Summary of the National Advisory Committee on Immunization (NACI) Seasonal Influenza Vaccine Statement for 2022–2023

Angela Sinilaite[1], Jesse Papenburg[2,3,4,5] on behalf of the National Advisory Committee on Immunization (NACI)*

Abstract

Background: The National Advisory Committee on Immunization (NACI) reviews the evolving evidence on influenza immunization and provides annual recommendations regarding the use of authorized seasonal influenza vaccines to the Public Health Agency of Canada.

Objective: To summarize the NACI seasonal influenza vaccine recommendations for 2022–2023 and to highlight new recommendations and supporting evidence.

Methods: In the preparation of the Statement on Seasonal Influenza Vaccine for 2022–2023, NACI's Influenza Working Group followed the NACI evidence-based process for developing recommendations. The recommendations were then considered and approved by NACI in light of the available evidence.

Results: The following key updates and new recommendations have been made for the 2022–2023 season: 1) updated information/guidance on influenza vaccination in the context of the coronavirus disease 2019 (COVID-19) has been incorporated; 2) Supemtek™ recombinant influenza vaccine may be considered for use among the quadrivalent influenza vaccines offered to adults 18 years of age and older for annual influenza immunization; and 3) Flucelvax® Quad may be considered among the quadrivalent influenza vaccines offered to adults and children two years of age and older.

Conclusion: NACI continues to recommend that an age-appropriate influenza vaccine should be offered annually for all individuals aged six months of age and older who do not have contraindications to the vaccine, with particular focus on people at high risk of influenza-related complications or hospitalization, people capable of transmitting influenza to those at high risk, and other groups for whom influenza vaccination is particularly recommended.

Affiliations

[1] Centre for Immunization Readiness, Public Health Agency of Canada, Ottawa, ON

[2] NACI Influenza Working Group Chair

[3] Division of Pediatric Infectious Diseases, Department of Pediatrics, Montréal Children's Hospital of the McGill University Health Centre, Montréal, QC

[4] Division of Microbiology, Department of Clinical Laboratory Medicine, Optilab Montréal - McGill University Health Centre, Montréal, QC

[5] Department of Epidemiology, Biostatistics, and Occupational Health, School of Population and Global Health, McGill University, Montréal, QC

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

Suggested citation: Sinilaite A, Papenburg J, on behalf of the National Advisory Committee on Immunization (NACI). Summary of the National Advisory Committee on Immunization (NACI) Seasonal Influenza Vaccine Statement for 2022–2023. Can Commun Dis Rep 2022;48(9):373–82. https://doi.org/10.14745/ccdr.v48i09a01
Keywords: National Advisory Committee on Immunization, NACI, influenza, influenza vaccine, guidance

Introduction

Seasonal influenza epidemics lead to significant morbidity and mortality in the Canadian population (1) and increase the demand on the healthcare system in the fall and winter months. Influenza circulation has been at a historical low since the onset of the coronavirus disease 2019 (COVID-19) pandemic, which has been associated with various reasons including the implementation of non-pharmaceutical public health measures (e.g. masking, social distancing) against COVID-19. Prior to the COVID-19 pandemic, the global annual attack rate was estimated to be 5%–10% in adults and 20%–30% in children (2). Although the burden of influenza can vary from year to year, it is estimated that in Canada there are an average of 12,200 hospitalizations related to influenza and approximately 3,500 deaths attributable to influenza annually (3,4). Current information on influenza activity internationally can be found on the World Health Organization's Global Influenza Program

website (5) and nationally on the Public Health Agency of Canada's (PHAC) FluWatch website (6).

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 annual update of the *NACI Statement on Seasonal Influenza Vaccine* 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.

This article provides a concise summary of NACI's recommendations and supporting information for the 2022–2023 influenza season, including conclusions from evidence reviews on 1) a new, recombinant quadrivalent influenza vaccine (Supemtek™; RIV4) and 2) a mammalian cell-based influenza vaccine (Flucelvax® Quad; IIV4-cc). Updated guidance for use of influenza vaccines during the COVID-19 pandemic is also highlighted. 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 2022–2023* (the Statement) (7) and related publications.

Influenza vaccine abbreviations

The current abbreviations used by NACI to describe the defining features of various types of influenza vaccines are presented in **Table 1**. For the 2022–2023 Statement, recombinant influenza vaccine (RIV) has been added as a new category of influenza vaccines authorized for use in Canada.

