Influenza Disease Burden, Vaccine Benefits, and Current Vaccine Recommendations

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Summary Points

• Influenza activity increases seasonally in the U.S. each year, generally from fall through early spring (though timing varies year to year).

• Influenza severity and illness burden vary from season to season.

• Older adults, young children, pregnant persons, immunocompromised persons, and those with certain chronic medical conditions are among those at increased risk of severe/complicated illness.

• Routine vaccination has been recommended for some populations since 1960, and for all aged ≥6 months since 2010.

• Influenza vaccine effectiveness varies, depending upon factors such as age and health of the recipient and “match” between vaccine and circulating viruses.

• Even in a season of modest vaccine effectiveness, influenza vaccination can prevent substantial disease burden (illnesses, hospitalizations, and deaths).
Influenza Disease Burden
Influenza Complications

- **Moderate Illness:**
  - Otitis media (in young children), sinusitis.
  - Exacerbation of chronic disease.

- **Severe to Critical Illness:**
  - Exacerbation of chronic disease.
  - Respiratory: viral pneumonia, croup, status asthmaticus, bronchiolitis, tracheitis, Acute Respiratory Distress Syndrome.
  - Cardiac: myocarditis, pericarditis, myocardial infarction.
  - Neurologic: encephalopathy & encephalitis, stroke, Guillain-Barre syndrome (GBS), Acute Disseminated Encephalomyelitis (ADEM), Reye syndrome.
  - Bacterial co-infections (e.g. pneumonia).
  - Musculoskeletal: myositis, rhabdomyolysis.
  - Multi-organ failure (respiratory, renal failure, septic shock).
  - Healthcare-associated infections (e.g. ventilator-associated pneumonia).
Groups at Increased Risk for Influenza Complications and Severe Illness

• Children under 5 years and adults aged 65 years and older.
• Persons with chronic medical conditions, including pulmonary (including asthma) or cardiovascular (excluding isolated hypertension), renal, hepatic, neurologic (including persons who have had a stroke) and neurodevelopmental, hematologic, metabolic or endocrine disorders (including diabetes mellitus).
• Persons who are immunocompromised.
• Persons with extreme obesity (BMI ≥40).
• Children and adolescents who are receiving aspirin-or salicylate-containing medications (who might be at risk for Reye syndrome after influenza virus infection).
• Residents of nursing homes and other long-term care facilities.
• Pregnant persons and people up to 2 weeks postpartum.
• People from certain racial and ethnic minority groups, including non-Hispanic Black, Hispanic or Latino, and American Indian or Alaska Native persons.

https://www.cdc.gov/flu/highrisk/index.htm
CDC Influenza Surveillance

- Includes data from several systems examining various aspects of influenza activity (e.g., characteristics of circulating viruses; surveillance of outpatient illnesses, hospitalizations, and deaths).
- We’ll focus here on two indices of severe illness: hospitalizations and deaths.
Influenza-Associated Hospitalizations—FluSurv-NET

Cumulative hospitalizations/100,000 population
2022-23 season
Overall and by age group

≥65 yrs: 187.3
0-4 yrs: 80.6
50-64 yrs: 67.9
5-17 yrs: 29.4
18-49 yrs: 27.2
Overall: 61.4
Influenza-Associated Hospitalizations—FluSurv-NET

Cumulative hospitalizations/100,000 population
2009-10 through 2022-23 seasons
(Selected seasons labeled)
All age groups

2017-18: 102.9
2022-23: 62.4
2021-22: 17.6
2011-12: 8.7
2020-21: 0.8
Pediatric Influenza Mortality Surveillance

- Pediatric deaths associated with lab-confirmed influenza are reportable since 2004.
- Approx. 50% of deaths occur in children with no risk factors for severe influenza illness.
- Each season, approx. 80% of those eligible for vaccination were not vaccinated for the season.

