaccinated. An individual's decision to get vaccinated should be primarily informed by their risk of influenza complications as well as their risk of transmitting influenza virus to vulnerable individuals (3).

## Authors' statement

LZ — Conceptualization, writing – original draft, writing – review and editing
RS — Conceptualization, writing – review and editing
KY — Conceptualization, writing – review and editing

## Conflict of interest

None.

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# Canadian pandemic influenza preparedness: Public health measures strategy

B Henry[1] on behalf of the Canadian Pandemic Influenza Preparedness Task Group

## Abstract

Public health measures, also known as non-pharmaceutical interventions, are basic actions aimed at slowing the community spread of a communicable disease outbreak. In the event of an influenza pandemic, public health measures and antiviral drugs are the only tools available to mitigate the effects of the pandemic during the months before a vaccine becomes available. The *Canadian Pandemic Influenza Preparedness*: *Planning Guidance for the Health Sector* (CPIP) outlines how federal, provincial and territorial governments will work together to ensure a coordinated and consistent health sector approach to pandemic influenza preparedness and response.

This article summarizes Canada's pandemic public health measures strategy, as described in the recently updated CPIP Public Health Measures Annex. The strategy builds on lessons learned during the 2009 H1N1 pandemic. Key elements of the public health measures strategy include individual measures (e.g. hand hygiene, self-isolation when ill), community-based measures (e.g. school closures, cancellation of mass gatherings), management of cases and close contacts, travel and border-related actions and public education. Factors that influence the effectiveness of public health measures in a pandemic include the pandemic epidemiology, timing of implementation, how the measures are used (i.e. alone or in combination), their scalability and flexibility and public compliance. The CPIP is an evergreen guidance document and the Annex will be updated as new information warrants.



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## Introduction

Canada has a multifaceted approach to pandemic influenza preparedness and response that includes the use of public health measures. These measures are the primary non-pharmaceutical means to slow the rate of viral transmission. They are implemented at the beginning of a pandemic before a vaccine becomes available. Public health measures include individual protective measures (e.g. hand hygiene, self-isolation when ill) and community measures (e.g. school closures, cancellation of mass gatherings) to international border and travel-related actions (e.g. entry and departure screening).

The 2009 H1N1 influenza pandemic provided the opportunity for the first real test of Canada's pandemic planning efforts and provided many valuable lessons for future pandemic planning and response. It reinforced that public health measures are an effective and important element of a pandemic response. In addition, there were many valuable lessons to do with planning and implementing public health measures, for example, the importance of implementing measures early in the pandemic in a targeted and layered manner, and providing the public with clear and consistent messaging to support compliance with recommended measures.

The renewed approach to the use of public health measures in an influenza pandemic is described in the Public Health Measures Annex of the *Canadian Pandemic Influenza Preparedness: Planning Guidance for the Health Sector* (1,2). The Public Health Measures Annex provides technical advice for federal/provincial/territorial ministries of health and other government departments that have roles in providing health care services to specific populations, such as some Indigenous communities and military personnel. It underscores the importance of all

levels of government working together to help ensure the public's understanding and adoption of measures. The Annex outlines the specific roles and responsibilities of those involved in selecting and implementing individual and community-level measures aimed at preventing, controlling and mitigating pandemic influenza. The Annex is meant to facilitate a common approach to public health measures across jurisdictions (2).

The Canadian Pandemic Influenza Preparedness (CPIP) Task Group updated the Annex to incorporate the experience gained during the 2009 H1N1 influenza pandemic and to reflect Canada's pandemic goals, as outlined in the CPIP: "First, to minimize serious illness and overall deaths, and second, to minimize societal disruption" (2). The CPIP is an evergreen guidance document and the Annex will be updated as new information warrants. The Annex should be read in conjunction with the main body and the other technical annexes of the CPIP as they are intended to be used together.

This article summarizes Canada's pandemic public health measures strategy, as described in the recently updated CPIP Public Health Measures Annex (2). It is part of a series outlining Canada's approach to pandemic influenza preparedness published in the *Canada Communicable Disease Report* (3–8).

## Objectives of Canada's pandemic public health measures strategy

The objectives of the public health measures strategy are to support Canada's pandemic goals by:

- Reducing the overall transmission and slowing the rate of transmission of the novel or pandemic virus, thus lowering the number of severely ill cases and deaths and dispersing the accumulation of cases over time
- Reducing the peak demands on health care institutions to protect against both societal disruption and overwhelming of community services, and to buy time until a vaccine is available

### Canadian context

During an influenza pandemic, collaboration by all levels of government on the approach to selection and use of public health measures is crucial to the success of the response. In Canada, provinces, territories and local public health have the authority to implement public health measures within their jurisdictions. The federal government is responsible for international border and travel-related measures, as well as recommending public health measures for specific populations who are beneficiaries of federal health programs and services, such as some Indigenous communities and correctional facility inmates.

