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

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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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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; TIV, trivalent inactivated influenza vaccine; QIV, quadrivalent inactivated influenza vaccine; -, not applicable
IM, intramuscular; LAIV, live attenuated influenza vaccine; LAIV3, trivalent live attenuated influenza vaccine; LAIV4, quadrivalent live attenuated 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 • IIV3-Adj • 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 • If a quadrivalent vaccine is not available, any of the available trivalent vaccines should be used
2–17 years	• IIV3-SD • IIV4-SD • 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 • If IIV4-SD or LAIV4 is not available, IIV3-SD should be used • IIV4-SD should be used for children for whom LAIV is contraindicated, such as in children with: - severe asthma - medically attended wheezing in the seven days prior to vaccination - current receipt of Aspirin or Aspirin-containing therapy - immune compromising conditions • LAIV4 may be given to children with: - stable, non-severe asthma - cystic fibrosis who are not being treated with immunosuppressive drugs (e.g. prolonged systemic corticosteroids)
18–59 years	• IIV3-SD • IIV4-SD • LAIV4	• Any of the available influenza vaccines should be used in adults without contraindications • IIV should be used for adults for whom LAIV is contraindicated, such as in: - pregnant women - adults with any of the chronic health conditions identified in Table 2, including immune compromising conditions - HCWs
60–64 years	• IIV3-SD • IIV4-SD	• Any of the available influenza vaccines should be used
65 years and older[b]	• IIV3-SD • IIV3-Adj • IIV3-HD • 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 • 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

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Conflict of interest

None.

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