



Summary of the National Advisory Committee on Immunization (NACI) Seasonal Influenza Vaccine Statement for 2021–2022

Angela Sinilaite¹, Kelsey Young¹, Robyn Harrison^{2,3} on behalf of the National Advisory Committee on Immunization (NACI)*

Abstract

Background: Several influenza vaccines are authorized in Canada and the evidence on influenza immunization is continually evolving. The National Advisory Committee on Immunization (NACI) provides recommendations regarding the use of seasonal influenza vaccines annually to the Public Health Agency of Canada (PHAC).

Objective: To summarize NACI recommendations regarding the use of seasonal influenza vaccines for 2021–2022 and to highlight new recommendations.

Methods: Annual influenza vaccine recommendations are developed by NACI's Influenza Working Group for consideration and approval by NACI. The development of the recommendations is based on the NACI evidence-based process.

Results: The following new recommendations were made: 1) Influvac® Tetra may be considered as an option among the standard dose quadrivalent inactivated influenza vaccines (IIV4-SD) offered to adults and children three years of age and older; 2) FluZone High Dose Quadrivalent (IIV4-HD) may be considered an option for individuals 65 years of age and older who are currently recommended to receive FluZone® High Dose (trivalent); and 3) Flucelvax® Quad may be considered amongst the quadrivalent influenza vaccines offered to adults and children nine years of age and older for annual influenza immunization. Guidance for use of influenza immunizations during the coronavirus disease 2019 pandemic is also highlighted.

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. 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.

This work is licensed under a [Creative Commons Attribution 4.0 International License](#).



Affiliations

¹ Centre for Immunization and Respiratory Infectious Diseases, Public Health Agency of Canada, Ottawa, ON

² NACI Influenza Working Group Chair

³ University of Alberta, Alberta Health Services, Edmonton, AB

***Correspondence:**
naci-ccni@phac-aspc.gc.ca

Suggested citation: Sinilaite A, Young K, Harrison R, on behalf of the National Advisory Committee on Immunization (NACI). Summary of the National Advisory Committee on Immunization (NACI) Seasonal Influenza Vaccine Statement for 2021–2022. *Can Commun Dis Rep* 2021;47(9):372–80.

<https://doi.org/10.14745/ccdr.v47i09a04>

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

Introduction

Seasonal influenza is an infectious viral illness that occurs globally with an annual attack rate estimated at 5%–10% in adults and 20%–30% in children (1). Epidemics of seasonal influenza occur annually in Canada, generally in the late fall and winter months; however, the burden of influenza illness can vary from year to year. Current information on influenza activity globally can be found on the World Health Organization's FluNet website (2)

and nationally on the Public Health Agency of Canada's (PHAC) FluWatch website (3).

The National Advisory Committee on Immunization (NACI) provides PHAC with annual recommendations regarding the use of seasonal influenza vaccines, which reflect identified changes in influenza epidemiology, immunization practices and influenza



vaccine products authorized and available for use in Canada. The development of the annual influenza vaccine recommendations, which is led by the NACI Influenza Working Group (IWG), involves a thorough review and evaluation of the literature as well as discussion and debate at the scientific and clinical practice levels on a variety of issues, which can include the following: the burden of influenza illness and the target populations for vaccination, efficacy, effectiveness, immunogenicity and safety of influenza vaccines, vaccine schedules, and other aspects of influenza immunization. Issues related to ethics, equity, feasibility and acceptability are also systematically examined by NACI for comprehensive development of vaccine guidance (4).

The objective of this article is to provide a concise summary of NACI's recommendations and supporting information for the 2021–2022 influenza season, including conclusions from reviews of evidence on 1) a new, biosimilar, egg-based, quadrivalent inactivated influenza vaccine (Influvac® Tetra; IIV4-SD), 2) a new quadrivalent, egg-based high dose inactivated influenza vaccine (Fluzone® High Dose Quadrivalent; IIV4-HD), and 3) a mammalian cell culture-based influenza vaccine (Flucelvax® Quad; IIV4-cc). Complete details can be found on the PHAC website in the *NACI Advisory Committee Statement: Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2021–2022* (the Statement) (5) and related publications.

Influenza vaccine abbreviations

Updated abbreviations used by NACI to describe the defining features of various types of influenza vaccines are presented in Table 1.