Table 1: National Advisory Committee on Immunization 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
Recombinant influenza vaccine (RIV)	Quadrivalent (RIV4)	Recombinant[e], unadjuvanted, IM administered	RIV4
Live attenuated influenza vaccine (LAIV)	Trivalent (LAIV3)	Unadjuvanted, Nasal spray, egg-based	LAIV3
	Quadrivalent (LAIV4)	Unadjuvanted, Nasal spray, egg-based	LAIV4

Abbreviations: IM, intramuscular; 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; 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; RIV, recombinant influenza vaccine; RIV4, quadrivalent recombinant influenza vaccine

[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; "-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 Fluad® or Fluad 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

[e] 45 µg HA per strain

Source: Table reproduced from NACI Seasonal Influenza Vaccine Statement for 2022–2023 (7)

Methods

In the preparation of the Statement on Seasonal Influenza Vaccine for 2022–2023, the NACI 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 (8). More details regarding the strength of NACI recommendations and the grading of evidence is available in **Table A1** in the **Appendix**. 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 (9).

For the 2022–2023 influenza season, the NACI IWG reviewed evidence and developed new recommendations regarding the use of two vaccines: 1) Supemtek, a new, quadrivalent recombinant influenza vaccine (RIV4) and 2) Flucelvax Quad, a mammalian cell culture-based, inactivated seasonal influenza vaccine (IIV4-cc). Supemtek is the first and, to date, the only available recombinant influenza vaccine that was first authorized for use in Canada in adults 18 years of age and older on January 14, 2021. NACI has not previously made a recommendation on recombinant influenza vaccines in any population; therefore, the NACI IWG oversaw the completion of a systematic literature review and meta-analysis on the vaccine efficacy, effectiveness, immunogenicity and safety of RIV4 in adults 18 years of age and older to inform the development of guidance on its use among adults in Canada. The methodology was specified *a priori* in a written protocol that included the research questions, search strategy, inclusion and exclusion criteria and quality assessment. The search spanned publications from January 1, 2000, to January 12, 2021, with an update to August 8, 2021. The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework (10) was used to organize and analyze the quality of the body of evidence across studies in developing recommendations. The strength and certainty of evidence included in syntheses were assessed by two independent reviewers using the GRADE system. NACI provided a new recommendation based on assessment of the available evidence.

Flucelvax Quad (IIV4-cc) is the first and, to date, the only mammalian cell culture-based inactivated seasonal influenza vaccine available for use in Canada. It was first authorized for use in Canada in adults and children nine years of age and older on November 22, 2019. In support of the original recommendation for use of the Flucelvax Quad in adults and children nine years of age and older, NACI conducted a systematic review of the literature to examine vaccine efficacy, effectiveness, immunogenicity and safety data for this age group. The systematic review methodology was developed with the NACI IWG and specified *a priori* in a written protocol that included review questions, search strategy, inclusion and exclusion criteria and quality assessment. Further details, recommendations and supporting evidence on the use of Flucelvax Quad in adults and children nine years of age and older can be found in the *NACI Supplemental Statement – Mammalian Cell Culture-Based Influenza Vaccines* (11) and have also been incorporated into the Statement on Seasonal Influenza Vaccine for 2021–2022. On March 8, 2021, Health Canada approved an expanded age indication for the use of Flucelvax Quad in children down to two years of age and older. Following the review and analysis of Health Canada's assessments of clinical trial evidence submitted by the manufacturer in support of the age extension, the NACI IWG proposed new recommendations for vaccine use to NACI. NACI critically appraised the available evidence and approved the specific recommendations brought forward.

Results

Use of seasonal influenza vaccine in the presence of COVID-19

Influenza vaccination remains a critical tool to minimize the morbidity and mortality related to potential influenza and COVID-19 co-circulation and to reduce the burden on the Canadian healthcare system to enhance the capacity to respond to ongoing COVID-19 activity. Public Health Agency of Canada guidance on seasonal influenza vaccination, developed in consultation with NACI and the Canadian Immunization Committee, to support provincial and territorial vaccine programs and primary care providers offering influenza vaccine during the COVID-19 pandemic, is available on the *Guidance on the use of influenza vaccine in the presence of COVID-19* web page (12). The web content will continue to be reviewed regularly and updates will be made as necessary to align with the currently available scientific evidence, expert opinion and public health context.

