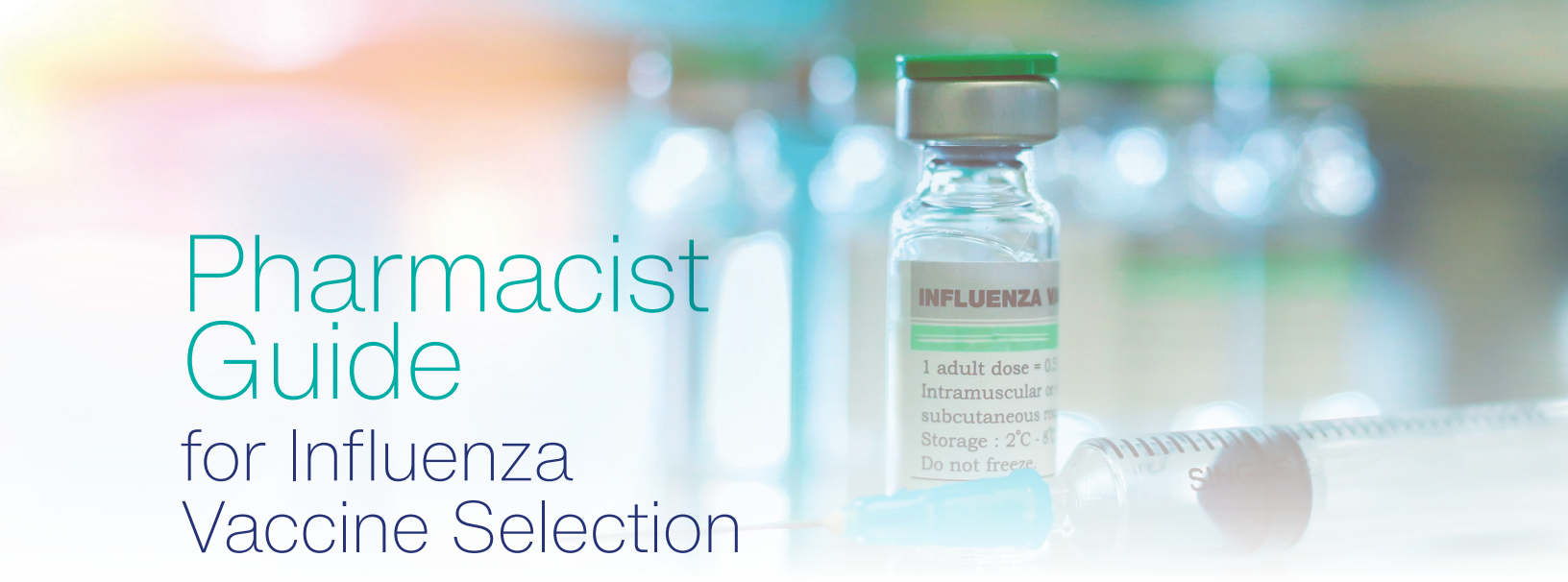

Pharmacist Guide for Influenza Vaccine Selection

FOR PATIENTS AGED 50 YEARS AND OLDER

The 2021–22 influenza vaccine will have several versions, all of which will be quadrivalent vaccines (Table 1). The Advisory Committee on Immunization Practices (ACIP) recommends influenza vaccine for all persons 6 months of age and older. According to ACIP, any age-appropriate brand of vaccine would be considered valid, provided that no contraindications or precautions exist.[1] Pharmacists have several options in influenza vaccines to offer to patients each flu season. This guide will help pharmacists choose a vaccine for people at higher risk for complications due to influenza, particularly those aged 50 years and older. While any age-appropriate vaccine would be valid, this guide discusses the technology and clinical data to assist pharmacists in assessing, recommending, counseling, and administering influenza vaccines to this patient population.