Canada is diverse in terms of language, religious beliefs, ethnicity, culture and lifestyle. In some cases, the needs of the population are not fully addressed by existing services. The CPIP highlights the need for health planners to tailor approaches for individuals who are unable to access and use standard resources and whose circumstances can influence their vulnerability in an influenza pandemic (e.g. persons who have physical or mental disabilities, low literacy skills, a limited understanding of English or French or income insecurity).

It is also important to tailor approaches to the circumstances (e.g. social, environmental, economic, access to health care) of individuals living in remote and isolated communities in pandemic planning. The Annex identifies the unique challenges faced by some of these communities (e.g. limited access to non-medical supplies such as soap, food, household items) and potential strategies for implementing public health measures in these communities (e.g. increasing individual and community awareness and the need to have surge capacity of these basic supplies).

### Key elements of the public health measures strategy

Public health measures are the most basic actions that can be taken to reduce community transmission of a pandemic influenza virus. The measures used in an influenza pandemic are based on existing practices for respiratory infectious disease, modified and intensified based on the epidemiology of the virus. During a pandemic, public health measures are implemented by many people in a variety of settings; therefore, the context in which they are used is important.

The CPIP identifies triggers for action, such as the use of public health measures, based on the level of pandemic virus activity in Canada. It is expected that the selection and timing of public health measures will vary across jurisdictions, as pandemic virus activity will vary across Canada, in terms of the timing and intensity of pandemic waves.

Factors that influence the effectiveness of public health measures in a pandemic response include the pandemic epidemiology (e.g. virus characteristics), timing of implementation, the approach to their use (i.e. alone or in combination) and public compliance. Measures need to be scalable, flexible and proportional to the pandemic threat to optimize their effectiveness.

### Individual measures

During a pandemic, personal protective measures protect individuals, their families and their communities. These measures are at the core of good public health practice for influenza and other respiratory illnesses, and are routinely recommended. Most of these measures are applicable to any pandemic scenario, irrespective of expected impact (ranging from low to high) based on the level of virus transmissibility and clinical severity.

Individual measures include:

- Hand hygiene (i.e. hand washing or hand antisepsis)
- Respiratory etiquette (i.e. covering sneezes and coughs)
- Cleaning and disinfecting of commonly used surfaces in the living environment
- The use of surgical masks by individuals with influenza
- Voluntary self-isolation (i.e. the sick person isolates themselves from other people from the time that influenza symptoms are recognized and for at least 24 hours after symptoms resolve)
- Voluntary home quarantine (i.e. the exposed person stays at home from the time of their initial exposure for up to three days after their last exposure)

Self-isolation and home quarantine can have unintended secondary consequences, for example, intolerance of employers regarding absences and loss of income if paid leave is not available. The Annex proposes possible strategies for addressing these challenges.

## Community-based measures

Community-based measures are disease control strategies aimed at reducing and slowing the transmission of influenza in communities. Decisions about implementing these measures will likely be made at the level of the local public health authority with coordination at the provincial/territorial or regional levels to ensure a consistent approach. The use of community-based measures will depend on the pandemic impact scenario as well as the local context. Community-based measures include:

- Environmental cleaning of public spaces in keeping with usual pre-pandemic practices (e.g. cleaning products used, surfaces cleaned)
- Social distancing measures that limit the frequency and duration of close contact among individuals of all ages in settings where people congregate, such as workplaces, daycares, schools, shelters, spiritual or cultural settings and mass gathering venues (e.g. concerts, sporting events)

Social distancing measures may have unintended secondary consequences for individuals, families and communities, such as loss of income, an elevated need for support services and potentially reduced availability of certain services. During a lower-impact pandemic scenario, the infection control benefits of implementing some community measures (e.g. proactive school closures) may not be offset by the cost and societal disruption caused by these measures. Hence, such measures are likely to be implemented only during a higher-impact pandemic scenario or in certain situations in some communities.

## Travel and border-related measures

The response to an emerging influenza pandemic includes the use of public health measures targeted to international travellers arriving in or departing from Canada. Such measures are based on existing federal programs and procedures. These include providing education, issuing travel health advisories and administering the *Quarantine Act* (9) at all international points of entry (e.g. implementing control measures with arriving or departing international travellers or conveyances). At the time of a pandemic, many factors will inform decisions about border measures, including the characteristics of the virus (e.g. transmissibility, virulence, risk factors), evidence of the effectiveness of the measures and the risk to the traveller and the public.

In accordance with the *Quarantine Act* (9), all ill travellers are subject to entry and departure screening at Canada's borders. Currently, identifying cases of novel or pandemic influenza at points of entry is difficult owing to the similarity of influenza symptoms to various other respiratory viruses. Departure screening is more effective than entry screening at decreasing influenza transmission because it reduces the number of ill travellers boarding conveyances.

## Case and contact management measures

When a novel or pandemic influenza virus is first detected in Canada or elsewhere, public health activities that aim to prevent or limiting the spread of the virus in Canada are triggered. Some circumstances may warrant public health management of cases of novel influenza and their close contacts (e.g. monitoring of health, providing advice on when to seek care).

Case and contact management by public health authorities are likely to be implemented most aggressively in the early stages of a pandemic, before transmission is sustained, in an effort to contain or delay the spread of the virus. If virus transmission is sustained, management activities will shift from individual management to public education in order to reinforce individual and community measures.

