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Vaccines for the 2022-23 Influenza Season

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Introduction

This document is intended to provide an overview of the publicly-funded influenza vaccines that are available in Ontario as part of the Universal Influenza Immunization Program[1] (UIIP) for the 2022-23 influenza season. It focuses on:

- The standard-dose quadrivalent vaccines (QIV) for individuals six months of age and older.
- The high-dose quadrivalent (QIV-HD) and standard-dose adjuvanted trivalent (TIV-adj) vaccines available for adults 65 years of age and older only.

Background

Most vaccine products provided through the UIIP this season are quadrivalent (QIV), meaning that they contain hemagglutinin antigen (HA) for each of the four influenza strains recommended by the World Health Organization (WHO) for the 2022-23 northern hemisphere influenza season. These strains include an influenza A(H3N2) and A(H1N1) strain and two influenza B strains, one from each B virus lineage (B/Yamagata and B/Victoria).[2] The four standard-dose QIVs contain 15 mcg of HA for each strain, whereas the high-dose quadrivalent (QIV-HD) – available only for adults 65 years of age and older – contains 60 mcg of HA for each strain.

In addition to the QIV products, adjuvanted trivalent vaccine (TIV-adj) is also provided through the UIIP this season for adults 65 years of age and over, which contains 15 mcg of HA for three influenza strains (i.e., an influenza A(H3N2) and A(H1N1) strain but only one influenza B strain from the B/Victoria lineage).

All vaccine products available through the UIIP for the 2022-23 season are egg-based vaccines. Canada's National Advisory Committee on Immunization (NACI) states that egg allergy is **not** a contraindication for influenza vaccination and individuals with egg protein allergies can receive any age-appropriate influenza product.[3]

The vaccines available through the UIIP for people 6 months of age and over are outlined in Table 1.

Note that the live attenuated, cell-culture based, and the recombinant quadrivalent influenza vaccines will not be available as part of the UIIP for the 2022-23 influenza season.

Table 1. Vaccines available through the UIIP for the 2022-23 influenza season

Ages	Type of influenza vaccines	Influenza vaccine products
6 months to 4 years	Standard-dose quadrivalent (QIV)	FluLaval Tetra Fluzone® Quadrivalent
5 years to 64 years	Standard-dose quadrivalent (QIV)	FluLaval Tetra Fluzone® Quadrivalent Afluria® Tetra
65 years and older	High-dose quadrivalent (QIV-HD)	Fluzone® High-Dose Quadrivalent
65 years and older	Adjuvanted trivalent (TIV-adj)	Fluad®
65 years and older	Standard-dose quadrivalent (QIV)	FluLaval Tetra Fluzone® Quadrivalent Afluria® Tetra

Influenza Vaccines for Adults 65 Years of Age and Over

For the 2022-2023 influenza season, one high-dose quadrivalent vaccine (QIV-HD), one adjuvanted trivalent vaccine (TIV-adj), and three standard-dose quadrivalent vaccines (QIV) are available in Ontario through the UIIP for adults 65 years of age and older.

CANADIAN RECOMMENDATIONS REGARDING INFLUENZA VACCINES FOR ADULTS 65 YEARS AND OLDER

Any of the available influenza vaccines would be preferable to remaining unvaccinated or requesting individuals to return for vaccine. Therefore, in the absence of a specific product, NACI recommends that any of the available influenza vaccines authorized for this age group should be used.[3]

High-Dose Quadrivalent Influenza Vaccine

Fluzone® High-Dose Quadrivalent[4] (Sanofi Pasteur Limited, Toronto, Ontario) is an egg-based, split virion, quadrivalent inactivated influenza vaccine. Fluzone® High-Dose Quadrivalent contains a high dose of hemagglutinin antigen (60 mcg) for each of the four influenza strains recommended by the WHO for the northern hemisphere's 2022-23 influenza season.[2]

KEY POINTS REGARDING THE USE OF FLUZONE® HIGH-DOSE QUADRIVALENT

- In Canada, Fluzone® High-Dose Quadrivalent is authorized for use only in **adults 65 years of age or older**.
- The recommended dose of Fluzone® High-Dose Quadrivalent is **0.7mL** (compared to 0.5mL for the standard-dose QIVs).