TABLE 1. Influenza Vaccines by Age Indication.[1]

Vaccine Type		0 through 6 months	6 through 23 months	2 through 17 years	18 through 49 years	50 through 64 years	≥ 65 years
IIV4	Standard-dose, unadjuvanted inactivated (IIV4)		Afluria Quadrivalent Fluarix Quadrivalent FluLaval Quadrivalent Fluzone Quadrivalent				
	Cell culture–based inactivated (ccIIV4)			Flucelvax Quadrivalent			
	Adjuvanted inactivated (aIIV4)						Fluad Quadrivalent
	High-dose inactivated (HD-IIV4)						Fluzone High-Dose Quadrivalent
RIV4	Recombinant (RIV4)				Flublok Quadrivalent		
LAIV4	Live attenuated (LAIV4)			FluMist Quadrivalent			

aIIV4 = adjuvanted quadrivalent inactivated influenza vaccine; **ccIIV4** = cell culture–based quadrivalent inactivated influenza vaccine; **HD-IIV4** = high-dose quadrivalent inactivated influenza vaccine; **IIV4** = quadrivalent inactivated influenza vaccine; **LAIV4** = quadrivalent live attenuated influenza vaccine; **RIV4** = recombinant quadrivalent influenza vaccine.

Not approved for age group | Not egg-based | Egg-based

Older adults are recognized as a high-risk group for severe influenza illness. Antibody response to influenza vaccination is decreased in older adults, and the duration of protection may not last as long compared with younger adults.

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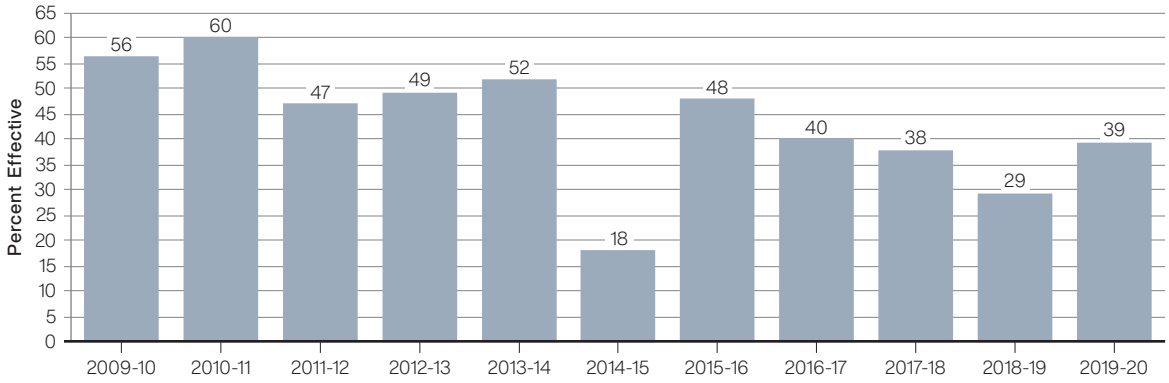
Persons Aged 50 Years and Older[2]

- Higher risk for complications due to influenza
- Antibody response to influenza vaccine may be decreased
- Waning immunity from influenza vaccine

Selecting the best vaccine depends on the patients who the pharmacist will vaccinate during the flu season. Pharmacists should aim to vaccinate their patients by the end of October and should avoid vaccinating patients too early in July and August. Data suggest that vaccinating too early may not provide enough protection later in the flu season. Observational studies suggest that the vaccine effectiveness is greater than zero for approximately 5 to 6 months after vaccination. However, older adults have more pronounced waning of protection.[3]

Figure 1 shows vaccine effectiveness of all seasonal influenza vaccines based on the U.S. Flu Vaccine Effectiveness Network. Vaccine effectiveness depends on several factors, including how well matched the circulating strains are with the components in the vaccine.[4]

FIGURE 1. Adjusted Influenza Vaccine Effectiveness by Season[4]



EVALUATING THE EVIDENCE

There are several things to consider when studying how well the influenza vaccination works. First is distinguishing between efficacy and effectiveness. Effectiveness outcomes mimic real-life situations, whereas efficacy data come from randomized controlled trials (RCTs). The outcomes of interest are also important to consider. Laboratory-confirmed influenza by either viral culture or reverse transcriptase–polymerase chain reaction is thought to provide the most persuasive evidence. Other outcomes such as influenza-like illness or medically attended acute respiratory illness are helpful but may include other pathogens that an influenza vaccine would not be expected to prevent. Serum antibody titers against hemagglutinin (hemagglutination-inhibition [HAI] antibody titers) represent another outcome for vaccination, typically for efficacy. HAI titer thresholds of 32 or 40 have been used to correlate with population-level immunity. In general, an HAI titer ≥40 correlates with approximately 50% clinical protection. However, individual patients may respond differently.[3]

Terminology[3]

Efficacy: prevention of illness among people who are vaccinated while enrolled in RCTs
Effectiveness: prevention of illness among people vaccinated under real-world conditions as measured in observational studies.