## Public education

During an influenza pandemic, public demand for information is expected to be extremely high and sustained as the illness spreads across Canada and into local communities. In the early stages of a pandemic, before a vaccine is available, public health measures are the primary means to slow transmission. Timely public education campaigns, grounded in a risk communications approach, are critical to promoting and supporting the implementation and adoption of measures at the individual and community levels. The strategies, interventions and products developed for seasonal influenza campaigns can be used as the building blocks for pandemic-related education campaigns. Communications will need to be tailored to reach individuals whose needs are not addressed by standard services or who are not able to access resources, which may increase their vulnerability in a pandemic.

## Risk management approach

Canada's pandemic public health measures strategy is subject to numerous risks, including the possibility of unintended secondary consequences of measures and uncertainty of adequate public

uptake of such measures. The Annex incorporates the CPIP risk management approach to support scalable and flexible pandemic planning by identifying risks and the proposing mitigation. Timely and transparent risk communications to the public and health care providers should be an integral part of the response to each event. **Table 1** provides an example of how the CPIP risk management approach is applied to the public health measures strategy.

**Table 1: Risks affecting the public health measures strategy, their implications and potential mitigation or response**

| Factor/event | Implications | Potential mitigation/response |
|---|---|---|
| Media report severe illness or a large number of cases | Sudden increase in demand for information about public health measure efficacy<br>Need for implementation of more public health measures (or perhaps more targeted measures) | Communicate and reinforce public education, i.e. individual public health measures and their rationales (e.g. hand hygiene, respiratory etiquette, voluntary self-isolation when ill, environmental cleaning, caring for the ill, seeking medical assessment). Use tailored approaches to communicate with vulnerable populations<br>Explain to the public how each additional measure increases personal and group protection and prevention<br>Advise the public that measures may change as new information becomes available |
| Differences in implementation of public health measures between jurisdictions and internationally | Selection and implementation of public health measures differ depending on local or regional situations<br>Public perception that another jurisdiction's approach is better<br>Public concern if there is a perception that public health resources are inequitably distributed | Acknowledge differences in local or regional approaches and provide rationale<br>Ensure that public health measures benefit all groups within a community or region and that burdens are equitably distributed |

Source: Pan-Canadian Public Health Network Council. Public Health Measures Annex: *Canadian Pandemic Influenza Preparedness: Planning guidance for the health sector* (2)

## Discussion

Canada's pandemic influenza preparedness and response requires a multifaceted approach, with public health measures an essential component throughout a pandemic. Public health measures, which require individual and community action to implement, are the most basic actions that can be taken to reduce transmission of a pandemic influenza virus; they are already used across Canada during outbreaks of seasonal influenza and other communicable diseases. Public health measures seek to reduce the occurrence and duration of human infections so as to delay the peak of pandemic influenza activity.

It is important for health planners to take into account that public health measures should be implemented early in a pandemic, in a targeted and layered manner. A communication approach that is transparent and consistent helps to ensure public trust and adoption of recommended measures. The potential benefits of specific measures need to be weighed against the practicality and feasibility of their implementation and potential unintended secondary social and economic impacts. Measures need to tailored for populations and settings whose circumstances may increase their vulnerability in an influenza pandemic.

### Conclusion

The guidance in the CPIP Public Health Measures Annex is intended to promote a scalable and consistent approach to pandemic planning. It is adaptable to different settings. Many of the recommended measures are contingent upon local triggers; therefore, the timing of their implementation depends on local circumstances that may not occur simultaneously across Canadian jurisdictions. However, a consistent approach to applying public health measures and the accompanying messaging will improve public perception, trust and adoption of guidance.

## Authors' statement

Canadian Pandemic Influenza Preparedness Task Group comprises B Henry (Chair), C Alfieri, I Gemmill, T Hatchette, E Henry, S Hota, A Lebans and B Schwartz.

### Conflict of interest

None.

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# Increase in ST-11 serogroup W *Neisseria meningitidis* invasive meningococcal disease in Canada, 2016–2018

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## Abstract

**Background:** Many countries have experienced increases in invasive meningococcal disease (IMD) due to a serogroup W *Neisseria meningitidis* (MenW) strain of the multilocus sequence type (ST)-11 clonal complex (CC). MenW ST-11 was first reported in Ontario, Canada, in 2014. By 2016, this strain caused IMD in five provinces and was responsible for 18.8% of the IMD cases in Canada.

**Objective:** To provide an update on invasive MenW disease in Canada including the strain characteristics, specimen source of isolates, age, sex and geographic distribution of cases.

**Methods:** *N. meningitidis* from culture-positive IMD cases are routinely submitted to the National Microbiology Laboratory (NML) for serogroup, serotype, serosubtype and sequence type analysis. The data from January 1, 2016 to December 31, 2018 were analyzed by calculating the proportion of IMD cases caused by MenW compared with other serogroups. In addition, trends based on age, sex and geographic distribution of cases and specimen source of isolates were analyzed based on information on specimen requisition forms.

