Summary and Work Group Considerations

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## Acknowledgments

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Influenza Vaccine Distribution Update
Influenza Vaccine Supply Update: Cumulative Doses of Influenza Vaccine Distributed by Month, by Season—United States, 2016-17 through 2019-20 Seasons
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>IIV</td>
<td>Inactivated Influenza Vaccine</td>
</tr>
<tr>
<td>ccIIV</td>
<td>Cell culture based Inactivated Influenza Vaccine</td>
</tr>
<tr>
<td>aIIV</td>
<td>Adjuvanted Inactivated Influenza Vaccine</td>
</tr>
<tr>
<td>HD-IIV</td>
<td>High-Dose Inactivated Influenza Vaccine</td>
</tr>
<tr>
<td>RIV</td>
<td>Recombinant Influenza Vaccine</td>
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<tr>
<td>LAIV</td>
<td>Live Attenuated Influenza Vaccine</td>
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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)
Influenza Immunization

The adult dosage recommended by the advisory committee for initial immunization is 1.0 cc. (500 c.c. units) of polyvalent vaccine, administered subcutaneously on two occasions separated by two or more months. Preferably, the first dose would be given no later than September 1 and the second no later than November 1. Persons previously immunized with polyvalent vaccine should be reimmunized with a single booster dose of 1.0 cc. subcutaneously each fall, prior to November 1. The only contraindication to vaccination would be a history of food allergy to eggs or chicken or a prior history of allergic reaction to an egg-produced vaccine, such as the commercial influenza product.

The time to start such a program is before the onset of the influenza season this fall. In the past, influenza vaccination has been sparse and sporadic, and primarily in response to an epidemic or the threat of an epidemic. The unpredictability of reoccurrence of influenza and its continued endemic occurrence are well known. Therefore, the Public Health Service strongly recommends that immunization of these high-risk groups be started now and continued annually, regardless of the predicted incidence of influenza for specific years.

The members of the Surgeon General’s Advisory Committee on Influenza Research are: Colin M. MacLeod, M.D., chairman, University of Pennsylvania, Fred M. Davison, M.D., University of Michigan, Morris Schneffer, M.D., bureau of laboratories of the City of New York Health Department, George Burch, M.D., Tulane University, Dorland J. Davis, M.D., National Institute of Allergy and Infectious Diseases, Public Health Service, Thomas F. Sellars, M.D., Georgia State Department of Health, and Glenn S. Usher, M.D., Communicable Disease Center, Public Health Service.
U.S. Seasonal Influenza Vaccines Since 2000-01
Number of unique products available by season
U.S.-Licensed Influenza Vaccines, 2019-20

Available vaccines by FDA-licensed age indication:

<table>
<thead>
<tr>
<th>Vaccine type</th>
<th>6 through 23 mos</th>
<th>2 through 3 yrs</th>
<th>4 through 17 yrs</th>
<th>18 through 49 yrs</th>
<th>50 through 64 yrs</th>
<th>≥65 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>IIV4s (egg-based)</td>
<td>Afluria Quadrivalent</td>
<td>Fluarix Quadrivalent</td>
<td>FluLaval Quadrivalent</td>
<td>Fluzone Quadrivalent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IIV4 (cell-based)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Flucelvax Quadrivalent</td>
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<tr>
<td>RIV4 (recombinant)</td>
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<td></td>
<td></td>
<td>Flublok Quadrivalent</td>
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<tr>
<td>Adjuvant IIV3 (egg-based)</td>
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<td>Fluad</td>
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<tr>
<td>High-dose IIV3 (egg-based)</td>
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<td></td>
<td></td>
<td></td>
<td>Fluzone High-dose</td>
</tr>
<tr>
<td>LAIV4 (egg-based)</td>
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</table>

