Immunizing older adults

The latest recommendations for protecting against flu, pneumococcal pneumonia, shingles, and other preventable conditions

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Alosa Health

Immunizing older adults

Activity Overview:

The goal of this educational program is to provide primary care clinicians with a review of immunizations recommended by the Advisory Committee on Immunization Practices (ACIP) for older adults (age 65 and up): influenza vaccine; pneumococcal vaccines; zoster vaccine; and tetanus and pertussis booster vaccines.

With the addition of a high-dose influenza vaccine for older adults and shifting recommendations regarding the use of PCV13 pneumococcal vaccines, primary care clinicians need to understand current evidence and practice guidelines. As COVID-19 has disrupted health care visits, understanding how to address an interrupted two-shot Zoster immunization series will provide timely guidance.

The education program has several components:

1. Written evidence report (print monograph)
2. Summary document of 4-5 key messages
3. “Academic detailing” educational sessions with trained outreach educators (pharmacists, nurses, physicians) who present the material interactively
4. Reference cards for easy access to key materials
5. Patient education information (brochure/tear off sheets)

Its goal is to critically review and synthesize the most current clinical information on these topics into accessible, non-commercial, evidence-based educational materials, to be taught interactively to providers by specially trained clinical educators.

Target Audience:

The educational program is designed for physicians practicing internal medicine, primary care, family medicine, and geriatrics, and nurses and other health care professionals who deliver primary care.

Learning Objectives:

Upon completion of this activity, participants will be able to:

- Discuss types of influenza vaccines and recommend an annual flu shot for adults 65 and over with a high-dose or adjuvanted vaccine
- Identify adults age 65 and older who should receive the pneumococcal polysaccharide vaccine (PPSV23) and the conjugate vaccine (PCV13)
- Distinguish between the recombinant zoster vaccine (Shingrix) and live zoster vaccine (Zostavax) regarding efficacy in preventing shingles and postherpetic neuralgia
- Review recent recommendations for tetanus protection with either Tdap or Td

Disclosures:

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Vaccination: a powerful way to prevent disease

Despite decades of advances in the science of vaccinations, infectious diseases remain a major worldwide cause of illness and death.[1] Older adults are more susceptible to these diseases due to age-related changes in their immune systems, changes that can sometimes render vaccinations less effective.[1] Deciding which vaccines to administer to older adults and timing vaccine administration can be challenging, but is a key opportunity for clinicians to prevent disabling disease and death.

This Evidence Document summarizes the latest recommendations from the Advisory Committee on Immunization Practices (ACIP) of the U.S. Centers for Disease Control and Prevention (CDC) for the use of vaccines to prevent influenza, pneumococcal disease, shingles, tetanus, and pertussis in older adults. It also provides evidence-based guidance for clinicians that goes beyond—but is consistent with—ACIP recommendations. In 2020 the ACIP announced several important updates to its recommendations, all of which will be explored in detail later in this document:

- Nearly all vaccines released for the 2020-2021 flu season in the US are quadrivalent vaccines. These include standard-dose inactivated vaccines, a high-dose inactivated vaccine (Fluzone), a high-dose recombinant vaccine (Flublok), and an adjuvanted vaccine (Fluad).
- ACIP does not make a formal recommendation to use high-dose vaccines in older adults, but a recent randomized controlled trial (see below) indicates that these vaccines are likely to be more efficacious than standard-dose vaccines in older adults.
- Pneumovax (PPSV23) is recommended for all adults aged 65 years and older, with an option to supplement with Prevnar (PCV13) for selected patients with risk factors.
- The live zoster vaccine (Zostavax) against shingles has been discontinued in favor of the recombinant vaccine (Shingrix).
- For tetanus booster, either Tdap (tetanus, diphtheria, pertussis) or Td (tetanus-diphtheria) is recommended, but Td is no longer preferred.

Influenza

The severity and extent of seasonal influenza outbreaks vary considerably from year to year. This variation is driven by the antigenic characteristics of the circulating viruses, the effectiveness of the vaccines developed each year against the actual (as opposed to predicted) viruses, and the extent and timing of mass influenza vaccinations.

In the 2019-2020 flu season, the CDC estimates that between 39 million and 56 million people in the U.S. became ill with flu, between 410,000 and 740,000 people were hospitalized for the flu, and between 24,000 and 62,000 people died of the flu.[2]

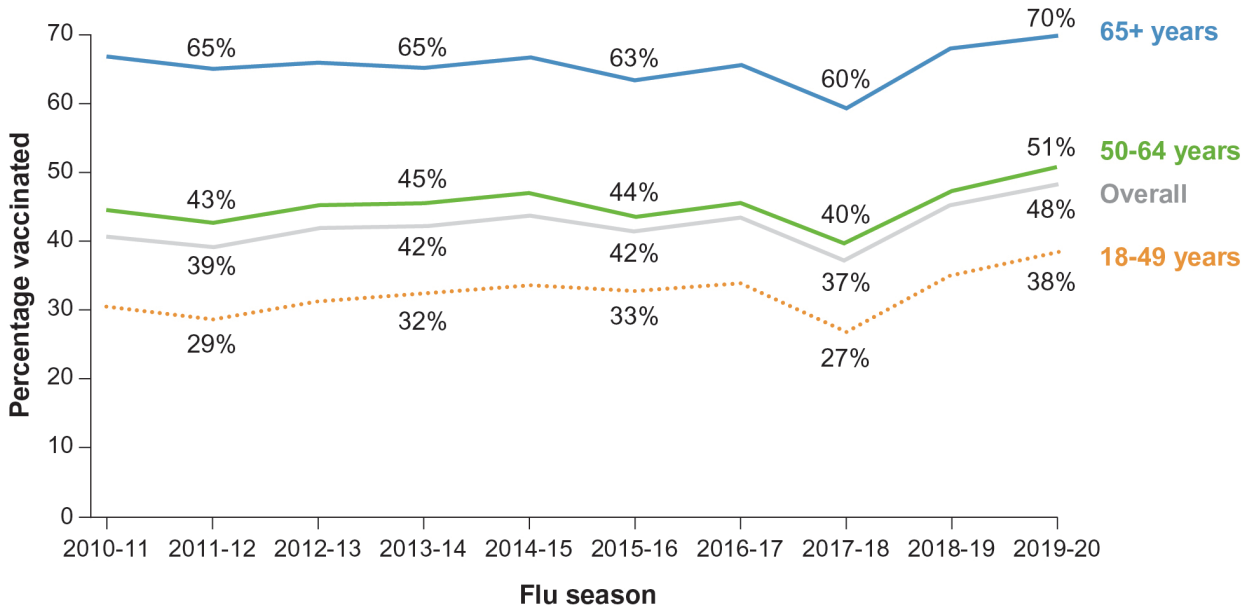
Although the flu vaccine was only 29% effective in 2018-2019, the CDC estimates that it still prevented 4.4 million illnesses, 2.3 million medical visits, 58,000 hospitalizations, and 3,500 deaths in that flu season.[3] Its benefits include reductions in:

- Cases of the flu[4]
- Hospitalizations for the flu[5]
- Flu severity[6]
- Cardiovascular events[7]

- COPD exacerbations[8]

