

**Update: CDC's Advisory Committee on Immunization Practices (ACIP) voted in favor of an interim recommendation that live attenuated influenza vaccine (LAIV), also known as the "nasal spray" flu vaccine, should not be used during the 2016-2017 flu season. ACIP continues to recommend annual flu vaccination, with either the inactivated influenza vaccine (IIV) or recombinant influenza vaccine (RIV) for everyone 6 months and older. The ACIP vote follows data showing poor or relatively lower effectiveness of LAIV from 2013 through 2016.**

**Summary Key Points:**

- Influenza causes substantial illness and death every year.
- Flu vaccines are the first and best way to prevent influenza.
- While how well flu vaccines work can vary from year to year, there are years of data showing that people who get vaccinated are, overall, better off than people who do not get vaccinated.
- Flu vaccines prevent flu illnesses, doctor's visits and hospitalizations.
- CDC presented data showing vaccine effectiveness for nasal spray vaccine among children 2 years through 17 years during 2015-2016 was 3 percent (with a 95 percent Confidence Interval (CI) of -49 percent to 37 percent). This estimate means no protective benefit could be measured.
- In comparison, flu shots IIV had a vaccine effectiveness estimate of 63 percent against any flu virus among children 2 years through 17 years with a 95 percent CI of 52 percent to 72 percent. (This estimate indicates flu shots provided measurable protection.)
- The disappointing LAIV VE data from 2015-2016 follows two previous seasons (2013-2014 and 2014-2015) showing poor and/or lower than expected vaccine effectiveness (VE) for LAIV.
- It's disheartening to see data suggesting that one flu vaccine is not working as well as expected, but fortunately, flu shots did perform well last season, offering substantial protection against influenza.
- Today's ACIP vote underscores the importance of ongoing efforts to measure and evaluate the effectiveness of public health interventions, including VE studies, which can have significant implications for public health policy.
- The change in the ACIP recommendation is an example of using new data to hone public health practice to be most beneficial.
- Today's ACIP vote may have implications for vaccine providers who have already placed flu vaccine orders for the 2016-2017 season.
- Vaccine manufacturers have projected that as many as 171 million - 176 million doses of flu vaccine will be made available for the 2016-2017 season.
- LAIV accounts for up to 14 million of those doses (about 8% of the total supply of flu vaccine).
- Based on manufacturer projections, health officials expect that supply of IIV for the 2016-2017 season should be sufficient to meet any increase in demand resulting from the ACIP recommendation, though providers may need to check more than one supplier or purchase a flu vaccine brand other than the one they normally select.
- Providers who have purchased or pre-ordered vaccine will need to consult with the manufacturer or vaccine distributor.
- Overall VE (all ages, all flu viruses) for IIV was 49 percent (CI 41 percent to 56 percent) indicating that millions of people were protected against flu last season.

### **Additional Key Points**

- On June 22, 2016, CDC's Advisory Committee for Immunization Practices (ACIP) was presented with vaccine effectiveness (VE) data from 2015-2016, including for the live attenuated influenza vaccine (LAIV), or Flumist Quadrivalent, also known as the "nasal spray vaccine."
- ACIP then reviewed previous VE data related to LAIV and IIV and subsequently discussed changes to the U.S. 2016-2017 seasonal influenza vaccine recommendations based on these data.
- CDC's Advisory Committee on Immunization Practices (ACIP) voted in favor of an interim recommendation that live attenuated influenza vaccine (LAIV), also known as the "nasal spray" flu vaccine, should not be used during the 2016-2017 flu season.
- ACIP is a panel of immunization experts that advises CDC.
- ACIP's recommendations must be reviewed and approved by CDC's director before it becomes official CDC policy.
- The final annual recommendations on the prevention and control of influenza with vaccines will be published in a CDC Morbidity and Mortality Weekly Report (MMWR), Recommendations and Reports, usually in late summer or early fall.
- LAIV is the only non-injection based flu vaccine currently available on the market.
- Vaccine manufacturers have projected that as many as 171 million - 176 million doses of flu vaccine will be made available for the 2016-2017 season.
- LAIV accounts for up to 14 million of those doses (about 8% of the total supply of flu vaccine).
- These projections reflect the possible doses of vaccine that manufacturers can produce, and actual supplies of vaccine may be lower.
- Health officials expect that supply of IIV for the 2016-2017 season should be sufficient to meet any increase in demand resulting from the ACIP recommendation, though providers may need to check more than one supplier or purchase a flu vaccine brand other than the one they normally select.
- The reason for the poorer overall performance of LAIV compared to IIV over the last few flu seasons is not well understood.
- CDC conducts vaccine effectiveness (VE) studies each season to measure the benefits provided by flu vaccination.

### **A Summary of Vaccine Effectiveness Data for LAIV during 2015-2016**

- During the 2015-2016 season, VE data provided by the U.S. Flu VE Network indicated that LAIV offered no significant protection against the predominant flu virus [i.e., influenza A (H1N1)pdm09] among study participants age 2 through 17 years of age.
  - Preliminary estimate of VE for LAIV against any virus was 3% (95% CI -49% to 37%), and for IIV was 63% (95% CI 52% to 72%).

