Influenza Vaccines available for Children and Older Adults for the 2018-19 Influenza Season

September, 2018

Purpose

This document is intended to help clinicians and public health unit staff assess the influenza vaccines that are publicly-funded for children and adults 65 years of age and over in Ontario as part of the Universal Influenza Immunization Program (UIIP) for the 2018-19 influenza season.

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 the B strain from the B/Victoria lineage. The high-dose product has a higher antigenic content for each of the three antigens it contains (60 µg versus 15 µg per antigen in the standard-dose quadrivalent products). The vaccines available through the UIIP are outlined in Table 1.

Table 1. Vaccines available through the UIIP for the 2018-19 influenza season

<table>
<thead>
<tr>
<th>Ages</th>
<th>Influenza Vaccine Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months to less than 2 years</td>
<td>• Standard-dose quadrivalent inactivated injectable (QIV)</td>
</tr>
<tr>
<td>2 to 17 years</td>
<td>• Standard-dose quadrivalent inactivated injectable (QIV)</td>
</tr>
<tr>
<td></td>
<td>• Live attenuated quadrivalent intranasal (Q-LAIV)</td>
</tr>
<tr>
<td>18 to 64 years</td>
<td>• Standard-dose quadrivalent inactivated injectable (QIV)</td>
</tr>
<tr>
<td>65 years and over</td>
<td>• High-dose trivalent inactivated injectable (high-dose TIV)</td>
</tr>
<tr>
<td></td>
<td>• Standard-dose quadrivalent inactivated injectable (QIV)</td>
</tr>
</tbody>
</table>

Additional information about vaccines available through the UIIP can be found on the Ministry of Health and Long Term Care website.

Influenza vaccines available for children and adults 65 years of age and over for the 2018-2019 influenza season.
Vaccines for Children 2 to 17 Years of Age: QIV versus Q-LAIV

The standard-dose quadrivalent inactivated injectable influenza vaccine (QIV) and live attenuated quadrivalent intranasal influenza vaccine (Q-LAIV) are both available for children 2 years up to and including 17 years of age. QIV is inactivated and given by injection, while Q-LAIV is a live attenuated product that is given via intranasal spray. Q-LAIV has additional specific contraindications compared to QIV that include immunocompromising conditions or taking immunocompromising medications, severe asthma or active wheezing, pregnancy or taking long term aspirin or aspirin-containing therapy.

For children less than 9 years of age who are receiving the influenza vaccine (QIV or Q-LAIV) for the first time ever, two doses are required in the current season, given at least four weeks apart.

Additional details comparing the two vaccines can be found in the Ministry of Health and Long Term Care fact sheet entitled: Health Care Provider Q&A: Information for individuals 6 months to 17 years of age.

Influenza vaccine considerations for children 2 to 17 years of age

- For children 2 years up to and including 17 years of age without contraindications specific to Q-LAIV, either Q-LAIV or QIV can be used.

- For children with contraindications specific to Q-LAIV (see list above and the Ministry of Health and Long Term Care fact sheet entitled: Health Care Provider Q&A: Information for individuals 6 months to 17 years of age), QIV should be used.

- For children who are very afraid of needles, Q-LAIV would be preferred.

Additional information is provided below.
National Recommendations Regarding QIV versus Q-LAIV

Recommendations from Canada
The Canadian National Advisory Committee on Immunization (NACI) indicates that either QIV or Q-LAIV can be used for children 2 to 17 years of age. Previously NACI expressed a preference for live attenuated influenza vaccine (LAIV) to be used in children 2 year to less than 6 years of age (without contraindications) compared to inactivated injectable vaccines, but that preference has been removed since the 2016-17 influenza season. The preferential recommendation for LAIV was removed as more recent studies showed the two types of vaccines to be performing similarly in Canada, which is in contrast to earlier studies that showed LAIV to be superior to inactivated vaccines.