**Results:** Over the three year period, 292 individual IMD case isolates were analyzed. The percentage of IMD case isolates typed as MenW more than doubled from 19% (n=15) to 44% (n=51) in 2018 when MenW became the most common serogroup, exceeded the number of MenB, MenC or MenY. In total, 93 MenW case isolates were identified, 91% (n=85) belonged to the ST-11 CC. The increase in MenW affected all age groups (but was most common in those older than 60) and both sexes, and occurred across the country but most prevalent in western Canada. The most common specimen source was blood.

**Conclusion:** In 2018, MenW was the most common serogroup for isolates received by the NML from culture-positive IMD cases in Canada. Over 90% of the MenW serogroup isolates belonged to the ST-11 CC. The quadrivalent ACWY meningococcal conjugate vaccine protects against IMD caused by strains in the A, C, W or Y serogroups and therefore may protect against IMD caused by the new MenW ST-11 strain; however, more research is needed. The emergence of variant strains highlight the importance of strain characterization in IMD surveillance and research.

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## Introduction

Invasive meningococcal disease (IMD) caused by the bacterium *Neisseria meningitidis* is a notifiable disease in most countries including Canada as well as by World Health Organization (1). The most severe forms of IMD include meningitis and septicemia, but the bacterium is also capable of causing pneumonia, septic arthritis and localized infections like conjunctivitis and urethritis. Before routine vaccination against meningococcal serogroup C (MenC) was introduced in Canada, incidence rates of IMD were about 1.0 case per 100,000 population with rates increasing during outbreaks of MenC disease (2). From 1989 to 1993, for example, incidences of IMD were 1.4–1.6 cases per 100,000 (3). Since the introduction of MenC conjugate vaccines in the mid-2000s, the overall average incidence rate of IMD in Canada decreased to about 0.6 per 100,000 population, with most cases due to MenB and MenY. Historically, MenW has not been a major cause of IMD (4).

In Canada, most IMD cases are confirmed by culture and/or polymerase chain reaction (PCR) at local hospitals and provincial public health laboratories. Invasive *N. meningitidis* isolates are also routinely sent to the National Microbiology Laboratory (NML) for further typing including antigenic analysis and genetic clonal analysis.

### Classification of *Neisseria meningitidis* bacteria

Based on the antigenicity of their surface capsular polysaccharides, 12 *N. meningitidis* serogroups have been identified. Most invasive diseases are caused by the six serogroups of A (MenA), B (MenB), C (MenC), W (MenW), X (MenX) and Y (MenY) (5,6). The prevalence of different serogroups varies geographically (5) and may be further affected by the local vaccination programs (7).

Besides the capsular serogroup polysaccharide that contributes to virulence, most strains with the potential to cause IMD outbreaks or epidemics belong to a limited number of hypervirulent clones or lineages and are classified into sequence types (STs). Related sequence types are grouped into clonal complexes (CCs). Some of the well-established hypervirulent clones have been described as ST-11, ST-32 and other sequence types (5,8). Two outer membrane protein antigens, PorB and PorA, are used to further classify strains into serotypes and serosubtypes, respectively (9). When these outer membrane proteins are used together with the capsular antigen, strains can be classified by their antigenic formula such as, for example, serogroup B:serotype 4:serosubtype P1.7,4. This helps to track the multiple variants and epidemiology of this disease.

### Emergence of MenW disease

Data collected at the NML over the last five years have shown the emergence of a MenW ST-11 clone in Canada, characterized by the antigens W:2a:P1.5,2. This clone was first detected in Ontario in 2014 (10). By 2016, four other provinces had reported IMD cases due to this MenW clone (11).

In this study, we report on the characterization of IMD isolates sent to the NML between 2016 and 2018. We analyzed the strains by antigenic and genetic typing and analyzed trends based on age, sex, geographic distribution of cases and specimen source.

## Methods

### Bacterial isolates

Invasive *N. meningitidis* cultured and identified at local hospitals and diagnostic laboratories are routinely submitted to their respective provincial public health laboratories for serogroup determination or confirmation. Provinces and territories submit such isolates to the NML for additional typing as part of the national surveillance of IMD.

This study made use of isolates of *N. meningitidis* obtained from individual IMD cases, and did not include cases diagnosed by PCR or antigen detection. Most of the isolates the NML receives are from culture-positive IMD cases. Previous studies have shown that 90% of IMD cases identified by provinces and territories could be matched to isolates received at the NML (12,13), suggesting that the NML has a robust and representative sample.

This study included all invasive *N. meningitidis* isolates obtained from culture-confirmed IMD cases submitted to the NML between January 1, 2016 and December 31, 2018. Duplicate isolates from the same patients were removed from the analysis.

### Typing of *Neisseria meningitidis*

At the NML, isolates were characterized by standard methods to determine their antigenic formula (serogroup:serotype: serosubtype). Multilocus sequence typing (MLST) was performed according to procedures described previously (14,15), and isolates were classified into sequence types and clonal complexes as per the procedures described by the Neisseria MLST website (16).