Methods

In the preparation of the 2020–2021 seasonal influenza vaccine recommendations, NACI's IWG identified the need for evidence reviews for new topics, and then reviewed and analyzed the available evidence, and proposed new or updated recommendations according to the NACI evidence-based process for developing recommendations (6). For a more detailed explanation of the strength of NACI recommendations and the grading of evidence refer to **Appendix Table A1**. A published, peer-reviewed framework and evidence-informed tools (including the Ethics Integrated Filters, Equity Matrix, Feasibility Matrix, and Acceptability Matrix) was applied to ensure that issues related to ethics, equity, feasibility and acceptability were systematically assessed and integrated into guidance (4).

For the 2020–2021 influenza season, the IWG reviewed evidence regarding the use of two new vaccines: 1) Influvac Tetra, a new biosimilar, egg-based, quadrivalent inactivated influenza vaccine; and 2) Fluzone High Dose (HD) Quadrivalent an egg-based high dose quadrivalent inactivated influenza vaccine (IIV4). Influvac Tetra (IIV4-SD) was first authorized for use in Canada in adults in March 2019 and subsequently in children three years of age and

Table 1: National Advisory Committee on Immunization (NACI) influenza vaccine abbreviations

Influenza vaccine category	Formulation	Type	Current NACI abbreviation ^a
Inactivated influenza vaccine (IIV)	Trivalent (IIV3)	Standard dose ^b , unadjuvanted, IM administered, egg-based	IIV3-SD
		Adjuvanted ^c , IM administered, egg-based	IIV3-Adj
		High dose ^d , unadjuvanted, IM administered, egg-based	IIV3-HD
	Quadrivalent (IIV4)	Standard dose ^b , unadjuvanted, IM administered, egg-based	IIV4-SD
		Standard dose ^b , unadjuvanted, IM administered, cell culture-based	IIV4-cc
		High dose ^d , unadjuvanted, IM administered, egg-based	IIV4-HD
Live attenuated influenza vaccine (LAIV)	Trivalent (LAIV3)	Unadjuvanted, Nasal spray, egg-based	LAIV3
	Quadrivalent (LAIV4)	Unadjuvanted, Nasal spray, egg-based	LAIV4

Abbreviations: IIV, inactivated influenza vaccine; IIV3, trivalent inactivated influenza vaccine; IIV3-Adj, adjuvanted egg-based trivalent inactivated influenza vaccine; IIV3-HD, high-dose egg-based trivalent inactivated influenza vaccine; IIV3-SD, standard-dose egg-based trivalent inactivated influenza vaccine; IIV4, quadrivalent inactivated influenza vaccine; IIV4-cc, standard-dose cell culture-based quadrivalent inactivated influenza vaccine; IIV4-HD, high-dose egg-based quadrivalent inactivated influenza vaccine; IIV4-SD, standard-dose egg-based quadrivalent inactivated influenza vaccine; IM, intramuscular; LAIV, live attenuated influenza vaccine; LAIV3, egg-based trivalent live attenuated influenza vaccine; LAIV4, egg-based quadrivalent live attenuated influenza vaccine; NACI, National Advisory Committee on Immunization

^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 HA per strain and are administered as a 0.5 mL dose by intramuscular injection; "-cc" refers to an IIV product that is made from influenza virus grown in cell cultures instead of chicken eggs (Flucelvax® Quad); "-Adj" refers to an IIV with an adjuvant (IIV3-Adj for Fluzad® or Fluzad Pediatric®); and "-HD" refers to an IIV that contains higher antigen content than 15 µg HA per strain (IIV3-HD for Fluzone® High-Dose or IIV4-HD for Fluzone® High-Dose Quadrivalent)

^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

Source: Table reproduced from *NACI Seasonal Influenza Vaccine Statement for 2021–2022* (5)

older in February 2020. Fluzone High Dose (HD) Quadrivalent was first authorized for use in Canada in adults in June 2020. A trivalent formulation, Fluzone High-Dose, was previously authorized for use in adults 65 years of age and older in Canada, and recommended by NACI, but marketing of the vaccine was discontinued as of February 2021. Following the review and



analysis of available pre-licensure clinical trial data and Health Canada's Clinical Review Reports for these two vaccines, the IWG proposed new recommendations for vaccine use to NACI. NACI critically appraised the available evidence and approved the specific recommendations brought forward.

