Influenza Vaccination Updates for the 2022–23 Season

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Massachusetts Chapter, American Academy of Pediatrics
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Disclosures/Unlabeled Use

- Nothing to disclose.

- Though not covered specifically in this presentation, ACIP makes recommendations for vaccination of persons with a history of egg allergy.
  - A history of severe allergic reaction (e.g., anaphylaxis) to the vaccine or any of its components (which include egg for some vaccines) is a labeled contraindication for egg-based inactivated influenza vaccines (IIV4s) and the live attenuated influenza vaccine (LAIV4).
  - However, ACIP recommends that persons with egg allergy of any severity should receive any licensed, recommended influenza vaccine that is appropriate for their age and health status.
  - Persons with a history of severe allergic reaction to egg who receive egg-based vaccines—i.e., vaccines other than cell culture–based inactivated influenza vaccine (cclIV4) or recombinant influenza vaccine (RIV4) should be vaccinated in an inpatient or outpatient medical setting, supervised by a health care provider who is able to recognize and manage severe allergic reactions.
Overview

- 2021-22 influenza activity
- 2022-23 ACIP influenza vaccination updates
U.S. Influenza Activity Update
U.S. Influenza Virologic Surveillance—2021-22

Influenza Positive Tests Reported to CDC by U.S. Clinical Laboratories, National Summary, October 3, 2021 – August 27, 2022

- **B**
- **A**
- Percent Positive
- % Positive Flu A
- % Positive Flu B

Influenza Positive Tests Reported to CDC by U.S. Public Health Laboratories, National Summary, October 3, 2021 – August 27, 2022

- A (subtyping not performed)
- A (H1N1)pdm09
- A (H3N2)
- B (Victoria Lineage)
- B (Yamagata Lineage)

CDC FluView (Weekly U.S. Influenza Surveillance Report | CDC)
Laboratory-confirmed Influenza Hospitalizations (FluSurv-NET)
ACIP Influenza Vaccination Update
General Vaccines Types and Abbreviations

IIVs  Inactivated Influenza Vaccine—contain inactivated viruses, and their HAs

ccIIV  Cell culture based Inactivated Influenza Vaccine

aIIV  Adjuvanted Inactivated Influenza Vaccine

HD-IIV  High-Dose Inactivated Influenza Vaccine

RIV  Recombinant Influenza Vaccine—contains recombinant HA

LAIV  Live Attenuated Influenza Vaccine—contains live viruses

Numbers indicate the number of influenza virus antigens:
3 for trivalent: an A(H1N1), an A(H3N2), and one B (from one lineage)
4 for quadrivalent: an A(H1N1), an A(H3N2), and two Bs (one from each lineage)

Note: all currently available vaccines are quadrivalent, but the trivalent abbreviations are used when describing information specific to trivalent vaccines
Core recommendation (unchanged):

- Annual influenza vaccination is recommended for all persons aged 6 months and older who do not have contraindications.
2022–23 ACIP Influenza Statement

Updates on the following topics:

• Influenza vaccines expected to be available for the 2022-23 season.
• U.S. influenza vaccine viral composition for the 2022-23 season.
• Change in FDA-approved age indication for Flucelvax Quadrivalent from ≥2 years to ≥6 months.
• Updated recommendations for vaccination of persons aged ≥65 years.
U.S. Seasonal Influenza Vaccines Since 2000-2001

Number of unique products available by season

- IIV3
- IIV4
- LAIV3
- LAIV4
- HD-IIV3
- HD-IIV4
- id-IIV3
- id-IIV4
- cc-IIV3
- cc-IIV4
- RIV3
- RIV4
- aIIV3
- aIIV4
<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>0 through 6 months</th>
<th>6 through 23 months</th>
<th>2 through 17 years</th>
<th>18 through 49 years</th>
<th>50 through 64 years</th>
<th>≥65 years</th>
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<tbody>
<tr>
<td>IIV4s</td>
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<tr>
<td>Standard-dose, unadjuvanted inactivated (IIV4)</td>
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<tr>
<td>Cell culture-based inactivated (ccIIV4)</td>
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<td>Flucelvax Quadrivalent</td>
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<td>Adjuvanted inactivated (aIIV4)</td>
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<td>Fluad Quadrivalent</td>
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<td>High-dose inactivated (HD-IIV4)</td>
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<td>Fluzone High-Dose Quadrivalent</td>
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<td>RIV4</td>
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<td>Recombinant (RIV4)</td>
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<td>Flublok Quadrivalent</td>
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<td>LAIV4</td>
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<tr>
<td>Live attenuated (LAIV4)</td>
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<td>FluMist Quadrivalent</td>
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All vaccines expected for 2022-23 are quadrivalent (i.e., contain hemagglutinin derived from four viruses: one influenza A(H1N1), one influenza A(H3N2), one influenza B/Victoria and one influenza B/Yamagata.
Influenza Vaccine Types—2022-23 U.S. Season

