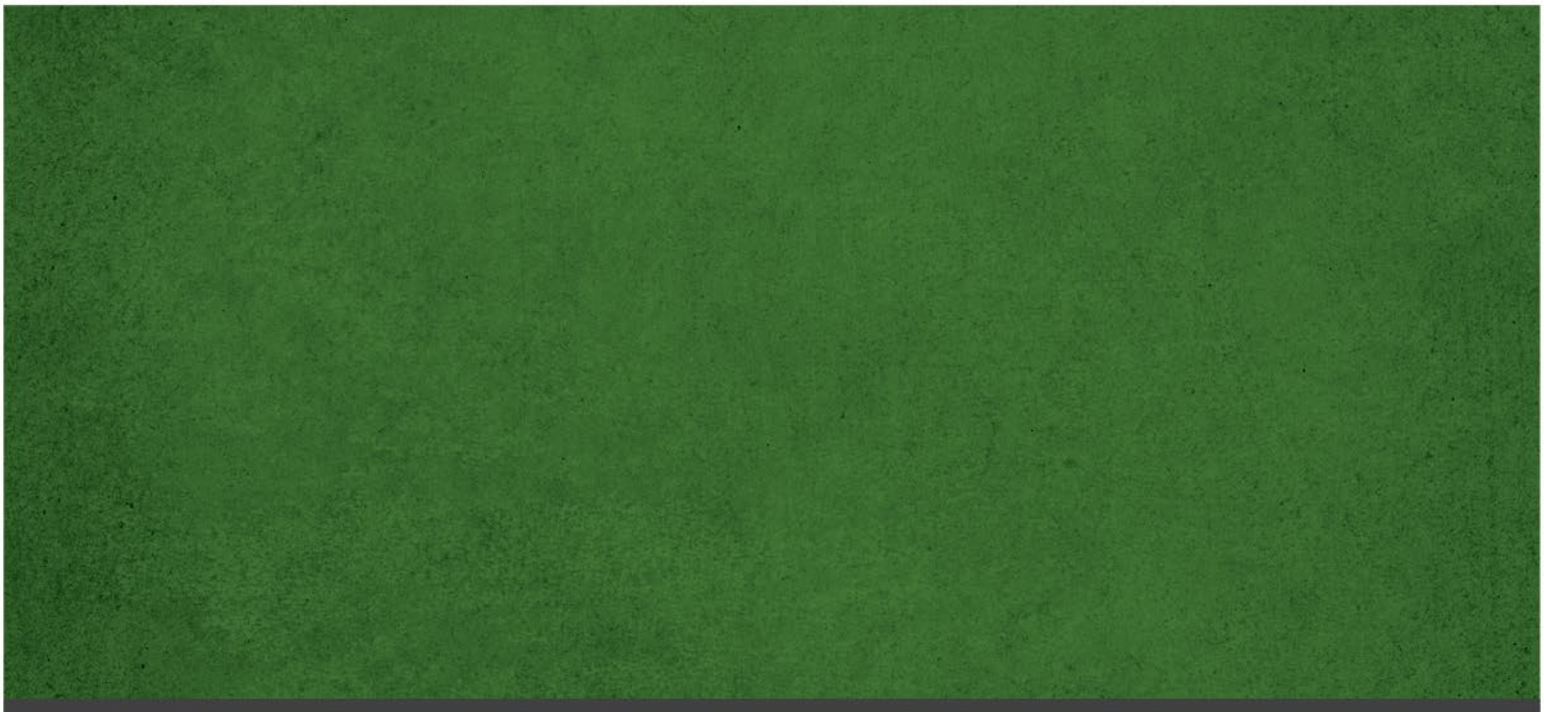
An Advisory Committee Statement (ACS) National Advisory Committee on Immunization (NACI)

Statement on seasonal influenza vaccines for 2026–2027



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Preamble

The National Advisory Committee on Immunization (NACI) is an External Advisory Body that provides the Public Health Agency of Canada (PHAC) with independent, ongoing, and timely medical, scientific, and public health advice in response to questions from PHAC relating to immunization.

In addition to burden of disease and vaccine characteristics, PHAC has expanded the mandate of NACI to include the systematic consideration of programmatic factors in developing evidence-based recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels.

The additional factors to be systematically considered by NACI include: economics, ethics, equity, feasibility, and acceptability. Not all NACI Statements will require in-depth analyses of all programmatic factors. While systematic consideration of programmatic factors will be conducted using evidence-informed tools to identify distinct issues that could impact decision-making for recommendation development, only distinct issues identified as being specific to the vaccine or vaccine-preventable disease will be included.

This statement contains NACI's independent advice and recommendations, which are based upon the best current available scientific knowledge. This document is being disseminated for information purposes. People administering the vaccine should also be aware of the contents of the relevant product monograph. Recommendations for use and other information set out herein may differ from that set out in the product monographs of the Canadian manufacturers of the vaccines. Manufacturer(s) have sought approval of the vaccines and provided evidence as to its safety and efficacy only when it is used in accordance with the product monographs. NACI members and liaison members conduct themselves within the context of PHAC's Policy on Conflict of Interest, including yearly declaration of potential conflict of interest.

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Summary of information contained in the NACI statement

The following highlights key information for immunization providers on seasonal influenza vaccines. Refer to the remainder of the statement for details.

What

- Influenza is a respiratory infection caused by influenza A and B viruses. Seasonal influenza epidemics occur annually in Canada, in the late fall and winter months. Each year, there are approximately 3 to 5 million cases of severe influenza illness and 290,000 to 650,000 deaths from influenza worldwide[1].
- Most people will recover from influenza within 7 to 10 days, but some people are at greater risk of severe complications, such as pneumonia. Influenza infection can also worsen certain chronic conditions, such as cardiovascular diseases (CVD)[2].
- Inactivated influenza vaccines (IIV) (which include standard dose [SD], high dose [HD], cell culture-based [cc] or adjuvanted [Adj] vaccines), and live attenuated influenza vaccine (LAIV) are all authorized for use in Canada. See Appendix A for a list of abbreviations used for the different vaccines.
- Influenza vaccines are the best protection against influenza, and their benefits outweigh their risks. Reactions following immunization are generally mild and of short duration. Very rarely, an individual may have an allergic reaction to a vaccine component. Monitoring of the safety and effectiveness of influenza vaccines is ongoing.

Who

NACI makes both individual-level and public health program-level recommendations. Individual-level recommendations are intended for people wishing to protect themselves from influenza and for their health care providers. Program-level recommendations are intended for provinces and territories making decisions about publicly-funded immunization programs. Individual-level and program-level recommendations may differ.

Recommendation for individual-level decision making

- NACI recommends that influenza vaccine should be offered annually to anyone 6 months of age and older who does not have a contraindication to the vaccine. Patients and providers should also be aware that risks of acquiring influenza are higher in some settings and risks from influenza infection are higher in some individuals. Immunization is particularly important for the following groups (see List 1):
- People at high risk of severe disease or serious influenza-related complications;
- People capable of transmitting influenza to those at high risk;
- People who provide essential community services [(including healthcare workers (HCWs)];
- People whose occupational or recreational activities increase their risk of exposure to avian influenza A viruses (e.g., H5N1).

In infants less than 6 months of age, evidence demonstrating the efficacy of influenza vaccine is lacking and currently authorized influenza vaccines are not indicated for use in this age group[3]. Thus, NACI recommends that influenza vaccine should not be offered to these infants. Since

infants less than 6 months of age are at high risk of severe or complicated influenza, the influenza vaccine should be offered to pregnant women and pregnant individuals, breastfeeding women and breastfeeding individuals, and household contacts of and care providers for young infants.

Recommendation for public health program-level decision-making

The national goal of the annual influenza immunization programs in Canada is to prevent serious illness and death caused by influenza. Provincial and territorial decisions about eligibility for publicly funded programs vary depending on many factors.

- NACI recommends that influenza vaccine should be offered as a priority to the groups for whom influenza vaccination is particularly important (see List 1).

How

The benefits and risks of influenza vaccination should be discussed prior to vaccination, including the risks of not being immunized.

Choice of influenza vaccine

A variety of influenza vaccines are authorized for use in Canada, some of which are authorized for use only in specific age groups. Not all products are available in all jurisdictions and publicly funded provincial and territorial programs may include only some vaccines, which may vary from year to year. For information regarding specific influenza vaccine availability, consult local, provincial or territorial public health.

Following an evidence review, NACI recommends that high-dose inactivated influenza vaccine, adjuvanted inactivated influenza vaccine, or recombinant influenza vaccine (RIV) should be offered over other influenza vaccines for adults 65 years of age and older. If a preferred product is not available, any of the available age-appropriate influenza vaccine should be offered.

For more information, refer to the NACI Supplemental guidance on influenza vaccination in adults 65 years of age and older.

Schedule, dose and route of administration

The dose and route of administration vary by influenza vaccine product. See Appendix B for information on characteristics of all influenza vaccines expected to be available for use in Canada for the 2026-2027 influenza season.

NACI recommends that:

- Adults and children 9 years of age and older should receive 1 dose of seasonal influenza vaccine each year; and
- Children 6 months to less than 9 years of age who have never received a dose of influenza vaccine should be given 2 doses of influenza vaccine for the current season, with a minimum interval of 4 weeks between doses. Those who previously received influenza vaccine dose(s) should receive only one dose per season moving forward.

Contraindications

For all influenza vaccines (IIV, RIV and LAIV), NACI recommends that influenza vaccination is contraindicated for:

- People who have had an anaphylactic reaction to influenza vaccine, or to any of the components of a specific influenza vaccine or its container, with the exception of egg;
    - If an individual is found to have an anaphylactic reaction to a component in one influenza vaccine, consideration may be given to offering another influenza vaccine that does not contain the implicated component, in consultation with an allergy specialist.
    - Safety data confirm that egg-allergic individuals may be vaccinated using any influenza vaccine, including egg-based vaccines and LAIV, without prior influenza vaccine skin test and with the full dose, irrespective of a past severe reaction to egg and without any particular considerations, including vaccination setting.

For LAIV, in addition to the above-mentioned contraindication, NACI also recommends that LAIV be considered contraindicated for:

- People with severe asthma (defined as currently on oral or high-dose inhaled corticosteroids);
- People with active wheezing or medically attended wheezing in the 7 days prior to vaccination;
- People who are immunocompromised due to underlying disease and/or therapy, except children living with stable HIV infection receiving antiretroviral therapy (ART) and with adequate immune function;
- Children less than 24 months of age;
- Children 2 to 17 years of age receiving long-term aspirin or aspirin-containing therapy;
- Pregnant women and pregnant individuals.

Additional Precautions or Warnings

- For LAIV, NACI additionally recommends precautions for the following situations:
    - In the presence of significant nasal congestion or discharge that might impede delivery of LAIV to the nasopharyngeal mucosa;
    - For close contacts, including workers, of people with severe immune compromising conditions;
    - When the person to be vaccinated is receiving an antiviral active against influenza virus (e.g., oseltamivir, zanamivir); and
    - LAIV is not recommended for adults with chronic health conditions identified in List 1 due to the potentially better immune response following IIV compared to LAIV in healthy adults in some studies
- Persons with contraindications or precautions specific to LAIV administration should be offered a parenteral inactivated or recombinant influenza vaccine.
- NACI generally recommends people who have developed Guillain-Barré Syndrome (GBS) within 6 weeks of a previous influenza vaccination should not receive influenza vaccine unless another cause was found for the GBS.

- Individuals who have developed oculorespiratory syndrome (ORS) with lower respiratory tract symptoms should consult a healthcare provider with expertise in the diagnosis and management of allergic reactions before subsequent influenza vaccination.
- Influenza vaccination should usually be postponed in people with serious acute illnesses until their symptoms have abated.

More information on contraindications and precautions can be found in Vaccine Safety and Adverse Events and in the Influenza vaccine chapter of the Canadian Immunization Guide's (CIG) section on contraindications and precautions.

Concurrent administration with other vaccines

Inactivated or recombinant influenza vaccines, or LAIV may be administered concurrently with (i.e., same day) or at any time before or after any other vaccines.

For additional information on specific concurrent administration of vaccines with influenza vaccines, refer to the Concurrent administration section of the statement.

Different injection sites and separate needles and syringes should always be used for concurrent parenteral injections. If multiple injections in the same limb are required, the injection sites should be separated by at least 2.5 cm (1 inch).

Why

- Influenza is a common vaccine-preventable disease which, together with pneumonia, is among the top 10 causes of death in Canada. Vaccination is the most effective way to prevent influenza and its complications.
- Vaccination helps prevent severe influenza illness and related complications, such as heart attacks and strokes, and can also help reduce the spread of influenza, reducing the overall burden.
- Annual vaccination is required because protection may not last beyond a single season, and vaccine strains are reviewed by the WHO and updated each year to match the expected circulating viruses.

Introduction

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. This document, the "National Advisory Committee on Immunization (NACI) Statement on Seasonal Influenza Vaccine for 2026-2027," updates NACI's recommendations regarding the use of seasonal influenza vaccines.

For a summary of clinical information on seasonal influenza vaccine administration for vaccine providers, refer to the updated Influenza vaccines chapter of the CIG.

A note on terminology

Throughout this document, the term 'influenza vaccine' refers specifically to the seasonal influenza vaccine, unless explicitly stated otherwise.

New or updated information for 2026-2027

Intraseasonal Waning of Influenza Vaccine Effectiveness and Optimal Timing for Seasonal Influenza Vaccination

The body of available evidence examining how factors such as the durability of influenza vaccine-induced protection, prior immunity, health status, and timing of administration may influence vaccine performance continues to grow. However, important uncertainties persist, especially around how best to tailor timing for different populations and how to balance the benefits of early protection with sustained immunity through the end of the season.

Considering the growing evidence base, a review was conducted to summarize the available information and key considerations related to optimal timing of seasonal influenza vaccine administration. This review considers seasonality of influenza activity across Canada, intraseasonal waning of influenza vaccine-induced immunity, and relevant programmatic factors. Overall, findings indicate that influenza vaccination in early fall provides sustained protection for most of the season, and maintaining high population coverage remains the most critical factor. Current evidence is insufficient to establish optimal timing for different populations, and given seasonal variability in influenza activity and operational constraints, significant changes to timing of existing annual influenza vaccination programs are not currently warranted nor feasible.

For more information, refer to Appendix D of this statement.

Seasonal influenza vaccination in the context of avian influenza

Although seasonal influenza vaccines do not protect against avian influenza A(H5N1) viruses, they may mitigate the severity of seasonal influenza and reduce the risk of co-infection with seasonal and avian influenza strains. NACI recommends that all individuals whose occupational or recreational activities increase their risk of exposure to avian influenza A(H5N1) viruses should receive an authorized, age-appropriate seasonal influenza vaccine.

In February 2025, NACI published preliminary guidance on human vaccination against avian influenza in a non-pandemic context. The guidance offers a framework to inform Canadian provinces and territories' decision-making on the use of human vaccines against avian influenza (HVAI), with the objective of preventing human infection with avian influenza A(H5N1) viruses. NACI will continue to monitor the evolving epidemiology of avian influenza, and scientific developments related to HVAI, and will update its recommendations as needed.

For more information on NACI guidance, refer to the Rapid response: Preliminary guidance on human vaccination against avian influenza in a non-pandemic context as of December 2024. For updates and details on Canada's prevention, preparedness, and response initiatives, refer to Avian influenza A(H5N1): Canada's response.

Background

The World Health Organization's (WHO) recommendations on the composition of influenza virus vaccines are typically available in February of each year for the upcoming season in the Northern Hemisphere, which allows time for vaccine manufacturers to produce the quantity of vaccine required. Currently, the WHO recommends that 3 influenza strains be included in the trivalent seasonal influenza vaccine: 1 influenza A(H1N1), 1 influenza A(H3N2), and 1 influenza B (B/Victoria lineage). Due to the absence of confirmed detections of naturally occurring B/Yamagata lineage viruses since March 2020, the WHO has recommended the removal of the B/Yamagata antigen as a component of all live and non-live influenza vaccines[4,5].

Health care providers in Canada should offer the seasonal influenza vaccine as soon as feasible after it becomes available in the fall, since seasonal influenza activity may start as early as October in the Northern Hemisphere. Decisions regarding the precise timing of vaccination in a given setting or geographic area should be made according to local epidemiologic factors (influenza activity, timing, and intensity), opportune moments for vaccination, as well as programmatic considerations. Further advice regarding the timing of influenza vaccination programs may be obtained through consultation with local public health agencies.