Recommendations and supporting evidence on the use of mammalian cell culture-based, inactivated seasonal influenza vaccine (Flucelvax Quad) from the *NACI Supplemental Statement – Mammalian Cell Culture-Based Influenza Vaccines* (7) were also incorporated into the *Statement on Seasonal Influenza Vaccine for 2021–2022*. Flucelvax Quad is the first and only available mammalian cell culture-based inactivated seasonal influenza vaccine in Canada; it was first authorized for use in adults and children nine years of age and older on November 22, 2019. The IWG oversaw the completion of a systematic review to inform the development of guidance on the use of Flucelvax Quad (IIV4-cc). Six electronic databases (EMBASE, MEDLINE, Scopus, ProQuest Public Health and ClinicalTrials.gov) were searched from inception until February 12, 2019, using a predefined search strategy to identify relevant literature on the efficacy, effectiveness, immunogenicity and safety in adults and children four years of age and older. Registered clinical trials and grey literature from international public health authorities and National Immunization Technical Advisory Groups were also considered. Additionally, hand-searching of the reference lists of included articles was performed by one reviewer to identify additional relevant publications. Two reviewers independently screened the titles and abstracts of records retrieved from the search and eligible full-text articles for inclusion. One reviewer extracted data from eligible studies and appraised the methodological quality of these studies using the criteria outlined by Harris *et al.* (8). A second reviewer independently validated the data extraction and quality assessment. A narrative synthesis of the extracted data was performed. NACI provided new recommendations based on assessment of the evidence.

Results

Use of seasonal influenza vaccine in the presence of the novel coronavirus disease 2019 (COVID-19)

In light of the ongoing coronavirus disease 2019 (COVID-19) pandemic, PHAC, in consultation with NACI and the Canadian Immunization Committee, has developed the following additional guidance on the delivery of influenza vaccination programs and administration of seasonal influenza vaccine to support provincial and territorial vaccine programs and primary care providers during the COVID-19 pandemic for 2021–2022:

- *Guidance for Influenza Vaccine delivery in the presence of COVID-19* (9)
- *Guidance on the use of seasonal influenza vaccine in the presence of COVID-19* (10)

This guidance is based on currently available scientific evidence and expert opinion. The content will be reviewed regularly, and updates will be made as necessary throughout the upcoming influenza season as the public health context evolves and new evidence and policy issues emerge.

New egg-based quadrivalent influenza vaccine

NACI concluded that Influvac Tetra is safe and has non-inferior immunogenicity to the trivalent Influvac formulation. Therefore, NACI recommended that **Influvac Tetra may be considered among the standard dose quadrivalent inactivated influenza vaccines (IIV4-SD) offered to adults and children three years of age and older (Discretionary NACI Recommendation)**.

New egg-based high dose quadrivalent influenza vaccine

NACI concluded that Fluzone High Dose Quadrivalent is comparably safe and has non-inferior immunogenicity to the previously authorized trivalent Fluzone High Dose formulation. Therefore, NACI has issued the following discretionary individual-level recommendation on the use of Fluzone High Dose Quadrivalent (IIV4-HD): **For individuals 65 years of age and older whom are currently recommended to receive Fluzone High Dose (trivalent), NACI recommends that Fluzone High Dose Quadrivalent (IIV4-HD) may be considered as an option (Discretionary NACI Recommendation)**. Recommendations for public health programs remain unchanged at this time.

Inclusion of mammalian cell culture-based quadrivalent influenza vaccine

The peer-reviewed published evidence on the effectiveness, immunogenicity and safety of IIV4-cc manufactured using fully cell-derived viruses was sparse. The systematic review identified four observational studies (11–14) investigating the vaccine effectiveness of IIV4-cc compared with egg-based IIV and two peer-reviewed randomized controlled trials that assessed the immunogenicity and safety of IIV4-cc compared with different IIV3-cc formulations (produced using the same Madin-Darby Canine Kidney [MDCK] cell culture-based manufacturing process). There was evidence indicating that IIV4-cc may be more effective than egg-based IIV3 and IIV4 influenza vaccines against non-laboratory confirmed influenza-related outcomes, including influenza-related health care interactions and influenza-like-illness (ILI). Although some data suggest that IIV4-cc may be more effective against laboratory-confirmed influenza A(H3N2) virus infection than egg-based IIV, there was no consistent and statistically significant difference in effectiveness identified for adults or children vaccinated with IIV4-cc compared with egg-based IIV. Two studies that assessed the immunogenicity and safety of IIV4-cc compared with different IIV3-cc formulations (produced by Seqirus using the same MDCK cell culture-based manufacturing process) were identified in this review (15,16). There was also evidence indicating that IIV4-cc has a comparable



immunogenicity and safety profile to egg-based influenza vaccines already licensed in Canada and the trivalent formulation of this cell culture-based influenza vaccine that has been licensed in the United States and Europe, but for which licensure has never been sought in Canada (17–22).