Inactivated Influenza Vaccines (IIV4s)
- Contain inactivated virus (split or subunit)
- Most are egg-based (one is cell culture-based—ccIIV4)
- Most contain 15 mcg of hemagglutinin per virus (one contains 60 mcg per virus—HD-IIV4)
- Most are unadjuvanted (one contains the adjuvant MF59—aIIV4)

Recombinant influenza vaccine (RIV4)
- No viruses used in production
- 45 mcg HA per virus
- Contains HA made through recombinant methods

Intramuscular Vaccines

Live attenuated influenza vaccine (LAIV4)
- Egg-based
- Contains live, attenuated influenza viruses which must replicate in the nasopharynx in order to promote an immune response
  - Attenuated—to not cause clinical illness
  - Cold-adapted
  - Temperature-sensitive
- For ages 2 through 49 years
- Not recommended in pregnancy and for those with some medical conditions

Intranasal Vaccine
Egg-based IIV4s and LAIV4 will contain HA derived from:
- an influenza A/Victoria/2570/2019 (H1N1)pdm09-like virus;
- an influenza A/Darwin/9/2021 (H3N2)-like virus;
- an influenza B/Austria/1359417/2021 (Victoria lineage)-like virus; and
- an influenza B/Phuket/3073/2013 (Yamagata lineage)-like virus.

ccIIV4 and RIV4 will contain HA derived from:
- an influenza A/Victoria/2570/2019 (H1N1)pdm09-like virus;
- an influenza A/Darwin/9/2021 (H3N2)-like virus;
- an influenza B/Austria/1359417/2021 (Victoria lineage)-like virus; and
- an influenza B/Phuket/3073/2013 (Yamagata lineage)-like virus.
Updated Age Indication for Flucelvax Quadrivalent (ccIIV4)

- Cell culture-based quadrivalent in activated influenza vaccine, ccIIV4
  - May 2016—approved for ages 4 years and older
    - Ages ≥18 yrs based on efficacy/safety
    - Ages 4 through 17 years based on immunogenicity/safety
  - March 2021—approved for ages 2-17 yrs based on efficacy/safety
  - October 2021—approved for ages 6 through 23 months based on immunogenicity/safety

- Now approved for ages 6 months and older

- Dose volume is 0.5mL for all age groups
Brief Aside: IIV4s for 6- through 35-Month-Olds

• All unadjuvanted, standard-dose IIV4s are now approved for ages ≥6 months.

• Still some differences in the dose volumes:
  • Fluarix Quadrivalent: 0.5 mL
  • Flucelvax Quadrivalent: 0.5 mL
  • FluLaval Quadrivalent: 0.5 mL
  • Fluzone Quadrivalent: 0.25 mL or 0.5 mL
    – 0.25 mL prefilled syringes no longer available.
  • Afluria Quadrivalent: 0.25 mL
    – 0.25 mL prefilled syringes no longer available.

• Dose volume is distinct from number of doses needed:
  • As previously, some children aged 6 months through 8 years need two doses.
  • For example, a first-time influenza vaccinee who is 1 year old,
  • And who gets 0.5mL FluLaval Quadrivalent for a first dose—
  • Still needs a second dose of influenza vaccine, ≥4 weeks later.
Children in this age group who have never received influenza vaccine, who have not had ≥2 doses of trivalent of quadrivalent vaccine before July 1, 2022, or whose vaccination history is not known need 2 doses ≥4 weeks apart for 2022-23.

- Previous doses can be from different/non-consecutive seasons.

- 8-year-olds determined to need 2 doses should receive second even if they turn age 9 years between dose 1 and dose 2.