### Demographic data and specimen source

Information on the age and sex of each patient and geographic origin and source of each specimen was obtained from the requisition forms provided with specimens by the provincial public health laboratories. For geographic origin, we combined the data for Atlantic Canada (New Brunswick, Newfoundland and Labrador, Nova Scotia, Prince Edward Island) as well as for northern Canada (Northwest Territories, Nunavut, Yukon Territory).

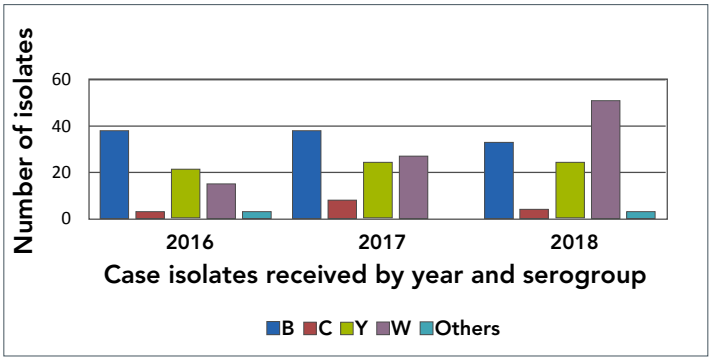
## Results

During the period January 1, 2016 to December 31, 2018, a total of 292 individual case isolates were sent to the NML: 80 in 2016, 97 in 2017 and 115 in 2018.

### Serogroup distribution

There was a change in the serogroup distribution of culture-confirmed IMD cases over the three-year period. The number of MenC case isolates remained low, fluctuating between three and eight isolates per year, and the proportion of IMD isolates that were typed as MenB and MenY showed a downward trend over the three-year period. The number of isolates that were typed as MenW increased from 15 in 2016 to 51 in 2018, and exceeded the number of MenB or MenY isolates in 2018 (**Figure 1**).

**Figure 1: Distribution of *Neisseria meningitidis* serogroups from invasive meningococcal disease cases in Canada, 2016–2018**




### Strain characteristics

Of the 93 invasive MenW isolates, 85 (91%) were assigned to ST-11 CC, six (6%) to ST-22 CC and one to ST-60 CC (ST-11739); one was not assigned to any known clonal complex (ST-1308). The majority (n=83 or 98%) of the MenW ST-11 CC isolates were typed as ST-11, with only two identified as single locus variants of ST-11. Of these variants, one was typed as ST-12818 and the other as ST-13250. Most MenW of the ST-11 CC were found to have the serotype antigen 2a (n=76; 89%) and most were typed as either 2a:P1.5,2 (n=42; 49%) or 2a:P1.2 (n=31; 36%). All six MenW of the ST-22 CC were typed as NT (non-typeable):P1.6. The MenW that did not classify into any known CC was typed as 4:P1.16 and the MenW of the ST-60 CC was typed as 2a:P1.5,2.

Five sequence types were identified among the six MenW of ST-22 CC: there was one isolate of ST-22; two of ST-184 and one each of ST-1158; ST-1124; and ST-8974. The five non ST-22 isolates had sequence types with six of their seven housekeeping genes identical to that of ST-22 (single locus variants of ST-22).

### Demographic data and specimen source

Between 2016 and 2018, over half (n=55, 65%) of the MenW ST-11 CC cases were adults aged over 30 (including 34 cases, or 40%, aged over 60), while 19% (n=16) were aged 16–30 years (**Table 1**). In 2018, nine (19%) of 47 cases were under six years; five were under 12 months old (Table 1). In contrast, there were only two cases aged less than six years in 2016 and 2017 combined. Of the 85 cases during the study period, 46 were female.

**Table 1: Age and sex distribution of invasive meningococcal disease cases caused by serogroup W *Neisseria meningitidis* (MenW) ST-11 clonal complex, 2016–2018, Canada**

| Age and sex of cases | | Number of cases per year | | | Total number of cases |
|---|---|---|---|---|---|
| | | 2016 | 2017 | 2018 | |
| Sex | Male | 9 | 12 | 18 | 39 |
| | Female | 4 | 13 | 29 | 46 |
| Age | Less than 12 months | 0 | 1 | 5 | 6 |
| | 1–5 years | 1 | 0 | 4 | 5 |
| | 6–15 years | 1 | 2 | 0 | 3 |
| | 16–30 years | 2 | 7 | 7 | 16 |
| | 31–60 years | 3 | 5 | 13 | 21 |
| | More than 60 years | 6 | 10 | 18 | 34 |
| | All ages | 13 | 25 | 47 | 85 |

The increase in MenW was particularly significant in western Canada (**Table 2**). The proportion of MenW among all IMD isolates from 2016 to 2018 was 57% in British Columbia, 50% in Alberta, 43% in Saskatchewan and 46% in Manitoba. In contrast, overall percentages of IMD isolates typed as MenW were 25% in Ontario and 17% in Quebec. In Atlantic Canada, there was only one MenW case isolate in the same three-year period. Only one MenW out of a total of two IMD isolates was received at the NML from northern Canada.