- ACIP recommends that a licensed, age-appropriate influenza vaccine should be used.
- No preferential recommendations are made for any specific influenza vaccine for any age group, where there is more than one that is appropriate.
Challenges in Assessing Relative Benefits of Specific Vaccines for Older Adults

- Large variety of available influenza vaccines
  - 8 are appropriate for this age group by licensed indications

- Growing canon of studies comparing individual vaccine types, but data limited for some relevant comparisons

- Vaccine effectiveness (and relative effectiveness of different vaccines) varies from season to season
  - Cannot be certain that results from one or a few high-quality studies will generalize across all or most influenza seasons
### HD-IIV3, allV3 and RIV4 for Older Adults

#### Summary of studies examining laboratory-confirmed influenza outcomes:

<table>
<thead>
<tr>
<th>Study Year published</th>
<th>Ages</th>
<th>Season(s)</th>
<th>Comparison</th>
<th>Design</th>
<th>N</th>
<th>Relative Efficacy/effectiveness</th>
</tr>
</thead>
<tbody>
<tr>
<td>DiazGranados 2013</td>
<td>≥65 years</td>
<td>1 2009-10</td>
<td>HD-IIV3 vs SD-IIV3</td>
<td>RCT</td>
<td>~9,100</td>
<td>Not evaluable because of pandemic</td>
</tr>
<tr>
<td>DiazGranados 2014</td>
<td>≥65 years</td>
<td>2 2011-12, 2012-13</td>
<td>HD-IIV3 vs SD-IIV3</td>
<td>RCT</td>
<td>~32,000</td>
<td>24.2% (95% CI = 9.7–36.5)</td>
</tr>
<tr>
<td>Dunkle 2017</td>
<td>≥50 years</td>
<td>1 2014-15</td>
<td>RIV4 vs SD-IIV4</td>
<td>RCT</td>
<td>~8,600</td>
<td>30% (95% CI = 10–47)</td>
</tr>
<tr>
<td>Van Buynder 2013</td>
<td>≥65 years</td>
<td>1 2011-12</td>
<td>allV3 vs SD-IIV3</td>
<td>observational</td>
<td>227</td>
<td>63% (95% CI = 4–86)</td>
</tr>
</tbody>
</table>

1. DiazGranados CA et al, Vaccine 2013;31:861-866
Do the relative benefits and harms of HD-IIV, aIIV, and RIV as compared with one another and with other influenza vaccines favor the use of these vaccines over others for persons aged 65 years and older?
**Planned Systematic Review/Meta-analysis--Summary**

**Population:** Adults aged ≥65 years

**Interventions:** Trivalent/quadrivalent high dose IIV, adjuvanted IIV, or RIV  
(U.S.-licensed, or similar in formulation/manufacture to U.S.-licensed)

**Comparators:** Other trivalent or quadrivalent influenza vaccine  
(U.S.-licensed, or similar in formulation/manufacture to U.S.-licensed)  
Non-influenza control vaccine  
Placebo  
No vaccine
Planned Systematic Review/Meta-analysis--Summary

Outcomes: (To be finalized early November)

Efficacy/Effectiveness
- All influenza -- A and B
  (sub-analysis stratified by virus type and subtype as feasible)
- Influenza-associated outpatient/emergency visits
- Influenza-associated hospitalizations
- Influenza-associated deaths

Safety
- Systemic and injection site adverse events
- Serious adverse events
- Guillain-Barre syndrome
- Severe hypersensitivity or anaphylaxis
Inclusion/Exclusion Criteria

- Peer-reviewed literature; no language restriction
- Publication dates from 1990 forward
- Include:
  - Randomized studies (including cluster-randomized)
  - Retrospective case-control and cohort studies
  - Prospective cohort studies
- Exclude:
  - Case series, case reports, registry reports without comparator information.
  - Studies/data on vaccines not licensed in the United States
  - Animal studies
  - Studies/data for which entire population falls outside of designated age range
  - Duplicate reports
  - Interim reports superseded by final reports