From MMWR 71(RR-1), August 26, 2022.
Persons aged ≥65 years are at increased risk of severe illness, hospitalization, and death due to influenza.

Target population for annual influenza vaccination since the early 1960s.

Influenza vaccines are often less effective compared with younger populations.

### Influenza and Older Adults (Aged ≥65 Years)

<table>
<thead>
<tr>
<th>Season</th>
<th>Overall VE, % (all ages, viruses, and vaccine types)</th>
<th>≥65 yrs (all viruses and vaccine types)</th>
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<tbody>
<tr>
<td>2019-20</td>
<td>39 (32, 44)</td>
<td>39 (9, 59)</td>
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<tr>
<td>2018-19</td>
<td>29 (21, 35)</td>
<td>12 (-31, 40)</td>
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<tr>
<td>2017-18</td>
<td>38 (31, 43)</td>
<td>17 (-14, 39)</td>
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<tr>
<td>2016-17</td>
<td>40 (32, 46)</td>
<td>20 (-11, 43)</td>
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<tr>
<td>2015-16</td>
<td>48 (41, 55)</td>
<td>42 (6, 64)</td>
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<tr>
<td>2014-15</td>
<td>19 (10, 27)</td>
<td>32 (3, 52)</td>
</tr>
<tr>
<td>2013-14</td>
<td>52 (44, 59)</td>
<td>50 (16, 71)</td>
</tr>
<tr>
<td>2012-13</td>
<td>49 (43, 55)</td>
<td>26 (-10, 50)</td>
</tr>
<tr>
<td>2011-12</td>
<td>47 (36, 56)</td>
<td>43 (-18, 72)</td>
</tr>
</tbody>
</table>

Influenza Vaccines for Persons Aged ≥65 Years

- All influenza vaccines currently available in the US, with the exception of the live attenuated influenza vaccine, are approved for ages ≥65 years.
  - Five standard-dose, unadjuvanted inactivated influenza vaccines (SD-IIVs).
  - One high-dose inactivated influenza vaccine (HD-IIV).
  - One adjuvanted inactivated influenza vaccine (aIIV).
  - One recombinant influenza vaccine (RIV).

- ACIP had previously expressed no preferential recommendation for any specific vaccine(s) for this age group.
Fluzone High-Dose Quadrivalent (HD-IIV4)

- Approved as a trivalent (HD-IIV3) in 2009 for ages ≥65 years.
  - Four times the hemagglutinin (HA) dose/virus compared with SD-IIVs (60 µg vs. 15 µg).
- Initial approval in 2009 based on superior immunogenicity to SD-IIV3.
- Demonstrated superior efficacy to standard-dose vaccine in a two-season randomized trial among ~32,000 participants ages ≥65 years.
- HD-IIV4 approved in 2019 based on noninferior immunogenicity to HD-IIV3, and replaced HD-IIV3 for the 2020-21 season.
**Fluad Quadrivalent (aIIV4)**

- Approved in US as a trivalent (aIIV3) in 2015 for ages ≥65 years; in use in Europe as early as 1997.
  - Contains the adjuvant MF59.
- Approved in 2015 based on noninferior immunogenicity to unadjuvanted SD-IIV3.
- Quadrivalent (aIIV4) was compared with Tdap in two-season randomized trial among ~6,700 persons ages ≥65 years.
  - Primary efficacy endpoint—prevention of PCR-confirmed protocol-defined influenza like illness (ILI) due to any influenza—not met (88% of antigenically characterized viruses from cases in aIIV4 arm were antigenically mismatched).
  - Efficacy was noted against PCR-confirmed CDC- and WHO-defined ILI due to any virus.
  - aIIV4 replaced aIIV3 for the 2021-22 season.
- More effective compared with SD-IIVs in some observational studies.
Flublok Quadrivalent (RIV4)

- Approved as a trivalent (RIV3) in 2013 for ages 18 through 49 years.
  - Recombinant HA (no viruses or eggs used in production).
  - Three times the HA dose/virus compared with SD-IIVs (45 µg vs. 15 µg).
- Initially approved based on efficacy demonstrated in a randomized placebo-controlled study among persons aged 18 through 49 years.
- Approved for ≥50 years in 2014 based on immunogenicity studies.
- RIV4 demonstrated improved efficacy relative to SD-IIV4 in a single-season randomized study conducted among ~8600 persons ages ≥50 years.
  - RIV4 replaced RIV3 for the 2018-19 season.
Summary—Review of Influenza Vaccines for ≥65 Years

- Review of randomized and observational studies of HD-IIV, aIIV, and RIV compared with unadjuvanted SD-IIVs and with one another, focusing on persons aged ≥65 years.