Administration of COVID-19 vaccines may occur at the same time as, or at any time before or after, influenza immunization (including all seasonal influenza vaccines or LAIV) for those aged 12 years and older as of September 2021. Readers should consult the Canadian Immunization Guide COVID-19 chapter (13) for updated NACI guidance on the concomitant administration of influenza and COVID-19 vaccines as the number of authorized COVID-19 vaccines and the age groups eligible to receive them expand.

Inclusion of quadrivalent recombinant seasonal influenza vaccine (RIV4)

Recombinant protein technology is a novel, alternative platform for influenza vaccine manufacturing that differs considerably from existing egg-based and mammalian cell culture-based

technologies. Although Supemtek is the first, and currently the only, recombinant seasonal influenza vaccine authorized in Canada, recombinant protein technology is a well-established vaccine-manufacturing platform that may allow for faster, more flexible production times, yields a highly pure product, and mitigates the risk of mismatch between the vaccine and circulating influenza virus strains. These advantages can help to overcome challenges associated with conventional egg-based influenza vaccine production and to improve the development process and quality of influenza vaccines for reducing and preventing future influenza epidemics and pandemics. However, they are also counterbalanced by barriers that may restrict feasibility, including limited RIV manufacturing infrastructure and higher cost of production (14).

Ten eligible studies were included in the evidence synthesis. Two vaccine efficacy and effectiveness outcomes were ranked as critical to decision making during the outcome prioritization process: efficacy or effectiveness against laboratory-confirmed influenza (LCI)-related mortality and efficacy or effectiveness against LCI. The peer-reviewed published evidence on the efficacy of RIV4 against LCI illness was sparse. No studies reporting on the efficacy of RIV4 against LCI-related mortality were identified. One randomized controlled trial (RCT) that assessed the efficacy of RIV4 against LCI in adults aged 50 years and older provided evidence that RIV4 may potentially offer improved protection against laboratory-confirmed influenza A infection compared to standard egg-based influenza vaccines (15). However, all the relative vaccine efficacy analyses were conducted using data only from the 2014–2015 influenza season in the United States (US), which was influenza A(H3N2)-dominant, and in adults aged 50 years and older. Peer-reviewed, published clinical data pertaining to the efficacy or effectiveness of vaccination with RIV4 during pregnancy or including breastfeeding were not available at the time of this review. Overall, there is fair evidence (of low certainty) that the efficacy of RIV4 is non-inferior to traditional egg-based comparators, based on data in adults aged 50 years and older.

Three vaccine immunogenicity outcomes were ranked as critical during the outcome prioritization process of this review: seroprotection rate; seroconversion rate; and geometric mean titre ratio. Eight RCTs that assessed the immunogenicity of RIV4 compared to different vaccines, including IIV3-HD, IIV3-Adj, IIV4-SD and IIV4-cc, were identified in this review. Of these studies, two were conducted during the 2014–2015 influenza season (15,16), three were conducted over the 2017–2018 influenza season (17–19) and three were conducted over the 2018–2019 influenza season (20–22). The RCTs were of good quality overall. Non-inferiority was assessed using the criteria specified by the US Food and Drug Administration (23). Across studies, RIV4 demonstrated non-inferiority compared to egg-based influenza vaccines against influenza A(H1N1), most strains of A(H3N2), and B/Yamagata lineage (15–22). Findings differed across studies regarding the non-inferiority of RIV4 compared to egg-based influenza vaccines against influenza B/Victoria lineage based on seroconversion rates, seroprotection rates and geometric mean titre ratio (15,16). Overall, there is fair evidence (of moderate certainty) that the immunogenicity for RIV4 is non-inferior to traditional egg-based comparators, based on data in adults aged 18 years and older.

Two vaccine safety outcomes were ranked as critical during the outcome prioritization process for this review: serious adverse events (SAEs) and solicited systemic adverse events (AEs). Six eligible studies were identified that assessed the safety of RIV4 in adults, including five RCTs and one review of post-marketing surveillance data from the US. Of these studies, two were conducted during the 2014–2015 influenza season (15,16), two were conducted during the 2017–2018 influenza season (18,24), one was conducted during the 2018–2019 influenza season (21) and one study (25) reported data from the Vaccine Adverse Event Reporting System (VAERS) from July 1, 2017, through June 30, 2020. The five RCTs found that Supemtek is a safe, well-tolerated and immunogenic alternative to conventional egg-based influenza vaccines for adults (noting that no published clinical data pertaining to the safety of vaccination with RIV4 during pregnancy were available at the time of this review to inform vaccine-associated risks) (15,16,18,21,24). No elevated risk of severe allergic reactions compared to traditional egg-based influenza vaccines was identified; however, lack of egg proteins in RIV4 does not eliminate the risk of allergic reactions following vaccine administration, as allergic reactions can occur following exposure to any drug or vaccine (26). Overall, there is evidence of moderate certainty that RIV4 is a safe and well-tolerated alternative to conventional egg-based influenza vaccines for adults.