Although vaccination before the onset of the influenza season is strongly preferred, influenza vaccine may still be administered throughout the season. Delayed administration results in lost opportunities to prevent infection prior to vaccination. Individuals seeking or considering vaccination should be informed that vaccine administered during an influenza outbreak will not provide immediate optimal protection, as it can take up to two weeks after vaccination to develop a protective antibody response. Vaccine providers should use every opportunity to administer influenza vaccine to individuals at risk who have not already been vaccinated during the current season. Vaccination remains beneficial even after the onset of influenza activity and should continue as long as influenza viruses are circulating in the community.

Every year, individuals with influenza and influenza-related complications require urgent health care and increase the pressures on the health care system in the fall and winter months, particularly during times when other respiratory viruses, such as COVID-19 and respiratory syncytial virus (RSV), are co-circulating. Effective prevention of influenza by vaccination is a critical tool to mitigate ongoing health system stress.

Methods

In brief, the broad stages in the preparation of this NACI advisory committee statement included:

- Synthesis of the body of evidence of benefits and harms, considering the quality of the synthesized clinical evidence along with data on economics, ethics, equity, feasibility and acceptability;
- Translation of evidence into recommendations.

For more information, please see NACI's evidence-based methods.

Annual influenza vaccine recommendations are developed by the Influenza Working Group (IWG) for consideration by NACI. Recommendation development includes review of a variety of issues including the burden of influenza illness and the specific ~~target~~ populations identified for vaccination; safety, immunogenicity, efficacy, and effectiveness of influenza vaccines; and vaccine schedules. In addition, PHAC has expanded the mandate of NACI to include the consideration of programmatic factors in developing their recommendations to facilitate timely decision-making for publicly funded vaccine programs at provincial and territorial levels. These programmatic factors include consideration of ethics, equity, feasibility, and acceptability (EEFA) and cost-effectiveness. NACI uses a published, peer-reviewed framework and evidence-informed tools to ensure that issues related to EEFA are systematically assessed and integrated into its guidance. The NACI Secretariat applied this framework with accompanying evidence-informed tools (Ethics Integrated Filters, Equity Matrix, Feasibility Matrix, Acceptability Matrix) to systematically consider these programmatic factors for the development of clear, comprehensive, appropriate recommendations for timely, transparent decision-making. For details on the development and application of NACI's EEFA Framework and evidence-informed tools, see A framework for the systematic consideration of ethics, equity, feasibility, and acceptability in vaccine program recommendations. For details on when and how NACI incorporates economic evidence for vaccine recommendations, refer to the NACI Process for incorporating economic evidence into federal vaccine recommendations.

The annual update of the NACI Statement on Seasonal Influenza Vaccine led by the NACI IWG involves a thorough review and evaluation of the literature as well as discussion at the scientific and clinical practice levels. In the preparation of the 2026-2027 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.

On September 24, 2025, the available evidence and updates for this year's seasonal influenza statement proposed by the IWG were presented for consideration and approval by NACI. Following a thorough review of the evidence, the committee approved the updated guidance. The description of relevant considerations, rationale for specific decisions, and identified knowledge gaps are described in this statement.

A note on language

NACI recognizes that not all people giving birth or breastfeeding will identify as women or mothers. The writing in this statement uses a gender additive approach where the term 'woman' is used alongside gender-neutral language. This is intended to demonstrate a commitment to

redress the historic exclusion of trans and non-binary people, whilst avoiding the risk of marginalizing or erasing the experience of women within the health care environment. In addition, much of the research available currently uses gendered language (e.g., “women”) or gender-neutral language (e.g., pregnant people) when discussing pregnancy. When citing research, NACI refers to the language used in the study. For the purposes of this statement, the terms “woman,” and “women,” should be considered to also apply to those individuals who do not specifically identify as female gender but are the parent gestating the fetus or breastfeeding or chestfeeding the infant. However, in line with best practice, it is recognized that when discussing or caring for individuals in a one-on-one capacity language and documentation should reflect the gender identity of the individual.

Finally, NACI acknowledges the dynamic nature of language. It is likely that language deemed to be suitable or affirming in one context may not translate across others, and over the coming years will likely change and evolve with respect to appropriate representations.

Epidemiology

Disease description

Influenza is a respiratory infection that can cause mild to severe illness, including hospitalization or death. Certain populations, such as young children, older adults, and those with chronic health conditions are at higher risk for serious influenza complications such as viral pneumonia, secondary bacterial pneumonia, and worsening of underlying medical conditions.

Infectious agent

There are 2 main types of influenza virus that cause seasonal epidemics in humans: A and B. Influenza A viruses are classified into subtypes based on 2 surface proteins: hemagglutinin (HA) and neuraminidase (NA). Three subtypes of HA (H1, H2, and H3) and 2 subtypes of NA (N1 and N2) are recognized among influenza A viruses as having caused widespread human disease over the past decades, most commonly A(H1N1) and A(H3N2). Immunity to the HA and NA proteins reduces the likelihood of infection and together with immunity to the internal viral proteins, lessens the severity of disease if infection occurs. Influenza B viruses are classified into two lineages that evolved in the early 1980s: B/Victoria and B/Yamagata. However, human B/Yamagata lineage infections have not been detected since March 2020. Both influenza A and B viruses can be further classified into clades and sub-clades.

Over time, antigenic variation (i.e., drift) of strains occurs within an influenza A subtype or a B lineage. The possibility of antigenic drift, which may occur in 1 or more circulating virus strains, requires the formulation of seasonal influenza vaccines to be re-evaluated annually.

Transmission

Influenza is primarily transmitted by aerosols and droplets spread through coughing or sneezing, and through direct or indirect contact with respiratory secretions.

The incubation period of seasonal influenza is usually about 2 days but can range from 1 to 4 days[6]. Adults may be able to spread influenza to others from 1 day before symptom onset to approximately 5 days after symptoms start. Children and people with weakened immune systems may be infectious longer.

Spectrum of clinical illness

Classically, influenza causes “influenza-like illness” with sudden onset of fever, cough, and muscle aches, commonly accompanied by headache, chills, loss of appetite, fatigue, and sore throat. Nausea, vomiting, and diarrhea may also occur, especially in children. However, the severity of influenza ranges from completely asymptomatic infection through mild acute upper respiratory illness (a “cold”) to severe influenza pneumonia. Older adults and individuals with immunocompromising conditions may present with atypical symptoms that do not meet standard case definitions for influenza-like illness (ILI). While most people will recover within a week or 10 days, complications including bacterial pneumonia, respiratory failure, cardiovascular (CV) complications, delirium, or worsening of underlying chronic medical conditions may occur. Influenza is associated with a significantly increased risk of myocardial infarction and stroke in the first 15 days after infection[7,8]. It has also been rarely associated with GBS, with onset typically 1 to 6 weeks after infection[9,10].

People at higher risk

The people at greatest risk of influenza-related complications are adults and children with chronic health conditions (see List 1), residents of nursing homes and other chronic care facilities, adults 65 years of age and older (particularly frail older adults), children 0 to 59 months of age, pregnant women and pregnant individuals, and individuals in or from First Nations, Inuit, or Métis communities.

Disease frequency

Global

Each year, there are approximately 3 to 5 million cases of severe influenza illness and 290,000 to 650,000 deaths from influenza worldwide[1]. Global influenza circulation was at a historical low during the COVID-19 pandemic (2020-2021 and 2021-2022 seasons) due in part to the implementation of public health measures such as physical distancing and the use of face masks [11,12]. By the 2022-2023 season, global influenza activity returned to circulation patterns resembling pre-pandemic seasons, except for the absence of B/Yamagata lineage virus detections after March 2020. During the most recent 2024-2025 Northern Hemisphere influenza season, influenza activity peaked in late January 2025, with influenza A outnumbering influenza B detections for the whole season[12]. For current international influenza activity information, refer to WHO's Global Influenza Program website.

National

Together, influenza and pneumonia are ranked among the top 10 leading causes of death in Canada[13]. The burden of influenza-associated illness and death varies every year, depending on various factors such as the type of circulating viruses in the season and the populations affected. Prior to the COVID-19 pandemic (2010-2011 to 2018-2019 seasons), influenza caused an estimated 15,000 hospitalizations annually, more than any other seasonal respiratory virus[14]. FluWatch+ is Canada's national surveillance system, which monitors the spread of influenza and other respiratory viruses continually throughout the year. In the 2024-2025 season, a total of 139,834 laboratory-confirmed influenza (LCI) detections were reported from 1,452,090 tests, with many of these detections are being among more severe cases (emergency department cases and hospitalizations)[15]. However, a large proportion of influenza infections are not laboratory- confirmed; therefore, the number of detections reported to the FluWatch+ surveillance system is a significant underestimate of the true number of infections.

Seasonal and temporal patterns

Influenza activity in Canada is usually low in the late spring and summer, begins to increase over the fall, and peaks in the winter months. The influenza season in Canada usually begins in mid to late- November and lasts an average of 27 weeks, although seasons can start as early as October or as late as February[16]. One or more peaks may occur during a season. Even though multiple influenza strains typically circulate each season, one strain often predominates. Additionally, there are often differences in the timing of influenza activity observed across regions in Canada.

The 2024-2025 influenza season in Canada began later than usual in mid-December 2024, with influenza activity peaking in late February 2025. Influenza A accounted for most detections

overall (88%) and predominantly circulated all season. Influenza A(H1N1)pdm09 was the predominant strain for the second season in a row[15]. Influenza B (Victoria) activity circulated later in the season at much lower levels than the previous season and was primarily detected among younger age groups. There were no detections of B/Yamagata[17]. For details on current national influenza activity, refer to the FluWatch+ website.

Changing epidemiology of Influenza B viruses

In the years prior to the emergence of SARS-CoV-2, the B/Yamagata and B/Victoria virus lineages circulated simultaneously globally[18]. Between 2012 and 2017, B/Yamagata viruses were responsible for a larger proportion of influenza B infections than B/Victoria, but in the last two years prior to the COVID-19 pandemic (i.e., after a major outbreak of B/Yamagata in 2017-2018 in most countries, including Canada), the B/Victoria lineage started becoming dominant[17,18]. As of March 2020, there have been no confirmed naturally occurring cases of B/Yamagata influenza lineage viruses worldwide, and any sporadic specimens reported to yield B/Yamagata have either been linked to individuals vaccinated with LAIV or errors in lineage determination upon investigation[18,19].

Historically, B/Yamagata viruses have been more prevalent in adults, while B/Victoria viruses have been more prevalent in children and adolescents[18,20,21]. This demographic trend related to B/Victoria is apparent in historical Canadian surveillance data where in recent seasons of B/Victoria predominance in Canada, individuals under 19 years of age accounted for approximately half (48 to 54%) of influenza B cases[15]. These trends continue in the most recent 2024-2025 season, where individuals less than 19 years of age accounted for 50% of influenza B detections with age information (compared to 7% in adults 65 years of age and older)[22].The extinction of B/Yamagata has not yet been declared; thus, epidemiological and virological monitoring of influenza viruses continues to be important[23].

Burden of disease in children

Influenza poses a significant disease burden on children. Infants, especially those under 6 months old, are disproportionately vulnerable to influenza infection and its complications due to their lack of prior immunity and ineligibility for the influenza vaccine. Across 7 influenza seasons (2012-2013 to 2018-2019) in Quebec, infants under 6 months old had a 2- and 5-fold higher risk of hospitalization (416 per 100,000 population per season) compared to children aged 6 to 23 months and 2 to 4 years, respectively[24]. For additional information regarding the impact of influenza on infants, refer to the NACI statement: Updated guidance on influenza vaccination during pregnancy.

In recent seasons of B/Victoria predominance in Canada, individuals under 19 years of age accounted for approximately half (48 to 54%) of influenza B cases[15]. Between the 2004 and 2013 (excluding the 2009-2010 H1N1 pandemic) seasons, influenza B was associated with 15.5 to 58.3% of influenza-related hospitalizations and higher mortality rates than influenza A (1.1% and 0.4%, respectively) among children admitted to Canadian Immunization Monitoring Program Active (IMPACT) centres[25]. During the 2024-2025 season in Canada, among hospitalizations with age information, children under 5 years of age had the second-highest cumulative influenza-associated hospitalization rate (119 per 100,000 population)[17]. Children and adolescents under 19 years of age accounted for 12% of all hospitalizations overall but accounted for 43% of influenza B hospitalizations[22]. Depending on the dominant type and subtype circulating in a particular season, the burden in children can fluctuate season to season. Between the 2004 and 2013 (excluding the 2009-2010 H1N1 pandemic), influenza B

was associated with 15.5 to 58.3% of influenza-related hospitalizations and higher mortality rates than influenza A (1.1% and 0.4%, respectively) among children admitted to Canadian IMPACT centres[25].

Burden of disease in adults

Adults aged 65 years and older have a disproportionately greater risk of severe influenza disease, hospitalization, intensive care unit admission, and death, compared to younger adults[26]. Specifically, older adults face a higher burden of influenza A infection than other age groups[17,26]. During the 2024-2025 season in Canada, adults aged 65 years and older accounted for most influenza-associated hospitalizations (59%) and deaths (83%) and had the highest cumulative hospitalization rate (315 per 100,000 population) overall[15]. For additional information regarding influenza in older adults, refer to the Supplemental guidance on influenza vaccination in adults 65 years of age and older.

Seasonal influenza vaccines

Vaccine products authorized for use in Canada

The following sections describe the influenza vaccine products that are authorized for use in Canada for the 2026-2027 season. Should the availability of a specific vaccine change (i.e., be made available or unavailable) after the release of this statement and prior to the 2026-2027 influenza season, NACI will communicate relevant information regarding the influenza vaccine changes if required. All influenza vaccines available in Canada have been authorized by Health Canada. However, not all products authorized for use are available in the marketplace. Vaccine manufacturers determine whether they will make any or all of their products available in each market. Provincial and territorial health jurisdictions determine which of the products available for purchase will be used in their respective publicly funded influenza immunization programs and for which population groups, recognizing that not all products will be offered in every jurisdiction and some may have limited availability. Not all products will be made available in all jurisdictions and availability of some products may be limited. Officials in individual provinces and territories should be consulted regarding the products available in individual jurisdictions.

The antigenic characteristics of circulating influenza virus strains provide the basis for selecting the strains included in each year's vaccine. All manufacturers that distribute influenza vaccine products in Canada confirm to Health Canada that the vaccines to be marketed in Canada for the upcoming influenza season contain the WHO's recommended antigenic strains for the Northern Hemisphere. Vaccine producers may use antigenically equivalent strains because of their growth properties. The strains recommended for egg-based products may differ somewhat from the strains chosen for cell-culture based products to account for differences in the production platforms.

There are 2 categories of influenza vaccine authorized for use in Canada: IIV and LAIV. Trivalent (3-strain) vaccines contain 1 A(H1N1) strain, 1 A(H3N2) strain, and 1 influenza B strain from the Victoria lineage. Quadrivalent (4-strain) vaccines contain the strains in the trivalent vaccine plus an influenza B strain from the Yamagata lineage. Most influenza vaccines currently authorized for use in Canada are made from influenza viruses grown in chicken eggs, with one exception: the influenza viruses used to produce Flucelvax® (IIV3-cc) are propagated in a mammalian cell line (Madin-Darby Canine Kidney [MDCK] cells). Supemtek® (RIV), which was previously authorized in Canada and used recombinant HA produced in a proprietary insect cell line using a baculovirus vector for protein expression, is no longer authorized or available.

A summary of the characteristics of influenza vaccines that are currently authorized for use in Canada and expected to be available for the 2026-2027 season can be found in Appendix B. For complete prescribing information, readers should consult the product monographs available through Health Canada's Drug Product Database.

Refer to Contents of Immunizing Agents Available for Use in Canada in Part 1 of the CIG for a list of all vaccines authorized for use in Canada.

Inactivated influenza vaccine (IIV)

IIVs contain standardized amounts of the HA protein from representative seed strains of the 2 human influenza A subtypes (H3N2 and H1N1) and either 1 (for trivalent vaccines) or both (for quadrivalent vaccines) of the 2 influenza B lineages (Victoria and Yamagata). IIVs currently

authorized for use in Canada are a mix of split virus and subunit vaccines, both consisting of disrupted virus particles. In split virus vaccines, the virus has been disrupted by a detergent. In subunit vaccines, HA and NA have been further purified by removal of other viral components. The amount of neuraminidase (NA) in the vaccines is not standardized and not reported. HA-based serum antibody produced to one influenza A subtype provides no protection against strains belonging to another subtype. The potential for trivalent vaccine to stimulate antibody protection across B lineages is affected by factors such as age and prior antigenic experience with the 2 B lineages[27-32].

