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August 2020 ~ Resource #360801

Flu Vaccines for 2020-21

CDC has released information about the 2020-21 influenza season. This information (and the specific strains covered in this year's vaccines) can be found at: https://www.cdc.gov/flu/season/faq-flu-season-2020-2021.htm. Items that are addressed include the following:

- **Influenza vaccination is recommended for everyone ages six months and older** who do not have contraindications, using any age-appropriate vaccine.[4]
  - In light of COVID-19, it's more important than ever to get a flu vaccine.[4] The flu vaccine won't protect against COVID-19, but getting the flu vaccine can help conserve healthcare resources, by reducing the risk of flu illnesses, hospitalizations, and death.[4] See the CDC guidance for vaccinating during a pandemic at https://www.cdc.gov/vaccines/pandemic-guidance/index.html.
  - The LAIV4 (live, quadrivalent, intranasal flu vaccine; *FluMist*) is an option endorsed by the American Academy of Pediatrics for the 2020-21 flu season.[13] Advisory Committee on Immunization Practices recommendations for the 2020-21 season are not available at the time of publication.
- Encourage patients to try to complete vaccination in September or October.[4] However, don't miss an opportunity to vaccinate due to fears the vaccine's effectiveness will not last throughout the entire flu season. Though delayed vaccination may lead to increased immunity later in the season, it could also lead to missed opportunities to vaccinate, and is not recommended.[19] Some evidence suggests that vaccination early in the season may lead to "waning" or "wearing off" before the end of the flu season.[23] However, this has not been consistently seen from year to year, nor among different patient populations. In addition, the timing of flu outbreaks is unpredictable. Note, it is not recommended (due to lack of data) to repeat a flu vaccine in a fully vaccinated patient due to fears of waning from vaccinating early in the season (e.g., August, September).[11]
- Continue to vaccinate as long as flu viruses are circulating.[4]

Continue to the end of this document for information about when two doses of influenza vaccine are needed; vaccination with an acute illness; vaccinating immunocompromised, pregnant, or breastfeeding patients; live vaccine information, and managing patients with an egg allergy. The chart below provides information about approved influenza vaccines for the 2020-21 season including FDA-approved ages for use, route of administration, dose, and cost.

Abbreviations: IM = intramuscular; MDV = multidose vial; PFS = pre-filled syringe; SDV = single-dose vial.

Brand Name Manufacturer[a]	Route[a]	Approved Ages for Use[a]	Availability[a] (Cost/dose[b])	Contains Thimerosal?[a]	Dose[a]	Comments[a]
Quadrivalent inactivated (IIV4): protects against two influenza A-like viruses and two influenza B-like viruses.[4]						
Afluria Quadrivalent Seqirus	IM	≥6 months	0.25 mL and 0.5 mL PFS ($18.65) 5 mL MDV ($17.26)	Yes (MDV only)	6-35 months: • 0.25 mL ≥36 months: • 0.5 mL	• No latex • Once entered, the MDV should be discarded within 28 days. • *PharmaJet* Stratis needle-free injector approved for ages 18-64 years.

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Brand Name Manufacturer[a]	**Route**[a]	**Approved Ages for Use**[a]	**Availability**[a] **(Cost/dose**[b]**)**	**Contains Thimerosal?**[a]	**Dose**[a]	**Comments**[a]
Quadrivalent inactivated (IIV4), continued (Protects against two influenza A-like viruses and two influenza B-like viruses.[4])						
Fluad Quadrivalent Seqirus	IM	≥65 years	0.5 mL PFS ($53.63)	No	0.5 mL	• No latex • This **adjuvanted vaccine** may be abbreviated **aIIV4**.[17] • Adverse effects (e.g., injection site reactions, fatigue, myalgias, headache) seem similar to the trivalent inactivated, adjuvanted vaccine (aIIV3; see *Fluad* row below). • Coadministration with other **adjuvanted vaccines** (e.g., *Heplisav-B*, *Shingrix*) has not been studied. There are theoretical concerns about more side effects. Don't delay flu vaccination if *Fluad Quadrivalent* is the only flu vaccine available.[19]
Fluarix Quadrivalent GSK	IM	≥6 months	0.5 mL PFS ($17.30)	No	0.5 mL	• No latex
Flucelvax Quadrivalent Seqirus	IM	≥4 years	0.5 mL PFS ($25.76) 5 mL MDV ($24.42)	Yes (MDV only)	0.5 mL	• This **cell-cultured** vaccine may be abbreviated **ccIIV4**.[16] • No latex • **Egg-free**[4]
FluLaval Quadrivalent GSK	IM	≥6 months	0.5 mL PFS ($17.30)	No	0.5 mL	• No latex

More. . .