Based on assessment of the available pre-licensure and post-market clinical trial and observational data, NACI concluded that IIV-cc is an effective, safe, well-tolerated and immunogenic alternative to conventional egg-based influenza vaccines for children and adults. Therefore, NACI has made the following recommendation, supplementing NACI's overarching recommendation for influenza vaccination, which is available in the *NACI Seasonal Influenza Vaccine Statement* (5):

NACI recommends that Flucelvax Quad may be considered among the IIV4 offered to adults and children nine years of age and older (Discretionary NACI Recommendation).

- NACI concludes that there is fair evidence to recommend vaccination of adults and children nine years of age and older with Flucelvax Quad (Grade B Evidence)

For complete details of this review, rationale, relevant considerations and additional information supporting this recommendation, refer to the *NACI Supplemental Statement: Mammalian Cell Culture-Based Influenza Vaccines* (7). Notably, Flucelvax Quad was recently authorized by Health Canada for use in adults and children two years of age and older. This updated authorized age indication supersedes the information for Flucelvax Quad found in relevant sections within the *NACI Statement on Seasonal Influenza Vaccine for 2021–2022* (5). Further details are available in the new product monograph for this vaccine (23).

Summary of National Advisory Committee on Immunization recommendations for the use of influenza vaccines for the 2021–2022 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 **List 1**.

Recommended influenza vaccine options by age group and by dosage and route of administration by age are summarized in **Table 2** and **Table 3**, respectively.

List 1: Groups for whom influenza vaccination is particularly recommended

People at high risk of influenza-related complications or hospitalization

- All children 6–59 months of age
- Adults and children with the following chronic health conditions^a:
 - 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, such as solid organ transplant or hematopoietic stem cell transplant recipients)
 - Renal disease
 - Anemia or hemoglobinopathy
 - Neurologic or neurodevelopment conditions (includes neuromuscular, neurovascular, neurodegenerative, neurodevelopmental conditions, and seizure disorders [and, for children, includes febrile seizures and isolated developmental delay], but excludes migraines and psychiatric conditions without neurological conditions)
 - Morbid obesity (body mass index of 40 and over)
 - Children six 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
- All pregnant women
- People of any age who are residents of nursing homes and other chronic care facilities
- Adults 65 years of age and older
- 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 0–59 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 Refer to Immunization of Persons with Chronic Diseases and Immunization of Immunocompromised Persons in Part 3 of the Canadian Immunization Guide for additional information about vaccination of people with chronic diseases (24).

Source: List reproduced from *NACI Seasonal Influenza Vaccine Statement for 2021–2022* (5).



ADVISORY COMMITTEE STATEMENT

Table 2: Recommendations on choice of influenza vaccine type for individual- and public health program-level decision-making by age group