Despite the proven efficacy of flu vaccines and the risks of influenza, only 48% of adults in the U.S. received the flu vaccine in the 2019-2020 flu season.[9] The rate of flu vaccination varied by age, with nearly 70% of adults aged ≥ 65 years getting a flu shot, but only 38% of adults aged 18-49 years doing so (Figure 1).[9] Disturbing racial and ethnic disparities in rates of flu vaccination persist. In the 2019-20 flu season 55% of white individuals received a flu vaccine, compared with only 46% of black and 47% of Hispanic individuals.[9]

Figure 1: Flu vaccination coverage by age in U.S. adults aged ≥ 18 years[9]



With the COVID-19 pandemic, influenza vaccination has become even more important, since concomitant spread of influenza and SARS CoV-2 could cause additional burden of disease and could stretch limited health care resources. (As of December, 2020, seasonal flu activity in the US was unusually low, possibly because of precautions being taken to reduce COVID transmission, according to the CDC, although it warns that incidence may still increase as the season progresses.)[10]

Influenza structure

Influenza virions consist of an outer lipid membrane encapsulating the viral RNA in a roughly spherical shell. The membrane is studded with three proteins crucial for its function: hemagglutinin (HA), neuraminidase (NA), and M2 ion channels.[11]

Influenza types A and B can cause human epidemics, while type C usually causes only mild symptoms and is not thought to cause epidemics.[12]

Influenza mutations

The influenza virus is constantly evolving, primarily in two ways. “Antigenic drift” describes changes due to small mutations in viral genes that lead to changes in the HA and NA surface proteins of the virus. This usually results in viruses that are closely related antigenically and may therefore respond similarly to vaccines.[13] As mutations caused by antigenic drift accumulate, however, the resulting viruses may become antigenically distinct enough that a person’s existing antibodies won’t recognize and neutralize the new virus.

The mutations caused by antigenic drift are the primary reason people can become infected with influenza repeatedly from one year to the next, and is why new flu vaccines must be developed for each flu season.

By contrast, “antigenic shift” describes sudden, significant changes to the HA and/or NA proteins of an influenza A virus. It can occur, for example, when an influenza virus common in animals suddenly acquires the capacity to infect humans. Such a shift occurred in the spring of 2009, when an H1N1 virus common in swine gained the capability of infecting humans, leading to a pandemic.

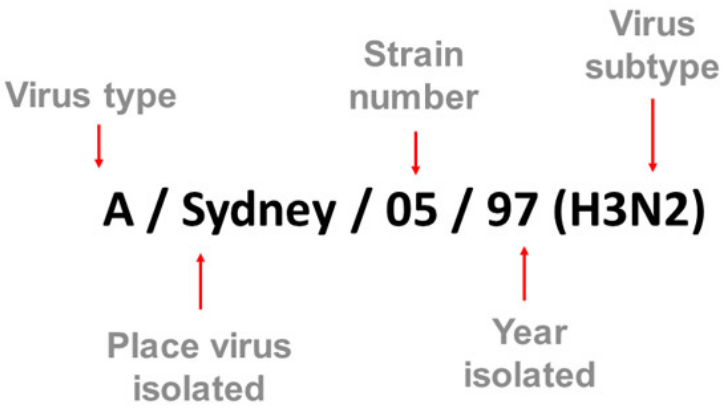
Compared to the continuous small changes resulting from antigenic drift, antigenic shifts (and resulting pandemics) occur much less frequently. Only four flu pandemics have occurred in the past century, for example.[13] Influenza B viruses appear to mutate only via antigenic drift. Influenza A, however, can undergo both antigenic drift and antigenic shift and is therefore the main flu virus to cause pandemics.[13]

Nomenclature

A naming convention for human influenza viruses was adopted by the World Health Organization in 1979 and uses the following components:

- The antigenic type (i.e., A, B, C)
- Geographical origin (e.g., Denver, Taiwan)
- Strain number (e.g., 7, 15)
- Year of collection (e.g., 2009)
- Virus subtype. For influenza A viruses, the HA and NA antigens are listed in parentheses, for example influenza A (H1N1), influenza A (H5N1). For influenza B viruses, subtypes are described in terms of their “lineage,” i.e., either Victoria lineage or Yamagata lineage.

Figure 2: Example of influenza A nomenclature



Influenza vaccines

Effectiveness

Flu vaccines are developed months in advance of flu seasons based on predictions about which viral strains are likely to emerge. Vaccines that protect against three influenza strains are termed "trivalent," while those that protect against four strains are known as "quadrivalent" vaccines. Trivalent vaccines provide coverage for two strains of influenza A and one strain of influenza B, while quadrivalent vaccines provide coverage for two strains of influenza A and two strains of influenza B. Average flu vaccine effectiveness, which varies across age groups, has ranged from 19% to 52% during the past decade (Table 1).

Table 1: Vaccine effectiveness in recent years[14]

Flu Season	Average Effectiveness
2011-2012	47%
2012-2013	49%
2013-2014	52%
2014-2015	19%
2015-2016	48%
2016-2017	40%
2017-2018	38%
2018-2019	29%
2019-2020	45%

Standard-dose vaccines

Most standard-dose quadrivalent flu vaccines are made with processes involving incubation in eggs, although there are options that do not involve eggs (see below). Afluria Quadrivalent, Fluarix Quadrivalent, FluLaval Quadrivalent, and Fluzone Quadrivalent are all egg-based vaccines and are FDA-approved for people 6 months of age and older. Although most flu vaccines are administered via intramuscular injection into the deltoid, the Afluria quadrivalent vaccine can also be given by jet injector (for people aged 18 through 64 years only).

ACIP recommends that patients with an egg allergy of any severity nonetheless receive any age-appropriate influenza vaccine.[15] However, the Committee does recommend that patients who have previously experienced an allergic reaction to eggs more severe than hives (e.g., angioedema, respiratory distress, lightheadedness, or requiring IV epinephrine) only receive egg-derived vaccines under the supervision of a medical provider.

For patients with severe egg allergies or those who prefer to avoid an egg-derived vaccine, two influenza vaccines use egg-free technology: a standard-dose cell culture vaccine (Flucelvax) and a higher dose recombinant vaccine (Flublok).

A live attenuated influenza vaccine (FluMist Quadrivalent), which is given intranasally, is approved only for people aged 2 through 49 years.[16] FluMist should also not be given to people who are pregnant, immunocompromised, asplenic, have cochlear implants or cerebrospinal fluid leaks, or who have recently received influenza antiviral medications.[16]

Newer influenza vaccines for older adults

Three newer vaccines are designed to boost the immune response in older adults and, hence, improve effectiveness.

High-dose vaccines

The Fluzone High-Dose Quadrivalent vaccine (the only high-dose vaccine licensed at the time of this publication) contains 60 mcg hemagglutinin, or four times the antigen in the standard-dose Fluzone Quadrivalent vaccine and other standard-dose inactivated flu vaccines.

The efficacy of high-dose vs. standard-dose vaccine was evaluated in a 2014 trial that randomized 31,989 adults aged ≥65 years to Fluzone high-dose (trivalent inactivated 60 mcg hemagglutinin/dose) vs. Fluzone standard-dose (trivalent inactivated 15 mcg hemagglutinin/dose).[17] The primary efficacy outcome was flu symptoms plus lab-confirmed influenza. These occurred in 1.4% of patients who received the high-dose vaccine vs. 1.9% of those who received the standard-dose vaccine, giving a relative risk reduction of 24.2% (95% CI: 9.7%-36.5%). Mortality during the surveillance period was identical between the arms (0.5% in both groups), and the rate of hospitalization for respiratory illness, regardless of laboratory confirmation, was not significantly lower in the high-dose group (12.76 per 1000 subject-seasons) vs. the standard-dose group (14.69 per 1000 subject-seasons) (RR 0.87; 95% CI: 0.72-1.05).

