Annual vaccination against influenza A and B viruses is recommended for everyone ≥6 months old without a contraindication. Available vaccines and recommendations for specific patient populations for the 2019-2020 season are listed in Tables 2 and 3.

**TIMING** — In the US, influenza vaccine should be offered by the end of October and continue to be offered for as long as influenza is circulating in the community. In most adults, serum antibody levels peak about two weeks after vaccination. Early vaccination (i.e., in July or August) may result in suboptimal immunity before the end of the influenza season, especially in older adults. Children who require 2 doses (see Table 3, footnote 2) should receive the first dose as early as possible, so that the second dose can be given by the end of October.

**COMPOSITION** — All seasonal influenza vaccines available in the US contain antigens of the same two influenza A viruses. Influenza A viruses are responsible for the majority of influenza-related morbidity and mortality, particularly in infants and older adults.

**Trivalent** vaccines contain only one influenza B virus antigen. **Quadrivalent** vaccines contain influenza B virus antigens from both genetic lineages that have been circulating globally since the 1980s, increasing the likelihood that the vaccine will provide protection against currently circulating strains. Children are more likely than adults to become infected with influenza B.

**EFFECTIVENESS** — Influenza vaccination reduces the incidence of laboratory-confirmed influenza and can reduce the risk of serious complications and death associated with influenza illness in children and adults.

Table 1. 2019-2020 Influenza Vaccine Composition

<table>
<thead>
<tr>
<th>Vaccine Type</th>
<th>Antigens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trivalent Vaccine</td>
<td>A/Brisbane/02/2018 (H1N1)pdm09-like, A/Kansas/14/2017 (H3N2)-like, B/Colorado/06/2017-like</td>
</tr>
<tr>
<td>Quadrivalent Vaccine</td>
<td>A/Brisbane/02/2018 (H1N1)pdm09-like, A/Kansas/14/2017 (H3N2)-like, B/Colorado/06/2017-like, B/Phuket/3073/2013-like</td>
</tr>
</tbody>
</table>

The effectiveness of seasonal influenza vaccine in preventing laboratory-confirmed influenza illness depends on several factors, including the match between the vaccine and circulating strains and the immunologic response of the recipient. Vaccine effectiveness is greatest when the match is close, but even when it is suboptimal, vaccination can still substantially reduce the risk of influenza-related hospitalization and death. The antigens selected for inclusion in the seasonal vaccine can be altered slightly during production of egg-based vaccines, possibly resulting in a less desirable match between the vaccine and circulating strains.

The interim adjusted overall effectiveness of the influenza vaccine in preventing laboratory-confirmed influenza infection during the 2018-2019 season was 47% (61% in children 6 months-17 years old and 24% in adults ≥50 years old). Effectiveness against group A viruses was 44% (H3N2) and 46% (H1N1). The live-attenuated vaccine, FluMist Quadrivalent, the intranasally administered live-attenuated influenza vaccine, is FDA-approved for use in healthy nonpregnant persons 2-49 years old (see Table 2, footnote 19 for contraindications and precautions). The Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics (AAP) recommend the live-attenuated vaccine as an option this season. In previous seasons, there were concerns about the efficacy of the live-attenuated vaccine against influenza A(H1N1)pdm09-like viruses, and the ACIP advised against its use during the 2016-2017 and 2017-2018...
For the 2018-2019 season, the ACIP recommended the live-attenuated vaccine once again as an option based on a change in the A(H1N1)pdm09-dominant 2014-2015 season, the recombinant quadrivalent vaccine was 30% more effective than a standard-dose unadjuvanted quadrivalent vaccine in preventing polymerase chain reaction (PCR)-
Table 3. Choice of Vaccine

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Vaccine Choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children 6 months—2 years old</td>
<td>Age-appropriate inactivated vaccine (Afluria Quadrivalent, Fluvarix Quadrivalent, Flulaval Quadrivalent, or Fluzone Quadrivalent)</td>
</tr>
<tr>
<td>Children 2-17 years old</td>
<td>Any age-appropriate inactivated or live-attenuated vaccine</td>
</tr>
<tr>
<td>Adults &gt;50 years old</td>
<td>Any age-appropriate inactivated, recombinant, or live-attenuated vaccine</td>
</tr>
<tr>
<td>Pregnant Women</td>
<td>Any age-appropriate inactivated or recombinant vaccine</td>
</tr>
<tr>
<td>Persons with Egg Allergy</td>
<td>Afluria Quadrivalent with needle-free injector or intranasal live-attenuated vaccine</td>
</tr>
<tr>
<td>Immunocompromised Persons</td>
<td>Any age-appropriate inactivated or recombinant vaccine</td>
</tr>
</tbody>
</table>

ACIP = Advisory Committee on Immunization Practices

1. See Table 2 for available vaccines in the US during the 2019-2020 influenza season and specific age recommendations.

2. Children 6 months to 8 years old who are being vaccinated for the first time or who have not received at least 2 lifetime doses of the trivalent or quadrivalent vaccine before July 1, 2019 should receive 2 doses at least 4 weeks apart. They should receive their first dose as soon as possible after the vaccine becomes available so that the second dose can be administered by the end of October. Children in this age group who received ≥2 doses of trivalent or quadrivalent vaccine at any time before July 1, 2019 require only 1 dose.

