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FACT SHEET

2017-2018 Influenza vaccination recommendations for children and adolescents: Information for health care providers

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This document reviews the influenza vaccine recommendations for children and adolescents. This includes the recommendations for live attenuated influenza vaccine (LAIV) given by nasal spray, (FluMist®, produced by AstraZeneca). It provides information for healthcare providers to support parents and patients in their influenza vaccination decisions for 2017-2018.

Summary of influenza vaccine recommendations for children and adolescents

- All children and adolescents 6 months to <18 years of age should receive a quadrivalent influenza vaccine.
- Children 6 months to <2 years of age should receive injectable quadrivalent inactivated influenza vaccines (IIV).
- Children and adolescents 2 years to < 18 years of age can receive either quadrivalent live attenuated influenza vaccine (LAIV) by nasal spray or quadrivalent IIV by injection. For children with no contraindications for LAIV, this choice may depend on whether the child prefers a nasal spray or injection.

Canadian influenza vaccine recommendations

Current Recommendation: The National Advisory Committee on Immunization (NACI) recommends that children 6 months to <18 years of age receive a quadrivalent influenza vaccine. A quadrivalent vaccine is composed of two influenza A and two influenza B strains. Protection against the extra B strain in this vaccine compared to the trivalent vaccine is particularly important for children and adolescents, who are more likely to acquire influenza B than adults. The quadrivalent influenza vaccine products recommended by NACI for children and adolescents are either:

- an injectable IIV for children and adolescents 6 months to <18 years of age, or
- the LAIV given by nasal spray for children and adolescents 2 years to <18 years of age.[1]

Previous Recommendations: Prior to August 2016, NACI had preferentially recommended LAIV over IIV for children 2 years to <6 years of age. NACI removed the preferential recommendation for LAIV and recommended that either inactivated or live attenuated vaccine could be used.[2]

U.S. recommendations

Current Recommendations: In June 2016, the Advisory Committee on Immunization Practices (ACIP) in the United States made an interim recommendation that the LAIV not be used for the 2016-2017 influenza season.[3] For the 2017-2018 season, ACIP also recommended against the use of LAIV.[4]

Previous Recommendations*:* For the 2014-2015 influenza season, ACIP had made a preferential recommendation for LAIV over the IIV for children 2 to 8 years of age. For the 2015-2016 influenza season, ACIP removed this preferential recommendation, stating that either LAIV or IIV could be used.

Why have recommendations changed for the live attenuated influenza vaccine (LAIV)?

The concerns about the LAIV were first raised based on data from the 2013-2014 influenza season in the United States (U.S.). In that season, information from three U.S. vaccine effectiveness sentinel surveillance networks/studies found poor quadrivalent LAIV effectiveness against the circulating influenza A(H1N1)pdm09 strain. However, three Canadian studies from that predominantly A(H1N1)pdm09 season found that the trivalent LAIV performed as well as [5, 6] or better [7] than IIV (although one study had very few children receiving LAIV, making the results of this study less conclusive[5]).

Investigations in the U.S. suggested that the A(H1N1)pdm09 strain used to make LAIV in 2013-2014 and earlier seasons may have been particularly sensitive to inactivation by heat exposure.[8] Exposure to heat may occur in the U.S. when vaccines are shipped during the hotter summer months. As a result of these investigations, the manufacturer changed the A(H1N1)pdm09 strain in all of its LAIV from an A/California/7/2009(H1N1)pdm09-like strain to an antigenically similar strain, A/Bolivia/559/2013, which was believed to be more heat stable.[2]

However, in the 2015-2016 influenza season, with a predominance of the A(H1N1)pdm09 strain circulating, the U.S. again found poor vaccine effectiveness for quadrivalent LAIV against this strain in two of the three U.S. sentinel surveillance networks/studies. Results from the third U.S. study, and studies from Canada and other countries where A(H1N1)pdm09 circulated in 2015-2016 showed higher vaccine effectiveness for quadrivalent LAIV against A(H1N1)pdm09 than found in the two U.S. studies. However, when assessing results from the third U.S. study and other countries, vaccine effectiveness for LAIV was somewhat lower than IIV (Please see Table 1 for details).

The 2016-2017 influenza season will likely add no additional information regarding the effectiveness of LAIV against A(H1N1)pdm09. This strain did not circulate to any great extent in Canada,[9] the United Kingdom (UK) or Finland,[10] where LAIV continued to be used.

To address the less than optimal vaccine effectiveness of LAIV against A(H1N1)pdm09, the manufacturer has replaced the A/Bolivia/559/2013 strains with a new strain, A/Slovenia/2903/2015, for all the vaccine produced for the 2017-2018 season. [11, 12]

Why did Canada make a different recommendation than the U.S. regarding live attenuated influenza vaccine (LAIV)?

The U.S. recommendation was based on their experience with quadrivalent LAIV effectiveness against A(H1N1)pdm09 in 2013-2014 and 2015-2016. Canada did not have a problem with the effectiveness of the trivalent LAIV against A(H1N1)pdm09 in 2013-2014. In 2015-2016, vaccine effectiveness of quadrivalent LAIV against A(H1N1)pdm09 in Canada, the UK and Finland was higher than in the U.S., although not as high as the vaccine effectiveness with IIV. Given the acceptable performance of LAIV in these countries, Canada, the UK and Finland continued to use LAIV. Canadian recommendations supported either the quadrivalent LAIV or quadrivalent IIV for children and adolescents 2 years to <18 years of age for the 2016-2017 and 2017-2018 seasons.

Why did Canada remove the preferential recommendation for the live attenuated influenza vaccine (LAIV) in August 2016?