Recombinant Vaccines

Flublok is a quadrivalent recombinant vaccine that contains 45 mcg hemagglutinin per dose, or three times the antigen in standard-dose inactivated vaccines (though less than the Fluzone high-dose vaccine). The Flublok recombinant vaccine was evaluated in a randomized controlled trial (RCT) in adults aged 50 years and older during the 2014-2015 flu season. Only 2.2% of patients randomized to the recombinant vaccine developed lab-confirmed influenza illness, compared to 3.2% in the standard-dose inactivated vaccine group (P=0.006). On pre-specified subgroup analysis, the recombinant vaccine was 42% more effective than the standard-dose inactivated vaccine among people aged 50-64 (95% CI: 15%-61%). However, in those 65 and older, there was no statistically significant difference in the efficacy of the two vaccines (efficacy difference 17%; 95% CI: -20% to 43%), though the trial was not powered to detect a difference in this subgroup.

Adjuvant Vaccines

A quadrivalent flu vaccine (FLUAD) using an adjuvant (an ingredient that promotes a stronger immune response) was approved in the U.S. in 2020 for people aged ≥65 years. It became available for the first time during the 2020-21 season (adjuvanted trivalent versions of FLUAD have been available since FDA approval in 2015). The adjuvanted quadrivalent vaccine is manufactured using an egg-based process, and with the MF59 adjuvant, which is an emulsion of water and squalene oil.

A 2014 trial randomized 7,082 participants to an MF59-adjuvanted trivalent flu vaccine vs. a non-adjuvanted version of the same vaccine in adults aged ≥65 years.[18] The adjuvanted group showed a significantly higher antibody response compared to the non-adjuvanted group, but clinical outcomes did not differ between the two groups. Influenza-like illness was reported by 322 in the adjuvant group vs. 314 in the standard group, a non-significant difference. No significant between-group differences were observed in rates of exacerbations of pre-existing chronic diseases, healthcare use, or mortality. Local adverse reactions, however, were reported by 32% of subjects in the adjuvanted group and by 17% in standard group, and systemic adverse reactions by 32% of subjects in the adjuvanted group and 26% in the standard vaccine group.

To date, there have been no randomized studies comparing adjuvant and high-dose flu vaccines.[19] A retrospective cohort study, however, evaluated egg-based quadrivalent vaccines against both the egg-based adjuvanted vaccine and the high-dose vaccine in 12,777,214 Medicare beneficiaries aged ≥65 years during the 2018-2019 flu season.[20] The study found that the adjuvanted and high-dose vaccines were both slightly more effective in this population than the standard quadrivalent vaccines (relative vaccine effectiveness 7.7% [CI: 3.9%-11.4%] and 4.9% [CI: 1.7%-8.1%] higher, respectively, compared to quadrivalent.)

Flu vaccines for 2020-2021

In the 2020-2021 season, all except one vaccine are quadrivalent, targeting the following strains:

- Influenza A/Hawaii/70/2019 (H1N1) pdm09-like virus
- Influenza A/Hong Kong/45/2019 (H3N2)-like virus
- Influenza B/Washington/02/2019 (Victoria-lineage)-like virus
- Influenza B/Phuket/3073/2013 (Yamagata lineage)-like virus

The Fluad trivalent vaccine for 2020-2021 includes the first three inactivated viruses, but not influenza B/Phuket.

Table 2: Influenza vaccines for 2020-2021[16]

Type of influenza vaccine	Trade name
Standard-Dose	Afluria
	Fluarix
	FluLaval
	Fluzone
	Flucelvax*
High-Dose	Fluzone High Dose
Recombinant	Flublok*
Adjuvanted	Fluad
Live attenuated	FluMist

* These products do not use egg in the manufacturing process.

Adverse events

In general, standard-dose non-adjuvanted flu vaccines elicit rates of side effects comparable to those reported by participants in clinical studies receiving a placebo injection.[21] For example, a 1996 trial randomized 849 healthy adults to inactivated flu vaccine or placebo and assessed for symptoms of fever, myalgia, fatigue, malaise, and headaches.[22] 34.1% of those getting the vaccine reported at least one symptom vs. 35.2% of the placebo group, and 6.2% of the vaccine group reported fever vs. 6.1% of the placebo group (no significant differences). A comparison of high-dose vs. standard-dose vaccine also found no significant differences in adverse events.[17] As noted above, however, rates of adverse events appear higher with adjuvanted vaccines compared to non-adjuvanted vaccines, although severe reactions such as Guillain-Barre syndrome are rare.[18]

Which flu vaccine for older patients?

For the 2020-2021 flu season, CDC recommendations express no preferences for any particular influenza vaccine. Any age-appropriate vaccine may be used, including inactivated standard-dose vaccines, inactivated high-dose vaccines, recombinant vaccines, and adjuvanted vaccines.[15]

That said, emerging clinical trial data can help guide an evidence-based approach for older adults. In a large randomized controlled trial of adults 65 and older, high-dose inactivated vaccines (Fluzone) yielded better clinical outcomes than standard-dose inactivated vaccines.[17] Though the trial compared high-dose trivalent vaccines to standard-dose trivalent vaccines, it may be possible to extrapolate these findings to quadrivalent vaccines. Our recommendation is to offer a high-dose quadrivalent flu vaccine to patients aged 65 years and older rather than standard-dose quadrivalent vaccines. Likewise, there are high-quality data to support preferentially offering the recombinant quadrivalent vaccine (Flublok) to adults aged 50 and older rather than the standard-dose inactivated quadrivalent vaccine.[23] Because subgroup analyses in this trial showed no benefit for those aged 65 and above, we favor high-dose inactivated quadrivalent vaccine (Fluzone) in this older age group when available (see Figure 3).

Finally, the evidence supporting the adjuvanted vaccine (Fluad) in adults aged 65 and older comes from immunogenicity studies rather than studies demonstrating clinical benefit. It may therefore be reasonable to favor the high-dose inactivated influenza vaccine in this age group rather than the adjuvanted vaccine.

Note that the preference for the high-dose inactivated flu vaccines, as described in Figure 3, is *not* based on head-to-head comparisons between high-dose, adjuvanted, and recombinant vaccines. Rather, it is based on the quality of currently-available evidence. Studies have found that all three vaccines—high-dose, recombinant, and adjuvanted—may be better in older adults than standard-dose inactivated vaccines, but the data for the high-dose vaccine are the strongest. If recombinant and adjuvanted vaccines are limited by local availability, vaccination with standard dose flu vaccine should not be delayed.