The IIVs available in Canada are in a standard dose formulation or in a formulation designed to enhance the immune response in specific age groups, using a higher dose of HA antigen or the inclusion of an adjuvant. Refer to Basic Immunology and Vaccinology in Part 1 of the CIG for more information about inactivated vaccines.

There are 4 standard dose IIVs currently authorized and available for use in Canada: IIV3-SD: Fluzone®, Fluviral, and Influvac®; and IIV3-cc: Flucelvax®. These vaccines are un-adjuvanted, contain a standard dose of antigen (15 µg HA per strain), and are administered as a 0.5 mL dose by intramuscular (IM) injection. Influvac® may be administered by IM or deep subcutaneous injection.

The adjuvanted IIV currently authorized for use in Canada is a trivalent subunit vaccine (IIV3-Adj) that contains the adjuvant MF59, which is an oil-in-water emulsion composed of squalene as the oil phase that is stabilized with the surfactants polysorbate 80 and sorbitan triolate in citrate buffer.

IIV3-Adj contains 7.5 µg HA per strain administered as a 0.25 mL dose by IM injection for children 6 to 23 months of age (Fluad Pediatric™) or 15 µg HA per strain administered as a 0.5 mL dose by IM injection for adults 65 years of age and older (Fluad®). Other IIVs do not contain an adjuvant. Although authorized, Fluad® Pediatric has not been available in Canada since 2019.

There is 1 high-dose IIV (IIV-HD) currently authorized and available for use in Canada: Fluzone® High-Dose Trivalent (IIV3-HD), a trivalent unadjuvanted, split virus seasonal influenza vaccine containing 60 µg HA per strain and administered as a 0.5 mL dose by IM injection for adults 65 years of age and older.

Recombinant influenza vaccine (RIV)

Supemtek® (RIV4) is a quadrivalent, baculovirus-expressed seasonal influenza vaccine that contains 45 µg HA per strain and is administered as a 0.5 mL dose by IM injection for adults 18 years of age and older. RIV contains recombinant HAs produced in an insect cell line using genetic sequences from cell-derived influenza viruses. The production of RIV does not depend on egg supply as it does not require egg-grown candidate vaccine viruses. Supemtek® was the first and, to date, the only seasonal influenza vaccine in Canada made with recombinant technology. RIV is not currently authorized for use or available in Canada.

Live attenuated influenza vaccine (LAIV)

LAIV contains standardized quantities of fluorescent focus units (FFU) of live-attenuated influenza virus reassortants. As a live replicating whole virus formulation administered intranasally by spray, it elicits mucosal immunity, which may more closely mimic natural infection. The virus strains in

LAIV are cold-adapted and temperature sensitive, so they replicate in the nasal mucosa rather than the lower respiratory tract, and they are attenuated, so they do not produce ILI. To date, there have been no reported or documented cases of transmission of vaccine virus to individuals administering LAIV. In rare instances, shed vaccine viruses can be transmitted from vaccine recipients to unvaccinated persons.

There is currently 1 LAIV authorized and available for use in Canada for children 2 to 17 years of age and adults 18 to 59 years of age: FluMist® (LAIV3), a trivalent nasal spray influenza vaccine given as a 0.2 mL dose (0.1 mL in each nostril).

Efficacy, effectiveness, and immunogenicity

Efficacy and effectiveness

Influenza vaccine has been shown in randomized controlled clinical trials (RCT) to be efficacious in providing protection against influenza infection and illness. However, the effectiveness of the vaccine—that is, how it performs in settings that are more reflective of usual health care practice— can vary from season to season and by influenza vaccine strain type and subtype. Influenza vaccine effectiveness (VE) depends on how well the vaccine strains match with circulating influenza viruses, the type and subtype of the circulating virus, as well as the health and age of the individual receiving the vaccine. Even when there is a less-than-ideal match or lower VE against 1 strain, the possibility of lower VE should not preclude vaccination, particularly for people at high risk of influenza-related complications and hospitalization, since vaccinated individuals are still more likely to be protected compared to those who are unvaccinated.

The Canadian Sentinel Practitioner Surveillance Network (SPSN) monitors influenza VE against medically attended LCI in Canada, using data from British Columbia, Alberta, Ontario and Quebec. Secondary objectives are to monitor and characterize circulating influenza and other respiratory viruses contributing to influenza-like illness in the community. Findings by the SPSN are also submitted to the World Health Organization to inform influenza vaccine strain selection for the northern and southern hemispheres. For more information on SPSN's annual VE estimates and other scientific publications, see the BC Centre for Disease Control's Sentinel Practitioner Surveillance Network website.

Immunogenicity

Immune Antibody responses after vaccination depends on several factors, including the age of the recipient, prior and subsequent exposure to antigens, and the presence of immune compromising conditions. Protective levels of humoral serum antibodies, which correlate with protection against influenza infection, are generally achieved by 2 weeks after vaccination; however, there may be some protection afforded before that time.

Additional information

Refer to Appendix C for further information on the efficacy and effectiveness, immunogenicity, and safety of influenza vaccines that are authorized for use in Canada by type: IIV and LAIV.

Because of potential changes in the circulating influenza virus from year to year and waning immunity in vaccine recipients, annual influenza vaccination is recommended. Although some studies suggest vaccine induced protection may be greater in some circumstances in individuals

who have not received a previous influenza vaccine recently, overall, the evidence shows no difference in the VE of repeated influenza vaccination compared to vaccination in the current season only. Importantly, optimal protection against influenza is best achieved through annual influenza vaccination, as repeated vaccination including the current season is consistently more effective than no vaccination in the current season[33,34]. Additional information regarding the effects of repeated influenza vaccination on VE, vaccine efficacy, and immunogenicity can be found in the NACI Recommendation on Repeated Seasonal Influenza Vaccination. NACI will continue to monitor this issue.

NACI acknowledges that evidence related to influenza vaccine performance, particularly with respect to vaccine efficacy and effectiveness, is constantly evolving with advances in research methodology and accumulation of data over many influenza seasons. Therefore, the evidence summarized in Appendix C may not include the latest studies. However, NACI continues to closely monitor the emerging evidence on the efficacy and effectiveness, immunogenicity, and safety of influenza vaccines to update and make recommendations when warranted.

Vaccine administration

Dose, route of administration, and schedule

With the variety of influenza vaccines available for use in Canada, it is important for vaccine providers to note the specific differences in age indication, route of administration, dosage, and schedule for the products that they will be using (see Table 1). Key relevant details and differences between vaccine products are also highlighted in Appendix B.
For influenza vaccines given by the IM route, the anterolateral thigh muscle is the recommended site in infants 6 to 12 months of age. The anterolateral thigh or the deltoid muscle can be used for toddlers and older children. The deltoid muscle is the preferred injection site in adolescents and adults. For more information on vaccine administration, refer to Vaccine Administration Practices in Part 1 of the CIG.

The first time that children 6 months to less than 9 years of age receive seasonal influenza vaccination, a 2-dose schedule is required to achieve protection[35-37]. Because children 6 to 23 months of age are less likely to have had prior priming exposure to an influenza virus, special effort is warranted to ensure that a 2-dose schedule is followed for previously unvaccinated children in this age group.

Table 1: Recommended dose and route of administration, by age, for influenza vaccine types authorized for the 2026–-2027 influenza season

Age group	Influenza vaccine type (route of administration)					Number of doses required
	IIV-SD[a] (IM)	IIV-cc[b] (IM)	IIV-Adj[c] (IM)	IIV-HD[d] (IM)	LAIV[e] (intranasal)	
6 to 23 months	0.5 mL[f]	0.5 mL	0.25 mL	-	-	1 or 2[g]
2 to 8 years	0.5 mL	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1 or 2[g]
9 to 17 years	0.5 mL	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1
18 to 59 years	0.5 mL	0.5 mL	-	-	0.2 mL (0.1 mL per nostril)	1
60 to 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	-	1

Abbreviations: IIV-Adj: adjuvanted inactivated influenza vaccine; IIV-cc: mammalian cell culture based inactivated influenza vaccine; IIV-HD: high-dose inactivated influenza vaccine; IIV-SD: standard-dose inactivated influenza vaccine; IM: intramuscular; LAIV: live attenuated influenza vaccine.

[a] Fluzone® (6 months and older), Influvac® (6 months and older), Fluviral (6 months and older).
[b] Flucelvax® (6 months and older)
[c] Fluad Pediatric™ (6 to 23 months) or Fluad® (65 years and older). Although authorized, Fluad® Pediatric has not been available in Canada since 2019.
[d] Fluzone® High-Dose (65 years and older)
[e] FluMist® (2 to 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. This 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.
[g] Children 6 months to less than 9 years of age receiving influenza vaccine for the first time in their life should be given 2 doses, with a minimum interval of 4 weeks between doses. Children who have been vaccinated with 1 or more doses of influenza vaccine in the past should receive 1 dose of influenza vaccine per season thereafter.

Booster doses and revaccination

Booster doses are not required within the same influenza season. There is currently no evidence that two doses of influenza vaccine in the same season improves protection against influenza sufficiently to warrant a recommendation for a second dose for the same season in any adult population[38].

Serological testing

Serological testing is not necessary or recommended before or after receiving seasonal influenza vaccine.

Storage requirements

Influenza vaccine should be stored at +2°C to +8°C and should not be frozen. Refer to the individual product monographs and Storage and Handling of Immunizing Agents in Part 1 of the CIG for additional information.

Concurrent administration with other vaccines

All seasonal influenza vaccines, including LAIV, may be given at the same time as, or at any time before or after administration of other vaccines (either live or non-live), including COVID-19 vaccines. NACI will continue to monitor the evidence base and update its recommendations as needed.

No studies were found on potential immune interference between LAIV and other live attenuated vaccines (oral or parenteral) administered within 4 weeks.

Studies on concurrent administration of LAIV3 with measles, mumps, rubella (MMR); measles, mumps, rubella, varicella (MMRV); or live oral polio vaccines did not find evidence of clinically significant immune interference[39-41]. One study reported a statistically significant but not clinically meaningful decrease in seroresponse rates to rubella antigen when administered concurrently with LAIV.

In theory, the administration of 2 live vaccines sequentially within less than 4 weeks could reduce the immunogenicity of the second vaccine. Possible immune mechanisms include: the inhibitory and immunomodulatory effects of systemic and locally produced cytokines on B- and T-cell response and viral replication; immunosuppression induced by certain viruses (such as measles); and direct viral interference as a result of competition for a common niche. Mucosal vaccines may have less impact on a parenteral vaccine and vice versa. The immune response with a mucosal vaccine may be compartmentalized to the mucosa while that to a parenteral vaccine is systemic. It is likely that there is some interaction between the systemic and mucosal compartments; however, the extent to which this interaction occurs is not known.

Given the lack of data for immune interference, and based on expert opinion, NACI recommends that LAIV can be given together with or at any time before or after the administration of any other live attenuated or non-live vaccine. While some vaccine providers have given LAIV and other live vaccines separated by at least 4 weeks based on the theoretical possibility of immune interference, NACI does not believe that this precaution is necessary for LAIV. The use of a parenteral inactivated or recombinant influenza vaccine would avoid this theoretical concern. Note that the timing rules related to 2 parenteral live vaccines (e.g., MMR and varicella vaccines) still apply. For more information, refer to Timing of vaccine administration in Part 1 of the CIG.

The specific groups prioritized for influenza and pneumococcal vaccines overlap considerably. A recent study showed that compared to administration alone, concurrent administration of IIV4 with 15-valent pneumococcal conjugate vaccine (PCV15) in adults demonstrated non-inferiority of pneumococcal- and influenza-specific antibody responses[42]. Vaccine providers should take the opportunity to vaccinate eligible people against pneumococcal disease when influenza vaccine is given.

NACI guidance indicates that the concurrent administration of an RSV vaccine with another adult vaccine, including seasonal influenza vaccines, is acceptable and supported. Readers

should consult the RSV vaccines chapter in Part 4 Immunizing Agents of the CIG and NACI's Statement on the prevention of respiratory syncytial virus (RSV) disease in older adults for more information.

When more than 1 injection is given at a single clinic visit, it is preferable to administer them in different limbs. If it is not possible to do so, injections given in 1 limb should be separated by a distance of at least 2.5 cm (1 inch). A separate sterile needle and syringe should always be used for each injection. For more information regarding vaccination administration timing rules, refer to Timing of vaccine administration in Part 1 of the CIG.

Concurrent administration with COVID-19 vaccines

NACI reviewed the most recent literature on the impact of concurrent administration of seasonal influenza and COVID-19 vaccines on efficacy/effectiveness, safety and immunogenicity outcomes, including the potential safety signal of ischemic stroke. Overall, available evidence supports the concurrent administration of seasonal influenza and COVID-19 vaccines. NACI guidance as of December 2022 outlines that administration of COVID-19 vaccines may occur at the same time as, or at any time before or after influenza immunization (with any parenteral or intranasal seasonal influenza vaccine). Readers should consult the COVID-19 vaccines chapter in Part 4 Immunizing Agents of the CIG and the latest NACI COVID-19 vaccine guidance for updated guidance and further information on concurrent administration of COVID-19 vaccines with influenza vaccines and across all eligible age groups.

Efficacy and effectiveness

Although data are limited, evidence suggests that concurrent administration of influenza and COVID-19 vaccines does not result in a difference in vaccine efficacy/effectiveness against COVID-19 or influenza compared to separate administration of COVID-19 or influenza vaccines[43,44].

Safety

Although some studies have reported increased reactogenicity after concurrent administration of COVID-19 vaccines and influenza vaccines compared to influenza vaccination alone, reactogenicity was comparable to COVID-19 vaccination alone[44-47]. Although a large self-controlled case series in the United States (US) on adults 65 years of age and older showed that concurrent administration of the bivalent COVID-19 vaccine and a high-dose or adjuvanted influenza vaccine was associated with a higher risk of ischemic stroke, this observation was inconsistent with results from other analyses in the US and other countries[48-50]. Most analyses, from several countries, did not show an association between concurrent administration of bivalent mRNA vaccines with influenza vaccines and ischemic stroke[48-53]. The totality of data available at this time does not support an association between ischemic stroke and concurrent administration of bivalent mRNA COVID-19 vaccines with influenza vaccines.

Immunogenicity

Most studies have showed that the concurrent administration of COVID-19 and seasonal influenza vaccines induces non-inferior immune responses against SARS-CoV-2 and HA compared to sequential administration[54-59]. Although some studies reported lower immune responses against SARS-CoV-2 following concurrent administration of COVID-19 and influenza vaccines, the clinical significance of these results is unknown[45,46,60,61].

NACI will continue monitoring emerging evidence and update guidance accordingly.

Concurrent administration with other adjuvanted or newer vaccines

Data are limited regarding concurrent administration of newer or adjuvanted influenza vaccines with other adjuvanted or non-adjuvanted vaccines. Specifically, studies investigating concurrent administration of IIV-cc or RIV with adjuvanted or newer vaccines are scarce.

For example, RZV is a recombinant adjuvanted subunit herpes zoster vaccine (Shingrix®, GlaxoSmithKline) that is authorized for use in Canada in adults 50 years of age and older, and adults 18 years of age and older who are or will be at increased risk of HZ due to immunodeficiency or immunosuppression caused by known disease or therapy; therefore, the target age group for herpes zoster vaccine and influenza vaccine overlap. RZV has been shown to be safe and effective when given concurrently with unadjuvanted, standard dose influenza vaccines[62]. However, studies assessing the concurrent administration of RZV with adjuvanted or high-dose influenza vaccines are limited[63]. It should be noted that RZV and IIV-Adj currently authorized for use in Canada contain the adjuvants $AS01_B$ and MF59, respectively. How these adjuvants may interact when RZV and IIV-Adj are administered concurrently is not yet known.