Brand Name Manufacturer[a]	**Route**[a]	**Approved Ages for Use**[a]	**Availability**[a] **(Cost/dose**[b]**)**	**Contains Thimerosal?**[a]	**Dose**[a]	**Comments**[a]
Quadrivalent inactivated (IIV4), continued (Protects against two influenza A-like viruses and two influenza B-like viruses.[4])						
Fluzone Quadrivalent Sanofi Pasteur	IM	≥6 months	0.25 mL PFS ($18.14) 0.5 mL PFS and SDV ($18.14) 5 mL MDV ($16.94)	Yes (MDV only)	6-35 months: • 0.25 mL or 0.5 mL ≥36 months: • 0.5 mL	• No latex
Fluzone Quadrivalent High-Dose Sanofi Pasteur Contains 60 mcg of each virus strain compared to 15 mcg in standard-dose IM vaccines.[21]	IM	≥65 years	0.7 mL PFS ($53.62)	No	0.7 mL	• No latex • Higher risk of adverse effects (injection site reactions, myalgia, headache) than the previous high-dose, inactivated, trivalent formulation (IIV3) (which had higher risk of adverse effects vs standard dose vaccine). • The trivalent version provided modestly greater protection against lab-confirmed flu vs standard-dose trivalent vaccine in patients ≥65 years of age (n=31,989; NNT=200), [Evidence level A-1].[3,19] There is no comparative data for the quadrivalent vaccines.
Trivalent inactivated (IIV3): Protects against two influenza A-like viruses and one influenza B-like viruses.[4]						
Fluad Seqirus *Continued…*	IM	≥65 years	0.5 mL PFS ($52.23)	No	0.5 mL	• No latex • This **adjuvanted vaccine** may be abbreviated **aIIV3**.[16] • May provide modestly greater protection against laboratory confirmed flu vs non-adjuvanted trivalent vaccine in patients ≥65 years of age (n=227, unable to calculate NNT), [Evidence Level B-2].[5,19] • Higher risk of adverse effects (injection site reactions, fatigue, myalgias, headache) than inactivated trivalent formulation (IIV3).[19]

More. . .

Brand Name Manufacturer[a]	**Route**[a]	**Approved Ages for Use**[a]	**Availability**[a] **(Cost/dose**[b]**)**	**Contains Thimerosal?**[a]	**Dose**[a]	**Comments**[a]
Trivalent inactivated (IIV3), continued (Protects against two influenza A-like viruses and one influenza B-like viruses.[4])						
***Fluad*, continued**						• Coadministration with other **adjuvanted vaccines** (e.g., *Heplisav-B*, *Shingrix*) has not been studied. There are theoretical concerns about more side effects. Don't delay flu vaccination if *Fluad* is the only flu vaccine available.[19]
Quadrivalent recombinant (RIV4): protects against two influenza A-like viruses and two influenza B-like viruses.[4]						
Flublok Quadrivalent Sanofi Pasteur Contains 45 mcg of each virus strain compared to 15 mcg in standard-dose IM vaccines.[19]	IM	≥18 years	0.5 mL PFS ($53.62)	No	0.5 mL	• No latex • **Egg-free** • May be slightly more effective in preventing laboratory confirmed flu than IIV4 vaccines in patients ≥50 years of age (N=8,604; NNT=100), [Evidence Level A-1].[2,19]
Quadrivalent live-attenuated (LAIV4): protects against two influenza A-like viruses and two influenza B-like viruses.[4]						
FluMist Quadrivalent MedImmune *Has not been studied in patients with severe asthma or active wheezing.	Intranasal	2 to 49 years	0.2 mL prefilled intranasal sprayer ($23.70)	No	0.1 mL per nostril	• No latex • For healthy, non-pregnant patients.[18] • Avoid in patients with contraindications to live vaccines (e.g., chronic diseases, immunosuppression, severely immunosuppressed close contacts).[19] • Avoid in children between the ages of 2 and 4 years with asthma or a history of wheezing in the last 12 months.[18] • Avoid in patients who have recently received influenza antivirals (e.g., oseltamivir, zanamivir).[18,c] • Should NOT be used in people with asplenia, cochlear implants, or active cerebrospinal fluid leaks.[1]