The source of specimens for MenW of the ST-11 CC were mainly from blood cultures (n=79 or 93%); three were found in cerebrospinal fluid (including one in both blood and cerebrospinal fluid). In 2018, there were two cases with the MenW ST-11 CC in the joint fluid; in one case, the organism was isolated from a subarachnoid specimen.

**Table 2: Temporal and geographic distribution of culture-positive invasive meningococcal disease for all serogroups and serogroup W *Neisseria meningitidis* (MenW) isolates in Canada according to clonal complex[a]**

| Region | 2016 | | | 2017 | | | 2018 | | | 2016–2018 |
|---|---|---|---|---|---|---|---|---|---|---|
| | All IMD isolates | ST-11 MenW | Non ST-11 MenW | All IMD isolates | ST-11 MenW | Non ST-11 MenW | All IMD isolates | ST-11 MenW | Non ST-11 MenW | Total IMD isolates |
| BC | 11 | 2 | 0 | 23 | 13 | 1 | 22 | 14 | 2 | 56 |
| AB | 7 | 1 | 1 | 8 | 4 | 0 | 19 | 11 | 0 | 34 |
| MB, SK | 6 | 2 | 1 | 8 | 2 | 0 | 6 | 3 | 1 | 20 |
| ON | 24 | 5 | 0 | 26 | 4 | 0 | 31 | 11 | 0 | 81 |
| QC | 25 | 3 | 0 | 24 | 2 | 1 | 26 | 6 | 1 | 75 |
| NB, NL, NS, PE | 6 | 0 | 0 | 8 | 0 | 0 | 10 | 1 | 0 | 24 |
| NT, NU, YT | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 0 | 2 |
| Total | 80 | 13 | 2 | 97 | 25 | 2 | 115 | 47 | 4 | 292 |

Abbreviations: AB, Alberta; BC, British Columbia; IMD, invasive meningococcal disease; MB, Manitoba; MenW, *Neisseria meningitidis* serogroup W; NB, New Brunswick; NL, Newfoundland and Labrador; NS, Nova Scotia; NT, Northwest Territories; NU, Nunavut; ON, Ontario; PE, Prince Edward Island; QC, Quebec; SK, Saskatchewan; ST, sequence type; YT, Yukon Territory
[a] Either ST-11 clonal complex (ST-11) or non ST-11 clonal complex (non ST-11)

# Discussion

In the last three years, the number of invasive *N. meningitidis* isolates received at the NML has increased by 44%, from 80 isolates in 2016 to 115 isolates in 2018. The increase was mainly due to MenW, with number of case isolates more than tripling, from 15 in 2016 to 51 in 2018. This increase in MenW shifted the serogroup distribution of IMD in Canada, which since the introduction of MenC conjugate vaccines, has been predominantly MenB. The increase in MenW in Canada is due to the continuing expansion and spread of the hypervirulent ST-11 CC. This increase was particularly evident in the western provinces where MenW accounted for 43–57% of their IMD isolates.

The MenW ST-11 CC isolates in Canada are similar to the strains currently circulating globally (17). Parallel findings have been reported in Australia (18), parts of the United States (US) (19,20) and the Central African Republic (21). In Australia, 44% of IMD cases in 2016 were due to MenW, an almost three-fold increase from 2015 (18). In the Central African Republic, 65% of culture-positive IMD cases were due to MenW, with the median age of MenW patients 60 years in 2015 and 66 years in 2016 (21).

The predominance of the ST-11 CC strain is relatively new, but changes are starting to be seen in its serotype antigen. Prior to 2014, the predominant strain was ST-22 CC (10,11). From 2009 to 2016, 100% of the ST-11 CC MenW were found to express the serotype antigen 2a. From 2017 to 2018, however, nine of 72 isolates (13%) did not express the serotype antigen 2a. Previously, we had observed a hot-spot mutation in the serotype 2a antigen of MenC strains (22).

Our finding of one invasive ST-60 CC (W:2a:P1.5,2 isolate of ST-11739) in MenW was unusual because most meningococci of the ST-60 CC in Canada belong to MenB (23,24) and previous studies of MenC or MenW that expressed serotype 2a antigen had been typed mostly as ST-11 CC (11,25). Further studies are required to understand the origin of this unusual W:2a:P1.5,2 ST-11739 strain.

## Limitations

There are some limitations to our study that should be considered when interpreting the findings. First, we only examined culture-confirmed cases, and did not include cases diagnosed by molecular means alone (i.e. PCR). Although this might affect the proportion of IMD cases caused by MenW, since PCR-diagnosed cases only constitute approximately 10% of all IMD cases identified in Canada (4), the overall effect on the results would probably not alter the current trend of increase in MenW IMD cases.

Second, we did not collect clinical data or disease outcomes of the MenW cases, and therefore we do not know if fatality rates were as high as those reported in other countries or regions (24% in Georgia, US; 20% in England, United Kingdom; and 21% in Australia) (19,26,27). Similarly, we do not know if the Canadian cases had unusual clinical presentations such as gastrointestinal symptoms or epiglottitis (26,28).