A rapid review was conducted by NACI in May 2024 to retrieve relevant articles on the concurrent administration of enhanced influenza vaccines (i.e., IIV-HD, IIV-Adj, IIV-cc and RIV) with other newer vaccines, adjuvanted vaccines, or vaccines using newer technologies. Few studies were identified through the database search and environmental scanning that evaluated the immunogenicity and/or safety of concurrent administration of IIV-Adj (n=1) or IIV-HD (n=2) with newer vaccines or other adjuvanted vaccines[64-66]. A RCT in adults 60 years of age and older demonstrated a good safety profile and no interference in immune response with the concurrent administration of IIV-Adj and another adjuvanted vaccine, the 13-valent pneumococcal conjugate vaccine (Prevnar®13, Pfizer), containing the adjuvant $AlPO_4$[64]. Two recent RCTs evaluated the concurrent administration of IIV-HD with newer RSV vaccines in adults 50 years of age and older[65,66]. No safety concerns were identified with the concurrent administration of IIV-HD and the RSV prefusion F (RSVpreF) vaccine (Abrysvo™, Pfizer) and the $AS01_E$ adjuvanted RSV prefusion protein F3 (RSVPreF3) vaccine (Arexvy, GlaxoSmithKline). No immune interference was reported with the concurrent administration of IIV-HD and the adjuvanted RSVpreF3 vaccine[65]. A reduced immune response to IIV-HD was observed with the concurrent administration of the RSVpreF vaccine; however, the clinical significance of this reduction is currently unknown[66]. Additional research is ongoing to further inform guidance on same-day administration of RSV vaccines and other adult vaccines, including influenza vaccines. NACI will continue to review the evidence and update guidance accordingly.

Vaccine safety and adverse events

Post-marketing surveillance of the safety of influenza vaccines in Canada is a continuous process. In addition to routine surveillance, every year during the seasonal influenza vaccination campaigns, PHAC, through its vaccine safety surveillance division (in collaboration with Health Canada), and the Federal/Provincial/Territorial Vaccine Vigilance Working Group (VVWG) of the Canadian Immunization Committee, conduct weekly expedited surveillance of adverse events following immunization (AEFI) for the currently distributed influenza vaccines to identify vaccine safety signals in a timely manner. Refer to the section Guidance on reporting adverse events following immunization below for more information on mandatory reporting of AEFIs. Refer to the Canadian Adverse Events Following Immunization Surveillance System (CAEFISS) web

page for more information on post-marketing surveillance and AEFIs in Canada. In addition, the Canadian National Vaccine Safety (CANVAS) Network, one of the networks of the Canadian Immunization Research Network (CIRN) sites across Canada that conducts active vaccine safety surveillance, collects and analyzes information on AEFIs after influenza vaccination at sites across Canada to provide influenza vaccine safety information to public health authorities during the core weeks of the annual influenza vaccination campaign.

All seasonal influenza vaccines have a favourable and stable safety profile. Some multi-dose vial formulations of inactivated influenza vaccine that are authorized for use in Canada contain thimerosal as a preservative to prevent bacterial and fungal contamination from multiple punctures of the vial[67]. Over the past 25 years, multiple well-designed studies using various epidemiological study designs conducted in several countries. In addition, large cohort studies of administrative health databases have found no association between childhood vaccination with thimerosal-containing vaccines and neurodevelopmental outcomes, including autistic-spectrum disorders[68]. All single dose formulations of IIV and LAIV are thimerosal-free. Refer to Vaccine Safety in Part 2 of the CIG for additional information.

Contraindications

Table 2 outlines the contraindications by vaccine type and specifies exceptions, rationale, and additional information. Contraindications specific to LAIV administration should not be used as a reason to withhold or delay immunization; rather, a parenteral inactivated or recombinant influenza vaccine should be offered.

Table 2: Influenza vaccine contraindications

Influenza vaccine type	Contraindication	Exceptions (i.e., not contraindicated)	Rationale and/or additional information
All (IIV, RIV, LAIV)	Anaphylactic reaction to influenza vaccine, or to any of the components of a specific influenza vaccine or its container	Egg allergy	If an individual is found to have an anaphylactic reaction to a component in 1 influenza vaccine or its container, consideration may be given to consulting an allergy specialist to offer another influenza vaccine that does not contain the implicated component. Refer to the section on Allergic reactions to previous vaccine doses under "Other reported adverse events (AEs) and conditions". Egg allergy is neither a contraindication nor precaution to influenza vaccine. Refer to the section on Egg-allergic individuals under "Other reported AEs and conditions".
LAIV	Severe asthma (defined as currently on oral or high-dose inhaled glucocorticosteroids) Active wheezing, or medically attended wheezing in the 7 days prior to the proposed date of vaccination	People with a history of stable asthma or recurrent wheeze which is not active	Due to increased risk of wheezing following administration of LAIV.
	People who are immunocompromised due to underlying disease and/or therapy	Children living with stable HIV infection receiving antiretroviral therapy (ART) and with adequate immune function	Refer to the Recommendation on the use of live attenuated influenza vaccine (LAIV) in HIV infected individuals.
	Children less than 24 months of age		LAIV not authorized for this age group due to increased risk of wheezing following administration of LAIV.
	Children 2 to 17 years of age currently receiving long-term aspirin or aspirin-containing therapy		Due to the association of Reye's syndrome with aspirin and wild-type influenza infection.
	Pregnant women and pregnant individuals		While there has been no identified safety signal regarding the use of LAIV in pregnancy, there are more data on the safety of other influenza vaccine products in pregnancy. Refer to the Updated guidance on influenza vaccination during pregnancy.

Abbreviations: IIV: inactivated influenza vaccine; RIV: recombinant influenza vaccine; LAIV: live attenuated influenza vaccine.

Warnings and Precautions

Table 3 outlines the precautions to influenza vaccine by vaccine type and specifies exceptions, rationale, and additional information. A precaution is defined in the CIG as a condition that may increase the risk of an adverse reaction following immunization or that may compromise the ability of the vaccine to produce immunity. In general, vaccines are deferred when a precaution is present. However, there may be circumstances when the benefits of giving the vaccine outweigh any potential risks, or when reduced vaccine immunogenicity may still result in significant benefit to an immunocompromised host. Product monographs will also include clinically significant information to promote safe and effective use of the drug.

Precautions specific to LAIV administration should not be used as a reason to withhold or delay immunization with an alternate influenza vaccine. In such cases, a parenteral inactivated or recombinant influenza vaccine can be offered.

Table 3: Influenza vaccine precautions

Influenza vaccine type	Precaution	Rationale and/or additional information
All (IIV, RIV, LAIV)	Guillain-Barré Syndrome (GBS) within 6 weeks of a previous influenza vaccination	NACI generally recommends people who have developed GBS within 6 weeks of a previous influenza vaccination should not receive influenza vaccine unless another cause was found for the GBS. The potential risk for a recurrent episode of GBS associated with influenza vaccination must be balanced against the risk of GBS associated with influenza infection itself and the benefits of influenza vaccination. Refer to the section on Guillain-Barré Syndrome under “Other reported adverse events (AEs) and conditions”.
	Oculorespiratory syndrome (ORS) with lower respiratory tract symptoms	Such individuals should consult a health care provider with expertise in the diagnosis and management of allergic reactions before subsequent influenza vaccination. Refer to the section on ORS under “Other reported AEs and conditions”.
	Serious acute illness	Influenza vaccination should usually be postponed until their symptoms have abated. More information on vaccinating individuals during acute illness can be found in the Canadian Immunization Guide's section on Contraindications and precautions associated with specific conditions: Acute Illness.
LAIV	Presence of significant nasal congestion or discharge	May impede delivery of LAIV to the nasopharyngeal mucosa and prevent vaccine from acting.
	Close contacts, including health care workers (HCWs), of people with severe immune compromising conditions	Due to viral shedding and the rare possibility of transmission of virus to people with severe immune compromise. Refer to the section on HCWs under “Choice of seasonal influenza vaccine”.
	Concurrent receipt of antivirals active against influenza virus (e.g., oseltamivir, zanamivir)	Antivirals may inactivate the vaccine viruses, and result in reduced response to the vaccine. Refer to the section on Drug interactions under “Other reported AEs and conditions”.
	Adults with any of the chronic health conditions identified in List 1	Due to the potentially better immune response following IIV compared to LAIV in healthy adults in some studies. Refer to the section on younger adults (18 to 64 years of age) under “Choice of seasonal influenza vaccine”.

Abbreviations: IIV: inactivated influenza vaccine; RIV: recombinant influenza vaccine; LAIV: live attenuated influenza vaccine.

More information on contraindications and precautions can be found in the Influenza vaccine chapter of the CIG's section on contraindications and precautions.

Common adverse events

With IM administered influenza vaccines, injection site reactions are common but are generally classified as mild and transient. IIV-Adj tends to produce more extensive injection site reactions than un-adjuvanted IIV, but these reactions are also generally mild and resolve spontaneously within a few days. IIV-HD tends to induce higher rates of systemic reactions compared to IIV-SD, but most of these reactions are mild and short-lived. Recombinant vaccines appear to have a similar safety profile to IIV-SDs. The most common AEs experienced by recipients of LAIV are nasal congestion and runny nose.

Less common and serious or severe adverse events

Serious adverse events (SAEs) are rare following influenza vaccination, and in most cases, data are insufficient to determine a causal association.

Allergic reactions to previous vaccine doses

Allergic responses to influenza vaccine are a rare consequence of hypersensitivity to a component of the vaccine or its container. Refer to the CIG chapter on Contents of immunizing agents authorized for use in Canada for a comprehensive list of contents of immunizing agents authorized for marketing in Canada. Expert review of the benefits and risks of vaccination should be sought for those who have previously experienced severe lower respiratory symptoms (wheeze, chest tightness, difficulty breathing) within 24 hours of influenza vaccination, an apparent significant allergic reaction to the vaccine, or any other symptoms that could indicate a significant allergic reaction (e.g., throat constriction, difficulty swallowing) that raise concern regarding the safety of revaccination. This advice may be obtained from experts in infectious disease, allergy, and immunology, or public health that can be found in various health settings, including the Special Immunization Clinic (SIC) network of CIRN.

In view of the considerable morbidity and mortality associated with influenza and rarity of true vaccine allergy, individuals with suspected allergy to an influenza vaccine or its container should consult a healthcare provider with expertise in the diagnosis and management of anaphylaxis.

Egg-allergic individuals

After careful review of clinical and post-licensure safety data, NACI has concluded that egg-allergic individuals may be vaccinated against influenza using any influenza vaccine, including egg-based vaccines and LAIV, without prior influenza vaccine skin test and with the full dose, irrespective of a past severe allergic reaction to egg and without any particular consideration, including vaccination setting. The amount of trace ovalbumin allowed in influenza vaccines that are authorized for use in Canada is associated with a low risk of AE, and in addition, 2 of the authorized products (i.e., IIV-cc and RIV) do not contain any ovalbumin. For more guidance on vaccinating egg-allergic individuals, refer to the Statement on Seasonal Influenza Vaccine for 2018–2019 and the egg allergy LAIV addendum for safety data supporting this recommendation for IIV and LAIV. The observation period post-vaccination is as recommended in Vaccine Safety in Part 2 of the CIG. As with all vaccine administration, vaccine providers should be prepared with the necessary equipment, knowledge, and skills to respond to allergic reactions, including anaphylaxis, at all times.

Guillain-Barré syndrome

In a review of studies conducted between 1976 and 2005, the United States Institute of Medicine concluded that the 1976 “swine flu” vaccine was associated with an elevated risk of GBS. However, evidence was inadequate to accept or to reject a causal relation between GBS in adults and seasonal influenza vaccination[69]. The attributable risk of GBS in the period following seasonal and/or monovalent pandemic 2009 influenza vaccination is about 1 excess case per million vaccinations[10,70]. In a self-controlled study that explored the risk of GBS after seasonal influenza vaccination and after influenza health care encounters (a proxy for influenza illness), the attributable risks were 1.03 GBS admissions per million vaccinations compared with 17.2 GBS admissions per million influenza-coded health care encounters[10]. Another cohort study found a risk of approximately 2 GBS cases per 1 million doses in the 4 weeks following administration of the 2009 pandemic influenza A H1N1 vaccine[71].

These findings suggest that both influenza vaccination and influenza illness are associated with small attributable risks of GBS, but the risk of GBS associated with influenza illness is notably higher than with influenza vaccination. The self-controlled study also found that the risk of GBS after vaccination was highest during weeks 2 to 4, whereas for influenza illness, the risk was greatest within the first week after an influenza-coded health care encounter and decreased thereafter but remained significantly elevated for up to 4 weeks[10].

At this time, it appears prudent to avoid subsequent influenza vaccination of individuals known to have had GBS without other known etiology within 6 weeks of a previous influenza vaccine. However, the potential risk of GBS recurrence associated with influenza vaccination must be balanced against the risk of GBS associated with influenza infection itself and the other benefits of influenza vaccination[72-74].

Oculorespiratory syndrome

Oculorespiratory syndrome (ORS), the presence of bilateral red eyes and 1 or more associated respiratory symptoms (cough, wheeze, chest tightness, difficulty breathing, difficulty swallowing, hoarseness, or sore throat) that starts within 24 hours of vaccination, with or without facial edema, was identified during the 2000-2001 influenza season[75]. In the two decades since then, there have been far fewer cases per year reported to CAEFISS[76]. ORS is not an allergic response. People who have an occurrence or recurrence of ORS upon vaccination do not necessarily experience further episodes with future vaccinations.

Individuals who have experienced ORS without lower respiratory tract symptoms may be safely revaccinated with influenza vaccine. Health care providers who are unsure whether an individual previously experienced ORS versus an immunoglobulin E (IgE) mediated hypersensitivity immune response should seek advice from a health care provider with expertise in the diagnosis and management of anaphylaxis. Data on clinically significant AEs do not support the preference of 1 vaccine product over another when revaccinating those who have previously experienced ORS.

Drug interactions

Although influenza vaccine can inhibit the clearance of warfarin and theophylline, clinical studies have not shown any adverse effects attributable to these drugs in people receiving influenza vaccine. Statins have effects on the immune system in addition to their therapeutic cholesterol-

lowering actions. Two published studies have found that adults who are regular statin users (at least 65 years of age in 1 study and 45 years and older in the other) had a decreased response to influenza vaccination as measured by reduced geometric mean titres (GMT) or reduced VE against medically attended acute respiratory illness[77,78]. Statins are widely used in the same adult populations who are also at-risk for influenza-related complications and hospitalizations. Therefore, if these preliminary findings are confirmed in future studies, concurrent statin use in adult populations could have implications for influenza VE and how this use is assessed in the measurement of VE. NACI will continue to monitor the literature related to this issue.

Influenza antiviral agents (e.g., oseltamivir, zanamivir) may inactivate the replicating vaccine virus contained in LAIV and therefore reduce the VE. Administration of LAIV should be postponed until 48 hours after the last dose of an antiviral. If these antiviral agents are required for clinical management of an infection within 2 weeks after receiving a dose of LAIV vaccine, re-vaccination should take place either at least 48 hours after the antivirals are stopped. Antiviral agents do not interfere with immunogenicity of non-live influenza vaccines (inactivated or recombinant), which can be administrated at any time.

Guidance on reporting adverse events following immunization

To ensure the ongoing safety of influenza vaccines in Canada, reporting of AEFIs by vaccine providers and other clinicians is critical, and in most jurisdictions, reporting is mandatory under public health legislation.

An AEFI is any untoward medical occurrence that follows vaccination whether or not there is a causal relationship with the usage of a vaccine. The AEFI may be any unfavourable or unintended sign, abnormal laboratory finding, symptom, or disease. Any AEFI temporally related to vaccination and for which there is no other clear cause at the time of reporting should be reported. Vaccine providers are asked to report AEFIs through local public health officials and to check for specific AEFI reporting requirements in their province or territory. If there is any doubt as to whether or not an event should be reported, a conservative approach should be taken, and the event should be reported.

For influenza vaccines, the following AEFIs are of particular interest:

- ORS; and
- GBS within 6 weeks following vaccination.

Refer to Reporting Adverse Events Following Immunization (AEFI) in Canada for additional information about AEFI reporting and to Vaccine Safety in Part 2 of the CIG for general vaccine safety information, including information on the management of AEs.

Recommendations

NACI makes the following recommendations for individual-level and public health program-level decision making. Individual-level recommendations are intended for people wishing to protect themselves from influenza or for vaccine providers wishing to advise individual patients about preventing influenza. Program-level recommendations are intended for provinces and territories responsible for making decisions on publicly funded immunization programs. Individual-level and program-level recommendations may differ, as the important factors to consider when recommending a vaccine for a population (e.g., population demographics, economic considerations) may be different than for an individual.