Annual Influenza Burden Estimates

While not all seasonal influenza is reportable, influenza burden can be estimated using modeling methods, including information drawn from:

- Surveillance data
- Testing practices
- Test characteristics
- Death certificate data

From 2010-11 through 2021-22, estimated annual influenza burden ranged from:
U.S. Influenza Vaccination Recommendations
Influenza Immunization

The adult dosage recommended by the advisory committee for initial immunization is 1.0 cc. (500 cca 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 reinoculated 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 recurrence 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. Davenport, M.D., University of Michigan; Morris Schaefer, 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 Institutes of Allergy and Infectious Diseases; Public Health Service; Thomas P. Sellers, M.D., Georgia State Department of Health, and Glenn S. Usher, M.D., Communicable Disease Center, Public Health Service.

Vaccination recommended for:
- Persons of any age with chronic debilitating conditions.
- Pregnant women.
- All persons aged 65 years or older.
Ages ≥65 years
Pregnant women 2\textsuperscript{nd}/3\textsuperscript{rd} trimester
Any age with chronic medical conditions
Contacts of recommended groups
Health care personnel

\textbf{ACIP Influenza Vaccine Recommendations Expansion, 2000-2010}

- Ages ≥65 years
- Pregnant women 2\textsuperscript{nd}/3\textsuperscript{rd} trimester
- Any age with chronic medical conditions
- Contacts of recommended groups
- Health care personnel

+ Healthy children ages 6-23 months
+ Healthy children ages 24-59 months
+ Healthy children ages 5-18 years—Vaccination recommended for all ≥6 months

- Healthy adults ages 19-49 years—Vaccination recommended for all ≥6 months

- Healthy children ages 6-23 months
- Pregnant women in all trimesters
- Healthy children ages 24-59 months
- Healthy children ages 5-18 years
- Healthy adults ages 19-49 years—Vaccination recommended for all ≥6 months

Pre-2000
2000
2003
2004
2006
2008
2010

+ Healthy adults ages 50-64 years
Pregnant women in all trimesters
+ Healthy children ages 5-18 years
Annual Influenza Vaccination

• Recommended for all ages 6 months and older who do not have contraindications.
• Children 9 years and older and adults need one dose for the season.
• Some children ages 6 months through 8 years need two doses:
  - If they have not received a total of ≥2 doses by the July 1 prior to the start of the season,
  - Or, if their influenza vaccination history is unknown.

Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023–24 Influenza Season | MMWR (cdc.gov)
Influenza Vaccine Types

- Currently 3 vaccine types (inactivated, recombinant, live attenuated); 9 brands.
- Inactivated vaccines include standard dose unadjuvanted, high-dose unadjuvanted, and standard-dose adjuvanted.
- All are quadrivalent (contain 1 A(H1N1), 1 A(H3N2), 1 B/Victoria, 1 B/Yamagata).
- Approved ages vary; none are approved for under age 6 months.
- Any age-appropriate vaccine can be used.
  - Live attenuated vaccine not recommended in pregnancy or for those with some medical conditions
  - No preferential recommendations for persons ages 6 months through 64 years.
  - High-dose inactivated, recombinant, and adjuvanted inactivated are preferred for ages ≥65 years.

- Pre-2003-04: Standard-dose inactivated (egg-based)
- 2003-04: Live attenuated (nasal spray; egg-based)
- 2010-11: High-dose inactivated (egg-based)
- 2013-14: Cell culture inactivated and Recombinant (nonegg-based)
- 2016-17 adjuvanted inactivated (egg-based)
<table>
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<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>
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<td>Standard-dose, unadjuvanted inactivated (IIIV4)</td>
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<td>Fluarix Quadrivalent</td>
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<td>High-dose inactivated (HD-IIIV4)</td>
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<tr>
<td>Live attenuated (LAIV4)</td>
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</tbody>
</table>

IIIV4=quadrivalent inactivated influenza vaccine  RIV4=quadrivalent recombinant influenza vaccine  LAIV4=quadrivalent live attenuated influenza vaccine

![Not approved for age group](image)
![Egg-based](image)
![Not egg-based](image)
Influenza Season Timing

Flu activity peak months in the U.S. from the 1982-1983 through 2021-2022 flu seasons*

* There was no discernible peak in activity during the 2020-2021 season due to the uncharacteristically low level of influenza virus circulation that season.

CDC. The Flu Season. https://www.cdc.gov/flu/about/season/index.html
Waning of Vaccine-Induced Immunity

• Observed in many studies.
  – Variability in rate and degree to which waning occurs across seasons, as well as among different age groups.
  – Most consistently observed among older adults.
  – Noted among children in a few studies.
    › However, fewer studies provide results for children.
  – In some studies, more pronounced for H3N2 viruses than for H1N1 viruses.