Figure 3: Preferred quadrivalent influenza vaccines for adults aged ≥65 years[15]

Encouraging immunization

Although the influenza vaccine is recommended routinely for nearly all patients, individual counseling by a clinician may increase use. Patient reminders, such as phone calls or emails, as well as postcards and leaflets increased flu vaccination rates in one study by 11%.[24] Using pharmacists, nurses, and receptionists to encourage vaccination more than doubled the likelihood of patients getting vaccinated — not just for flu but other adult immunizations as well.[25]

Flu Shot Myths & Realities

Ill-founded "vaccine hesitancy" prevents many patients from getting the protection they need. Talk to patients about concerns they may have, bearing in mind the following common myths and possible responses.

Myth: "I don't get the flu."
Reality: Anyone can get the flu in a given year. Talking points:

- Just because you haven't had a car accident before doesn't mean you shouldn't wear a seatbelt today.
- In addition to reducing the risk of death, the flu vaccine can prevent major complications, like pneumonia, especially in older adults.

Myth: "The flu shot gives you a case of the flu."
Reality: Flu shots don't give you the flu. Talking points:

- Most patients have very minor local injection site reactions, and that's all.
- Injectable flu vaccines for older adults are made from inactivated virus and do not contain live virus, so they can't "cause the flu."
- The vaccine is given at the beginning of cold and flu season, so many people contract viral upper respiratory infections around the time they get their flu shot. This is not a result of the vaccination, but of other circulating viral illness in the community.

Myth: "In many years, the flu vaccine doesn't work well at all."
Reality: The flu vaccine benefits patients, even though it is not 100% effective. Talking points:

- The efficacy of the flu vaccine varies year to year based on the composition of the vaccine and the strain of virus circulating in the community.

- Patients may be skeptical because the reported efficacy is often in the 30-50% range. But even at this level, the flu shot really reduces the risk of death, severity of illness, and length of hospitalization.
- Studies have shown that even if someone who was vaccinated gets influenza, the disease is likely to be less severe than it would be otherwise.[26]

Myth: "The flu isn't that serious; it's just like a bad cold."
Reality: Viral influenza can be a severe and sometimes fatal disease, especially in people over 65. In the 2019-2020 flu season, between 24,000 and 62,000 people died from flu.

BOTTOM LINE: Two types of influenza cause seasonal flu: Influenza A and B. Quadrivalent vaccines are directed at two strains of influenza A and two strains of influenza B, while trivalent vaccines target two strains of influenza A and one strain of influenza B. A high-dose vaccine is preferred for older adults, but any standard flu vaccine is acceptable.

Pneumococcal vaccine

Pneumococci (*Streptococcus pneumoniae*) inhabit the respiratory tract of roughly 90% of healthy people.[27] The surfaces of pneumococci are composed of complex polysaccharides, which are one source for the organism's pathogenicity and are how the 90 known serotypes are differentiated.[27] Antibodies to some pneumococcal capsular polysaccharides may cross-react with related types as well as with other bacteria, providing protection against additional serotypes.

Two vaccine types protect against pneumococcal disease: polysaccharide and conjugate vaccines.

Pneumococcal Polysaccharide Vaccine

Purified pneumococcal polysaccharide is used to produce the polysaccharide vaccine. In 1977, a polysaccharide vaccine containing 14 serotypes was licensed in the United States, and in 1983 a 23-valent polysaccharide vaccine (Pneumovax) replaced the 14-valent vaccine. Pneumovax is given by injection intramuscularly or subcutaneously. It contains 12 serotypes in common with Prevnar (see below), a 13-valent pneumococcal conjugate vaccine (PCV13), along with 11 additional serotypes.

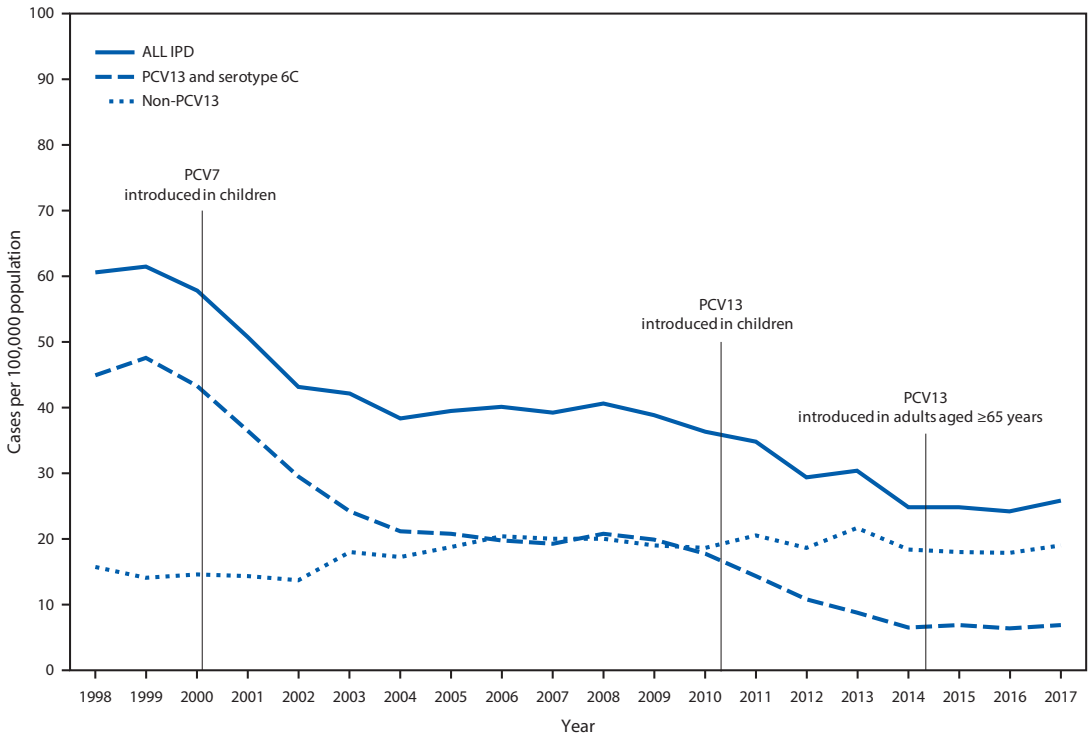
Most studies evaluating Pneumovax effectiveness have shown that it protects against invasive pneumococcal disease (IPD) in healthy younger adults and in older adults.[28] Effectiveness estimates for preventing IPD range from roughly 50% to 80% in immunocompetent older adults and those with a variety of chronic illnesses.[29] A Cochrane meta-analysis of 15 RCTs and seven nonrandomized observational studies of Pneumovax effectiveness suggested an overall vaccine efficacy of 74% against IPD (CI: 56%–85%), based on pooled results from 10 of the RCTs.[30]

Pneumococcal Conjugate Vaccine

In 2011 the U.S. FDA approved Prevnar (PCV13) for the prevention of pneumococcal pneumonia and invasive disease in persons 50 years of age and older.