Previous preferential recommendations for LAIV over IIV were based on three randomized controlled trials.[13-15] However, recent studies have shown LAIV and IIV to have similar vaccine effectiveness against influenza A(H3N2) and B, and in some studies, IIV performs somewhat better than LAIV against influenza A(H1N1)pdm09. Based on this information, the National Advisory Committee on Immunization (NACI) removed the preferential recommendation for LAIV over IIV.

Why is the live attenuated influenza vaccine (LAIV) showing lower vaccine effectiveness than the inactivated vaccine (IIV) against A(H1N1)pdm09 in some studies? Why is it working particularly poorly in the U.S. ?

As the name implies, the LAIV is a live, weakened influenza vaccine that works by growing in the nasopharynx and inducing an immune response. In this way, it mimics the immune response induced by natural infection. It is uncertain why LAIV is working particularly poorly against A(H1N1)pdm09 in the U.S., although a number of theories have been postulated.[10] Possible explanations for the lower vaccination effectiveness in some studies in 2015-2016 is that the vaccine strain is inhibited from growing in the nasopharynx because:

- it must compete with the three other strains that are part of the quadrivalent formulation; or
- immunity to A(H1N1)pdm09 from either past vaccination or infection is inhibiting the growth of the vaccine strain in the nasopharynx;[10] or
- the A/Bolivia A(H1N1)pdm09 strain in the 2015-2016 influenza vaccine had properties that did not allow it to grow well in the nasopharynx.[11]

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Studies conducted by the manufacturer of FluMist® suggest that the impaired ability of the A/Bolivia A(H1N1)pdm09 strain to replicate in the nasopharynx was the cause of the lower vaccine effectiveness in 2015-2016.[11] They have therefore replaced this strain with an A/Slovenia strain for the 2017-2018 influenza vaccine.[12] Further research is ongoing in this area.

What does this mean for Ontario children and adolescents?

In Canada, NACI recommends a quadrivalent vaccine for children 6 months to <18 years of age. A trivalent vaccine should only be used if a quadrivalent vaccine is not available. For children 6 months to <2 years of age, the only authorized quadrivalent vaccine is inactivated (IIV). Children 2 years to <18 years of age can receive either a quadrivalent IIV product or LAIV, as long as the child has no contraindications. See Contraindications.

Consistent with NACI's recommendation, Ontario offers the following quadrivalent vaccines for children and adolescents as part of its publicly-funded influenza immunization program:

- **FluLaval Tetra®:** an injectable quadrivalent IIV from 6 months to <18 years of age
- **Fluzone® Quadrivalent:** an injectable quadrivalent IIV from 6 months to <18 years of age
- **Flumist® Quadrivalent:** a LAIV given by nasal spray from 2 to <18 years of age

Children 6 months to <9 years of age who have never received an influenza vaccine in their life should receive two doses of vaccine given at least four weeks apart.

Contraindications for Vaccines

Contraindications for all influenza vaccines are:

- Anaphylactic reaction to a past influenza vaccine
- Guillain-Barré Syndrome within six weeks of a previous influenza vaccine
- Anaphylaxis to a component of the vaccine (other than egg). Note that egg allergy is NOT a contraindication for either LAIV or the IIV. [1, 16]

Contraindications particular to LAIV include:

- Less than two years of age
- Immunocompromised by disease or medication;
- Severe asthma or active wheezing;
- Taking long-term aspirin or aspiring-containing medication (because of the potential concern regarding Reye's syndrome);
- Pregnant;
- Taking an influenza antiviral medication (i.e., oseltamivir or zanamivir) in the preceding 48 hours.

Conclusion

Children and adolescents 6 months to <18 years of age should receive a quadrivalent influenza vaccine. For children 6 months to <2 years of age, only IIV are authorized. For children and adolescents 2 to <18 years of age with no contraindications, either the LAIV or IIV can be used. The choice may depend on whether the child prefers a nasal spray or injection.

Additional Information

More information is available from your local public health unit or the following sources:

- Universal Influenza Immunization Program (Ministry of Health and Long-Term Care)
- Canadian Immunization Guide Chapter on Influenza and Statement on Seasonal Influenza Vaccine for 2017-2018 (National Advisory Committee on Immunization)

For information about this document, contact CD@oahpp.ca.

Appendix

Table 1: Summary of 2015-2016 vaccine effectiveness (VE) results for the quadrivalent live attenuated influenza vaccine (LAIV), including comparisons to the inactivated influenza vaccine (IIV) where available

Study	Quadrivalent LAIV VE	IIV VE
U.S. Flu Vaccine Effectiveness Network – CDC - U.S. [17] A/H1N1pdm09; 2-17 years of age; adjusted analysis	-19% (95% CI: -113 to 33)	63% (95% CI: 45 to 75)
Department of Defense dependents - U.S. [18] A/H1N1pdm09; 2-17 years of age	15% (Not statistically significant)*	68% (Statistically significant)^
Influenza Clinical Investigation for Children (ICICLE) - MedImmune – U.S. [19] A/H1N1pdm09; 2-17 years of age	50% (Not statistically significant)*	71% (Statistically significant)^
Sentinel Practitioner Surveillance Network (SPSN) – Canada [2] A/H1N1pdm09; age not specified	Approximately 50% (Not statistically significant)*	Not provided
United Kingdom [20] A/H1N1pdm09; 2-17 years of age; adjusted analysis	41.5% (95% CI: -8.5 to 68.5)	100% (95% CI: 13.3 to 100)
Finland [21] Influenza A - A(H1N1)pmd09 predominated; 2 year olds; adjusted analysis	47.9% (95% CI: 21.6 to 65.4)	79.5% (95% CI: 50.3 to 91.6)

*Not statistically significant indicates that the confidence interval contains the vaccine effectiveness value of zero

^Statistically significant indicates that the confidence interval does not contain the vaccine effectiveness value of zero

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