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a. **Information is from the following U.S. product labeling unless otherwise specified**: *Afluria Quadrivalent* (March 2020); *Fluarix Quadrivalent* (July 2020); *Flucelvax Quadrivalent* (March 2020); *FluLaval Quadrivalent* (July 2020); *Fluzone Quadrivalent* (July 2020); *Fluad* (June 2020); *Fluad Quadrivalent* (June 2020); *Fluzone Quadrivalent High-Dose* (July 2020); *Flublok Quadrivalent* (July 2020); *FluMist Quadrivalent* (August 2020).
b. Pricing based on wholesale acquisition cost (WAC). Medication pricing by Elsevier when available and the CDC Vaccine price list (https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html), accessed August 2020.
c. There are no data available about LAIV use after antivirals. Most sources advise avoiding LAIV within 48 hours of an antiviral. However, based on antiviral half-lives, it is possible antivirals could interfere with LAIV effectiveness if LAIV is given within 48 hours (oseltamivir and zanamivir), five days (peramivir), or 17 days (baloxavir) AFTER the antiviral.[22]

Information and Clinical Pearls about Influenza Vaccine Administration

- Live-attenuated* and inactivated influenza vaccines can be given at the same time as other vaccines, using separate administration sites.[15] (See the *Fluad* rows above concerning co-administration of two adjuvanted vaccines.) *If two live vaccines (including LAIV4) are NOT given on the same day, they should be administered at least four weeks apart.[15]
- To provide optimal protection, **children between the ages of 6 months and eight years** should receive two doses of influenza vaccine (separated by at least four weeks) if they have not received at least two doses of influenza vaccine (separated by at least four weeks) prior to July 1, 2020.[20] For children who should receive two doses, if the child turns nine years old between doses one and two of the vaccine, two doses are still recommended.[11]
- **Immunocompromised patients** may receive any licensed, recommended, age-appropriate injectable flu vaccine.[14]
- Vaccinate **pregnant women** (any trimester) with any licensed, recommended, age-appropriate injectable flu vaccine, regardless of thimerosal content.[6,19]
  - Risk of influenza and potential complications in pregnant woman and/or the fetus exceeds possible risks associated with influenza vaccination.[7,8]
  - Flu vaccination is safe during breastfeeding. Vaccinate post-partum women who did not receive an influenza vaccine while pregnant.[6,9,10]
- **Patients with a history of severe egg allergy** (symptoms more severe than hives [e.g., angioedema, respiratory distress, requiring epinephrine]) can usually tolerate any flu vaccine. But they should receive the vaccine in a medical setting under the supervision of a healthcare professional who can identify and treat severe allergic reactions, if necessary. *Flublok Quadrivalent* and *Flucelvax Quadrivalent* are the only influenza vaccines considered egg-free.[19] See our chart, *Flu Vaccination and Egg Allergy*, for answers to questions about vaccinating egg-allergic patients.
- **Avoid missed opportunities to vaccinate** by giving the influenza vaccine to patients who cannot remember if they received this season's influenza vaccine, even if this means giving a second dose to some patients.[11]
- **Continue to give the flu vaccine to patients with mild acute illnesses** in order to avoid missed opportunities to vaccinate. Mild acute illness with or without fever (e.g., diarrhea, upper respiratory infection) is not a contraindication to receiving the vaccine.[12] Consider delaying vaccination in patients with moderate to severe illness as vaccination side effects (e.g., fever, malaise) may make it difficult to assess management of acute illness.[12] In addition, though mild illness is not a contraindication, defer flu vaccination in patients with confirmed or suspected COVID-19 (regardless of symptoms), to avoid exposing healthcare personnel and other patients.[4]

More. . .

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*****	1. High-quality RCT 2. SR/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*****	1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).
RCT = randomized controlled trial; **SR** = systematic review
[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. http://www.aafp.org/afp/2004/0201/p548.pdf.]