Recipient by age group	Vaccine types authorized for use	Recommendations on choice of influenza vaccine	
6–23 months	IIV3-SD ^a IIV3-Adj IIV4-SD	<ul style="list-style-type: none"> A quadrivalent influenza vaccine licensed for this age group should be used in infants and young children without contraindications, 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 licensed for this age group should be used. 	
2–17 years ^b	IIV3-SD ^a IIV4-SD IIV4-cc (nine years of age and over) LAIV4	<ul style="list-style-type: none"> An age appropriate IIV4-SD, LAIV4, or IIV4-cc (IIV4-cc only authorized for nine years of age and older) should be used in 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. <ul style="list-style-type: none"> There are currently no IIV4-cc vaccines licensed for children younger than nine years of age. LAIV4 may be given to children with: <ul style="list-style-type: none"> Stable, non-severe asthma Cystic fibrosis who are not being treated with immunosuppressive drugs (e.g. prolonged systemic corticosteroids) Stable HIV infection, if the child is currently being treated with HAART and has adequate immune function LAIV should not be used in children for whom it is contraindicated for, such as those with: <ul style="list-style-type: none"> Severe asthma (defined as currently on oral or high-dose inhaled glucocorticosteroids or active wheezing) Medically attended wheezing in the seven days prior to vaccination Current receipt of aspirin or aspirin-containing therapy Immune compromising conditions, with the exception of stable HIV infection, i.e. if the child is treated with HAART (for at least four months) and has adequate immune function LAIV is contraindicated in pregnant adolescents. IIV4-SD or IIV4-cc^c should be used instead. If IIV4-SD, IIV4-cc^c, and LAIV4 are not available, IIV3-SD should be used. 	
18–59 years	IIV3-SD ^a IIV4-SD IIV4-cc LAIV4	<ul style="list-style-type: none"> Any of the available influenza vaccines should be used in adults without contraindications. <ul style="list-style-type: none"> There is some evidence that IIV may provide better efficacy than LAIV in healthy adults LAIV is not recommended for the following: <ul style="list-style-type: none"> Pregnant women Adults with any of the chronic health conditions identified in List 1, including immune compromising conditions Healthcare workers 	
60–64 years	IIV3-SD ^a IIV4-SD IIV4-cc	Any of the available influenza vaccines should be used in those without contraindications.	
65 years and older ^d	IIV3-SD ^a IIV3-Adj IIV3-HD ^e IIV4-SD IIV4-cc	Individual-level decision-making <ul style="list-style-type: none"> IIV-HD should be used over IIV-SD, given the burden of influenza A(H3N2) disease and the good evidence of IIV3-HD providing better protection compared to IIV3-SD in adults 65 years of age and older. <ul style="list-style-type: none"> Other than a recommendation for using IIV-HD over IIV-SD formulations, NACI has not made comparative individual-level recommendations on the use of the other available vaccines in this age group. In the absence of a specific product, any of the available age appropriate influenza vaccines should be used. 	Public health program-level decision-making <ul style="list-style-type: none"> Any of the available influenza vaccines should be used. <ul style="list-style-type: none"> There is insufficient evidence on the incremental value of different influenza vaccines (i.e. cost-effectiveness assessments have not been performed by NACI) to make comparative public health program-level recommendations on the use of the available vaccines.

Abbreviations: HAART, highly active antiretroviral therapy; IIV, inactivated influenza vaccine; IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4-cc, quadrivalent mammalian cell-culture based inactivated influenza vaccine; IIV4-HD, high-dose quadrivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; LAIV, live attenuated influenza vaccine; LAIV4, quadrivalent live attenuated influenza vaccine; NACI, National Advisory Committee on Immunization

^a IIV3-SD formulations will not be available for use in Canada during the 2021–2022 influenza season

^b Refer to Table 4 of the NACI *Seasonal Influenza Vaccine Statement for 2021–2022* for a summary of vaccine characteristics of LAIV compared with IIV in children 2–17 years of age

^c IIV4-cc is currently authorized for use in adults and children nine years of age and older

^d Refer to Table 5 of the NACI *Seasonal Influenza Vaccine Statement for 2021–2022* for a comparison of the vaccine characteristics of influenza vaccine types available for use in adults 65 years of age and older (5)

^e IIV3-HD formulations will not be available for use in Canada during the 2021–2022 influenza season

Source: Table reproduced from the NACI *Seasonal Influenza Vaccine Statement for 2021–2022* (5)



Table 3: Recommended dose and route of administration, by age, for influenza vaccine types authorized for the 2021–2022 influenza season

Age group	Influenza vaccine type (route of administration)						Number of doses required
	IIV3-SD ^a or IIV4-SD ^b (IM)	IIV4-cc ^c (IM)	IIV3-Adj ^d (IM)	IIV3-HD ^e (IM)	IIV4-HD ^f (IM)	LAI4 ^g (intranasal)	
6–23 months	0.5 mL ^h	–	0.25 mL	–	–	–	1 or 2 ⁱ
2–8 years	0.5 mL	–	–	–	–	0.2 mL (0.1 mL per nostril)	1 or 2 ⁱ
9–17 years	0.5 mL	0.5 mL	–	–	–	0.2 mL (0.1 mL per nostril)	1
18–59 years	0.5 mL	0.5 mL	–	–	–	0.2 mL (0.1 mL per nostril)	1
60–64 years	0.5 mL	0.5 mL	–	–	–	–	1
65 years and older	0.5 mL	0.5 mL	0.5 mL	0.5 mL	0.7 mL	–	1

Abbreviations: IIV3-Adj, adjuvanted trivalent inactivated influenza vaccine; IIV3-HD, high-dose trivalent; IIV4-cc, quadrivalent mammalian cell-culture based inactivated influenza vaccine; IIV4-HD, high-dose quadrivalent inactivated influenza vaccine; IIV3-SD, standard-dose trivalent inactivated influenza vaccine; IIV4-SD, standard-dose quadrivalent inactivated influenza vaccine; IM, intramuscular; LAI4, quadrivalent live attenuated influenza vaccine; –, not applicable

