FACT SHEET

Influenza Vaccines for the 2019–20 Influenza Season - Focus on Adults 65 Years of Age and Over

Purpose
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 (UIIP) for the 2019–20 influenza season. It will focus on the vaccines available for adults 65 years of age and over.

Available Vaccines
Most vaccine products provided through the UIIP this season are quadrivalent, meaning they contain an A(H3N2) and A(H1N1) strain and two influenza B strains, one from each B virus lineage (B/Victoria and B/Yamagata). The exception is the high-dose influenza vaccine for adults 65 years of age and over, which is trivalent and contains an A(H3N2), A(H1N1) and only one B strain (from the B/Victoria lineage). The high-dose product has a higher hemagglutinin content for each of the three strains it contains (60µg per strain in the high-dose trivalent product versus 15µg per strain in the standard-dose quadrivalent products). The vaccines available through the UIIP for people 6 months of age and over are outlined in Table 1.

Table 1. Vaccines available through the UIIP for the 2019-20 influenza season

<table>
<thead>
<tr>
<th>Ages</th>
<th>Type of influenza Vaccines</th>
<th>Influenza Vaccine Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months up to and including 4 years</td>
<td>Standard-dose quadrivalent (QIV)</td>
<td>• FluLaval Tetra</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Fluzone® Quadrivalent</td>
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<tr>
<td>5 years up to and including 64 years</td>
<td>Standard-dose quadrivalent (QIV)</td>
<td>• FluLaval Tetra</td>
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<td></td>
<td>• Fluzone® Quadrivalent</td>
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<td></td>
<td>• Afluria® Tetra</td>
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<tr>
<td>65 years and over</td>
<td>High-dose trivalent (TIV)</td>
<td>• Fluzone® High-Dose</td>
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<tr>
<td></td>
<td>Standard-dose quadrivalent (QIV)</td>
<td>• FluLaval Tetra</td>
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<td>• Fluzone® Quadrivalent</td>
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<td></td>
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<td>• Afluria® Tetra</td>
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</table>

Additional information about vaccines available through the UIIP can be found on the Ministry of Health website.
Vaccines for Adults 65 Years of age and Over – High Dose Trivalent versus Quadrivalent

The high-dose trivalent vaccine (TIV) and standard dose quadrivalent vaccines (QIV) are both available for adults 65 years of age and over. Table 2 provides an overview of the considerations when assessing the high-dose TIV compared to standard-dose QIV. More detailed information is provided following Table 2.

Table 2. Overview of the high-dose trivalent vaccine compared to the quadrivalent vaccines

<table>
<thead>
<tr>
<th>Factors</th>
<th>Considerations</th>
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<tbody>
<tr>
<td><strong>Influenza A</strong></td>
<td>• The high-dose TIV provides better protection than standard-dose TIV against the A(H3N2) strain as demonstrated in a large randomized-controlled trial. The A(H3N2) strain is the same in the standard-dose TIV and standard-dose QIV vaccines.</td>
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<td></td>
<td>• In adults 65 years of age and over, the burden of influenza A(H3N2) is higher compared to influenza A(H1N1) and influenza B. Seasons with circulation of influenza A(H3N2) result in more outbreaks, hospitalizations and deaths, which occur most commonly among older adults.</td>
</tr>
<tr>
<td><strong>Influenza B</strong></td>
<td>• Although the high-dose TIV contains one less influenza B strain than the QIV, influenza B occurs less frequently in adults 65 years of age and over than influenza A.</td>
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<tr>
<td></td>
<td>• There may be cross protection against B lineages, such that a TIV vaccine that contains B/Victoria may offer some protection against B/Yamagata and vice versa. Therefore, high-dose TIV may afford some protection against the B lineage not included in that vaccine.</td>
</tr>
<tr>
<td><strong>Safety</strong></td>
<td>• QIV and high-dose TIV are expected to have a generally similar safety profile. Local reactions and systemic adverse events occur somewhat more frequently with high-dose TIV than standard-dose TIV. The systemic reactions are described as generally mild and resolved within three days.</td>
</tr>
</tbody>
</table>
Canadian Recommendations Regarding High-Dose TIV

The individual-level recommendation of the National Advisory Committee on Immunization (NACI) regarding high-dose TIV is summarized below based on NACI’s 2019-2020 influenza statement.

At the individual level, high-dose TIV should be used over standard-dose TIV, given the burden of influenza A (H3N2) disease and the good evidence of better efficacy compared to standard dose TIV in this age group. There is insufficient evidence to make comparative individual-level recommendations among high-dose TIV and QIV.

Vaccine Effectiveness of High-Dose TIV

A large randomized, double-blinded controlled clinical trial involving almost 32,000 individuals 65 years of age and over compared high-dose TIV to standard-dose TIV over two influenza seasons. The trial showed high-dose TIV to be 24.2% (95% confidence interval (CI): 9.7% to 36.5%) more efficacious compared to standard-dose TIV in preventing laboratory-confirmed influenza. The improved efficacy for high-dose TIV was particularly notable for A(H3N2), with high-dose TIV being 23.3% (95% CI: 6.0% to 37.5%) more efficacious. Two NACI literature reviews, one published in May 2018 and the other published in 2016, identified a number of other studies that support NACI’s recommendation to offer high-dose TIV over standard-dose TIV at the individual level. There are currently no studies that have directly compared high-dose TIV to standard-dose QIV.

Burden of Influenza A (H3N2) Compared to Influenza B

Figure 1 demonstrates the relative contribution of influenza strains by age in Ontario from laboratory-confirmed influenza reported through the reportable disease system (the integrated Public Health Information System) averaged over eight influenza seasons (2010–11 to 2017–18). The figure illustrates that the distribution of strains varies by age. In adults 65 years of age and over, 75.8% of strains were influenza A and only 24.0% were influenza B. Approximately 46% of the influenza A strains among these older adults were further subtyped – 92.4% of these were A(H3N2) and only 7.6% were influenza A(H1N1).

Trivalent Influenza Vaccines May Provide Some Protection against the Opposite B Lineage

Some recent studies (e.g., McLean HQ et al., Pebody R et al., Ohmit SE et al., Beyer WEP et al.) 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.), 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.

Additional information on influenza vaccines, including for adults 65 years of age and over, is available on the Ministry of Health’s website.
Figure 1. Proportion of influenza cases by type and subtype for influenza A, by age group: Ontario, 2010–11 to 2017–18 influenza seasons

- **< 5 years**
  - Influenza A (H3N2): 61.1%
  - Influenza A (H1N1): 38.9%
  - Influenza B: 27.4%

- **5-19 years**
  - Influenza A (H3N2): 72.1%
  - Influenza A (H1N1): 27.9%
  - Influenza B: 46.2%

- **20-64 years**
  - Influenza A (H3N2): 61.5%
  - Influenza A (H1N1): 38.5%
  - Influenza B: 28.3%

- **65+ years**
  - Influenza A (H3N2): 92.4%
  - Influenza A (H1N1): 7.6%
  - Influenza B: 24.0%

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Data Caveats and Technical Notes for Figure 1

- Data source: Ontario Ministry of Health and Long-Term Care, integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario on September 10, 2019.

- The data only represent laboratory-confirmed cases of influenza reported to public health and recorded in iPHIS.

- Influenza A subtype information is only available for 29.6% to 45.9% of influenza A, depending on age group.

- Data for the 2018-19 season is not included in the analysis, as data entry and/or data cleaning may not be complete.

- The possibility of duplicates exists because duplicate sets were not identified and excluded unless they were resolved prior to data extraction either at the local or provincial level.
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