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References

1. American Academy of Pediatrics. AAP news: CDC committee addresses COVID-19, flu, MenACWY vaccines. June 25, 2020. https://www.aappublications.org/news/2020/06/25/acip062520#:~:text=The%20CDC's%20policy%20will%20clarify,or%20active%20cerebrospinal%20fluid%20leaks. (Accessed July 17, 2020).
2. Dunkle LM, Izikson R, Patriarca P, et al. Efficacy of recombinant influenza vaccine in adults 50 years of age or older. *N Engl J Med* 2017;376:2427-36.
3. DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. *N Engl J Med* 2014;371:635-45.
4. CDC. Influenza (flu). Frequently asked influenza (flu) questions: 2020-2021 season. Updated August 31, 2020. https://www.cdc.gov/flu/season/faq-flu-season-2020-2021.htm. (Accessed September 3, 2020).
5. Domnich A, Arata L, Amicizia D, et al. Effectiveness of MF59-adjuvanted seasonal influenza vaccine in the elderly a systematic review and meta-analysis. *Vaccine* 2017;35:513-20.
6. CDC. Flu vaccine safety and pregnancy. October 16, 2019. https://www.cdc.gov/flu/highrisk/qa_vacpregnant.htm. (Accessed July 10, 2020).
7. Zerbo O, Modaressi S, Chan B, et al. No association between influenza vaccination during pregnancy and adverse birth outcomes. *Vaccine* 2017;35:3186-90.
8. CDC. Addressing concerns pregnant women might have about influenza vaccine safety. October 22, 2019. https://www.cdc.gov/flu/professionals/vaccination/vaccination-possible-safety-signal.html. (Accessed July 10, 2020).
9. Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2018-2019. *Pediatrics* 2018;142:e20182367.
10. The American College of Obstetricians and Gynecologists. The flu vaccine and pregnancy. October 2015. https://www.acog.org/patient-resources/faqs/pregnancy/the-flu-vaccine-and-pregnancy. (Accessed July 10, 2020).
11. Immunization Action Coalition. Ask the experts: influenza. Updated November 7, 2019. https://www.immunize.org/askexperts/experts_inf.asp. (Accessed July 10, 2020).
12. Immunization Action Coalition. Ask the experts: precautions and contraindications. Updated July 11, 2019. http://www.immunize.org/askexperts/precautions-contraindications.asp. (Accessed July 10, 2020).
13. Jenco M. AAP: no flu vaccine preference for 2020-'21season. March 27, 2020. https://www.aappublications.org/news/2020/03/27/fluvaccine032720. (Accessed July 10, 2020).
14. CDC. Altered immunocompetence: general best practice guidelines for immunization. Best practices guidance of the Advisory Committee on Immunization Practices (ACIP). Last reviewed August 20, 2019. https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html. (Accessed July 10, 2020).
15. CDC. Influenza (flu). Influenza vaccination: a summary for clinicians. September 18, 2019. https://www.cdc.gov/flu/professionals/vaccination/vax-summary.htm#:~:text=Inactivated%20or%20live%20

More. . .

vaccines%20can,another%20live%20vaccine%20is%20administered. (Accessed July 13, 2020).
16. Immunization Action Coalition. Influenza vaccine products for the 2019-2020 influenza season. September 2019. https://www.immunize.org/catg.d/p4072.pdf. (Accessed July 13, 2020).
17. Blue Cross Blue Shield of Rhode Island. Payment policy: immunizations adult and pediatric. Updated February 2019. https://www.bcbsri.com/providers/sites/providers/files/policies/2019/12/2019%20Immunizations%20Adult%20and%20Pediatric2_0.pdf. (Accessed July 13, 2020).
18. CDC. Influenza (flu). Live attenuated influenza vaccine [LAIV] (the nasal spray flu vaccine). Updated November 7, 2019. https://www.cdc.gov/flu/prevent/nasalspray.htm. (Accessed July 13, 2020).
19. CDC. Prevention and control of seasonal influenza with vaccines: recommendations of the advisory committee on immunization practices – United States, 2020-21 influenza season. August 21, 2020. https://www.cdc.gov/mmwr/volumes/69/rr/pdfs/rr6908a1-H.pdf. (Accessed September 3, 2020).
20. American Academy of Pediatrics. Influenza implementation guide. Updated September 2019. https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/immunizations/Influenza-Implementation-Guidance/Pages/Annual-AAP-Influenza-Policy.aspx. (Accessed July 14, 2020).
21. National adult and influenza immunization summit. ACIP influenza update. May 21, 2020. https://www.izsummitpartners.org/content/uploads/2020/05/1e-1-grohskopf-acip-influenza-update.pdf. (Accessed July 17, 2020).
22. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. 2020. http://www.clinicalkey.com. (Accessed July 17, 2020).
23. Ray GT, Lewis N, Klein NP, et al. Intraseason waning of influenza vaccine effectiveness. *Clin Infect Dis* 2019;68:1623-30.

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