^a IIV3-SD formulations (Agriflu[®] [six months and older], Fluviral[®] [six months and older] and Influvac[®] [three years and older]) are authorized but will not be available for use in Canada during the 2021–2022 influenza season

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

^c Flucelvax[®] Quad (nine years and older)

^d Fluad Pediatric[®] (6–23 months) or Fluad[®] (65 years and older)

^e Fluzone[®] High-Dose (65 years and older) was previously authorized, but marketing of the vaccine has been discontinued as of February 2021

^f Fluzone[®] High-Dose Quadrivalent (65 years and older)

^g FluMist[®] Quadrivalent (2–59 years)

^h 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 (25,26). 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* (27)

ⁱ 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 younger 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

Source: Table reproduced from NACI *Seasonal Influenza Vaccine Statement for 2021–2022* (5)

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. For the 2021–2022 influenza season, NACI newly recommends that Influvac Tetra and Flucelvax Quad may be considered as options among the quadrivalent inactivated influenza vaccines offered to adults and children for their annual vaccination. NACI also newly recommends that Fluzone High-Dose Quadrivalent may be considered as an option for adults 65 years of age and older.

In addition, people capable of transmitting to high-risk individuals, people who provide essential community services and people in direct contact during culling operations with poultry infected with avian influenza are particularly recommended to receive the influenza vaccine.

Authors' statement

AS — Writing, original draft, review, editing

KY — Review, editing

RH — Review, editing

The NACI *Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2021–2022* was prepared by K Young, L Zhao, A Sinilaita, R Stirling and R Harrison, on behalf of the NACI Influenza Working Group, and was approved by NACI.

Competing interests

None.

Acknowledgements

Influenza Working Group members: R Harrison (Chair), I Gemmill, K Klein, D Kumar, J Langley, J McElhaney, A McGeer, D Moore and B Warshawsky

Former members: N Dayneka, S Smith



ADVISORY COMMITTEE STATEMENT

NACI members: S Deeks (Chair), R Harrison (Vice-Chair), J Bettinger, P De Wals, E Dubé, V Dubey, K Hildebrand, K Klein, J Papenburg, C Rotstein, B Sander, S Smith and S Wilson

Former members: C Quach (Chair), N Dayneka, S Gant

Liaison representatives: LM Bucci (Canadian Public Health Association), E Castillo (Society of Obstetricians and Gynaecologists of Canada), A Cohn (Centers for Disease Control and Prevention, United States), L Dupuis (Canadian Nurses Association), J Emili (College of Family Physicians of Canada), D Fell (Canadian Association for Immunization Research Evaluation), M Lavoie (Council of Chief Medical Officers of Health), D Moore (Canadian Paediatric Society), M Naus (Canadian Immunization Committee) and A Pham-Huy (Association of Medical Microbiology and Infectious Disease Canada)

Ex-officio representatives: D Danoff (Marketed Health Products Directorate, Health Canada [HC]), E Henry (Centre for Immunization and Respiratory Infectious Diseases [CIRID], Public Health Agency of Canada [PHAC]), M Lacroix (Public Health Ethics Consultative Group, PHAC), J Pennock (CIRID, PHAC), R Pless (Biologics and Genetic Therapies Directorate, HC), G Poliquin (National Microbiology Laboratory, PHAC), V Beswick-Escanlar (National Defense and the Canadian Armed Forces) and T Wong (First Nations and Inuit Health Branch, Indigenous Services Canada)

The National Advisory Committee on Immunization acknowledges and appreciates the contribution of A House, M Laplante, C Tremblay and M Tunis to this statement.

Funding

The work of the National Advisory Committee on Immunization is supported by the Public Health Agency of Canada.