3. FDA-approved only for use in nonpregnant persons 2-49 years old. Not recommended for persons who are immunocompromised, children 2-4 years old who have asthma or have had a wheezing episode in the previous 12 months, children or adolescents taking aspirin or salicylate-containing therapy, close contacts of severely immunocompromised persons who require a protected environment, or patients treated with influenza antiviral drugs in the previous 48 hours.

4. See Table 4. Fluad, Fluzone High-Dose, and Flublok Quadrivalent have been shown to be more effective in preventing laboratory-confirmed influenza in randomized controlled trials (the recombinant vaccine in adults ≥50 years old and the high-dose vaccine in adults ≥65 years old). The ACIP has not preferentially recommended any vaccine for this age group and states that vaccination should not be delayed if a specific product is not readily available.

5. A history of a severe allergic reaction to any component of the vaccine is a contraindication in the labeling of all influenza vaccines. However, the ACIP states that any age-appropriate inactivated influenza vaccine, recombinant influenza vaccine, or live-attenuated vaccine may be administered to persons with egg allergy of any severity. Persons who have severe egg allergy should be vaccinated in a healthcare setting with supervision by a healthcare provider experienced in recognizing and managing severe allergic reactions. The recombinant inactivated vaccine (Flublok Quadrivalent) and the cell culture-based inactivated vaccine (Flucelvax Quadrivalent) are not prepared by propagation of virus in embryonated eggs.

6. Delivery of Afluria Quadrivalent via the PharmaJet Stratis needle-free injection system is FDA-approved only for persons 18-64 years old.

Confirmed influenza illness in 8604 adults ≥50 years old (42% more effective in persons 50-64 years old and 17% more effective in those ≥65 years old).21

High-Dose Vaccine – Fluzone High-Dose, an inactivated trivalent vaccine that contains four times the amount of antigen included in standard-dose influenza vaccines, is FDA-approved for use in persons ≥65 years old. In a randomized, double-blind trial in 31,989 adults ≥65 years old during two influenza seasons, the high-dose vaccine induced significantly greater antibody responses than a standard-dose trivalent inactivated vaccine, and was 24.2% more effective in preventing laboratory-confirmed influenza illness.22 In observational studies and one meta-analysis in adults ≥65 years old, the high-dose influenza vaccine was associated with reduced risk of respiratory-related and all-cause hospital admissions and death compared to standard-dose vaccines.23-26

Adjuvanted Vaccine – Fluarix, an adjuvanted inactivated trivalent influenza vaccine, is FDA-approved for use in persons ≥65 years old.27 It contains MF59, an oil-in-water emulsion of squalene oil that increases the immune response by recruiting antigen-presenting cells to the injection site and promoting uptake of influenza virus antigens. In a randomized trial in 7082 adults ≥65 years old, the adjuvanted vaccine elicited significantly greater antibody responses against all three influenza strains than an unadjuvanted trivalent vaccine, but the prespecified criteria for superiority was not met.28 In observational studies, older adults who received the adjuvanted trivalent influenza vaccine were less likely than those who received an unadjuvanted standard-dose trivalent vaccine to develop symptomatic influenza illness or be hospitalized for influenza or pneumonia.29,30 Randomized controlled trials demonstrating the efficacy of the adjuvanted vaccine in preventing laboratory-confirmed influenza are lacking.

PREGNANCY – Vaccination protects pregnant women against influenza-associated illness, which can be especially severe during pregnancy, and protects their infants for up to the first 6 months of life.31-33 Most studies have not found an association between influenza vaccination and adverse pregnancy outcomes, but data demonstrating the safety of vaccination during the first trimester are limited. In one case-control study of 485 cases of spontaneous abortion (gestational age 5 to <20 weeks) that occurred during the 2010-2011 and 2011-2012 influenza seasons, administration of an inactivated influenza vaccine containing an A/H1N1pdm09 antigen was modestly, but statistically significantly, associated with spontaneous abortion in the 28 days after vaccination among women who had received an A/H1N1pdm09-containing vaccine during the previous season.34 In a larger follow-up study during the 2012-2013, 2013-2014, and 2014-2015 influenza seasons, influenza vaccine was not associated with spontaneous abortion regardless of previous season vaccination.35 The ACIP and the American College of Obstetricians and Gynecologists recommend vaccinating pregnant
women against influenza without regard to the trimester of pregnancy but they should not receive the live-attenuated vaccine.