CANADIAN RECOMMENDATIONS REGARDING HIGH-DOSE QIV

The National Advisory Committee on Immunization has provided the following recommendation for individual-level decision making for adults 65 years of age and older regarding high-dose QIV:

> For individual-level decision-making, "IIV-HD [*high-dose inactivated influenza vaccine]* should be used over IIV-SD [*standard-dose inactivated influenza vaccine]*, given the burden of influenza A(H3N2) disease and the good evidence of IIV3-HD [*high-dose TIV]* providing better protection compared to IIV3-SD [*standard-dose TIV]* in adults 65 years of age and older."[3]

BURDEN OF INFLUENZA A (H3N2) COMPARED TO INFLUENZA B

Figure 1 illustrates the proportion of laboratory-confirmed influenza cases by type, sub-type and age reported through Ontario's reportable disease information system (the integrated Public Health Information System (iPHIS)) averaged over twelve influenza seasons (2010–11 to 2021–22, as of July 25, 2022).[5] The figure illustrates that the distribution of strains varies by age. In adults 65 years of age and over, 79.2% of strains were influenza A and only 20.7% were influenza B. Further subtyping of a subset (42.2%) of laboratory confirmed influenza A strains among these older adults revealed 86.3% were A(H3N2) and only 13.7% were influenza A(H1N1). Thus, in adults 65 years of age and older in Ontario, the greatest burden of influenza disease over the past twelve influenza seasons is due to influenza A (H3N2).

VACCINE EFFECTIVENESS OF HIGH-DOSE QIV

A phase 3 randomized clinical trial[6] involving 2,670 adults 65 years of age and older compared the safety and immunogenicity of the high-dose QIV (QIV-HD) to that of two high-dose trivalent vaccines, each containing a different influenza B strain (TIV-HD1 and TIV-HD2) over one influenza season. The results demonstrated that the hemagglutination inhibition antibody responses of the QIV-HD were non-inferior to those induced by the TIV-HD1 and TIV-HD2 for the three shared strains, and superior for the additional B-lineage strain. The authors concluded that the addition of a second B-lineage strain did not inhibit the immunogenicity induced by the other three strains or compromise the vaccine's tolerability.

Standard-Dose Adjuvanted Trivalent Vaccine

Fluad®[7](Seqirus Inc., Kirkland, Quebec) is an egg-based, surface antigen, trivalent inactivated influenza vaccine that is adjuvanted with MF59C.1 (an oil-in-water emulsion composed of squalene as the oil phase, stabilised with the surfactants polysorbate 80 and sorbitan trioleate, in citrate buffer). Fluad® contains a standard dose of hemagglutinin antigen (15 mcg) for each of three influenza strains recommended by the WHO.

CANADIAN RECOMMENDATIONS REGARDING STANDARD-DOSE TIV-ADJ

The NACI Statement on Seasonal Influenza Vaccine for 2022-2023 does not include specific recommendations for individual-level decision making on the use of the TIV-adj.[3]