Based on the review of available pre-licensure and post-market clinical trial and surveillance data, NACI made the following recommendation, supplementing NACI's overarching recommendation for influenza vaccination, which is available in the NACI Seasonal Influenza Vaccine Statement (7):

NACI recommends that Supemtek may be considered among the seasonal influenza vaccines offered to adults 18 years of age and older (Discretionary NACI Recommendation).

- **NACI concludes that there is fair evidence to recommend vaccination of adults 18 years of age and older with Supemtek (Grade B Evidence)**

For complete details of this review, rationale, relevant considerations and additional information supporting this recommendation, refer to the *NACI Supplemental Statement: Recombinant Influenza Vaccines* (27). NACI will continue to monitor the evidence related to recombinant influenza vaccines and will update this supplemental statement as needed and as data on Supemtek from several different influenza seasons accumulates.

Updated recommendations on mammalian cell culture-based quadrivalent influenza vaccine (IIV4-cc)

The age extension for the use of Flucelvax Quad in adults and children two years of age and older was based on a phase 3/4 randomized clinical trial of efficacy, immunogenicity and safety of the vaccine in children two years to less than 18 years of age. The clinical trial was conducted in eight countries in Europe and South East Asia over three influenza seasons (Southern Hemisphere 2017 influenza season and Northern Hemisphere 2017–2018 and 2018–2019 influenza seasons). Overall, the quality of the evidence was considered good. NACI concluded that Flucelvax Quad is effective and safe compared to comparable vaccines, and elicits a robust immune response based on direct evidence in children two years to less than nine years of age. The quantity of direct safety and immunogenicity evidence for Flucelvax Quad in children two years to less than nine years of age is limited; however, the currently reviewed and previous clinical trial evidence provided fair evidence of efficacy, immunogenicity, and safety in children. Therefore, NACI recommended that **Flucelvax Quad may be considered among the IIV4 offered to adults and children two years of age and older (Discretionary NACI Recommendation).**

Additional information supporting this recommendation can be found in Section IV.1 of the NACI Seasonal Influenza Vaccine Statement for 2022–2023 (7). Notably, Flucelvax Quad was recently authorized by Health Canada for use in adults and children six months 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 2022–2023. Further details are available in the new product monograph for this vaccine (28).

Summary of National Advisory Committee on Immunization recommendations for the use of influenza vaccines for the 2022–2023 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 kg/m^2 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 individuals
- 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

- Healthcare 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 childcare 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 CIG for additional information about vaccination of people with chronic diseases (29)

Source: Table reproduced from NACI Seasonal Influenza Vaccine Statement for 2022–2023 (7)

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	• 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 LAIV4	• An age-appropriate quadrivalent influenza vaccine (IIV4-SD, LAIV4 or IIV4-cc) should be used in children without contraindications or precautions (see text below applicable to LAIV), including those with 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 • 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) ◦ Stable HIV infection, if the child is currently being treated with ART (i.e. HAART) and has adequate immune function • LAIV should not be used in children or adolescents for whom it is contraindicated or for whom there are warning and precautions such as those with: ◦ 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 4 months) and has adequate immune function ◦ Pregnancy ◦ In pregnancy, IIV4-SD or IIV4-cc should be used instead • If IIV4-SD, IIV4-cc and LAIV4 are not available, IIV3-SD should be used	
18–59 years	IIV3-SD[a] IIV4-SD IIV4-cc RIV4 LAIV4	• Any of the available influenza vaccines authorized for this age group should be used in adults 18–59 years without contraindications or precautions, noting the following consideration and exceptions: ◦ There is some evidence that IIV may provide better efficacy than LAIV in healthy adults • LAIV is not recommended for: ◦ Pregnant individuals ◦ 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 RIV4	• Any of the available influenza vaccines authorized for this age group should be used in adults 60–64 years without contraindications	
65 years and older[c]	IIV3-SD[a] IIV3-Adj IIV3-HD[d] IIV4-SD IIV4-cc RIV4	**Individual-level decision-making** • 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 ◦ 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** • Any of the available influenza vaccines authorized in this age group should be used ◦ 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: ART: antiretroviral therapy; HAART, highly active antiretroviral therapy; 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-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; RIV4, quadrivalent recombinant influenza vaccine