**ALLERGY** — A history of severe allergic reaction to any component of the influenza vaccine is listed as a contraindication in the labeling of all influenza vaccines. In 28 studies that included 4315 patients with egg allergy (656 with a history of a severe allergic reaction), there were no reports of anaphylaxis after administration of egg-based inactivated influenza vaccines; some mild reactions did occur. The ACIP, the American Academy of Allergy, Asthma and Immunology, and the American College of Allergy, Asthma and Immunology state that any age-appropriate influenza vaccine can be administered to persons who report a history of hives related to egg exposure. Persons with more severe egg allergy can also receive any age-appropriate influenza vaccine, but they should be vaccinated in a healthcare setting with supervision by a healthcare provider experienced in recognizing and managing severe allergic reactions. The recombinant vaccine (Flublok Quadrivalent) and the cell culture-based inactivated vaccine (Flucelvax Quadivalent) are not prepared by propagation of virus in embryonated eggs.

**IMMUNOCOMPROMISED PERSONS** — The live-attenuated influenza vaccine should not be used in immunocompromised persons. Inactivated vaccines are generally considered safe for use in such persons, but the immune response may be reduced. Separation in time of influenza vaccination from an immunocompromising intervention might be considered.

In a randomized trial in 172 solid-organ transplant recipients ≥18 years old, the high-dose vaccine induced significantly greater antibody responses than a standard-dose vaccine. In a randomized trial in 279 patients with rheumatoid arthritis, immune responses to the influenza vaccine were higher in patients given a high-dose vaccine than in those given a standard-dose vaccine.

**ADVERSE EFFECTS** — Influenza vaccination has been associated with Guillain-Barré syndrome, but the absolute risk is very low (about 1-2 additional cases per million persons vaccinated). Influenza infection itself has been associated with the syndrome (about 17 cases per million influenza infection encounters).

Except for soreness at the injection site, adverse reactions to inactivated influenza vaccines are uncommon. In clinical trials, Fluzone High-Dose caused more injection-site reactions than standard-dose influenza vaccines. Pain and tenderness at the injection site occurred more frequently with Fluzone than with an unadjuvanted vaccine. Delivery of Afluria by needle-free jet injector has resulted in more mild to moderate local reactions than delivery by standard needle and syringe.

The most common adverse reactions associated with the live-attenuated vaccine are runny nose, nasal congestion, fever, and sore throat. The vaccine can increase the risk of wheezing, especially in children <5 years old with recurrent wheezing and in persons of any age with asthma. Persons vaccinated with the live-attenuated vaccine may shed the vaccine-strain virus for a few days after vaccination, but

---

1. No studies directly comparing these vaccines are available. The Advisory Committee on Immunization Practices (ACIP) has not preferentially recommended any vaccine for older persons and states that vaccination should not be delayed if a specific product is not readily available. Any age-appropriate inactivated or recombinant vaccine can be used (see Table 2).
person-to-person transmission has been rare, and serious illness resulting from transmission has not been reported. Nevertheless, persons who care for severely immunocompromised patients in protected environments should not receive the live-attenuated vaccine or should avoid contact with such patients for 7 days after receiving it.

WITH OTHER VACCINES — Inactivated and recombinant influenza vaccines can be administered concomitantly or sequentially with live or other inactivated vaccines. The live-attenuated influenza vaccine can be given simultaneously with inactivated or other live vaccines. Other live vaccines not administered on the same day should be given at least 4 weeks later. Use of an unadjuvanted influenza vaccine might be considered in persons receiving another adjuvanted vaccine (e.g., Shingrix, Heplisav B) because of the theoretical possibility of increased reactogenicity.

WITH INFLUENZA ANTIVIRALS — Use of influenza antiviral drugs (a neuraminidase inhibitor or baloxavir) within 48 hours before or <2 weeks after administration of the intranasal live-attenuated influenza vaccine could inhibit replication of the vaccine virus, reducing the vaccine’s efficacy.

CONCLUSION — Vaccination against seasonal influenza is recommended for all persons ≥6 months old, including pregnant women. Quadrivalent vaccines offer broader coverage against influenza B viruses. The intranasal live-attenuated vaccine is a recommended option for the 2019-2020 season. Recombinant, high-dose, and adjuvanted vaccines elicit greater antibody responses than standard-dose unadjuvanted vaccines in persons ≥65 years old, and the high-dose and recombinant vaccines have been shown to be more effective for prevention of laboratory-confirmed influenza in older persons in randomized controlled trials.