The **CAPiTA** randomized trial conducted in the Netherlands demonstrated 75% (95% CI: 41%–91%) efficacy against PCV13-type IPD and 45% (CI: 14%–65%) efficacy against noninvasive PCV13-type pneumonia among adults aged ≥65 years.[31] Three RCTs[31-33] assessing the safety of Prevnar showed that rates of severe adverse events were similar among participants vaccinated with PCV13 versus placebo or PPSV23. Commonly-reported adverse events include pain, redness, and swelling at the injection site, movement impairment in the affected arm, fatigue, headache, chills, decreased appetite, generalized muscle pain, and joint pain. The ACIP has stated that PCV13 is safe and effective for preventing PCV13-type IPD and noninvasive pneumonia.[34]

Figure 4: Invasive pneumococcal disease (IPD) in adults aged ≥65 years by serotype[34]



Re-evaluation of Prevnar for older adults

When PCV7 was first introduced in children in 2000, there was a sharp decline in cases of IPD in adults older than 65, likely due to decreased carriage and transmission of these pneumococcal strains. Conversely, after the introduction of PCV13 in 2014 for older adults, the incidence of IPD on a population level did not change significantly, leading some experts to speculate whether Prevnar was necessary for all older adults.[34]

The cost-effectiveness of using Prevnar in series with Pneumovax vs. using Pneumovax alone was assessed in two economic models. In a population of 2.7 million adults aged 65 years, only an estimated 76–175 cases of PCV13-type illness and 4,000–11,000 cases of PCV13-type pneumonia would be avoided by using Prevnar/Pneumovax compared with Pneumovax alone.[34]

In view of the high cost of Prevnar, these results raised concerns that continuing to add Prevnar to Pneumovax vaccination in adults aged ≥65 years may not be cost-effective.[34] In 2020, based on this

evidence, ACIP changed its recommendations for Prevnar in older adults, recommending that it be administered based on shared decision-making rather than routinely to all patients.

What is shared decision-making?

According to the CDC, shared clinical decision-making involves individually-tailored discussions between the health care provider and the patient or parent/guardian about treatment choices.[35] This stands in contrast to usual decision-making around vaccination, where the recommended default is for physicians to vaccinate based on a patient's age or other indications, unless contraindicated. With shared clinical decision-making, however, there is no default—a decision to vaccinate can be based on available evidence of benefit; patient characteristics, values, and preferences; the health care provider's clinical judgement; concerns about cost; and/or the specific attributes of the vaccine under consideration.[35]

Discussing options with Prevnar

Clinicians should understand the factors that the ACIP considered when recommending "shared decision-making" for Prevnar.[36]

Here are some suggestions for the discussion:[36,37]

1. Present the option

   "In addition to Pneumovax, we have a second pneumonia vaccine, Prevnar. It protects against strains of bacteria that are uncommon in adults these days."

   For a patient who is open to vaccines: "I know you always make a point of getting your vaccines and screening tests promptly, so if you would like to do this one as well, then we can give it to you today."

   For a patient equivocal about vaccines: "I know you are reluctant about vaccines, but I wanted to make sure you were aware that this is an option for you."

2. Discuss the benefits and risks of vaccination

   Benefits: "Prevnar can help prevent a relatively rare cause of bacterial pneumonia."

   People who are more likely to benefit from Prevnar:

   - Residents in group living situations (e.g., nursing homes, assisted living)
   - Those living in areas with low rates of childhood Prevnar immunization
   - Those with other chronic conditions (e.g., smoker, alcohol dependence, heart disease, liver disease, lung disease, diabetes)
   - Those with risk factors such as substance use, prior pneumonia, or medications that increase the risk of pneumonia

   Risks: The risks of Prevnar are low and it is well-tolerated by most adults. Pain at the injection site is relatively common, but other possible side effects include redness, swelling, limitation of arm movement, and fatigue.

Recommendations

Pneumovax is recommended for all adults aged ≥65 years (Table 3). For those with certain underlying medical conditions or who are immunocompromised, Pneumovax is also recommended before the age of 65, and then a booster should be administered at age 65.

Immunocompromised patients should receive Prevnar before the age of 65. For everyone else, the decision to receive Prevnar should be made on a case-by-case basis at the age of 65.[34] In prior studies, those who received Pneumovax as the initial study vaccine had lower antibody responses after subsequent administration of a Prevnar dose one year later than those who had received Prevnar as the initial dose, which is why it is recommended that Prevnar be given first if both vaccines are going to be administered.[27,38,39]

Table 3: Recommendations for pneumococcal vaccination based on patient factors and age[37]

	Age 19-64	Age ≥65
Healthy adult	Not routinely indicated	**Pneumovax**
Underlying medical conditions*	**Pneumovax**	**Prevnar** (optional) + **Pneumovax** 1 year later
Immunocompromising conditions**	**Prevnar** + **Pneumovax** ≥8 weeks later + **Pneumovax** 5 years later	**Pneumovax**§

*e.g., smoking, alcohol dependence, chronic heart disease, chronic liver disease, chronic lung disease, diabetes
**including, but not limited to: chronic renal failure, HIV, solid organ transplant, malignancy and other cancers, asplenia, and use of immunocompromising medications
§Patients with immunocompromising conditions who did not receive pneumococcal vaccination before the age of 65 should receive Prevnar at the age of 65 followed by Pneumovax at least 8 weeks later.

BOTTOM LINE: Two vaccines can protect against pneumococcus: Pneumovax (PPSV23) and Prevnar (PCV13). Provide Pneumovax to all adults aged 65 years and older with the option to supplement with Prevnar (given first) for patients with risk factors.

Zoster vaccine

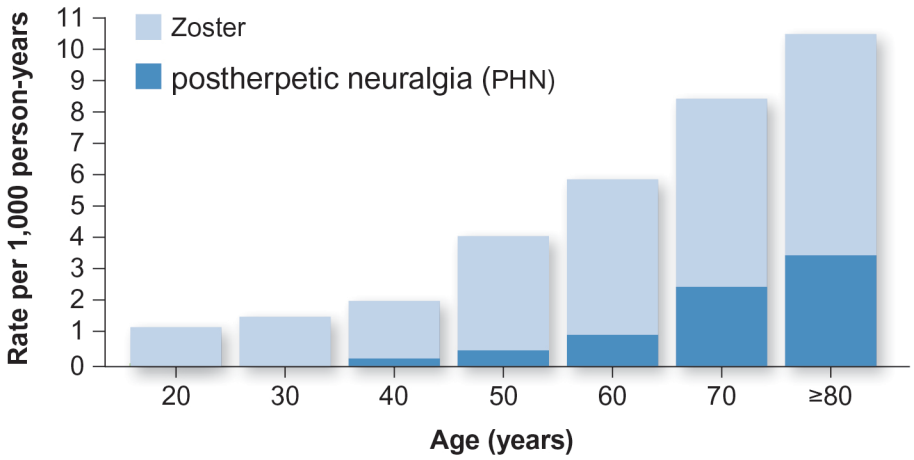
Shingles is an often-painful disease caused by the varicella zoster virus (VZV). Until the 1990s, nearly all people developed a primary infection with VZV (i.e., chicken pox) in childhood. A two-dose vaccine series

for preventing primary VZV infection has been available in the United States since 1995 and is recommended for all children.[40] Varicella cases declined 97% between 1995 and 2010, when vaccination coverage among children 19-35 was estimated to be 95%.[41] However, more than 99% of people aged 50 years and older have been infected with VZV. The ACIP therefore considers such people immune to new acute episodes of varicella.[42]

After primary infection, however, the varicella zoster virus remains latent in dorsal sensory or cranial nerve ganglia.[43] Reactivation of VZV later in life can causes shingles, a localized and generally painful cutaneous eruption that occurs most frequently in older adults. The individual lifetime risk of shingles is about 30%,[44] and approximately 1 million new cases of shingles occur in the United States annually.[45] The prevalence of shingles increases with advancing age (Figure 5).