Recommendations from the United States
Because of concerns regarding the performance of Q-LAIV against influenza A/H1N1 strains in recent years in the United States (US), the US Advisory Committee on Immunization (ACIP) advised against the use of LAIV for the 2016-17 and 2017-18 influenza seasons. For the 2018-19 season, ACIP reversed this decision and indicated that LAIV is recommended as an option for influenza vaccination for persons for whom it is otherwise appropriate. A summary of the consideration of the ACIP can be found in the June 8, 2018 Morbidity and Mortality Weekly Report.

Reasons for Changing Recommendations Regarding LAIV
Concerns about the effectiveness of LAIV against influenza A/H1N1 were first raised in 2015, as a result of low vaccine effectiveness demonstrated in the 2013-14 influenza season in US studies only. As a result of these concerns, the manufacturer changed the A/H1N1 strain in the vaccine from A/California to A/Bolivia for the 2015-16 influenza season; however, the A/Bolivia strain did not provide good vaccine effectiveness against influenza A/H1N1 in 2015-16 in the US, leading to the ACIP decision to not recommend LAIV for the 2016-17 and 2017-18 influenza seasons. Studies from Canada, the United Kingdom and Finland found higher vaccine effectiveness for LAIV against A/H1N1 than studies from the US; hence LAIV continued to be recommended for use in these countries.

It is believed that both the A/California and A/Bolivia H1N1 strains did not grow well in the nose and so did not produce a good immune response, resulting in low vaccine effectiveness. For the 2017-18 influenza season, the A/H1N1 strain in LAIV switched again to a strain called A/Slovenia. The A/Slovenia strain has been shown by the manufacturer to grow better in the nose and produce a higher immune response than the previous A/Bolivia strain. Effectiveness data against A/H1N1 of LAIV containing the A/Slovenia strain for the 2017-18 season is currently available from the United Kingdom; their data indicate that LAIV was 90.3% effective (adjusted analysis, 95% confidence intervals (CI): 16.4% to 98.9%) in children 2 to 17 years of age.
Vaccines for Adults 65 Years of Age and Over: High-Dose TIV versus QIV

The high-dose trivalent inactivated injectable influenza vaccine (high-dose TIV) and standard-dose quadrivalent inactivated injectable influenza vaccine (QIV) are both available for use in adults 65 years of age and over. While high-dose TIV contains only one B strain (from the B/Victoria lineage for the 2018-19 vaccine) compared to the QIV which contains B strains from both lineages, high-dose TIV contains four times as much antigen compared to QIV (60 µg versus 15 µg per antigen) for the three strains the vaccines share in common. The immune response, efficacy and effectiveness has generally been found to be better for high-dose TIV compared to standard-dose TIV, but no direct comparisons have been published for high-dose TIV and standard-dose QIV. Additional details comparing the two vaccines can be found in the Ministry of Health and Long Term Care fact sheet entitled Health Care Provider Q&A: Information for individuals 6 months to 17 years of age.

Influenza vaccine considerations for adults 65 years of age and over

The following are relevant considerations when vaccinating adults 65 years of age and over.

Influenza A:

- The burden of influenza A/H3N2 is higher in adults 65 years of age and over compared to other strains. Seasons with circulation of influenza A/H3N2 result in more outbreaks, hospitalizations and deaths, which occur most commonly among older adults.

- The high-dose TIV provides better protection than standard-dose TIV, including against the A/H3N2 strain as demonstrated in a large randomized trial. The A/H3N2 strain is the same in the standard-dose TIV and standard-dose QIV vaccines, so similar enhanced protection against the A/H3N2 found for high-dose TIV is also expected when compared to the standard-dose QIV.

Continued on next page
Influenza vaccine considerations for adults 65 years of age and over – continued

Influenza B:

- Although the high-dose TIV contains one less B strain than in the QIV, B strains occur less frequently in adults 65 years of age and over than A strains.

- There may be cross protection against B lineages, such that the TIV vaccine that contains B/Victoria may offer some protection against B/Yamagata and vice versa, although this may not always occur. Therefore, high-dose TIV may afford some protection against the B lineage not included in that vaccine.