Recommendation for individual-level decision making

NACI recommends that influenza vaccine should be offered annually to anyone 6 months of age and older who does not have a contraindication to the vaccine. Influenza vaccination is particularly important for the groups indicated in List 1.

Recommendations for public health program-level decision making

The national goal of the annual influenza immunization programs in Canada is to prevent serious illness caused by influenza and its complications, including death. Programmatic decisions to provide influenza vaccination to specific populations as part of publicly funded provincial and territorial programs depend on many factors, such as cost-effectiveness evaluation and other programmatic and operational factors, such as implementation strategies.

- **NACI recommends that influenza vaccine should be prioritized for the groups for whom influenza vaccination is particularly important (see List 1 in the section below).**

List 1: Groups for whom influenza vaccination is particularly important

People at high risk of influenza-related complications or hospitalization

- All children 6 to 59 months of age;
- Adults and children with the following chronic health conditions[a]:
  - Cardiac or pulmonary disorders (including 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 neurodevelopmental 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);
  - Class 3 obesity (defined as body mass index of 40 kg/m² and over); and
  - Children 6 months to 18 years of age undergoing long-term treatment with acetylsalicylic acid, because of the potential increase of Reye's syndrome associated with influenza;

- All pregnant women and pregnant individuals;
- All individuals of any age who are residents of nursing homes and other chronic care facilities;
- Adults 65 years of age and older; and
- Individuals in or from First Nations, Inuit, or Métis communities as a result of intersecting determinants of health rooted in historic and ongoing colonization and systemic racism.

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 6 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 to 59 months of age, whether in or out of the home; and
- Those who provide services within closed or relatively closed settings to people at high risk (e.g., crew on a cruise ship).

Others

- People who provide essential community services; and
- People whose occupational or recreational activities increase their risk of exposure to avian influenza A(H5N1) viruses.

[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.

Choice of seasonal influenza vaccine

Due to the evolving influenza vaccine landscape, including the introduction of new influenza vaccines, some of which are designed to enhance immunogenicity in specific age groups, the choice of product is now more complex. NACI recommends that any age-appropriate influenza vaccine should be used for individuals 6 months of age and older who do not have contraindications. For adults 65 years of age and older, NACI recommends offering IIV-HD, IIV-Adj, or RIV when available. If these are not available, any age-appropriate influenza vaccine should be used.

Table 4 provides age group-specific recommendations for the age-appropriate influenza vaccine types authorized for use in Canada for individual and public health program-level decision making. Additional information for these recommendations and considerations on choice of influenza vaccine are provided in the section below.

Table 4: 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[a] for use	Recommendations on choice of influenza vaccine
6 to 23 months	• IIV-Adj • IIV-SD • IIV-cc	• Any age-appropriate influenza vaccine should be used for infants and young children who do not have contraindications, noting the following considerations: ◦ Influvac® (IIV3-SD) is authorized for use in children 6 months of age and older; however, additional NACI evidence review is required before recommending its use in children younger than 3 years. Updated guidance will be provided once this review is complete.
2 to 17 years[b]	• IIV-SD • IIV-cc • LAIV	• Any age-appropriate influenza vaccine should be used for children and adolescents who do not have contraindications including those with chronic health conditions, noting the following considerations and exceptions: ◦ Influvac® (IIV3-SD) is authorized for use in children 6 months of age and older; however, additional NACI evidence review is required before recommending its use in children younger than 3 years. Updated guidance will be provided once this review is complete. LAIV is contraindicated in children or adolescents with: ▪ severe asthma (defined as currently on oral or high-dose inhaled corticosteroids); ▪ active wheezing, or medically attended wheezing in the 7 days prior to vaccination; ▪ immune compromising conditions, with the exception of stable HIV infection, i.e., if the child is currently being treated with ART for at least 4 months and has adequate immune function; ▪ current receipt of long-term aspirin or aspirin-containing therapy; and ▪ pregnancy
18 to 59 years	• IIV-SD • IIV-cc • LAIV	• Any age-appropriate influenza vaccine should be used for adults 18 to 59 years of age who do not have contraindications, noting the following considerations and exceptions: ◦ There is some evidence that IIV may provide better efficacy than LAIV in adults; ◦ LAIV is contraindicated in adults with: ▪ severe asthma (defined as currently on oral or high-dose inhaled corticosteroids); ▪ active wheezing, or medically attended wheezing in the 7 days prior to vaccination; ▪ immune compromising conditions; and ▪ pregnancy. ◦ LAIV is not recommended for: ▪ adults with any of the chronic health conditions identified in List 1; and ▪ healthcare workers (HCWs).
60 to 64 years	• IIV-SD • IIV-cc	• Any age-appropriate influenza vaccine should be used for adults 60 to 64 years of age who do not have contraindications.
65 years and older[c]	• IIV-Adj • IIV-SD • IIV-HD • IIV-cc	• IIV-HD, IIV-Adj, or RIV should preferentially be offered, when available, over IIV-SD or IIV-cc for adults 65 years of age and older without contraindications. If no preferred product is available, any available influenza vaccines authorized for this age group should be used.

Abbreviations: ART: antiretroviral therapy; IIV: inactivated influenza vaccine; IIV-Adj: adjuvanted inactivated influenza vaccine; IIV-SD: standard-dose inactivated influenza vaccine; IIV-cc: mammalian cell-culture-based inactivated influenza vaccine; IIV-HD: high-dose inactivated influenza vaccine; IIV4-SD: standard-dose quadrivalent inactivated influenza vaccine; RIV: recombinant influenza vaccine; LAIV: live attenuated influenza vaccine.

[a] Authorized products may or may not be marketed and available in Canada in a given season.
[b] Refer to Table 5 for a summary of vaccine characteristics of LAIV compared with IIV in children 2 to 17 years of age.
[c] Refer to the NACI Supplemental statement on influenza vaccination in adults 65 years of age and older for rationale, supporting evidence appraisal and additional details on the evidence reviews that were conducted to support this recommendation.

Children

Healthy children

Three types of influenza vaccine are authorized and available for use in children: IIV-SD, IIV-cc, and LAIV. Although authorized, Fluad® Pediatric (IIV-Adj) has not been available in Canada since 2019.

LAIV is not authorized for children under the age of 2 years.

Children with chronic health conditions

NACI recommends that any age-appropriate quadrivalent or trivalent influenza vaccine (IIV or LAIV) may be considered for children 2 to 17 years of age with chronic health conditions; however, LAIV should not be used for children with severe asthma (defined as currently on oral or high-dose inhaled glucocorticosteroids or with active wheezing, or with medically attended wheezing in the 7 days prior to vaccination, those currently receiving long-term aspirin or aspirin-containing therapy, and those with immune compromising conditions (excluding those with stable HIV infection on ART and with adequate immune function). LAIV is also contraindicated in adolescents who are pregnant (see vaccine use in pregnancy below). Children and adolescents for whom LAIV is contraindicated should receive IIV.

NACI recommends that LAIV may be given to children aged 2-17 years with stable, non-severe asthma.

Refer to the NACI Recommendations on the Use of Live, Attenuated Influenza Vaccine (FluMist®): Supplemental Statement on Seasonal Influenza Vaccine for 2011–2012 for additional information supporting these recommendations.

The comparison of the vaccine characteristics of IIV and LAIV, in Table 5 below, may be considered in deciding on the preferred vaccine option(s) for use by an individual or a public health program.

Table 5: Vaccine characteristics of live attenuated influenza vaccine (LAIV) compared with inactivated influenza vaccine (IIV) in children 2 to 17 years of age

Considerations[a]	LAIV compared with IIV[b]
Authorization/ Recommendations	IIV-SD, IIV-cc, and LAIV are authorized for use in Canada for children 2 to 17 years of age. Note: Influvac® (IIV3-SD) is authorized for use in children 6 months of age and older; however, additional NACI evidence review is required before recommending its use in children younger than 3 years. Updated guidance will be provided once this review is complete.
Efficacy and effectiveness	There was early evidence of superior efficacy of LAIV3 compared with IIV3-SD in children less than 6 years of age from RCTs, with weaker evidence of superior efficacy in older children. However, later post-marketing and surveillance studies across multiple influenza seasons found comparable protection against influenza for LAIV and IIV, with findings of reduced effectiveness for LAIV against A(H1N1) in some studies.
Immunogenicity	LAIV has been shown to be as immunogenic as IIV-SD, with some age-related differences.
Safety	Rhinitis (runny nose) and nasal congestion are more common with LAIV. Clinical and post-marketing studies showed a similar safety profile to IIV. Injection site reactions are common with IIV.
Contraindications	There are vaccine contraindications specific to LAIV. LAIV is contraindicated for children with severe asthma (currently on oral or high-dose inhaled glucocorticosteroids or active wheezing, or medically attended wheezing in the 7 days prior to vaccination), and immune compromising conditions (with the exception of children with stable HIV infection on ART and with adequate immune function), as well as those currently receiving long-term aspirin or aspirin-containing therapy. LAIV is also contraindicated for pregnant adolescents.
Acceptability	Delivery of LAIV as a nasal spray may be preferable for children who are averse to receiving the vaccine by needle injection.

Abbreviations: ART: highly active antiretroviral therapy; IIV: inactivated influenza vaccine; IIV-SD: standard-dose inactivated influenza vaccine; IIV-SD: standard-dose inactivated influenza vaccine; LAIV: live attenuated influenza vaccine.

[a] NACI has not assessed the comparative cost-effectiveness of authorized influenza vaccine types for children 2 to 17 years of age.
[b] Data comparing LAIV to IIV-cc are not available, however IIV-cc is comparable to egg-based IIV.

Adults

Younger Adults (18 to 64 years of age)

Two types of influenza vaccine are authorized and available for use in adults 18 to 64 years of age: IIV-SD and IIV-cc. Supemtek® (RIV) is not currently authorized or available for use since the 2025-2026 season. LAIV is authorized for adults aged 18-59 years.

NACI recommends that any of the authorized and available influenza vaccines should be used in adults 18 to 64 years of age without contraindications to the vaccine.

For adults with chronic health conditions identified in List 1, including those with immune-compromising conditions who are 18-64 years of age, NACI recommends that any age-appropriate IIV or RIV should be offered. LAIV is not recommended for adults with chronic health conditions due to the potentially better immune response following IIV compared to LAIV in healthy adults in some studies. For further information, refer to Recommendations on the use of live, attenuated influenza vaccine (FluMist®) Supplemental Statement on Seasonal Influenza Vaccine for 2011-2012.

Older adults (65 years of age and over)

Four types of influenza vaccine are authorized and available for use in adults 65 years of age and older: IIV-Adj, IIV-SD, IIV-cc and IIV-HD. Supemtek® (RIV) is not currently authorized or available for use since the 2025-2026 season.

NACI recommends that IIV-HD, IIV-Adj, or RIV should be offered, when available, over other influenza vaccines for adults 65 years of age and older. If no preferred product is available, IIV-SD or IIV-cc should be used. Where supply of IIV-HD, IIV- Adj, and RIV is limited, consideration can be given to prioritizing groups at highest risk of severe outcomes from influenza among adults 65 years of age and older, such as advanced-age older adults (e.g., 75 years of age and older), those with 1 or more comorbidities, older frail adults, and residents of nursing homes and other chronic care facilities.

Based on a review of the evidence to determine whether any age-appropriate influenza vaccines should be preferentially used in adults 65 years of age and older, the evidence supports IIV-HD, IIV-Adj, and RIV as having increased benefit as compared to IIV-SD, with no difference in safety. No study included in the review compared IIV-cc to other influenza vaccines against critical outcomes for decision-making. Consequently, it was not possible to make a recommendation on the preferential use of IIV-cc in adults 65 years of age and older.

Refer to the NACI Supplemental Statement on Influenza Vaccination in Adults 65 Years of Age and Older for additional information supporting these recommendations.

Other population groups

Pregnant women and pregnant individuals

NACI recommends that any age-appropriate IIV (i.e., IIV-SD, IIV-cc) or RIV, but not LAIV, should be offered to pregnant women and pregnant individuals. There has been no identified safety signal regarding the use of RIV during pregnancy, although published clinical data are limited. Additionally, there has been no identified safety signal regarding the use of LAIV in pregnancy, although there are more data on the safety of other influenza vaccine products in pregnancy and evidence that IIV has higher efficacy than LAIV in healthy adults. However, vaccination with LAIV should not be considered a reason to terminate pregnancy.

Breastfeeding women and breastfeeding individuals can receive either non-live or live-attenuated influenza vaccines. There have been no identified safety signals for influenza vaccination in breastfeeding, and no hypothesized biological mechanism for a safety issue with currently authorized products. For further details, refer to the Updated guidance on influenza vaccination during pregnancy.

Health care workers

NACI recommends that any age-appropriate IIV or RIV, but not LAIV, should be offered to health care workers (HCWs). Comparative studies in healthy adults have found IIV to be similarly or more efficacious or effective compared with LAIV[79]. LAIV is not recommended but if used, as a precautionary measure, LAIV recipients should avoid close association with people with severe immune compromising conditions (e.g., bone marrow transplant recipients requiring protective isolation) for at least 2 weeks following vaccination, due to the theoretical risk of transmitting a vaccine virus and causing infection.

Travellers

NACI recommends that a decision for or against revaccination of travellers to the Southern Hemisphere between April and October, if they had already been vaccinated in the preceding fall or winter with the Northern Hemisphere's vaccine, should depend on individual risk assessment, the similarity between the Northern and Southern Hemisphere vaccines, the similarity between the Northern Hemisphere vaccine strains and currently circulating strains in the Southern Hemisphere, and the availability of a reliable and safe vaccine at the traveller's destination.

Influenza occurs year-round in the tropics. In temperate northern and southern countries, influenza activity generally peaks during the winter season (November to March in the Northern Hemisphere and April to October in the Southern Hemisphere).

Vaccines prepared specifically for use in the Southern Hemisphere are not available in Canada, and the extent to which recommended vaccine components for the Southern Hemisphere may overlap with those in available Canadian formulations will vary.

Refer to Immunization of Travellers in Part 3 of the CIG for additional general information.

Groups for whom influenza vaccination is particularly important

The groups for whom influenza vaccination is particularly important are presented in List 1. Additional information is provided below.

People at high risk of influenza-related complications or hospitalization

All children 6 to 59 months of age

On the basis of existing data, NACI recommends the inclusion of all children 6 to 59 months of age among those for whom influenza vaccine is particularly important. Refer to the Statement on Seasonal Influenza Vaccine for 2011–2012 for additional details on children 6 to 23 months of age and to the Statement on Seasonal Influenza Vaccine for 2012–2013 for children 24 to 59 months of age.

Adults and children with chronic health conditions

Several chronic health conditions are associated with increased risk of influenza-related complications and can be exacerbated by influenza infection. Influenza vaccination can induce protective antibody levels in a substantial proportion of adults and children with immune-compromising conditions, including transplant recipients, those with proliferative diseases of the hematopoietic and lymphatic systems, and HIV-infected people. VE may be lower in people with immunocompromising conditions compared to healthy adults.

Influenza infection has been associated with an increased risk of CV events, including myocardial infarction, heart failure, and stroke, especially among individuals with pre-existing cardiac disorders[80]. A study from 2022 suggested that, globally, 3 to 5% of the total number of ischemic heart disease deaths could be attributed to influenza, corresponding to 200,000 to 400,000 ischemic heart disease deaths annually[81]. In addition to the prevention of influenza infection and its complications, influenza vaccination may also have a secondary protective

effect against the occurrence of CV events in those with acute and chronic heart disease[82,83]. NACI conducted a review of systematic reviews and meta-analyses assessing the effect of influenza vaccination on CV events. Overall, the findings provide evidence of a protective effect of influenza vaccination against CV events among high-risk populations, such as those with CV disease. For more information refer to Does influenza vaccination contribute to the prevention of cardiovascular events?

Pregnant women and pregnant individuals

Pregnant women and pregnant individuals, along with infants under 6 months of age, are particularly at risk of severe illness from influenza infection[84]. Overall, studies support the safety and effectiveness of influenza vaccines during pregnancy[85]. Vaccination reduces the morbidity and mortality associated with influenza infection during pregnancy[86]. Since influenza-related outcomes experienced during pregnancy can negatively impact the development of the fetus, vaccination during pregnancy also helps protect the fetus[86]. Furthermore, passive transfer of antibodies from vaccination during pregnancy protects newborns during their first months of life when they are at high risk of complications from influenza infection, and too young to be immunized.