References

1. World Health Organization. Fact sheet: Influenza (seasonal). Geneva (CH): WHO; 2014. <http://www.who.int/mediacentre/factsheets/fs211/en/>
2. World Health Organization. Tools and toolkits: FluNet. Geneva (CH): WHO; 2021. <https://www.who.int/tools/funet>
3. Public Health Agency of Canada. Flu (influenza): FluWatch surveillance. Ottawa (ON): PHAC; 2020. <https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance.html>
4. Ismail SJ, Hardy K, Tunis MC, Young K, Sicard N, Quach C. A framework for the systematic consideration of ethics, equity, feasibility, and acceptability in vaccine program recommendations. *Vaccine* 2020;38(36):5861–76. [DOI](#) [PubMed](#)
5. National Advisory Committee on Immunization. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2021–2022. Ottawa (ON): PHAC; 2021. <https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2021-2022.html>
6. National Advisory Committee on Immunization. Evidence-based recommendations for immunization—Methods of the National Advisory Committee on Immunization. *Can Commun Dis Rep*. 2009;35(ACS-1):1-10. <https://www.canada.ca/en/public-health/services/reports-publications/canada-communicable-disease-report-ccdr/monthly-issue/2009-35/methods-national-advisory-committee-immunization.html>
7. National Advisory Committee on Immunization. An Advisory Committee Statement. Supplemental Statement – Mammalian Cell-Culture Based Influenza Vaccines. Ottawa (ON): PHAC; 2020. <https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/mammalian-cell-culture-based-influenza-vaccines.html>
8. Harris RP, Helfand M, Woolf SH, Lohr KN, Mulrow CD, Teutsch SM, Atkins D; Methods Work Group, Third US Preventive Services Task Force. Current methods of the US Preventive Services Task Force: a review of the process. *Am J Prev Med* 2001;20(3 Suppl):21–35. [DOI](#) [PubMed](#)
9. National Advisory Committee on Immunization. Guidance for influenza vaccine delivery in the presence of COVID-19. Ottawa (ON): PHAC; 2020. <https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-influenza-vaccine-delivery-covid-19.html>
10. Public Health Agency of Canada. Guidance on the use of influenza vaccine in the presence of COVID-19. <https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-use-influenza-vaccine-covid-19.html>
11. Boikos C, Sylvester G, Sampalis J, Mansi J. Effectiveness of the Cell Culture- and Egg-Derived, Seasonal Influenza Vaccine during the 2017-2018 Northern Hemisphere Influenza Season. Canadian Immunization Conference. 2018. 2018 Dec 04-06; Ottawa, ON, Canada [poster presentation]. <https://www.izsummitpartners.org/content/uploads/2019/05/1-effectiveness-of-cell-culture-and-egg-derived-flu-vax-during-2017-2018-flu-season.pdf>
12. DeMarcus L, Shoubaki L, Federinko S. Comparing influenza vaccine effectiveness between cell-derived and egg-derived vaccines, 2017-2018 influenza season. *Vaccine* 2019;37(30):4015–21. [DOI](#) [PubMed](#)
13. Izurieta HS, Chillarige Y, Kelman J, Wei Y, Lu Y, Xu W, Lu M, Pratt D, Chu S, Wernecke M, MaCurdy T, Forshee R. Relative effectiveness of cell-cultured and egg-based influenza vaccines among elderly persons in the United States, 2017-18, 2017-18. *J Infect Dis* 2019;220(8):1255–64. [DOI](#) [PubMed](#)