Safety:

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 short lived.

Additional information is provided below.

Canadian Recommendations Regarding High-Dose TIV

NACI indicates the following in its 2018-19 influenza statement:

At the individual level, NACI recommends that high-dose TIV should be offered over standard-dose TIV to persons 65 years of age and older. NACI concludes that, given the burden of disease associated with influenza A(H3N2) and the good evidence of better efficacy compared to standard-dose TIV in this age group, high-dose TIV should be offered over standard-dose TIV to persons 65 years of age and older (Grade A). There is insufficient evidence to make comparative recommendations on the use of MF59-adjuvanted TIV and QIV over standard-dose TIV (Grade I).

Note: MF59 adjuvanted TIV (Fluad®) is not included in the publicly-funded UIIP program for the 2018-19 influenza season.
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% CI: 9.7% to 36.5%) more effective compared to standard dose TIV in preventing laboratory-confirmed influenza. For influenza A/H3N2 the findings were similar, with high-dose TIV being 23.3% (95% CI: 6.0% to 37.5%) more effective. Two NACI literature reviews, one published in May 2018 and the other published in 2016, identify 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 seven influenza seasons (2010-11 to 2016-17). The figure illustrates that the distribution of strains varies by age. In adults 65 years of age and over, 82.7% of strains were influenza A and only 17.2% were influenza B. Approximately half of the influenza A strains among these older adults were further subtyped - 91.5% of these were A/H3N2 and only 8.5% were influenza A/H1N1.

Trivalent Influenza Vaccines May Provide Some Protection against the Opposite 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.
Figure 1. Proportion of influenza cases by type and subtype for influenza A, by age group: Ontario, 2010-11 to 2016-17 influenza seasons

- **< 5 years**
  - Influenza A: 74.5%
  - Influenza B: 25.4%
  - Influenza A & B: 0.1%

- **5-19 years**
  - Influenza A: 55.4%
  - Influenza B: 44.5%
  - Influenza A & B: 0.1%

- **20-64 years**
  - Influenza A: 75.8%
  - Influenza B: 24.1%
  - Influenza A & B: 0.1%

- **65+ years**
  - Influenza A: 82.7%
  - Influenza B: 17.2%
  - Influenza A & B: 0.1%
Data Caveats and Technical Notes for Figure 1

- Data were obtained from the Ministry of Health and Long-Term Care (MOHLTC) integrated Public Health Information System (iPHIS) database, extracted by Public Health Ontario on August 10, 2018.

- Influenza A subtype information is only available for 31.9% to 49.2% of influenza A, depending on age group.

- Data for 2017-18 season is not included in the analysis as data entry and/or data cleaning may not be complete.

- Only confirmed cases of influenza are included in this request.

- Dates used for influenza cases are based on the ‘episode date’.

- Records for which the Diagnosing Health Unit was reported as ‘MOHLTC’ (to signify a case that is not a resident of Ontario) or ‘MUSKOKA PARRY SOUND’ (a health unit that no longer exists) have been excluded.

- Records for which the Episode Status or Diagnosis Status was reported as ‘ENTERED IN ERROR’, ‘DOES NOT MEET DEFINITION’, ‘DUPLICATE-DO NOT USE’ or any variation on these values have been excluded.

- Influenza A cases with a subtype identified as ‘INDETERMINATE’, ‘NOT SUBTYPED’, ‘OTHER (SPECIFY)’, ‘UNTYPEABLE’ or with missing subtype information were excluded from subtype analysis.
Public Health Ontario

Public Health Ontario is a Crown corporation dedicated to protecting and promoting the health of all Ontarians and reducing inequities in health. Public Health Ontario links public health practitioners, front-line health workers and researchers to the best scientific intelligence and knowledge from around the world.

For more information about PHO, visit publichealthontario.ca.

Public Health Ontario acknowledges the financial support of the Ontario Government.