[a] IIV3-SD formulations will not be available for use in Canada during the 2022–2023 influenza season

[b] Refer to Table 4 of the NACI Seasonal Influenza Vaccine Statement for 2022–2023 for a summary of vaccine characteristics of LAIV compared with IIV in children 2–17 years of age

[c] Refer to Table 5 of the NACI Seasonal Influenza Vaccine Statement for 2022–2023 for a comparison of the vaccine characteristics of influenza vaccine types available for use in adults 65 years of age and older

[d] IIV3-HD formulations will not be authorized or available for use in Canada during the 2022–2023 influenza season

Source: Table reproduced from NACI Seasonal Influenza Vaccine Statement for 2022–2023 (7)

Table 3: Recommended dose and route of administration, by age, for influenza vaccine types authorized for the 2022–2023 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)	IIV4-HD[e] (IM)	RIV4[f] (IM)	LAIV4[g] (intranasal)	
6–23 months	0.5 mL[h]	-	0.25 mL	-	-	-	1 or 2[i]
2–8 years	0.5 mL	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	-	-	0.5 mL	0.2 mL (0.1 mL per nostril)	1
60–64 years	0.5 mL	0.5 mL	-	-	0.5 mL	-	1
65 years and older	0.5 mL	0.5 mL	0.5 mL	0.7 mL	0.5 mL	-	1

Abbreviations: 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; IM, intramuscular; LAIV4, quadrivalent live attenuated influenza vaccine; RIV4:quadrivalent recombinant influenza vaccine

[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 (two years and older)

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

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

[f] Supemtek™ (18 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 (29,30). 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

[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 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

Source: Table reproduced from NACI Seasonal Influenza Vaccine Statement for 2022–2023 (7)

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, 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 2022–2023 influenza season, NACI newly recommend that Supemtek recombinant influenza vaccine may be considered for use among the quadrivalent influenza vaccines offered to adults 18 years of age and older. NACI also newly recommends that Flucelvax Quad may be considered among the quadrivalent influenza vaccines offered to adults and children two years of age and older.

Authors' statement

AS — Writing, original draft, review, editing
JP — Review, editing

The *NACI Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023* was prepared by A Sinilaite, R Stirling and R Harrison, on behalf of the NACI Influenza Working Group, and was approved by NACI.

Competing interests

J Papenburg reports grants to his institution from MedImmune, Sanofi Pasteur, Merck and AbbVie and personal fees from AbbVie, Astra-Zeneca and Merck; all of which were outside of the submitted work.

Acknowledgements

Influenza Working Group members: J Papenburg (Chair), P De Wals, D Fell, I Gemmill, R Harrison, J Langley, A McGeer, and D Moore

Former members: N Dayneka, K Klein, D Kumar, J McElhaney, S Smith, and B Warshawsky

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

Former member: C Quach (Chair)

Liaison representatives: L Bill (Canadian Indigenous Nurses Association), 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), J Comeau (Association of Medical Microbiology and Infectious Disease Control), L Dupuis (Canadian Nurses Association), E Adams (Indigenous Physicians Association of Canada), J Hu (College of Family Physicians of Canada), M Lavoie (Council of Chief Medical Officers of Health), D Moore (Canadian Paediatric Society), M Naus (Canadian Immunization Committee), and A Ung (Canadian Pharmacists Association)

Ex-officio representatives: V Beswick-Escanlar (National Defence and the Canadian Armed Forces), E Henry (Centre for Immunization and Respiratory Infectious Diseases [CIRID), Public Health Agency of Canada [PHAC]), M Lacroix (Public Health Ethics Consultative Group, PHAC), C Lourenco (Biologic and Radiopharmaceutical Drugs Directorate, Health Canada [HC]), D MacDonald (COVID-19 Epidemiology and Surveillance, PHAC), S Ogunnaike-Cooke (CIRID, PHAC), K Robinson (Marketed Health Products Directorate, HC), M Routledge (National Microbiology Laboratory, PHAC), and T Wong (First Nations and Inuit Health Branch, Indigenous Services Canada)

The NACI acknowledges and appreciates the contribution of A Gil, C Tremblay, M Tunis, M Xi, and K Young to this statement.