NACI continues to strongly recommend that inactivated (IIV-SD, IIV-cc) or recombinant (RIV) influenza vaccines be offered at any stage of pregnancy. NACI also continues to include pregnant women and pregnant individuals among those for whom influenza vaccination is particularly important. Finally, NACI reaffirms its recommendation that influenza vaccines may be administered concurrently with (i.e., same day), or at any time before or after, other vaccines recommended during pregnancy (e.g., pertussis or RSV).

For further details, refer to the Updated guidance on influenza vaccination during pregnancy.

People of any age who are residents of long-term care homes and other chronic care facilities

More than 90% of residents of long-term care homes are 65 or over 65 and have one or more chronic health conditions. The majority of patients in other residential or chronic care facilities have 1 or more chronic health condition. In addition, the congregate living setting facilitates the spread of influenza.

Adults 65 years of age and older

Although influenza-associated morbidity and mortality vary each season, there is generally an increased burden of severe disease such as influenza-associated hospitalizations, intensive care unit (ICU) admissions, and deaths in adults 65 years of age and older, especially in seasons when influenza A(H3N2) predominates[11]. For further details on estimated burden of influenza among this population, refer to the supplemental guidance on influenza vaccination in adults 65 years of age and older.

Individuals in or from First Nations, Inuit, or Métis communities

Based on a body of evidence indicating a higher rate of influenza-associated hospitalization among individuals in or from First Nations, Inuit, and Métis communities, NACI recommends the inclusion of this population among those for whom the influenza vaccine is particularly important, regardless of geographic location[87].

The increased risk of severe influenza among individuals in or from First Nations, Inuit, and Métis communities is a consequence of many upstream factors, including medical conditions resulting from intersecting determinants of health. These intersecting determinants of health include social, environmental, and economic factors, rooted in historic and ongoing colonization and systemic racism (i.e., structural inequity). To improve understanding of the disproportionate impact within the current landscape, culturally safe research in collaboration with Indigenous partners should be supported. Autonomous decisions should be made by Indigenous Peoples with the support of culturally safe public health and health care partners in accordance with the United Nations Declaration on the Rights of Indigenous Peoples Act (UNDRIP).

People capable of transmitting influenza to those at high risk of influenza-related complications or hospitalization

People who are potentially capable of transmitting influenza to those at high risk should receive annual vaccination, regardless of whether the high-risk individual has been vaccinated.

Health care workers and other care providers in facilities and community settings

For the purposes of this statement, HCWs are care providers in facilities and community settings, essential care providers, emergency response workers, those who work in continuing care or long-term care facilities or residences, those who provide home care for people at high risk, and students of related health care services. HCWs include any person, paid or unpaid, who provides services, works, volunteers, or trains in a hospital, clinic, or other health care facility. These care providers, through their service-related activities are at increased risk of transmitting influenza to those at high risk of severe disease and serious complications from influenza. In addition, due to their close contact with people who may be infected with influenza, HCWs are themselves at increased risk of infection[88].

Vaccination of HCWs decreases their own risk of illness, as well as the risk of death and other serious outcomes among the individuals for whom they provide care[89-94]. Vaccination of HCWs and residents of nursing homes is associated with decreased risk of ILI outbreaks[95]. Four cluster RCTs conducted in geriatric long-term care settings have demonstrated that vaccination of HCWs is associated with substantial decreases in ILI and all-cause mortality in the residents[89-92].

Given the potential for HCWs and other care providers to transmit influenza to individuals at high risk and knowing that vaccination is the most effective way to prevent influenza, NACI recommends that, in the absence of contraindications, HCWs and other care providers in facilities and community settings should be vaccinated against influenza annually. NACI considers the receipt of influenza vaccination to be an essential component of the standard of care for all HCWs and other care providers for their own protection and that of their patients. This group should consider annual influenza vaccination as part of their responsibilities to provide the highest standard of care.

Although the current influenza vaccine coverage rate for HCWs is higher than for the general public, it remains below the national goal of 80% coverage for HCWs in Canada[96-98]. Comprehensive vaccination programs should be adopted that address HCWs' acceptance of the vaccine and facilitate the process of vaccinating HCWs to improve uptake of the influenza vaccine beyond the current level. HCW influenza vaccination programs that have successfully increased vaccine coverage of HCWs have included a combination of education, increased awareness, accessible on-site vaccination delivery options for all HCWs, visible support from senior staff and

other leaders, and regular review and improvement of vaccination strategies[99-104].

As noted in PHAC's Guidance: Infection Prevention and Control Measures for Healthcare Workers in Acute Care and Long-term Care Settings for seasonal influenza, all health care organizations should have a written plan for preventing and managing influenza outbreaks in their facilities. Inherent in such plans should be policies and programs to optimize patient/resident/client, HCW, volunteer, other caregiver and visitor influenza vaccination[105]. As part of outbreak management, the above-mentioned PHAC guidance also suggests consideration of chemoprophylaxis for all unvaccinated HCWs, unless contraindications exist. Refer to the Association of Medical Microbiology and Infectious Disease Canada (AMMI Canada) website for guidelines regarding the use of antiviral medications for prophylaxis.

Contacts of individuals at high risk of influenza complications

Vaccination is recommended for contacts, both adults and children, of individuals at high risk of influenza-related complications or hospitalization (see List 1), whether or not the individual at high risk has been vaccinated. These contacts include: household contacts and care providers of individuals at high risk (including infants less than 6 months of age), members of a household expecting a newborn during the influenza season, household contacts and care providers (whether in or out of the home) of children 0 to 59 months of age, and providers of services within closed or relatively closed settings with people at high risk of influenza-related complications (e.g., crew on a passenger or cruise ship).

Others

People who provide essential community services

Vaccination for these individuals should be encouraged to minimize the disruption of services and routine activities during annual influenza epidemics. People who provide essential community services, including healthy working adults, should consider annual influenza vaccination, as this intervention has been shown to decrease work absenteeism due to respiratory and related illnesses[93,94,106-108].

People whose occupational or recreational activities increase their risk of exposure to avian influenza A(H5N1) viruses

Since late 2021, multiple outbreaks of avian influenza A(H5N1), specifically clade 2.3.4.4b, have occurred in poultry and wild birds in Canada and the United States (US), with spillover events in dairy cattle and swine in the US and to other mammals in Canada and elsewhere. In the US, documented transmission from cattle to humans and poultry to humans has been reported[109,110]. Some countries and provinces have recommended seasonal influenza vaccination on a yearly basis for those working with poultry, swine, cattle, goats, and wild birds[111-114]. For more information on avian influenza, refer to Rapid response: Preliminary guidance on human vaccination against avian influenza in a non-pandemic context as of December 2024.

Although seasonal influenza vaccines do not protect against avian influenza infection, they may reduce the risk of seasonal human and avian influenza A(H5N1) virus co-infection.

NACI particularly recommends seasonal influenza vaccination for people whose occupational and/or recreational activities increase their risk of exposure to avian influenza A(H5N1) viruses,

including contact with certain animal species or their environment. These occupations or activities may include:

- Working with poultry (e.g., chickens, turkeys, ducks) or other livestock (e.g., cattle, goats, swine, mink) on commercial farms including fur farms, small farms, and/or backyard flocks;
- Hunting or trapping wild birds or mammals;
- Handling and/or disposing of sick or dead wild birds, poultry, or mammals (e.g., culling operations), or involvement in the control of avian influenza outbreaks;
- Working with wild birds or mammals for research, conservation, or rehabilitation;
- Working in facilities processing animal products (e.g., meat processing, handling raw milk);
- Workers involved in the transportation of animals, animal products, or agricultural equipment or samples;
- Laboratory workers handling avian influenza viruses; and
- Veterinarians and veterinary staff.

Swine workers are included in this recommendation because bidirectional transmission of influenza A viruses between swine and humans is known to occur and may provide opportunity for emergence of a strain with higher pandemic potential through reassortment[115,116].

In addition to vaccination to help prevent seasonal influenza infection, biosecurity measures, personal protective equipment, and antivirals should be used as recommended for animal contact.

Refer to Human health issues related to avian influenza in Canada for PHAC recommendations on the management of domestic avian influenza outbreaks. NACI will continue to monitor the evolving evidence and update guidance as needed.

List of abbreviations

Adj	Adjuvanted
AE	Adverse event
AEFI	Adverse event following immunization
ART	Antiretroviral therapy
CAEFISS	Canadian Adverse Events Following Immunization Surveillance System
cc	Cell cultured
CI	Confidence interval
CIG	Canadian Immunization Guide
CV	Cardiovascular
CVD	Cardiovascular disease
DIN	Drug identification number
EMA	European Medicines Agency
FDA	Food and Drug Administration
FFU	Fluorescent focus units
GBS	Guillain-Barré syndrome
GMT	Geometric mean titre
GMTR	Geometric mean titre ratio
HA	Hemagglutinin
HCW	Healthcare worker
HD	High dose
HIV	Human immunodeficiency virus
Ig	Immunoglobulin
IIV	Inactivated influenza vaccine
IIV3	Trivalent inactivated influenza vaccine
IIV3-Adj	Adjuvanted trivalent inactivated influenza vaccine (egg-based)
IIV3-HD	High-dose trivalent inactivated influenza vaccine (egg-based)
IIV3-SD	Standard-dose trivalent inactivated influenza vaccine (egg-based)
IIV4	Quadrivalent inactivated influenza vaccine
IIV4-cc	Mammalian cell culture-based quadrivalent inactivated influenza vaccine
IIV4-HD	High-dose quadrivalent inactivated influenza vaccine (egg-based)
IIV4-SD	Standard-dose quadrivalent inactivated influenza vaccine (egg-based)

IM	Intramuscular
IMPACT	Immunization Monitoring Program Active
LAIV	Live attenuated influenza vaccine (egg based)
LAIV3	Trivalent live attenuated influenza vaccine (egg based)
LAIV4	Quadrivalent live attenuated influenza vaccine (egg based)
LCI	Laboratory-confirmed influenza
MDCK	Madin-Darby canine kidney
MMR	Measles, mumps, and rubella
NA	Neuraminidase
NACI	National Advisory Committee on Immunization
ORS	Oculorespiratory syndrome
PHAC	Public Health Agency of Canada
RCT	Randomized controlled trial
RIV	Recombinant influenza vaccine
RIV4	Recombinant quadrivalent influenza vaccine
RNA	Ribonucleic acid
rVE	Relative vaccine efficacy
RZV	Recombinant zoster vaccine
SAE	Serious adverse event
SPSN	Sentinel Practitioner Surveillance Network
UK	United Kingdom
US	United States
VE	Vaccine effectiveness
VRBPAC	Vaccines and Related Biological Products Advisory Committee
WHO	World Health Organization

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Appendix A: Abbreviations for influenza vaccines

Influenza vaccine category	Valency	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
		Standard dose[b], unadjuvanted, IM administered, mammalian cell culture-based	IIV3-cc
	Quadrivalent (IIV4)	Standard dose[b], unadjuvanted, IM administered, egg-based	IIV4-SD
		Standard dose[b], unadjuvanted, IM administered, mammalian 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: 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; IIV3-cc: standard-dose cell culture-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; RIV: recombinant influenza vaccine; RIV4: recombinant quadrivalent influenza vaccine; LAIV: live attenuated influenza vaccine; LAIV3: egg-based trivalent live attenuated influenza vaccine; LAIV4: egg-based quadrivalent live attenuated 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" (where "SD" is used to denote "standard dose" for an IIV) 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" (where "cc" denotes "cell culture") refers to an IIV product that is made from influenza virus grown in cell cultures instead of chicken eggs (IIV3-cc for Flucelvax® or IIV4-cc for Flucelvax® Quad); "- Adj" (where "Adj" is used to abbreviate "adjuvanted") 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 the 15 µg HA per strain that is contained in the standard IIV dose (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.

Appendix B: Characteristics of influenza vaccines available for use in Canada, 2026–-2027[a]

Note: Should the availability of a specific vaccine change (i.e., be made available or unavailable) after the release of this statement and prior to the 2026-2027 influenza vaccine season, NACI will communicate relevant information regarding the new vaccine preparations if required.

Product name (manufacturer)	Vaccine characteristic									
	Vaccine type	**Route of administration**	**Authorized ages for use**	**Antigen content for each vaccine strain**	**Adjuvant**	**Formats available**	**Post-puncture shelf life for multi-dose vials**	**Thimerosal**	**Antibiotics (traces)**	**Production medium**
Fluzone® (Sanofi)	IIV3-SD (split virus)	IM	6 months and older	15 µg HA/0.5 mL dose	None	Single-dose pre-filled syringe without attached needle	Up to expiry date indicated on vial label	Yes (multi-dose vial only)	None	Egg (Avian)
Fluzone® High-Dose (Sanofi)	IIV3-HD (split virus)	IM	65 years and older	60 µg HA/0.5 mL dose	None	Single dose pre-filled syringe without attached needle	Not applicable	No	None	Egg (Avian)
Flucelvax® (Seqirus)	IIV3-cc (subunit)	IM	6 months and older	15 µg HA /0.5 mL dose	None	5 mL multi-dose vial Single dose pre-filled syringe without attached needle	28 days	Yes (multi-dose vial only)	None	Cell culture (Mammalian)

FluMist® (AstraZeneca)	LAIV3 (live attenuated)	Intranasal	2 to 59 years	$10^{6.5\text{-}7.5}$ FFU of live attenuated reassortants /0.2 mL dose (given as 0.1 mL in each nostril)	None	Single use pre-filled glass sprayer	Not applicable	No	Gentamicin	Egg (Avian)
Fluad® (Seqirus)	IIV3-Adj (subunit)	IM	65 years and older	15 µg HA /0.5 mL dose	MF59	Single dose pre-filled syringe without a needle	Not applicable	No	Kanamycin and neomycin	Egg (Avian)
Fluviral (GSK)	IIV3-SD (split virus)	IM	6 months and older	15 µg HA /0.5 mL dose	None	5 mL multi-dose vial	28 days	Yes	None	Egg (Avian)
Influvac® (BGP Pharma ULC, operating as Mylan, d.b.a. Viatris Canada)	IIV3-SD (subunit)	IM	6 months and older	15 µg HA/0.5 mL dose	None	Single dose pre-filled syringe with or without attached needle	Not applicable	No	Gentamicin or neomycin and polymyxin Bb	Egg (Avian)

Abbreviations: FFU: fluorescent focus units; HA: hemagglutinin; IIV3-Adj: adjuvanted egg-based trivalent inactivated influenza vaccine; IIV3-cc: standard-dose cell culture-based quadrivalent inactivated influenza vaccine; IIV3-SD: standard-dose egg-based trivalent inactivated influenza vaccine; IM: intramuscular; LAIV3: quadrivalent live attenuated influenza vaccine; NA: neuraminidase.

[a] Full details of the composition of each vaccine authorized for use in Canada, including other non-medicinal ingredients, and a brief description of its manufacturing process can be found in the product monograph.

[b] Neomycin and polymyxin B are only used if gentamicin cannot be used. No trace amounts of neomycin or polymyxin B are present if gentamicin was used.

Appendix C: Additional information on vaccine efficacy, effectiveness, immunogenicity, and safety

Standard dose mammalian cell culture-based inactivated influenza vaccine (IIV-cc)

Vaccines currently authorized for use:

- Flucelvax® (Seqirus) (IIV3-cc)
- Flucelvax® Quad (Seqirus) (IIV4-cc)

Following the IIV4-cc vaccination recommendations published in the Statement on Seasonal Influenza Vaccine for 2022-2023, an expanded age indication for the use of IIV4-cc in children 6 months to 47 months was authorized.

Flucelvax® Quad was first authorized for use in adults and children 9 years of age and older on November 22, 2019. In support of this, NACI conducted a systematic review of the literature to examine vaccine efficacy, effectiveness, immunogenicity, and safety data for children in this age group. Refer to the NACI Supplemental Statement on Mammalian Cell Culture-Based Influenza Vaccines and the Statement on Seasonal Influenza Vaccine for 2022-2023 for further details.