## Clinical and public health implications

The quadrivalent ACWY meningococcal conjugate vaccine protects against IMD caused by strains expressing the serogroup antigens of A, C, W or Y. In theory, they should protect against IMD caused by the MenW ST-11 strain. In 2017, an outbreak in British Columbia prompted immunization with the meningococcal quadrivalent ACWY-conjugate vaccine of 15–19 years old in the affected region (29). This immunization was provided in addition to routine meningococcal quadrivalent conjugate vaccine booster given to Grade nine students, which had been implemented in September 2016 (30). Although most provinces and territories now have quadrivalent ACWY

meningococcal conjugate vaccine programs for primary or high school students (31), some populations are not covered, including adults over 30 years of age, the age group most affected in the past three years of data collection.

### Conclusion

Between 2016 and 2018, there has been an increase in invasive MenW disease that has altered the serogroup distribution of culture-confirmed IMD cases in Canada. The quadrivalent ACWY meningococcal conjugate vaccine protects against IMD caused by strains in the A, C, W or Y serogroups. The vaccine may also protect against IMD caused by the new MenW ST-11 strain, but additional research is needed. The emergence of newer clonal types and unusual strains highlight the importance of strain characterization in IMD surveillance and research.

## Authors' statement

All authors (RST, LH, GJT, JM, PVC, JVK, BL, DH, RG, GG, GZ and BH) are involved in the surveillance of IMD in Canada. RST prepared the first draft and all authors contributed to the final version with comments and suggestions.

### Conflict of interest

None.

## Acknowledgements

We thank the staff at the provincial public health laboratories for identifying and sending *N. meningitidis* isolates to the National Microbiology Laboratory (NML). We also thank D Law, J Zhou and S Deng for providing laboratory assistance in the analysis of strains, and the NML's DNA Core Service for providing assistance in nucleotide sequencing.

This publication made use of the Neisseria multilocus sequence typing website (16) developed by K Jolley and sited at the University of Oxford. The development of this site was funded by the Wellcome Trust and the European Union.

## Funding

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# 2018/19 influenza vaccine had low late-season effectiveness against the A(H3N2) influenza virus

**Source:** Vaccine effectiveness in: **FluWatch report: March 31 to April 6, 2019** (Week 14). https://www.canada.ca/en/public-health/services/publications/diseases-conditions/fluwatch/2018-2019/week14-march-31-april-6-2019.html

Given an atypical late-season wave of influenza A(H3N2), the community-based Canadian Sentinel Practitioner Surveillance Network (SPSN) has undertaken an additional interim analysis to assess effectiveness of the 2018/19 influenza vaccine against A(H3N2) illness. The Canadian SPSN includes participation by sentinel practitioners in the four most populous provinces of Canada: Alberta, British Columbia, Ontario and Quebec. Vaccine effectiveness (VE) monitoring methods are as described in prior publications, available at the SPSN website alongside historic and current VE findings.

Based on data collected as of March 30th, 2019 including more than 2,800 participants, the 2018/19 northern hemisphere vaccine has provided little or no protection against medically-attended outpatient A(H3N2) illness (VE of 23%; 95% CI: -9 to 46), including among working age adults 20-64 years old who comprise the majority of SPSN participants (VE of -16%; 95% CI: -76 to 23).

Consistent with expected patterns, VE estimates for this delayed A(H3N2) wave are considerably lower than reported earlier by the SPSN for the primary A(H1N1)pmd09 epidemic based on data collected as of January 12th, 2019. In that mid-season analysis, VE against A(H1N1)pdm09 was 72% (95% CI: 60 to 81) overall, with substantial protection observed in all age groups. In the most recent analysis spanning March 30th, estimates against A(H1N1)pmd09 have remained stable at approximately 70%. The SPSN continues to monitor and will further update VE estimates at end of season.

# Children under 10 years of age were more affected by the influenza A(H1N1) virus in 2018/19 than in previous years

**Source:** Skowronski DM, Leir S, De Serres G, Murti M, Dickinson JA, Winter AL, Olsha R, Croxen MA, Drews SJ, Charest H, Martineau C, Sabaiduc S, Bastien N, Li Y, Petric M, Jassem A, Krajden M, Gubbay JB. **Children under 10 years of age were more affected by the 2018/19 influenza A(H1N1)pdm09 epidemic in Canada: possible cohort effect following the 2009 influenza pandemic.** Euro Surveill. 2019 Apr;24(15). DOI

**Introduction:** Findings from the community-based Canadian Sentinel Practitioner Surveillance Network (SPSN) suggest children were more affected by the 2018/19 influenza A(H1N1)pdm09 epidemic.

**Aim:** To compare the age distribution of A(H1N1)pdm09 cases in 2018/19 to prior seasonal influenza epidemics in Canada.