14. Klein NP, Fireman B, Goddard K, Zerbo O, Asher J, Zhou J, King J, Lewis N. LB15. Vaccine Effectiveness of Flucelvax Relative to Inactivated Influenza Vaccine During the 2017–18 Influenza Season in Northern California. *Open Forum Infect Dis.* 2018;5(Suppl 1):S764. [DOI](#)
15. Bart S, Cannon K, Herrington D, Mills R, Forleo-Neto E, Lindert K, Abdul Mateen A. Immunogenicity and safety of a cell culture-based quadrivalent influenza vaccine in adults: A Phase III, double-blind, multicenter, randomized, non-inferiority study. *Hum Vaccin Immunother* 2016;12(9):2278–88. [DOI](#) [PubMed](#)
16. Hartwickson R, Cruz M, Ervin J, Brandon D, Forleo-Neto E, Dagnow AF, Chandra R, Lindert K, Mateen AA. Non-inferiority of mammalian cell-derived quadrivalent subunit influenza virus vaccines compared to trivalent subunit influenza virus vaccines in healthy children: a phase III randomized, multicenter, double-blind clinical trial. *Int J Infect Dis* 2015;41:65–72. [DOI](#) [PubMed](#)
17. Frey S, Vesikari T, Szymczakiewicz-Multanowska A, Lattanzi M, Izu A, Groth N, Holmes S. Clinical efficacy of cell culture-derived and egg-derived inactivated subunit influenza vaccines in healthy adults. *Clin Infect Dis* 2010;51(9):997–1004. [DOI](#) [PubMed](#)
18. Vesikari T, Block SL, Guerra F, Lattanzi M, Holmes S, Izu A, Gaitatzis N, Hilbert AK, Groth N. Immunogenicity, safety and reactogenicity of a mammalian cell-culture-derived influenza vaccine in healthy children and adolescents three to seventeen years of age. *Pediatr Infect Dis J* 2012;31(5):494–500. [DOI](#) [PubMed](#)
19. Ambrozaitis A, Groth N, Bugarini R, Sparacio V, Podda A, Lattanzi M. A novel mammalian cell-culture technique for consistent production of a well-tolerated and immunogenic trivalent subunit influenza vaccine. *Vaccine* 2009;27(43):6022–9. [DOI](#) [PubMed](#)
20. Szymczakiewicz-Multanowska A, Groth N, Bugarini R, Lattanzi M, Casula D, Hilbert A, Tsai T, Podda A. Safety and immunogenicity of a novel influenza subunit vaccine produced in mammalian cell culture. *J Infect Dis* 2009;200(6):841–8. [DOI](#) [PubMed](#)
21. Loebermann M, Fritzsche C, Geerdes-Fenge H, Heijnen E, Kirby D, Reisinger EC. A phase III, open-label, single-arm, study to evaluate the safety and immunogenicity of a trivalent, surface antigen inactivated subunit influenza virus vaccine produced in mammalian cell culture (Optaflu®) in healthy adults. *Infection* 2019;47(1):105–9. [DOI](#) [PubMed](#)
22. Nolan T, Chotpitayasunondh T, Capeding MR, Carson S, Senders SD, Jaehnig P, de Rooij R, Chandra R. Safety and tolerability of a cell culture derived trivalent subunit inactivated influenza vaccine administered to healthy children and adolescents: A Phase III, randomized, multicenter, observer-blind study. *Vaccine* 2016;34(2):230–6. [DOI](#) [PubMed](#)
23. Seqirus UK. Limited. Product monograph: Flucelvax® QUAD: Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures). 2021. <https://www.seqirus.ca/-/media/seqirus-canada/docs-en/flucelvax-quad-ca-pm-2-approved-8mar2021.pdf?la=en-us&hash=9504E4305DF163072338F3C307640B7379230DC8>
24. Public Health Agency of Canada. Canadian Immunization Guide: Part 3 – Vaccination of specific populations. Ottawa (ON): PHAC; 2015. <https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-3-vaccination-specific-populations.html>
25. Langley JM, Vanderkooi OG, Garfield HA, Hebert J, Chandrasekaran V, Jain VK, Fries L. Immunogenicity and safety of 2 dose levels of a thimerosal-free trivalent seasonal influenza vaccine in children aged 6–35 months: a randomized, controlled trial. *J Pediatric Infect Dis Soc* 2012;1(1):55–63. [DOI](#) [PubMed](#)
26. Skowronski DM, Hottes TS, Chong M, De Serres G, Scheifele DW, Ward BJ, Halperin SA, Janjua NZ, Chan T, Sabaiduc S, Petric M. Randomized controlled trial of dose response to influenza vaccine in children aged 6 to 23 months. *Pediatrics* 2011;128(2):e276–89. [DOI](#) [PubMed](#)
27. National Advisory Committee on Immunization (NACI). Statement on Seasonal Influenza Vaccine for 2011–2012. *Can Commun Dis Rep* 2011;37(ACS-5):1–55. [DOI](#)



Appendix

Table A1: Ratings for strength of National Advisory Committee on Immunization (NACI) recommendations and grade of evidence

Strength of NACI recommendation based on factors not isolated to strength of evidence (e.g. public health need)	Strong	Discretionary
Wording	"should/should not be offered"	"may be considered"
Rationale	Known/anticipated advantages outweigh known/anticipated disadvantages ("should"), OR known/anticipated disadvantages outweigh known/anticipated advantages ("should not")	Known/anticipated advantages closely balanced with known/anticipated disadvantages, OR uncertainty in the evidence of advantages and disadvantages exists
Implication	A strong recommendation applies to most populations/individuals and should be followed unless a clear and compelling rationale for an alternative approach is present	A discretionary recommendation may be considered for some populations/individuals in some circumstances Alternative approaches may be reasonable
Grade of evidence <i>based on assessment of the body of evidence</i>	A: good evidence to recommend B: fair evidence to recommend C: conflicting evidence, however other factors may influence decision-making D: fair evidence to recommend against E: good evidence to recommend against I: insufficient evidence (in quality or quantity), however other factors may influence decision-making	