An age indication extension for the use of Flucelvax® Quad in adults and children 2 years and older was authorized on March 8, 2021. Recommendations were developed based on a review of the Health Canada assessment of a multi-country phase 3/4 RCT on the efficacy, immunogenicity and safety of Flucelvax® Quad in children 2 years to less than18 years of age conducted over 3 influenza seasons (Southern Hemisphere 2017 influenza season and the 2017-2018 and 2018-2019 Northern Hemisphere influenza seasons). Refer to the Statement on Seasonal Influenza Vaccine for 2022-2023 for further details.

A second age indication extension to children 6 months to 47 months was authorized on March 8, 2022. To support this age indication extension, NACI reviewed the Health Canada assessment of a Phase 3 randomized clinical trial of the immunogenicity and safety of IIV4-cc compared to Afluria Tetra (IIV4-SD) in healthy children (n=2402) 6 to 47 months of age submitted by the manufacturer. The clinical trial was conducted in 47 sites across the United States during the 2019-2020 influenza season. The analysis of vaccine immunogenicity and safety in children 6 months to 47 months were consistent with the findings of the previous NACI systematic literature review and the Health Canada clinical assessment.

Adjuvanted inactivated influenza vaccine (IIV3-Adj)

Vaccines currently authorized for use:

- Fluad® (Seqirus)
- Fluad Pediatric™ (Seqirus)

Fluad® (adults 65 years of age and older)

Efficacy and effectiveness

Available evidence shows a protective effect of IIV3-Adj compared to IIV3-SD for influenza-associated hospitalization in older adults, with pooled rVE estimates of 12% (95% CI: 3 to 20%) and 25% (95% CI: 3 to 42%) against hospitalization and vaccine efficacy estimates of 25% (95% CI: -236 to 83%) against death. Refer to the Supplemental guidance on influenza vaccination in adults 65 years of age and older and Table 4 in the Statement on seasonal influenza vaccine for 2024–2025 for more detailed information on the efficacy and effectiveness of IIV3-Adj in adults 65 years of age and older.

Immunogenicity

The mechanism of action of MF59 is not fully determined and has primarily been studied using in vitro and mouse models. From these studies, it appears that MF59 may act differently from aluminum-based adjuvants. These studies show that MF59 acts in the muscle fibres to create a local immune-stimulatory environment at the injection site[117]. MF59 allows for an increased influx of phagocytes (e.g., macrophages, monocytes) to the site of injection. The recruited phagocytes are further stimulated by MF59, thereby increasing the production of chemokines to attract more innate immune cells and inducing differentiation of monocytes into dendritic cells[118,119]. MF59 further facilitates the internalization of antigen by these dendritic cells[117,119]. The overall higher number of cells available locally increases the likelihood of interaction between an antigen presenting cell and the antigen, leading to more efficient transport of antigen to the lymph nodes, with resulting improved T cell priming[118].

There is evidence from RCTs that IIV3-Adj elicits non-inferior immune responses compared to the un-adjuvanted subunit and split virus IIV3-SDs; however, superiority of IIV3-Adj to these vaccines by pre-defined criteria has not been consistently demonstrated. Refer to the Statement on Seasonal Influenza Vaccine for 2018–2019 for more information on the immunogenicity of IIV3-Adj in adults 65 years of age and older. for more information on the immunogenicity of IIV3-Adj in adults 65 years of age and older.

Safety

Evidence from RCTs shows that IIV3-Adj led to fewer solicited systemic reactions grade 3 or higher compared to IIV-SD (pooled risk ratio [RR] of 0.77, 95% CI: 0.34 to 1.76). Additionally, a meta-analysis of RCTs showed that IIV3-Adj led to more solicited injection site reactions grade 3 or higher compared to IIV-SD (pooled RR of 3.39, 95% CI: 1.32 to 8.72). However, there were no differences in SAEs between IIV3-Adj and IIV3-SD, though these estimates lacked precision (pooled RR of 1.07, 95% CI: 0.92 to 1.26). Lastly, an observational study comparing IIV3-Adj to IIV-SD found no cases of GBS among 170,988 recipients. Refer to the Supplemental guidance on influenza vaccination in adults 65 years of age and older and Table 4 in the Statement on seasonal influenza vaccine for 2024-2025 for more detailed information on the safety of IIV3-Adj in adults 65 years of age and older.

Fluad Pediatric™ (children 6 to 23 months of age)

Efficacy and effectiveness

A pre-licensure efficacy trial in children 6 to 71 months of age found a higher relative efficacy for IIV-Adj than the un-adjuvanted IIV3-SD[120]. However, the findings of this study should be interpreted with caution. The comparator un-adjuvanted IIV3 used in this trial was shown, in an unrelated study, to induce a lower immune response compared to another un-adjuvanted IIV3-SD. There were concerns raised by a European Medicines Agency inspection about the quality of diagnostic laboratory testing and validity of ascertainment of influenza cases. The study administered 0.25 mL doses of the comparator un-Adj IIV3-SD for children less than 36 months of age, which is lower than the dose of 0.5 mL of un-Adj IIV3-SD or IIV4-SD that is recommended for this age group in Canada. Refer to the NACI Literature Review on Pediatric Fluad Influenza Vaccine Use in Children 6 to 72 Months of Age for more information on the efficacy and effectiveness of IIV3-Adj in children. for more information on the efficacy and effectiveness of IIV3-Adj in children.

Immunogenicity

In children, there is limited but consistent evidence that IIV3-Adj is more immunogenic than IIV3-SD against both influenza A and B[120-125]. In particular, a single dose of IIV3-Adj is more immunogenic than a single dose of IIV3-SD and has been shown in 1 study to produce greater GMTs than 2 doses of IIV3-SD against influenza A[125]. However, similar to IIV3-SD, IIV3-Adj generally induced a weaker hemagglutination-inhibition antibody response against B strains compared to A strains and therefore 2 doses of IIV3-Adj are still necessary for first-time recipients to achieve a satisfactory immune response against influenza B.

Almost all of the pre-licensure pediatric studies used vaccine formulations of 0.25 mL in children 6 to 35 months of age, both for IIV3-Adj and the comparator un-adjuvanted influenza vaccine (NACI recommends 0.5 mL dosage of IIV3-SD or IIV4-SD for all age groups). There is limited immunogenicity evidence comparing IIV3-Adj at 0.25 mL dose to IIV3-SD or IIV4-SD at 0.5 mL dose in the 6-to-23-month age group. Refer to the NACI Literature Review on Pediatric Fluad Influenza Vaccine Use in Children 6 to 72 Months of Age for more information on the immunogenicity of IIV3-Adj in children. for more information on the immunogenicity of IIV3-Adj in children.

Safety

The safety data in children are consistent with what is known about IIV3-Adj's safety profile in adults. In pediatric trials, IIV3-Adj was more reactogenic than IIV3-SD, with recipients experiencing 10 to 15% more solicited local and systemic reactions. However, most reactions were mild and resolved quickly. A dose-ranging study of MF59-Adj and un-Adj IIV3 and IIV4 did not find an increased risk of AEs associated with increased MF59 dose, antigen dose, or the addition of a second B strain; however, the reactogenicity of 15 µg formulations were slightly higher for both Adj and un-Adj vaccines compared to the corresponding 7.5 µg formulations[123].

There are currently no data on the effects of long-term or repeated administration of Adj influenza vaccines in children. The most significant experience with an Adj influenza vaccine in children was the AS03-Adj A(H1N1) pandemic vaccine that has been associated with an increased risk of narcolepsy. A study comparing 2 AS03-Adj A(H1N1) vaccine products (Pandemrix and Arepanrix) has suggested that the underlying immune mediated mechanism associated with the increased

narcolepsy risk may not be initiated by the adjuvant, but by the A(H1N1) nucleoprotein viral antigen, given that the study found significant antigenic differences between the 2 A(H1N1) pandemic vaccines. However, the pandemic vaccine was a single strain Adj vaccine administered only during 1 season, and it is unknown what effects a multi-strain Adj vaccine or an Adj vaccine administered for more than 1 season may have in young children[126].

Refer to the NACI Literature Review on Pediatric Fluad Influenza Vaccine Use in Children 6-72 Months of Age for additional information on the safety of IIV3-Adj in children.

High-dose inactivated influenza vaccine (IIV-HD)

Vaccines currently authorized for use:

- Fluzone® High-Dose (Sanofi) (IIV3-HD)
- Fluzone® High-Dose Quadrivalent (Sanofi) (IIV4-HD)

Refer to the Supplemental guidance on influenza vaccination in adults 65 years of age and older and Table 4 in the Statement on seasonal influenza vaccine for 2024-2025 for more detailed information on the efficacy/effectiveness and safety of IIV3-HD in adults 65 years of age and older.

Methods

Fluzone® High-Dose Quadrivalent (IIV4-HD) builds on the clinical development of its trivalent predecessor Fluzone® High-Dose (IIV3-HD) since both vaccines have the same manufacturing process and overlapping compositions. Therefore, data on the efficacy, effectiveness, immunogenicity, and safety of IIV3-HD are relevant and inferred to IIV4-HD.

Efficacy and effectiveness

There is good evidence that Fluzone® High-Dose (IIV3-HD) provides better protection compared with IIV3-SD in adults 65 years of age and older. Two studies found that IIV3-HD may provide greater benefit in adults 75 years of age and older compared to adults 65 to 74 years of age[127,128]. The efficacy results for IIV3-HD are inferred to IIV4-HD based on the non-inferior immunogenicity, described in the next section.

Immunogenicity

There is evidence that immunization with IIV3-HD elicits a higher immune response compared to immunization with IIV3-SD in older adults[129-136]. Across all 3 influenza vaccine strains, rates of seroconversion were found to be about 19% higher (ranging from 8 to 39% higher) for the IIV3-HD group. The post-vaccination GMT ratios (GMTR) of participants' responses to IIV3-HD was about 1.5 to 1.8 times higher than those receiving IIV3-SD. There is good evidence that the immunogenicity for Fluzone® High Dose Quadrivalent (IIV4-HD) is non-inferior to IIV3-HD[137,138]. In a pivotal RCT, IIV4-HD met all non-inferiority criteria set by the US Food and Drug Administration, based on GMTR and seroconversion rates when compared to IIV3-HD[138]. Immunogenicity for IIV4-HD was superior for the influenza B strain not contained within the trivalent high dose vaccine[138].

Safety

IIV3-HD has been observed to produce a higher rate of some systemic and local reactions than IIV3-SD. Studies have reported higher rates of malaise, myalgia, and moderate to severe fever. Most systemic reactions were mild and resolved within 3 days. SAEs were rare and similar in frequency between standard-dose and high-dose vaccines. When comparing the 2 high dose vaccine products, IIV4-HD has been shown to produce a comparable rate of systemic and local reactions compared to IIV3-HD. A comparable proportion of study participants also experienced unsolicited and serious AEs[138].

Recombinant influenza vaccine (RIV)

Vaccines previously authorized for use:

- Supemtek® (Sanofi) (RIV4)

Methods

A systematic literature review and meta-analysis was conducted on the vaccine efficacy, effectiveness, immunogenicity, and safety of RIV4 in adults 18 years of age and older. NACI used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) framework to review the evidence and develop relevant recommendations on the use of RIV4. Further information on this framework can be found in the GRADE handbook.

The complete details of this review, rationale, relevant considerations and additional information supporting this recommendation can be found in the NACI Supplemental Statement – Recombinant Influenza Vaccines and the Statement on Seasonal Influenza Vaccine for 2022-2023.

Efficacy and effectiveness

One RCT that evaluated the efficacy of RIV4 demonstrated that Supemtek® was statistically significantly more efficacious than egg-based IIV4-SD in preventing laboratory confirmed influenza illness in adults 50 years of age and older[139]. Non-inferiority assessments suggested that RIV4 may be more effective than IIV4-SD influenza vaccines against LCI A virus infection, but not LCI B virus infection in older adults. 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.

Immunogenicity

Eight RCTs assessed the immunogenicity of RIV4. The immunogenicity outcomes reported included seroconversion rates, seroprotection rates, and GMTR[139-147]. Across the 8 studies, Supemtek® demonstrated non-inferiority compared to previously authorized IIVs (IIV3-HD, IIV3-Adj, IIV4-SD, and IIV4-cc) against A(H1N1), most strains of A(H3N2), and B/Yamagata lineage. In some studies, RIV4 did not meet non-inferiority criteria against B/Victoria lineage compared to previously authorized IIVs based on seroconversion, seroprotection, and GMTR[139,142,148].

Pooled seroconversion data from 3 of the 8 RCTs conducted in adult participants 50 years of age and older identified that RIV4 induced similar antibody responses compared to IIV4-SD, IIV3-HD, and IIV3-Adj[141,142,144].

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.

Safety

Six studies assessed the safety of RIV4 in adults, including 5 RCTs and 1 post-marketing surveillance study using data from the United States Vaccine Adverse Event Reporting System (VAERS)[139,141,142,144,149,150]. The 5 RCTs found RIV4 to be safe and well-tolerated compared to conventional egg-based IIVs (noting that no published clinical data pertaining to safety of vaccination with RIV4 during pregnancy were available at the time of the review). Most AEs reported to VAERS following RIV4 administration were non-serious. When data from 2 RCTs conducted among adult participants 50 years of age and older were pooled, no difference in the odds of experiencing a SAE following administration of RIV4 and traditional egg-based IIV3-HD and IIV4-SD vaccine comparators was detected[139,141]. Overall, there is evidence of moderate certainty that RIV4 is a safe and well-tolerated alternative to conventional egg-based influenza vaccines for adults.

Live attenuated influenza vaccine (LAIV)

Vaccine currently authorized for use:

- FluMist® (AstraZeneca) (LAIV3)

Efficacy and effectiveness

After careful review of the available Canadian and international LAIV VE data over many influenza seasons, NACI concluded that the current evidence is consistent with LAIV providing comparable protection against influenza to that afforded by IIV and does not support a recommendation for the preferential use of LAIV in children 2 to 17 years of age. Additionally, NACI concluded that there is insufficient evidence on the immunogenicity and safety supporting the use of LAIV in adults with immunocompromised conditions and does not support the use of LAIV in this group.

Observational studies from the United States found low effectiveness of LAIV against circulating post-2009 pandemic A(H1N1) [A(H1N1)pdm09], in 2013-2014 and 2015-2016; however, reduced LAIV effectiveness was not observed in Canada or any other countries that have investigated the issue. Manufacturer investigation identified potential reduced replicative fitness of the A(H1N1)pdm09-like LAIV viruses in the nasal mucosa from the 2 affected A(H1N1)-dominant seasons compared to pre-2009 pandemic influenza A(H1N1) LAIV viruses as contributing to the poor LAIV effectiveness against circulating A(H1N1)[79]. This finding led to the manufacturer replacing the A(H1N1)pdm09 component of LAIV with new strains, with the A/Slovenia/2903/2015 being the strain that has been used since the 2017–-2018 season. In adults, studies have found IIV-SD to be similarly or more efficacious or effective compared with LAIV. A recent systematic review and network meta-analysis found that LAIV was more efficacious against LCI in adults and older adults compared to placebo or no vaccination. As with other studies, LAIV showed similar efficacy against LCI compared to other influenza vaccines in adults and older adults[151].

Refer to the Statement on Seasonal Influenza Vaccine for 2018–2019 for detailed information supporting this recommendation.

Immunogenicity

LAIV, which is administered by the intranasal route, is thought to result in an immune response that mimics that induced by natural infection with wild-type viruses, with the development of both mucosal and systemic immunity. Local mucosal antibodies protect the upper respiratory tract and may be more important for protection than serum antibody.

Studies have demonstrated that the presence of a hemagglutination-inhibition antibody response after the administration of LAIV3 is predictive of protection. However, efficacy studies have shown protection in the absence of a significant antibody response as well[152]. In these studies, LAIV3 has generally been shown to be equally, if not more, immunogenic compared to IIV3-SD for all 3 strains in children, whereas IIV3-SD was typically more immunogenic in adults than LAIV3. Greater rates of seroconversion to LAIV3 occurred in baseline seronegative individuals compared to baseline seropositive individuals in both pediatric and adult populations, because pre-existing immunity may interfere with response to a live vaccine. Refer to the NACI Recommendations on the Use of Live, Attenuated Influenza Vaccine (FluMist®): Supplemental Statement on Seasonal Influenza Vaccine for 2011-2012 for further details regarding the immunogenicity of LAIV3.

LAIV4 has shown non-inferiority based on immunogenicity compared to LAIV3 in both children and adults. The immune response to the B strain found only in the quadrivalent formulation was better in children who received the quadrivalent vaccine[153-155].