ACIP Meeting June 22, 2016  
Influenza Session: **Key Points**

- Preliminary estimate of VE against A(H1N1)pdm09 virus for LAIV was -21% (95% CI -108% to 30%), and for IIV it was 65% (95% CI 49% to 76%).
- For influenza B viruses, preliminary estimate of VE of LAIV among children aged 2 through 17 years was -4% (95% CI -141% to 55%) for Yamagata-lineage viruses, and 31% (95% CI -62% to 70%) for Victoria-lineage viruses.
  - In contrast, VE of IIV was 64% (95% CI 31% to 81%) for Yamagata-lineage viruses, and 56% (95% CI 29% to 72%) for Victoria-lineage viruses.
- There was evidence that VE for IIV was statistically better than LAIV for influenza A(H1N1)pdm09 virus but not for influenza B viruses (lineages combined); VE for influenza A (H3N2) viruses could not be assessed due to too few infections.

**Background: LAIV and ACIP recommendations**

- LAIV (i.e., the nasal spray vaccine) is currently approved for use in healthy, non-pregnant people 2 through 49 years of age.
  - For more information on LAIV, including groups recommended to receive it or not receive it and other considerations, see <http://www.cdc.gov/flu/about/ga/nasalspray.htm>.
  - LAIV is manufactured by MedImmune, LLC, which is a subsidiary of AstraZeneca.
- LAIV was initially licensed in 2003 as a trivalent (three-component) vaccine for use among healthy, non-pregnant persons 5 through 49 years of age, and ACIP recommended its use in this age group from 2003-2007.
- On September 19, 2007, MedImmune received approval from the Food and Drug Administration (FDA) to expand the use of FluMist (LAIV) to include healthy children aged 2-4 years (i.e., 24-49 months).
- In 2012, a quadrivalent (four-component) formulation of LAIV was licensed, and it replaced the trivalent formulation in the United States beginning during the 2013-2014 season.
- From 2003 through the 2012-2013 season, ACIP and CDC expressed no preference for LAIV or inactivated influenza vaccine (IIV), otherwise known as the “flu shot.”
- For the 2014-2015 season, the ACIP and CDC issued a preferential recommendation for the use of LAIV, when immediately available, for healthy children 2 through 8 years of age, to be implemented as feasible for the 2014-2015 season but not later than the 2015-2016 season.
  - This recommendation was based on the “Grading of Recommendations, Assessment, Development, and Evaluation” (GRADE) framework.
    1. The GRADE framework was adopted by the ACIP in October 2010. It provides a standardized and explicit process for developing ACIP recommendations with the goal of enhancing transparency, consistency and communication.
    2. The GRADE framework was designed to help the ACIP systematically assess the type or quality of evidence about a vaccine’s expected health impacts and the balance of health benefits and risks, along with the values and preferences of people affected, and

health economic analyses. It groups evidence into four categories, with the order reflecting the level of confidence in the estimated effect of vaccination on health outcomes.

3. For more information on the GRADE framework, see

<https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6118a3.htm>

- The research-related justification for the LAIV preferential recommendation for healthy children 2-8 years old when immediately available relied predominantly on data from two randomized control trials of LAIV and IIV among young children which measured superior efficacy of LAIV (1,2). These studies were conducted during the 2002-2003 and 2004-2005 flu seasons, respectively.\*
  1. Ashkenazi S, Vertruyen A, Aristegui J, Esposito S, McKeith DD, Klemola T, et al. Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections. *Pediatr Infect Dis J*. 2006 Oct;25(10):870-9.
  2. Belshe RB, Edwards KM, Vesikari T, Black SV, Walker RE, Hultquist M, et al. Live attenuated versus inactivated influenza vaccine in infants and young children. *The New England journal of medicine*. 2007 Feb 15;356(7):685-96.
- \* Both of these studies were conducted prior to the 2009 H1N1 pandemic when the H1N1pdm09 virus first emerged and began circulating. In addition, during these early studies it is likely that most children were flu vaccine naïve (previously unvaccinated) at the time LAIV was given, as opposed to recent seasons during which many children getting LAIV have been previously vaccinated.
- In February 2015, the ACIP and CDC did not renew the preferential recommendation for LAIV over IIV for children 2 through 8 years of age.
  - This decision was informed by VE data for the 2013-2014 and 2014-2015 seasons.
  - Results showed poor vaccine effectiveness (VE) of LAIV against influenza A(H1N1)pdm09, which was the predominant virus that season for children 2 through 17 years of age (1).
    1. Grohskopf LA, Sokolow LZ, Olsen SJ, Bresee JS, Broder KR, Karron RA. Prevention and Control of Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices, United States, 2015-16 Influenza Season. *MMWR Morbidity and mortality weekly report*. 2015 Aug 7;64(30):818-25.
  - The 2013-2014 season was the first H1N1 predominant season since the 2009 pandemic
  - It was hypothesized that the reduced effectiveness of LAIV against the influenza A (H1N1)pdm09 virus was due to reduced vaccine stability of the LAIV vaccine virus, A/California/2009/(H1N1), caused by a single amino acid mutation (1).
    1. Cotter CR, Jin H, Chen Z. A single amino acid in the stalk region of the H1N1pdm influenza virus HA protein affects viral fusion, stability and infectivity. *PLoS Pathog*. 2014 Jan;10(1):e1003831.
  - As a result, a new H1N1 vaccine virus (A/Bolivia/559/2013) was used in LAIV formulations for the 2015-2016 season.

ACIP Meeting June 22, 2016  
Influenza Session: **Key Points**

- However, despite the change in the H1N1 virus component of the LAIV vaccine, VE data for the 2015-2016 season found that LAIV was less effective than IIV among study participants aged 2-17 years. Similar to the 2013-2014 season, influenza A (H1N1)pdm09 viruses also circulated predominantly during the 2015-2016 season.
- More information about past LAIV VE data is available at <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6332a3.htm>