- Overall, there is evidence of greater potential benefit HD-IIV, RIV, and aIIV over SD-IIVs.
  - Most evidence for HD-IIV3.
  - Less evidence for RIV and aIIV; no RCT including lab-confirmed outcomes for aIIV3.
  - Estimates of relative benefit of one vaccine over another vary with study/season.

- Few studies compare HD-IIV, RIV and aIIV with one another—insufficient to conclude that any one will be superior to the others across seasons.

- Limitations include:
  - Few randomized studies, covering few influenza seasons.
  - More data from observational studies, but most are retrospective cohort designs using diagnostic-code defined outcomes.
  - No data reflecting currently available formulations of HD-IIV and aIIV, which are now quadrivalents (HD-IIV4 and aIIV4).
“ACIP recommends that adults aged ≥65 years preferentially receive any one of the following higher dose or adjuvanted influenza vaccines: quadrivalent high-dose inactivated influenza vaccine (HD-IIV4), quadrivalent recombinant influenza vaccine (RIV4), or quadrivalent adjuvanted inactivated influenza vaccine (aIIV4). If none of these three vaccines is available at an opportunity for vaccine administration, then any other age-appropriate influenza vaccine should be used.”
Timing of Influenza Seasons

- Timing of the onset and peak of influenza activity varies from season to season.
- Timing of activity onset can also vary geographically.
- In the United States, localized areas of increased activity occur as early as October.
- Over the 38 seasons between 1982-83 and 2019-20, peak activity occurred in:
  - December: 7 (18%) seasons
  - January: 6 (16%) seasons
  - February: 17 (45%) seasons
  - March: 6 (16%) seasons

https://www.cdc.gov/flu/about/season/flu-season.htm
Factors Relevant for Timing of Vaccination

- Declines in influenza vaccine effectiveness over the course of the season have been observed in many observational studies.
- Has been noted in some studies for all age groups.
  - Appears to be more pronounced among older adults.
  - Less evidence for waning among children.
- Might be more of an issue for H3N2 viruses.
- Other considerations related to timing:
  - Unpredictability of timing of onset and peak of the influenza season.
  - Avoiding missed opportunities to vaccinate.
  - Programmatic constraints.
Guidance for Timing of Vaccination

- For most people who need only 1 dose of influenza vaccine for the season, September and October are good times to get vaccinated.
- For most adults (especially aged 65 years) and pregnant persons in the first or second trimester, July and August should be avoided—unless there is concern later vaccination might not be possible.
- Children who need 2 doses (those 6 months through 8 years who have never been vaccinated, who have not received ≥2 total doses, or whose vaccination history is unknown)—should receive first dose as soon as possible after vaccine is available.
- July and August vaccination can be considered for children who need only one dose and pregnant persons in third trimester during those months.
- Ideally, vaccination should be offered by the end of October, but—
- Vaccination of those not yet vaccinated for the season should continue after October, throughout the season, as long as influenza viruses are circulating and unexpired vaccine is available.
Estimated Benefits of Influenza Vaccination

- Vaccine effectiveness varies, affected by:
  - Season/predominant viruses.
  - Degree of match between circulating and vaccine viruses.
  - Age and immunity of the recipient.

- In a season during which most circulating viruses are similar to those represented in the vaccine, can expect 40%-60% effectiveness overall.
  - Generally better for older children and younger adults vs older adults.
  - Generally better for influenza A(H1N1) and influenza B viruses than for influenza A(H3N2) viruses.
  - But, vaccination still provides important benefits even in a season of low overall effectiveness.

Estimated Benefits of Influenza Vaccination—2019-20 Season

- CDC provides estimates of overall influenza burden and vaccine effectiveness after each season.
- Estimated vaccine effectiveness for 2019-20:
  - 39% overall
- Estimated burden averted through vaccination
  - 7.5 million illnesses
  - 105,000 hospitalizations
  - 6,300 deaths

Thank you!

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