Study design is another factor to consider. In any study, limitations may exist that would increase the risk of bias and therefore decrease the study quality. Bias can occur in studies when selecting patients, blinding the outcomes, using incomplete data, reporting selective outcomes, among other types of bias.[3,6] RCTs are the strongest quality of evidence, provided that they do not contain significant limitations. Observational studies, such as cohort studies, case–control studies, or controlled before–after studies, provide a slightly lower quality of evidence. Real-world evidence incorporates real-world data that are collected outside standard study design within routine clinical practice to assess benefits and risks.[5] Clinical experience and expert opinion offer the lowest quality of evidence.

EVIDENCE FOR INFLUENZA VACCINATION IN PATIENTS AGED 50 YEARS AND OLDER

Given the higher risk of severe influenza illness, newer influenza vaccines have been developed specifically targeting high-risk patients. The high-dose inactivated quadrivalent influenza vaccine (HD-IIV4) and adjuvanted inactivated quadrivalent influenza vaccine (aIIV4) are licensed for persons 65 years of age and older. The recombinant quadrivalent influenza vaccine (RIV4) is license for persons 18 years of age and older. There are no RCTs comparing these vaccines directly against one another, but they have been compared against standard-dose influenza vaccines. Some of the studies have been done with trivalent versions of the vaccine and benefits are inferred with a newer quadrivalent formulation.[3]

HD-IIV4 (Fluzone High-Dose)

HD-IIV4 contains 60 µg of hemagglutinin antigen per virus strain, which is four times the amount of a standard-dose vaccine. Higher HAI titers have been shown with the higher dose in persons 65 years of age and older. A RCT of over 31,000 people compared high-dose trivalent inactivated influenza vaccine (HD-IIV3) with standard-dose trivalent inactivated influenza vaccine (SD-IIV3) during the 2011–12 and 2012–13 influenza seasons. The primary endpoint of this study was laboratory-confirmed influenza. Results showed 1.4% of participants developed influenza in the high-dose group versus 1.9% in the standard-dose group. The relative efficacy was 24.2% (95% CI, 9.7 to 36.5), which satisfied a prespecified superiority criterion.[7] This is interpreted as HD-IIV3 is 24% more efficacious than SD-IIV3 in this population.

In a cluster-randomized trial of over 52,000 people ≥65 years during the 2013-14 influenza season, hospital admissions related to pulmonary or influenza-like illnesses were significantly lower in the HD-IIV3 group compared with SD-IIV3 (adjusted relative risk, 0.873; 95% CI, 0.776 to 0.982).[8] This is interpreted as HD-IIV3 had 13% fewer hospital admissions for influenza-like illness compared with SD-IIV3.

Other studies have been done with high-dose influenza vaccine that show a positive benefit compared with standard-dose influenza vaccines, including a probabilistic sensitivity analysis suggesting that HD-IIV3 is 93% likely to be cost saving compared with SD-IIV3.[3,9]

aIIV4 (Fluad Quadrivalent)

The aIIV4 is an adjuvanted, quadrivalent vaccine containing an oil-in-water adjuvant, MF59. Immunogenicity data were studied in aIIV3 and unadjuvanted IIV3 where the aIIV3 met the criteria for non-inferiority for all three vaccine virus strains based on predefined titer thresholds.[3]

A small observational study of 227 vaccinated people aged 65 years and older during the 2011–12 flu season compared aIIV3 with SD-IIV3. The results showed a relative aIIV3 effectiveness of 63% (95% CI, 4 to 86).[10] This is interpreted as the aIIV3 was 63% more effective than SD-IIV3 against laboratory-confirmed influenza. Other studies have shown in improvement for hospitalizations coded for pneumonia and influenza in certain age groups receiving aIIV3.[3]

RIV4 (Flublok Quadrivalent)

The RIV4 is a recombinant influenza vaccine manufactured using insect cells rather than eggs. It contains 45 µg, or three times the hemagglutinin antigen per virus strain. A randomized controlled trial of more than 8,600 people during the 2014–15 influenza season compared RIV4 with SD-IIV4 in people aged 50 years and older. The outcome of the study was laboratory-confirmed influenza and found a modified influenza rate of 2.2% in patients receiving RIV4 and 3.1% in patients receiving SD-IIV4. The relative efficacy was 30% (95% CI, 10 to 47).[11] This is interpreted as the RIV4 was 30% more efficacious than SD-IIV4 in preventing laboratory-confirmed influenza.