• Variability of results, combined with unpredictability of flu season timing, prevents determination of an ideal time to vaccinate that will generalize across seasons.
Timing of Vaccination

- Vaccination during July and August is not recommended for most groups because of the possible waning of immunity over the course of the influenza season.

- For most persons who need only 1 dose of influenza vaccine for the season, vaccination should ideally be offered during September or October.

- However, vaccination should continue after October and throughout the influenza season as long as influenza viruses are circulating and unexpired vaccine is available.

https://www.cdc.gov/mmwr/volumes/71/rr/rr7101a1.htm
Timing of Vaccination—2022-23

Considerations for specific groups:

• **Most adults (particularly ages ≥65 years) and pregnant persons in 1st or 2nd trimester:** July and August should be avoided unless there is concern that vaccination later in the season might not be possible.

• **Children who require 2 doses:** Should receive first dose as soon as possible (including during July and August, if vaccine is available) to allow the second dose (which must be administered ≥4 weeks later) to be received, ideally, by the end of October.

• **Children who require only 1 dose:** Vaccination during July and August can be considered for children of any age who need only 1 dose of influenza vaccine for the season.
  – Not as much evidence for waning as adults (though there are fewer studies including children).
  – Children in the group might visit healthcare providers in late summer.

• **Pregnant persons in 3rd trimester during July/August:** Vaccination during July and August can be considered (can reduce risk for influenza illness in infants during the first months after birth).

[https://www.cdc.gov/mmwr/volumes/71/rr/rr7101a1.htm](https://www.cdc.gov/mmwr/volumes/71/rr/rr7101a1.htm)
Benefits of Influenza Vaccination
Influenza Vaccine Effectiveness (VE)

- Varies dependent upon factors including
  - Predominant viruses,
  - “Match” between vaccine and circulating viruses,
  - Age and health of recipient.
- Typically greatest in older children and younger adults.
- Tends to be higher in H1N1-predominant seasons than in H3N2-predominant seasons.
- Assessed each season through several CDC networks.

<table>
<thead>
<tr>
<th>Season</th>
<th>VE, %</th>
<th>95% CI</th>
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<tbody>
<tr>
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<td>47</td>
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<tr>
<td>2012-13</td>
<td>49</td>
<td>(43--55)</td>
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<tr>
<td>2013-14</td>
<td>52</td>
<td>(44--59)</td>
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<td>2014-15</td>
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<td>(10--27)</td>
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<td>(41--55)</td>
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<td>2018-19</td>
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<td>(21--35)</td>
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<td>2019-20</td>
<td>39</td>
<td>(32--44)</td>
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<tr>
<td>2021-22</td>
<td>36</td>
<td>(21--48)</td>
</tr>
</tbody>
</table>
Influenza Vaccine “Match” and Vaccine Effectiveness

• Vaccine composition (the viruses that are represented) is considered each year.
  - Composition usually changes each season.
  - Must be determined months in advance (in the U.S., determined in early March).
  - Selection is based on review of global surveillance data.
  - Viruses selected are those anticipated to circulate in the coming season.
  - **However**, degree of match varies since influenza viruses **constantly change**.

• During seasons when influenza vaccine viruses are similar to circulating flu viruses, vaccination has been shown to reduce the risk of medically-attended influenza by 40% to 60%.
Estimated Annual Influenza Burden Averted through Vaccination

- Based on annual burden and vaccine effectiveness estimates.
- Substantial burden averted even with modest vaccine effectiveness:
- E.g., for the 2017-18 seasons
  - Vaccine effectiveness: 38%
  - Estimated burden averted:
    › 5.9 million illnesses
    › 8.2 thousand hospitalizations
    › 4.8 thousand deaths

From 2010-11 through 2021-22, estimated annual influenza burden averted through vaccination ranged from:

- 1 to 12 thousand deaths
- 22 to 100 thousand hospitalizations
- 1.4 to 7.0 million illnesses

Estimated Influenza Illnesses, Medical Visits, and Hospitalizations Averted by Vaccination | CDC
Thanks!

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.