Funding

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

References

1. Statistics Canada. The 10 leading causes of death, 2011. Ottawa (ON): Statistics Canada; 2018. http://www.statcan.gc.ca/pub/82-625-x/2014001/article/11896-eng.htm
2. World Health Organization. Fact sheet: Influenza (Seasonal). Geneva (CH): WHO; 2014. https://www.who.int/news-room/fact-sheets/detail/influenza-(seasonal)
3. Schanzer DL, McGeer A, Morris K. Statistical Estimates of Respiratory Admissions Attributable to Seasonal and Pandemic Influenza for Canada. Influenza Other Respir Viruses 2013;7(5):799-808. DOI
4. Schanzer DL, Sevenhuysen C, Winchester B, Mersereau T. Estimating Influenza Deaths In Canada, 1992–2009. PloS One 2013;8(11):E80481. DOI
5. World Health Organization. Global Influenza Programme. Geneva (CH): WHO; 2022. https://www.who.int/teams/global-influenza-programme
6. Public Health Agency of Canada. Flu (influenza): FluWatch surveillance. Ottawa (ON): PHAC; 2021. https://www.canada.ca/en/public-health/services/diseases/flu-influenza/influenza-surveillance.html
7. National Advisory Committee on Immunization. Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2022–2023. Ottawa (ON): PHAC; 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/canadian-immunization-guide-statement-seasonal-influenza-vaccine-2022-2023.html
8. 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/content/dam/phac-aspc/migration/phac-aspc/publicat/ccdr-rmtc/09pdf/ccdr-rmtc-vol-35-acs-dcc-1.pdf
9. 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
10. Grading of Recommendations, Assessment, Development and Evaluation (GRADE) Working Group. GRADE Handbook. 2013. https://gdt.gradepro.org/app/handbook/handbook.html
11. 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

12. National Advisory Committee on Immunization. Guidance on the use of influenza vaccine in the presence of COVID-19. Ottawa (ON): PHAC; 2022. https://www.canada.ca/en/public-health/services/immunization/national-advisory-committee-on-immunization-naci/guidance-use-influenza-vaccine-covid-19.html

13. National Advisory Committee on Immunization. Part 4 – Active Vaccines. COVID-19 vaccine: Canadian Immunization Guide. Ottawa (ON): PHAC; 2022. https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-26-covid-19-vaccine.html

14. Harding AT, Heaton NS. Efforts to Improve the Seasonal Influenza Vaccine. Vaccines 2018;6(2):E19. DOI

15. Dunkle LM, Izikson R, Patriarca P, Goldenthal KL, Muse D, Callahan J, Cox MMJ; PSC12 Study Team. Efficacy of Recombinant Influenza Vaccine in Adults 50 Years of Age or Older. N Engl J Med 2017;376(25):2427–36. DOI

16. Dunkle LM, Izikson R, Patriarca PA, Goldenthal KL, Muse D, Cox MMJ. Randomized Comparison of Immunogenicity and Safety of Quadrivalent Recombinant Versus Inactivated Influenza Vaccine in Healthy Adults 18–49 Years of Age. J Infect Dis 2017;216(10):1219–26. DOI

17. Belongia EA, Levine MZ, Olaiya O, Gross FL, King JP, Flannery B, McLean HQ. Clinical trial to assess immunogenicity of high-dose, adjuvanted, and recombinant influenza vaccines against cell-grown A(H3N2) viruses in adults 65 to 74 years, 2017–2018. Vaccine 2020;38(15):3121–8. DOI

18. Cowling BJ, Perera RAPM, Valkenburg SA, Leung NHL, Iuliano AD, Tam YH, Wong JHF, Fang VJ, Li APY, So HC, Ip DKM, Azziz-Baumgartner E, Fry AM, Levine MZ, Gangappa S, Sambhara S, Barr IG, Skowronski DM, Peiris JSM, Thompson MG. Comparative Immunogenicity of Several Enhanced Influenza Vaccine Options for Older Adults: A Randomized, Controlled Trial. Clin Infect Dis 2020;71(7):1704–14. DOI