VACCINE EFFECTIVENESS OF STANDARD-DOSE TIV-ADJ

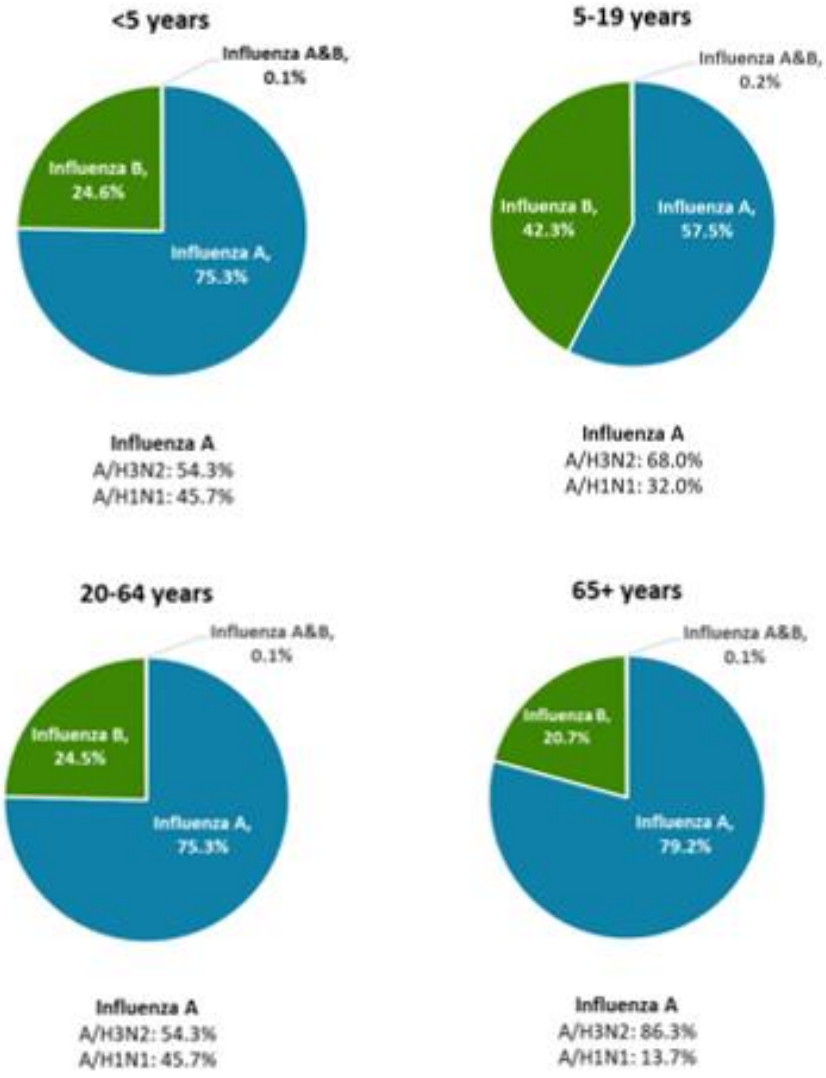
There are currently no studies that have directly compared the effectiveness of TIV-adj to standard- or high-dose QIVs. A literature review[8] published by NACI in May 2018 concluded that:

> "There is fair evidence that the MF59-adjuvanted Fluad® may be effective at reducing the risk of hospitalization for influenza and influenza complications in the elderly compared to unvaccinated individuals (Grade B Evidence);
>
> "There is insufficient evidence that Fluad® is effective at reducing the risk of hospitalization for influenza and influenza complications in the elderly compared to those who received unadjuvanted trivalent inactivated subunit vaccine (Grade I Evidence); and
>
> "There is no identified evidence on how the high-dose vaccine (*TIV-HD)* directly compares to the MF59-adjuvanted Fluad® (Grade I Evidence)."

TRIVALENT INFLUENZA VACCINES MAY PROVIDE SOME PROTECTION AGAINST THE OPPOSITE B-LINEAGE STRAIN

Some recent studies (e.g., McLean HQ et al., Pebody R et al., Ohmit SE et al., Beyer WEP et al.)[9-12] have demonstrated protection from the influenza B lineage in the vaccine against the opposite B lineage, referred to as cross-protection; however, cross protection may not always occur and may vary by season, age and past vaccination history. Examples of cross protection can be seen in Canadian data from the Sentinel Practitioner Surveillance Network. In the 2017-18 influenza season (Skowronski D et al.),[13] the B strain that circulated was predominantly B/Yamagata; the interim adjusted vaccine effectiveness against influenza B was 55% (95% CI: 38% to 68%) for both QIV and TIV together. The TIV contained B/Victoria (i.e., not the circulating strain) and TIV represented more than two-thirds of the vaccine doses distributed through the publicly-funded programs in the Canadian provinces that participated in the vaccine effectiveness study suggesting that there was some cross-protection.

Figure 1. Proportion of influenza cases by type and subtype for influenza A, by age group: Ontario, 2010–11 to 2021–22* influenza seasons (*as of July 25, 2022)



Data source: Ontario. Ministry of Health. Integrated Public Health Information System (iPHIS) [database]. Toronto, ON: Queen's Printer for Ontario; 2022 [data extracted 2022 Jul 26].
Notes: The data only represent laboratory-confirmed influenza cases reported to public health and recorded in iPHIS. Influenza A subtype information is only available for 42.2% of influenza A cases. The possibility of duplicates exists because duplicate sets were not identified and/or excluded unless they were resolved prior to data extraction either at the local or provincial level.

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