Safety

The most common AEs experienced by recipients of LAIV3 are nasal congestion and runny nose, which are also reported for LAIV4. In a large efficacy trial, rates of wheezing were statistically higher among children 6 to 23 months of age for LAIV3 compared to IIV3-SD[151]. This finding is expected to be the same for recipients of LAIV4; however, pre-licensure clinical studies for LAIV4 were conducted only in adults and children 2 years of age and older. LAIV4 is not authorized in children less than 2 years of age.

Studies on LAIV3 have shown that vaccine virus can be recovered by nasal swab in children and adults following vaccination (i.e., “shedding”). The frequency of shedding decreases with increasing age and time since vaccination. Shedding is generally below the levels needed to transmit infection, although in rare instances, shed vaccine viruses can be transmitted from vaccine recipients to unvaccinated people. Refer to the NACI Recommendations on the Use of Live, Attenuated Influenza Vaccine (FluMist®): Supplemental Statement on Seasonal Influenza Vaccine for 2011-2012 for more information on LAIV and viral shedding.

Appendix D: Evidence review on optimal timing of seasonal influenza vaccination

Background

Influenza requires annual public health vaccination campaigns that are strategically timed to align with anticipated virus circulation. The seasonality of influenza activity is influenced by environmental, demographic, and behavioural factors, as well as viral evolution and population susceptibility. These determinants contribute to variability in the onset, duration, and intensity of influenza activity across and within countries[156,157]. Vaccine formulations are updated annually based on global surveillance and strain characterization, with production and distribution coordinated to support fall immunization campaigns in the Northern Hemisphere. In Canada, most programs launch in October, with most vaccine uptake occurring in late October and November. Nationally, the influenza season most often begins in late-November, but the onset can vary from October to January. Nationally, seasons usually last 12 to16 weeks with some seasons extending beyond 20 weeks, however, regionally or locally, the duration may differ. Influenza surveillance is well-established through the FluWatch+ surveillance system, which informs public health decisions around vaccine timing and effectiveness. Year-to-year variability in seasonal onset continues to challenge long-term planning, necessitating ongoing adaptation of immunization strategies.

Internationally, jurisdictions generally recommend initiating influenza vaccination campaigns in September or October to align with expected virus circulation. In recent years, the United States Advisory Committee on Immunization Practices (ACIP) and the United Kingdom's (UK) Joint Committee on Vaccination and Immunisation (JCVI) have undertaken reviews on vaccination timing and issued updated guidance to help optimize national immunization efforts[158,159]. NACI currently recommends annual influenza vaccination for everyone six months of age and older without contraindications, ideally administered before the onset of the influenza season, but does not provide specific evidence-informed guidance on optimal immunization campaign timing in the context of waning protection. It is currently unknown whether current provincial and territorial seasonal influenza program timing is optimized for protection against influenza.

The body of available evidence examining how factors such as the durability of influenza vaccine-induced protection, prior immunity, health status, and timing of administration may influence vaccine performance continues to grow. However, important uncertainties persist, especially around how best to tailor timing for different populations and how to balance the benefits of early protection with sustained immunity through the end of the season.

The primary objective of this review is to summarize the available evidence regarding optimal timing of seasonal influenza vaccine administration, with consideration to seasonality of influenza activity across Canada, intraseasonal waning of influenza vaccine-induced immunity, and relevant programmatic factors.

Methods

The NACI IWG used an integrated, multi-source evidence approach to review the available information and key considerations pertaining to optimal timing of seasonal influenza vaccination, combining epidemiologic analyses, and systematic and scoping reviews.

The evidence base included:

1. **Epidemiologic Analysis:** FluWatch+ surveillance data were analyzed to describe geo-temporal variation in the onset and duration of influenza seasons across Canadian provinces and territories. This included assessment of interannual variability and strain-specific activity patterns to understand the timing of influenza circulation nationally and regionally.
2. **Systematic review and meta-analysis of immunogenicity evidence:** Evidence on the duration of influenza vaccine protection was obtained from a systematic review and meta-analysis by Doyon-Plourde et al. (2023), which synthesized Phase III/IV clinical trial data on the intraseasonal waning antibody responses following vaccination in individuals 6 months of age and older[160]. This review provided quantitative estimates of the persistence of vaccine-induced immunity up to six months post-vaccination.
3. **Scoping review of efficacy and effectiveness, and other considerations:** A complementary scoping review, conducted according to the Joanna Briggs Institute (JBI) guidelines[161], was undertaken to supplement the systematic review and meta-analysis with additional data on waning of efficacy/effectiveness and key considerations for optimal timing for influenza vaccination programs. A detailed description of the review methods, including study eligibility criteria, search strategy, study selection and data extraction processes, is available in the full publication[162].

To meet the objective of the review and contextualize findings, other *ad hoc* literature searches were conducted as needed to gather data and information, including epidemiologic factors, an environmental scan of recommendations and considerations for optimal timing of influenza vaccine programs in Canadian provinces and territories and in other high-income countries. Economic evaluations were not included in the scope of this review.

Together, these evidence streams were synthesized to assess whether the timing of current influenza vaccination programs in Canada aligns with observed patterns of influenza circulation and the expected duration of vaccine-induced protection, and to identify remaining knowledge gaps and priorities for future research. Knowledge synthesis was performed by the NACI Secretariat and supervised by the IWG.

Overview of evidence and considerations

This section provides an overview of the evidence reviewed and key considerations. For a comprehensive description of the methodology, study characteristics, detailed findings, and assessment of evidence quality, please refer to the accompanying systematic and scoping review publications[160,162].

Epidemiology

- Influenza activity in Canada typically follows a similar seasonal pattern across provinces and territories; however, some provinces or territories experience activity earlier than others during an annual influenza season[163]. An epidemiological analysis was performed using influenza laboratory data from the FluWatch+ surveillance system from seasons 2010-11 to 2018-19 to determine whether there were consistencies in the start of influenza epidemics in Canada. The start and end of the influenza epidemic were defined as the week when the cumulative number of influenza detections reaches 5% and 95% of the cumulative seasonal total.
- It was found that the median start week of seasonal influenza epidemics in provinces and territories can be as early as mid-November or as late as mid-January. There appears to be a trend towards a west to east progression of influenza activity, specifically between the

Western Provinces and Territories and Atlantic Provinces.

- Influenza B activity typically starts later in a season. It was found that an influenza B epidemic can start anywhere from early-January to late-February in Canada.
- On average, a whole influenza season can range between 14 and 24 weeks within the provinces and territories; epidemics caused by influenza A typically span 12 to 23 weeks, while those caused by influenza B span 13 to 22 weeks.
- These trends were determined based solely on laboratory data. Differing testing practices across provinces and territories and across seasons can greatly influence the trends and their comparability across provinces and territories and across seasons. The timing and length of a season can also be influenced by the timing and efficacy of vaccination programs.
- Although the results of this analysis suggest some seasonality trends, influenza is known to be unpredictable. In this analysis seasonality differed year-over-year (i.e. seasons rarely started at the exact same time each season within a province or territory). While sporadic influenza activity can begin as early as September in some parts of Canada, such early onset is uncommon. The unpredictable seasonality of influenza and regional variability makes developing guidance for planning the optimal timing of seasonal influenza vaccines challenging.

Intraseasonal waning and duration of protection

- Evidence from immunogenicity and effectiveness studies shows that influenza vaccination elicits a good immune response and provides protection against disease, both of which gradually decline over the course of a single season. Waning of protection could be due to waning of immunity, changes in the virus characteristics (antigenic drift), or both.
- Antibody levels typically peak within one month following vaccination and decline over the next six months, while remaining above pre-vaccination levels. VE follows a similar pattern, with the highest protection observed in the first two to three months after vaccination and gradual reductions thereafter. Despite measurable waning, protection against influenza illness and severe outcomes generally persist for the duration of a typical influenza season.
- Some evidence suggests that VE waning is more pronounced for influenza A(H3N2) viruses, which often show faster declines in VE than other subtypes. Protection against influenza A(H1N1)pdm09 and B viruses tends to remain more stable over the influenza season.
- The rate and magnitude of waning of protection seem to vary by host and viral factors, including age, and prior vaccination history. Evidence on the impact of specific underlying medical conditions and different vaccine types (e.g., IIV-HD, IIV-cc, RIV) on the duration of protection remains limited. Most evidence identified in the reviews pertains to standard-dose and adjuvanted vaccines, and no studies assessing IIV-HD were identified. However, some evidence suggests that adjuvanted vaccines enhance initial immune responses and may extend the duration of protection, particularly in children and older adults, although waning still occurs over time.
- In children, vaccine-induced protection remains robust and relatively stable across a typical influenza season. Antibody titers peak one-month post-vaccination and decline gradually over time but generally remain above seroprotective levels for at least six months. Evidence from VE studies shows minimal waning within a season, with protection remaining high through the peak of influenza activity.
- In adults, VE typically decreases by about 6-10% per month, though the rate and

magnitude of decline vary across studies and influenza subtypes. Despite this decline, vaccination continues to confer protection against illness and severe outcomes through most of the influenza season.

- Adults 65 years of age and older tend to experience a faster decline in influenza vaccine-induced protection compared with other age groups. Evidence from immunogenicity and effectiveness studies indicates that antibody levels and VE typically have a lower peak and also decrease more markedly in older adults, particularly against influenza A(H3N2). However, the magnitude of waning varies across studies, and not all differences are statistically significant. Biological factors such as age-related immune decline and comorbidities that impair immune function likely contribute to reduced persistence of protection.
- Across all populations, intraseasonal wanning represents a gradual, rather than abrupt, loss of protection and does not appear to compromise overall effectiveness during the influenza season in most years, as vaccination may continue to mitigate illness even when infection is not prevented.

Optimal timing of influenza vaccination

- Evidence from modelling studies indicates that the optimal timing of influenza vaccination depends on several interacting factors, including VE, rate of waning, timing of influenza activity, and vaccination coverage.
- Most models suggest that modest adjustments in the timing of influenza vaccination may influence the duration of protection and population-level outcomes, but these effects are generally small compared with the benefits of achieving and maintaining high vaccine coverage.
- Observational studies generally support these findings, showing that vaccination in early fall provides sustained protection through most influenza seasons.
- Delaying vaccination to align more closely with the expected peak of influenza activity may offer slight improvements in duration of effectiveness, particularly in seasons with late onset or faster waning of immunity; however, such benefits are offset if delayed vaccination reduces uptake or leaves populations unprotected during early influenza activity.
- Some evidence suggests that vaccinating children earlier in the season may help to optimize protection through the peak season, whereas delaying vaccination for older adults 65 years of age and older may slightly reduce late-season cases if overall coverage remains high[164,165].
    - Early vaccination in children may offer additional benefits given their role in initiating community transmission, however, evidence on indirect effects and the influence of waning is limited.
- Given annual variability in the timing, intensity, and dominant strains of influenza activity, flexible vaccination strategies would require robust surveillance and predictive systems to inform optimal implementation.

Environmental scan on international recommendations

- Internationally, jurisdictions in the Northern Hemisphere generally recommend initiating influenza vaccination campaigns in September or October to ensure protection before the onset of influenza activity.

- Differences in timing of administration may be advised for certain groups, as seen in guidance from the US and UK (Table 6).

Table 6: Summary of recommendations from the US and UK on timing of influenza vaccine administration and supporting rationale

Jurisdiction	Recommendations	Considerations and Rationale
JCVI/UKHSA[159]	Date: March 2024 1. Vaccinate children and pregnant women starting September 2. Delay the start of adult program until October	• The UK had not had an early season since the 2009 pandemic • 2022/23 VE data showed signs of waning in older adults despite the use of adjuvanted vaccine • No signal of waning VE was evident in children • Data on waning of VE against H1N1 was less clear as there were no recent data to look at waning VE against this subtype • Operational considerations (e.g. school based influenza vaccination program)
ACIP/CDC[166]	Date: August 2025 1. For most persons who need only 1 dose of influenza vaccine for the season, vaccination should ideally be offered in September or October 2. Vaccination should continue throughout the season as long as influenza viruses are circulating	• For most adults (particularly those aged ≥65 years) and during the first or second trimester of pregnancy, **vaccination during July and August should be avoided** unless there is concern that later vaccination might not be possible • Vaccination during July and August can be considered for children of any age who require only 1 dose, particularly if there is concern that later vaccination might not be possible • Flu vaccination during July and August can be considered during the third trimester of pregnancy

Abbreviations: JCVI: Joint Committee on Vaccination and Immunisation; UKHSA: United Kingdom Health Security Agency; ACIP: Advisory Committee on Immunization Practices; CDC: Centers for Disease Control and Prevention

Ethics, equity, feasibility, and acceptability

- In Canada, seasonal influenza vaccine deliveries typically begin in early to mid-September and are generally completed by the end of October, although timelines may vary depending on the supplier and product.
- The impact of an earlier vaccination campaign on overall uptake remains uncertain. Some experts have hypothesized that earlier availability could improve convenience for some individuals and providers, particularly when aligned with concurrent administration opportunities for other vaccines such as those targeting COVID-19 or respiratory syncytial virus (RSV).
- Although vaccinating older adults later in the season is feasible, changing influenza vaccine timing for older adult programs introduces logistical complexities that may hinder implementation.
- Reducing access barriers and enhancing uptake, particularly among vulnerable populations, should remain a core focus of program planning. Timing may serve as a complementary consideration in efforts to optimize overall program effectiveness.

Other considerations

- Vaccine providers are encouraged to use every available opportunity to immunize and to continue offering the vaccine through to the end of the season.
- Annual influenza vaccination programs should aim for timing that ensures individuals are protected before influenza activity starts, while taking into account program logistics, population needs, and seasonal variability.
- The precise timing can be tailored to a given setting or geographical area based on epidemiological trends, including influenza transmission dynamics, as well as programmatic considerations and opportunities for vaccination.

Knowledge gaps and research priorities

Epidemiology and Surveillance

- Where it is anticipated seasonal influenza and other pathogen combination vaccine candidates could come to market, such as a COVID-19 and influenza combination vaccine, it is essential to continue research and monitoring of the seasonality of the viral infections. Seasonal patterns for each of the pathogens targeted by the vaccine should be studied both nationally and within PT jurisdictions to ensure guidance still supports the optimal timing of vaccination. Other epidemiological characteristics such as age should also be considered when exploring optimal vaccination timing.
- There is limited understanding of how much the timing of influenza activity varies across different jurisdictions in Canada, and whether these differences justify tailoring the timing of vaccination programs to local patterns.
- There is limited understanding on how the timing of influenza activity varies across age groups in Canada and, whether these differences justify targeting vaccination of specific age populations at different times when balanced against programmatic considerations.
- The impact of vaccination timing and VE on the overall transmission dynamics of influenza remains insufficiently explored, given the challenges of studying these factors and their seasonal variability, leaving uncertainty about how these factors interact to influence outbreak severity and duration.

Immunogenicity and immunological mechanisms

- Data characterizing intra-seasonal waning of the immune response following influenza vaccination in adults and older children aged 8 to 17 years are limited.
- Further research is needed to clarify the immunologic mechanisms underlying waning protection, including the relative contributions of antibody declines, cellular immunity, and antigenic drift.

Vaccine efficacy/effectiveness

- There is limited evidence on how individual characteristics, such as high-risk medical conditions, frailty and the use of different vaccine types (e.g., IIV-HD, IIV-cc, RIV) affect the duration of protection against influenza.
    - Evidence on the impact of vaccine type on duration of protection is limited, with most data available for IIV-adjuvanted and IIV-standard dose vaccines.

- The relationship between waning antibody levels and reduction in influenza VE over time remains uncertain and warrants further investigation across populations and influenza subtypes.
- The duration of protection provided by novel vaccine platforms, such as multi-virus combination formulations and mRNA-based influenza vaccines, is not yet established and warrants further study.

Ethics, equity, feasibility, and acceptability

- Given current uncertainties around the optimal timing of vaccination, programmatic constraints and delivery schedules, continuing research into existing barriers and enablers associated with influenza vaccine uptake is important to addressing ongoing challenges. There remains a lack of research examining factors influencing immunization through an intersectionality lens, and their overall impact on health equity is often overlooked when these factors are considered in isolation. These insights can further strengthen existing influenza vaccination programs and inform the development of tailored strategies to help maximize protection while promoting efficient and equitable access to vaccines.

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