SAFETY

In comparative safety studies in older persons, some injection site and systemic reactions were observed more frequently with HD-IIV3 and aIIV3 compared with nonadjuvanted standard-dose influenza vaccine.[3] Serious adverse reactions to any influenza vaccine are rare, with approximately 1.31 cases per million doses.[12]

All egg-based influenza vaccines are contraindicated in persons with a history of severe allergic reaction, such as anaphylaxis, to any component of the vaccine or to a previous dose of any influenza vaccine (i.e., IIV, RIV, and LAIV). The cell culture–based quadrivalent inactivated influenza vaccine (ccIIV4) is contraindicated in persons with a history of severe allergic reaction to ccIIV4, ccIIV3, or any component of ccIIV4. RIV4 is contraindicated in persons with a severe allergic reaction to RIV4, RIV3, or any component of RIV4.1

CONCLUSION

There is some evidence that support the efficacy and effectiveness of certain influenza vaccines over others in older adults. Pharmacists may want to consider these data as they anticipate the vaccination needs of their patients during the influenza season. Annual influenza vaccination is recommended for all persons aged 6 months and older without contraindications. Any age-appropriate dose of influenza vaccine would be considered valid in a patient.

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REFERENCES

1. Grohskopf L. WG Considerations and Proposed Influenza Vaccine Recommendations, 2021-22. Presented at the meeting of the Advisory Committee on Immunization Practices; June 24, 2021. Available at: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-06/03-influenza-grohskopf-508.pdf. Accessed July 6, 2021.
2. Goodwin K, Viboud C, Simonsen L. Antibody response to influenza vaccination in the elderly: a quantitative review. Vaccine. 2006;24(8):1159–1169. doi: 10.1016/j.vaccine.2005.08.105
3. Grohskopf LA, Alyanak E, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2020–21 influenza season. MMWR Recomm Rep. 2020;69(No. RR-8):1–24. doi: 10.15585/mmwr.rr6908a1
4. Centers for Disease Control and Prevention. CDC seasonal flu vaccine effectiveness studies. December 11, 2020. Available at: https://www.cdc.gov/flu/vaccines-work/effectiveness-studies.htm. Accessed July 8, 2021
5. U.S. Food and Drug Administration. Real-World Evidence. 2020. Available at: https://www.fda.gov/science-research/science-and-research-special-topics/real-world-evidence. Accessed July 10, 2021
6. Ahmed F. U.S. Advisory Committee on Immunization Practices (ACIP) Handbook for Developing Evidence-Based Recommendations. 2013. Available at: https://www.cdc.gov/vaccines/acip/recs/grade/downloads/handbook.pdf. Accessed July 9, 2021.
7. 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(7):635–645. doi: 10.1056/NEJMoa1315727
8. Gravenstein S, Davidson HE, Taljaard M, et al. Comparative effectiveness of high-dose versus standard-dose influenza vaccination on numbers of US nursing home residents admitted to hospital: a cluster-randomised trial. Lancet Respir Med. 2017;5(9):738–746. doi: 10.1016/S2213-2600(17)30235-7
9. Chit A, Becker DL, DiazGranados CA, et al. Cost-effectiveness of high-dose versus standard-dose inactivated influenza vaccine in adults aged 65 years and older: an economic evaluation of data from a randomised controlled trial. Lancet Infect Dis. 2015;15(12):1459–1466. doi: 10.1016/S1473-3099(15)00249-2
10. Van Buynder PG, Konrad S, Van Buynder JL, et al. The comparative effectiveness of adjuvanted and unadjuvanted trivalent inactivated influenza vaccine (TIV) in the elderly. Vaccine. 2013;31(51):6122–6128. doi: 10.1016/j.vaccine.2013.07.059
11. Dunkle LM, Izikson R, Patriarca P, et al. Efficacy of recombinant influenza vaccine in adults 50 years of age older. N Engl J Med. 2017;376(25):2427–2436. doi: 10.1056/NEJMoa1608862
12. McNeil MM, Weintraub ES, Duffy J, et al. Risk of anaphylaxis after vaccination in children and adults. J Allergy Clin Immunol. 2016;137(3):868–878. doi: 10.1016/j.jaci.2015.07.048

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