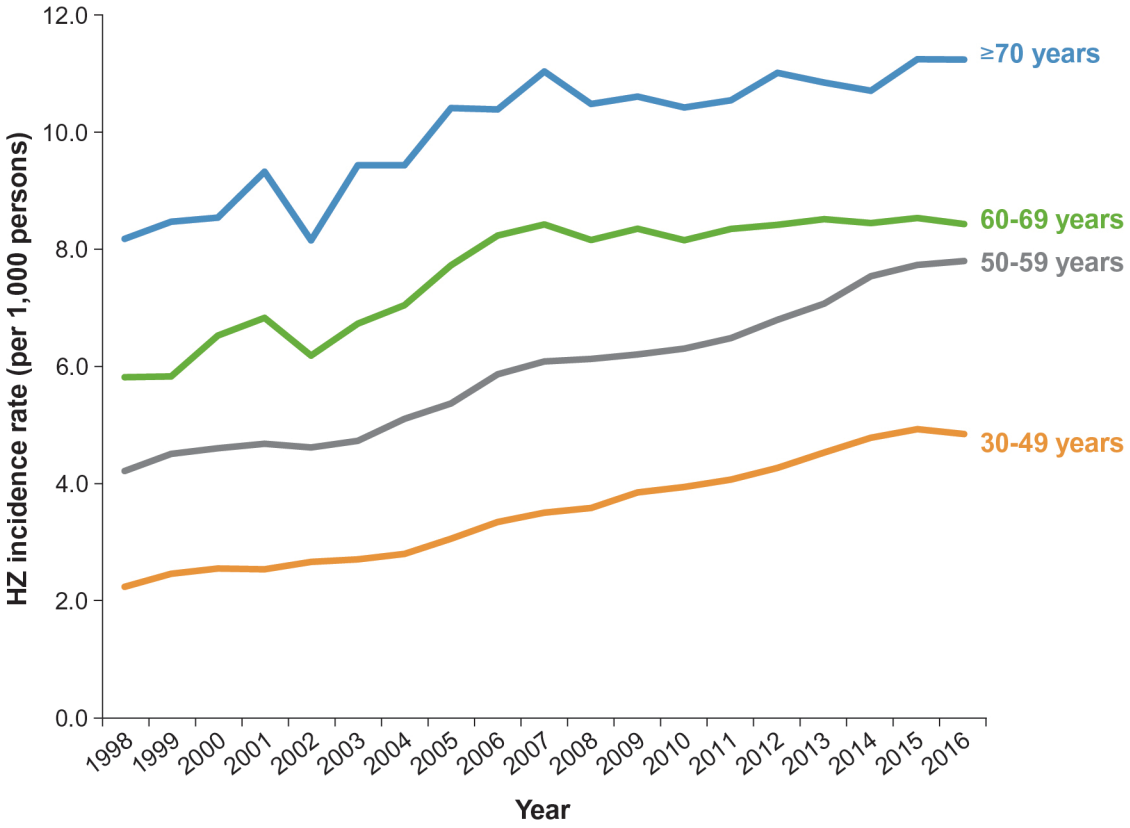
While shingles is self-limited and can be mild in some cases, it can also produce disabling symptoms and can lead to severe complications. The most common is persistent pain following the initial episode, known as postherpetic neuralgia (PHN). PHN can be very painful and burdensome for patients, with pain lasting months to years; it occurs in 10%-18% of those who develop shingles.[46] Ophthalmic involvement can be severe and potentially sight-threatening. Other rare but severe neurologic complications include meningitis, encephalitis, transverse myelitis, and Guillain-Barre syndrome.[43]

Figure 5: Rate of zoster and postherpetic neuralgia by age in the United States[40]



The rate of zoster infections has been increasing since 1998, although incidence has leveled off in recent years (Figure 6, next page).

Figure 6: Incidence of zoster by age and calendar year[47]



The first vaccine to prevent shingles was a live vaccine (Zostavax), which was recommended for all adults over age 60 starting in 2006. The live zoster vaccine was 51% effective in preventing shingles and 66% effective in preventing PHN. However, the vaccine is less effective among older adults, and longer-term follow-up data revealed that its effect waned substantially within 5-10 years.[41] Zostavax was taken off the market starting July 1, 2020, and all existing doses were removed from pharmacies when those doses expired on November 18, 2020.[48]

The recombinant zoster vaccine Shingrix was approved in 2017 and is recommended for all patients over age 50.[49] Two doses of Shingrix are more than 90% effective at preventing shingles and PHN. Protection stays above 85% for at least the first four years after vaccination.[49] Longer-term data are not yet available.

Table 4: Zoster Vaccines[50]

	Zoster live vaccine (discontinued)	Recombinant zoster vaccine
Brand name	Zostavax	Shingrix
Mechanism	Live attenuated	Recombinant, adjuvanted
FDA approval	2006	2017
Dose schedule	Single dose, age ≥60	Two doses, at least 2 months apart, age ≥50
Herpes zoster efficacy	51%	97% (≥50 years old) 90% (≥70 years old)
Postherpetic neuralgia efficacy	67%	89%
Longevity	Immunity wanes to 4.2% after 8 years	No waning immunity within first 3-4 years

The efficacy of Shingrix was evaluated in two RCTs, **ZOE-50** (N=5,411) and **ZOE-70** (N=13,900), both of which showed the vaccine to be highly effective (pooled effectiveness 91.3%) (Table 5).[51,52] Shingrix, however, does carry some risks for complications. In a subgroup analysis of the 2016 ZOE-70 trial (participants contacted up to 7 days after injection), 53% of participants in the vaccine group had any systemic reaction (e.g., fatigue, myalgia, headache, fever, and shivering) compared to 25.1% in the placebo group, and 74.1% had any injection-site reaction compared to 9.9% of the placebo group.[52] Only 11.9% of the vaccine group, however, had any moderate-to-severe (Grade 3) reaction, vs. 2% of the placebo group. The rates of other serious adverse events, potential immune-mediated diseases, and deaths were not significantly different between the two groups.

While these side effects should not prohibit giving the vaccination, adequate counseling is important so patients know what to expect. Additionally, for patients who express skepticism about vaccine side effects, it may be reasonable to separate this vaccine from other vaccines, especially the influenza vaccine, so that patients do not associate the systemic side effects with the flu vaccine, thereby reducing their readiness to get the flu vaccine in future years.

Table 5: Efficacy of recombinant zoster vaccine[51,52]

	ZOE-50 trial	ZOE-70 trial
Population	5,411 adults, age ≥50	13,900 adults, age ≥70
Mean follow-up	3.2 years	3.7 years
Pooled herpes zoster efficacy	91.3% (95% CI: 86.8-94.5%) 9.3 → 0.8 cases per 1000 person-years	
Pooled postherpetic neuralgia efficacy	91.2% (95% CI: 75.9-97.7%) 0.9 → 0.1 cases per 1000 person-years	

Recommendations

For adults aged ≥50 years give Shingrix in 2 doses spaced 2-6 months apart.[53] If the second dose is given less than 4 weeks after the first, it should be repeated after an appropriate amount of time has passed (i.e., after at least 2 months). If the second dose is given >6 months after the first, there is no need to re-start the series. Patients who were previously vaccinated with Zostavax should still receive the Shingrix vaccine, due to the waning efficacy of Zostavax over time.