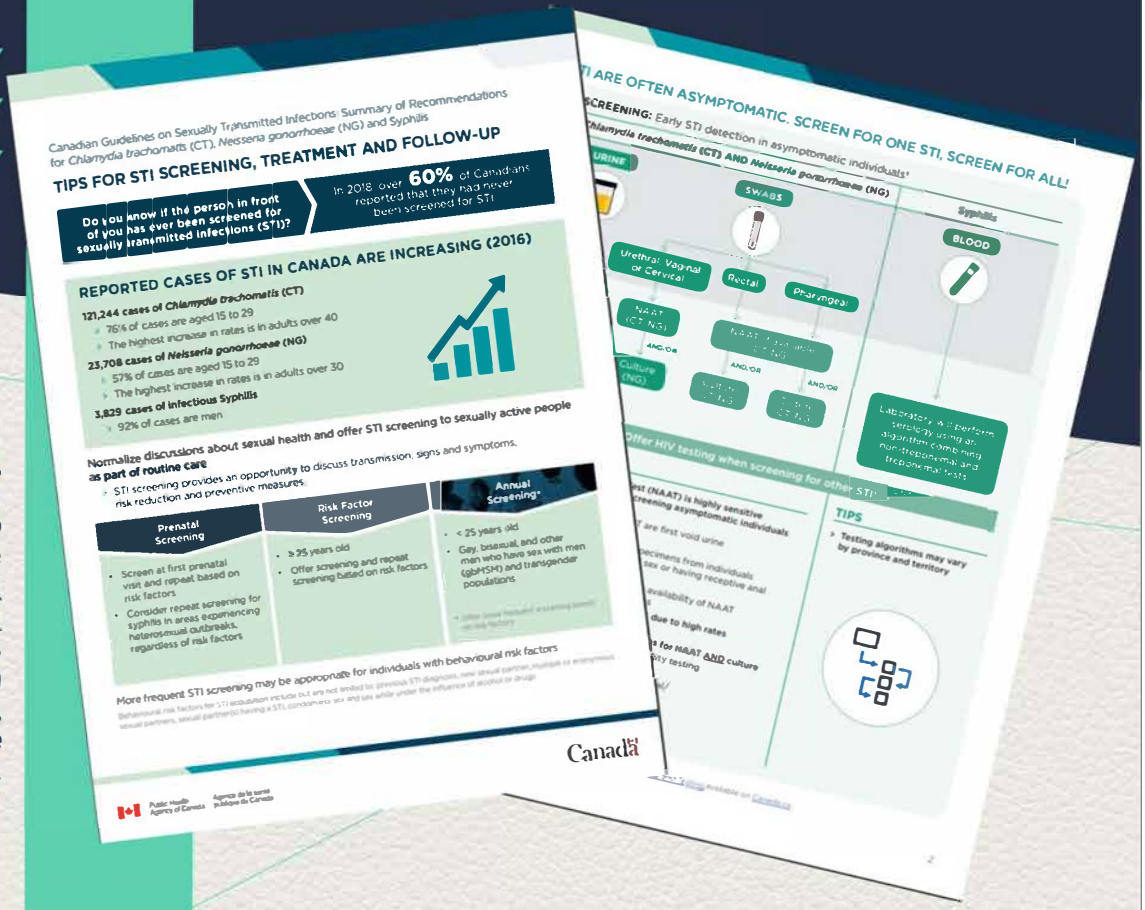
**Methods:** The age distribution of unvaccinated influenza A(H1N1)pdm09 cases and test-negative controls were compared across A(H1N1)pdm09-dominant epidemics in 2018/19, 2015/16 and 2013/14 and with the general population of SPSN provinces. Similar comparisons were undertaken for influenza A(H3N2)-dominant epidemics.

**Results:** In 2018/19, more influenza A(H1N1)pdm09 cases were under 10 years old than controls (29% vs 16%; $p < 0.001$). In particular, children aged 5-9 years comprised 14% of cases, greater than their contribution to controls (4%) or the general population (5%) and at least twice their contribution in 2015/6 (7%; $p < 0.001$) or 2013/14 (5%; $p < 0.001$). Conversely, children aged 10-19 years (11% of the population) were under-represented among A(H1N1)pdm09 cases versus controls in 2018/19 (7% vs 12%; $p < 0.001$), 2015/16 (7% vs 13%; $p < 0.001$) and 2013/14 (9% vs 12%; $p = 0.12$).

**Conclusion:** Children under 10 years old contributed more to outpatient A(H1N1)pdm09 medical visits in 2018/19 than prior seasonal epidemics in Canada. In 2018/19, all children under 10 years old were born after the 2009 A(H1N1)pdm09 pandemic and therefore lacked pandemic-induced immunity. In addition, more than half those born after 2009 now attend school (i.e. 5-9-year-olds), a socio-behavioural context that may enhance transmission and did not apply during prior A(H1N1)pdm09 epidemics.

For Healthcare Providers

# Canadian Guidelines on Sexually Transmitted Infections




**Tips for STI Screening, Treatment and Follow-up** summarises the Canadian Guidelines on STI recommendations for *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG) and Syphilis.

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## Summary of Recommendations for Chlamydia trachomatis (CT), Neisseria gonorrhoeae (NG) and Syphilis

- Sexually transmitted infections (STI) often have no symptoms.
- If you screen for one STI, screen for all!
- Normalize discussions about sexual health and offer STI screening to sexually active people.
- Discuss transmission, signs and symptoms, risk reduction and preventive measures.

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