19. Gouma S, Zost SJ, Parkhouse K, Branche A, Topham DJ, Cobey S, Hensley SE. Comparison of Human H3N2 Antibody Responses Elicited by Egg-Based, Cell-Based, and Recombinant Protein–Based Influenza Vaccines During the 2017–2018 Season. Clin Infect Dis 2020;71(6):1447–53. DOI

20. Wang W, Alvarado-Facundo E, Vassell R, Collins L, Colombo RE, Ganesan A, Geaney C, Hrncir D, Lalani T, Markelz AE, Maves RC, McClenathan B, Mende K, Richard SA, Schofield C, Seshadri S, Spooner C, Utz GC, Warkentien TE, Levine M, Coles CL, Burgess TH, Eichelberger M, Weiss CD. Comparison of A(H3N2) Neutralizing Antibody Responses Elicited by 2018–2019 Season Quadrivalent Influenza Vaccines Derived from Eggs, Cells, and Recombinant Hemagglutinin. Clin Infect Dis 2021;73(11):e4312–20. DOI

21. Shinde V, Cai R, Plested J, Cho I, Fiske J, Pham X, Zhu M, Cloney-Clark S, Wang N, Zhou H, Zhou B, Patel N, Massare MJ, Fix A, Spindler M, Thomas DN, Smith G, Fries L, Glenn GM. Induction of Cross-Reactive Hemagglutination Inhibiting Antibody and Polyfunctional CD4+ T-Cell Responses by a Recombinant Matrix-M–Adjuvanted Hemagglutinin Nanoparticle Influenza Vaccine. Clin Infect Dis 2021;73(11):e4278–87. DOI

22. Dawood FS, Naleway AL, Flannery B, Levine MZ, Murthy K, Sambhara S, Gangappa S, Edwards L, Ball S, Grant L, Belongia E, Bounds K, Cao W, Gross FL, Groom H, Fry AM, Rentz Hunt D, Jeddy Z, Mishina M, Kim SS, Wesley MG, Spencer S, Thompson MG, Gaglani M. Comparison of the Immunogenicity of Cell Culture-Based and Recombinant Quadrivalent Influenza Vaccines to Conventional Egg-Based Quadrivalent Influenza Vaccines Among Healthcare Personnel Aged 18–64 Years: A Randomized Open-Label Trial. Clin Infect Dis 2021;73(11):1973–81. DOI

23. US Food and Drug Administration. Guidance for Industry: Clinical Data Needed to Support the Licensure of Seasonal Inactivated Influenza Vaccines. FDA; 2007; (accessed 2021-06-05). https://Www.Fda.Gov/Downloads/Biologicsbloodvaccines/Guidancecomplianceregulatoryinformation/Guidances/Vaccines/Ucm091990.Pdf

24. Cowling BJ, Thompson MG, Ng TWY, Fang VJ, Perera RAPM, Leung NHL, Chen Y, So HC, Ip DKM, Iuliano AD. Comparative Reactogenicity of Enhanced Influenza Vaccines in Older Adults. J Infect Dis 2020;222(8):1383–91. DOI

25. Woo EJ, Moro PL. Postmarketing safety surveillance of quadrivalent recombinant influenza vaccine: Reports to the vaccine adverse event reporting system. Vaccine 2021;39(13):1812–7. DOI

26. Grohskopf LA, Alyanak E, Broder KR, Blanton LH, Fry AM, Jernigan DB, Atmar RL. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2020–21 Influenza Season. MMWR Recomm Rep 2020;69(8):1–24. DOI

27. National Advisory Committee on Immunization. An Advisory Committee Statement. Supplemental Statement – Recombinant Influenza Vaccines. Ottawa (ON): PHAC; 2022. https://www.canada.ca/en/public-health/services/publications/vaccines-immunization/recombinant-influenza-vaccines-supplemental-statement-canadian-immunization-guide-seasonal-influenza-vaccine-2022-2023.html

28. Seqirus UK. Product monograph: Flucelvax® QUAD: Influenza Vaccine (surface antigen, inactivated, prepared in cell cultures). Maidenhead (UK): Seqirus; 2022. https://pdf.hres.ca/dpd_pm/00065550.PDF

29. 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

30. 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

31. 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

Appendix

Table A1: National Advisory Committee on Immunization recommendations: strength of recommendation 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 (based on assessment of the body of evidence)	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	

Abbreviation: NACI, National Advisory Committee on Immunization