Counsel patients about expected side effects of Shingrix (i.e., fatigue, myalgia, headache, fever, and shivering) and consider giving Shingrix separately from annual flu shots to isolate side effects and avoid patients being disincentivized to have future flu vaccinations.

The ACIP recommends Shingrix for patients with previous shingles infections to prevent recurrent infections.[54] Wait to administer Shingrix until after an acute shingles infection resolves. There is no specific waiting period, but experts suggest waiting 3-6 months after infection.

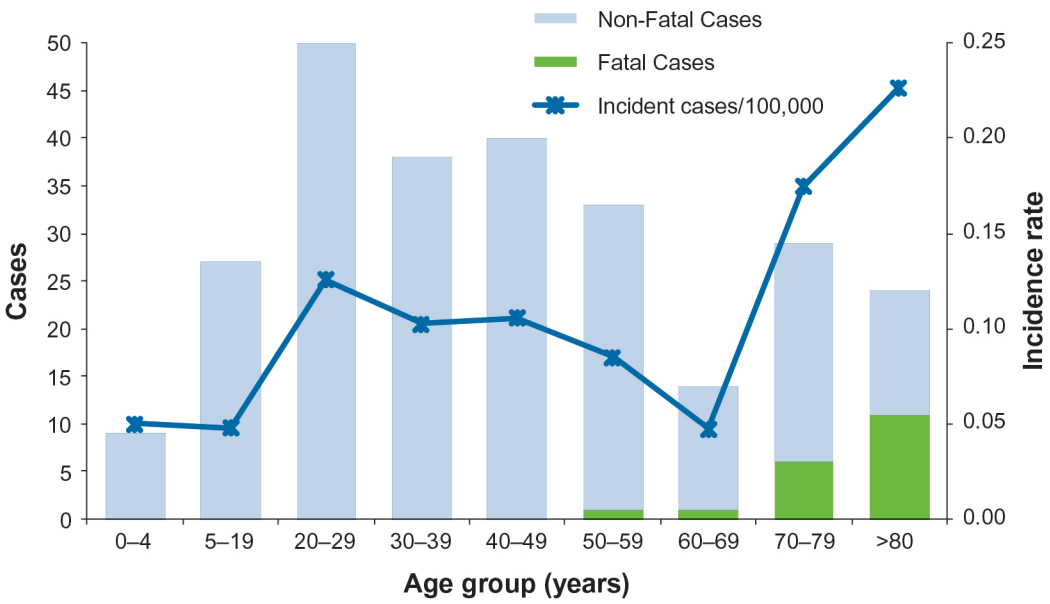
BOTTOM LINE: Shingles is a painful, potentially disabling condition largely preventable with vaccination. Shingrix is recommended for all adults over 50 in a 2-dose series separated by 2-6 months. Patients previously immunized with Zostavax should be re-immunized with Shingrix.

Tetanus and Pertussis Vaccination

Tetanus is a severe, life-threatening neurologic disease caused by the bacteria *Clostridium tetani.* While tetanus is not contagious, the *C. tetani* spores are widespread and commonly found in soil, dust, and manure and enter the body through a wound or breach in the skin.[55] In the presence of anaerobic conditions, the spores germinate and produce potent toxins, which act at several sites within the central nervous system, including peripheral motor end plates, spinal cord, brain, and the sympathetic nervous system. Tetanus toxin causes the typical clinical manifestations of tetanus by interfering with the release of neurotransmitters and blocking inhibitor impulses. This leads to unopposed muscle contraction and spasm. These spasms lead to the disease's common name – lockjaw – but the results can be more severe, including seizures, paralysis, and death.

In the post-vaccination era, tetanus is uncommon in the United States, with approximately 30 reported cases each year.[55] Elderly adults remain at risk for tetanus, however, and all fatal cases in recent years have occurred in adults over 50.[56] Nearly all cases of tetanus are among people who were not up-to-date on their tetanus vaccinations (Figure 7).

Figure 7: Cases, survival status, and incidence rates of tetanus by age group 2009-2017.[57]



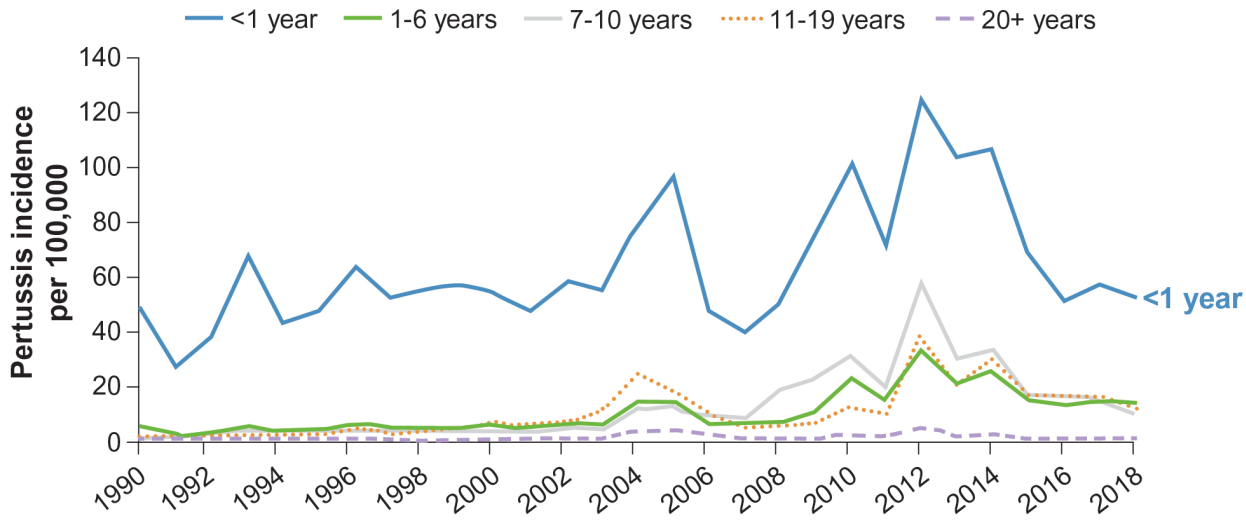
*Incidence rate is calculated as cases per 100,000 population.

Pertussis, also known as whooping cough, is a contagious disease caused by the bacterium *Bordetella pertussis*. Pertussis can affect people of all ages but is particularly dangerous for newborns and infants under age 1. In the U.S. in 2012, 15 of 18 pertussis deaths were among infants <1 year old.[58]

Despite nearly universal childhood vaccination, pertussis incidence has climbed in the past decade (Figure 8). In 2012 the CDC reported 48,277 cases of pertussis in the United States, the highest number of cases since 1955, but cases have since declined.[59]

Evidence suggests that the protection provided by pertussis vaccination wanes over time and that many cases of pertussis among infants and children may be linked to transmission from an adult or adolescent.[60] These two facts have raised concern that adults should be vaccinated against pertussis in addition to children.

Figure 8: Incidence of pertussis over the past two decades[61]



Tetanus vaccination – for which boosters are recommended every 10 years – can be provided either with (Tdap) or without concomitant pertussis vaccination (Td).

Two RCTs found similar levels of safety and efficacy between Td and Tdap vaccines.[62,63] For example, a 2019 trial randomized 1330 adults to either Tdap (n=1002) or Td (n=328) vaccine 8 to 12 years after a dose of Tdap vaccine administered previously.[62] Adverse events were monitored for 6 months. Adverse events were mostly mild, although at least one adverse event was reported by 87.7% of the Tdap group and 88.0% of Td vaccine recipients. No significant between-group differences were found in the rates of injection-site reactions, systemic reactions, or serious adverse events. Postvaccination concentrations of tetanus and diphtheria antibodies were similar in the Tdap and Td groups, and the rates of seroprotection against tetanus and diphtheria were >99% in both groups.

Recommendations

ACIP recommends a boosting dose of any tetanoid-containing vaccine (Td or Tdap) every 10 years, with no upper age limit.[53] Prior to 2020, guidelines had preferred Td over Tdap in many circumstances, but there is now no recommendation for any one tetanus vaccine. Every adult should have received one dose of Tdap after age 11 for boosted protection against pertussis. If a patient's vaccine history is unknown, Tdap may be preferred over Td to assure adequate protection against both pertussis and tetanus. ACIP currently recommends Tdap vaccination in women at each pregnancy to reduce risk to infants.[53]

Table 6; Tetanus/diphtheria/pertussis vaccines[60]

Vaccine	Brand	Dose	Comments
Tdap	Adacel	0.5 mL	Not approved for adults ≥65
Tdap	Boostrix	0.5 mL	
Td	Tenivac	0.5 mL	
Td	Generics	0.5 mL	Contains thimerosal

Note: all tetanus vaccines contain small amounts of formaldehyde.

BOTTOM LINE: Immunization against tetanus and pertussis can be provided in a single injection of Td or Tdap. If Tdap vaccination status is unknown, choose Tdap over Td. A booster with Tdap is recommended for all adults every 10 years.

Safe vaccine administration

Many vaccines for adults are given via intramuscular injection into the deltoid. Safe vaccine practice includes the selection of appropriate needle length for muscle penetration and using anatomic landmarks to determine the location of vaccination. Although seemingly routine, a survey of 100 physicians and nurses found that half could not name any structure at risk from improper deltoid vaccination technique and many used inappropriate depths of injection.[64]

Safe IM vaccine administration can be assured by using the midpoint of the deltoid muscle, located between the acromion and deltoid tuberosity with the arm abducted to 60 degrees.[65]

Vaccine Costs

These vaccinations are generally covered by Medicare and other insurance plans, although Medicare coverage is divided between Part B and Part D (Figure 9).

Figure 9: Medicare coverage of vaccinations

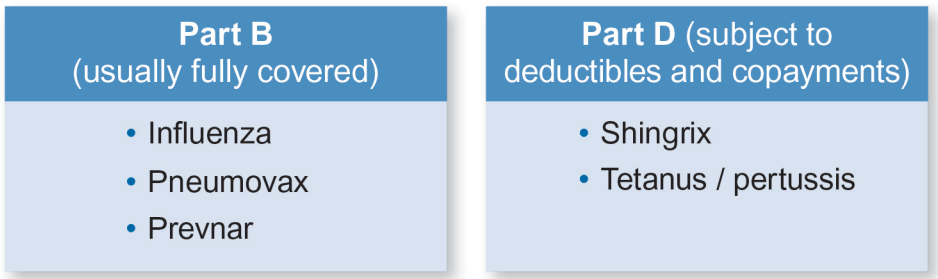
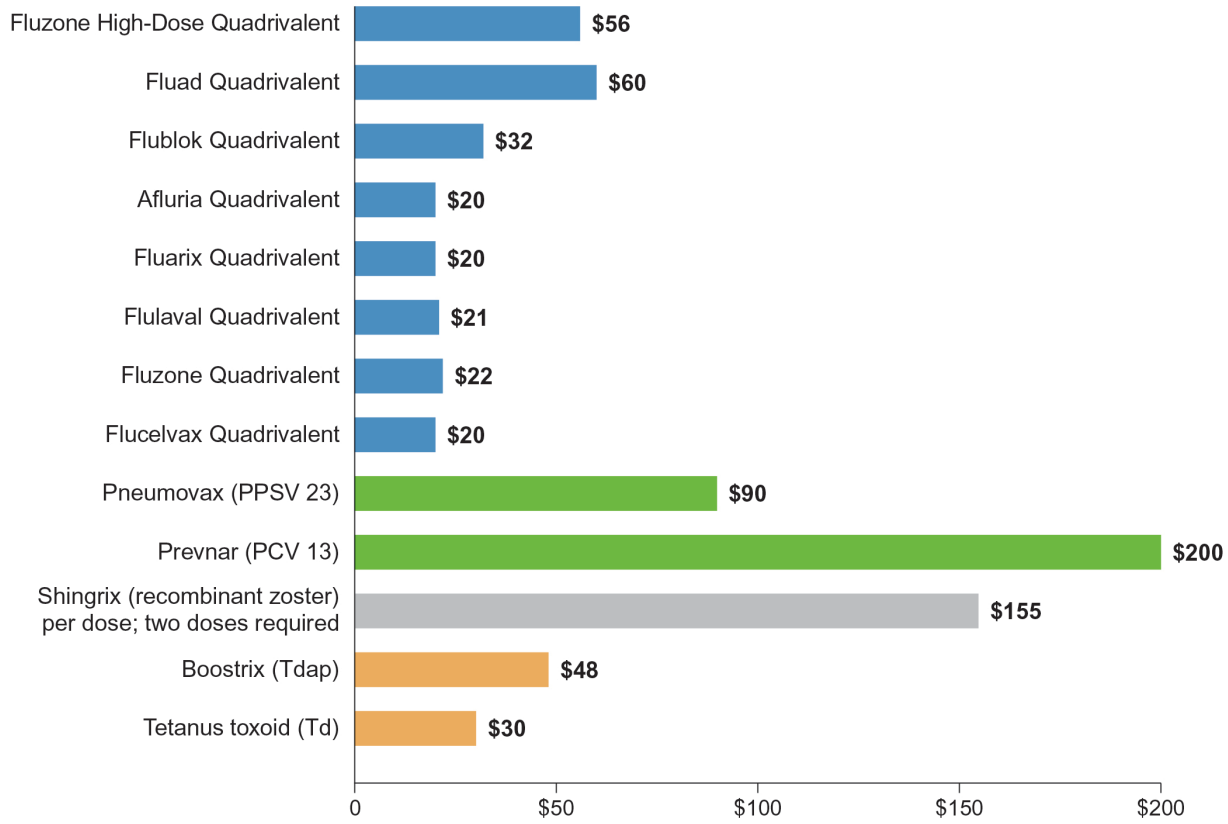


Figure 10: Prices for vaccinations recommended for older adults



Prices from goodrx.com, October 2020. Prices are the cost per one dose. Prices are a guide; patient costs will be subject to copays, rebates, and other incentives.

Summary and Conclusions

Vaccinating older adults is one of the most powerful, cost-effective, and direct ways to prevent a range of disabling, painful, or lethal illnesses and help reduce disease transmission to others. This evidence document has detailed the latest evidence-based recommendations from the ACIP, which can be summarized as:

- Immunization against influenza is vital for all patients over 65, especially during the COVID-19 pandemic. A high-dose or adjuvanted vaccine is preferred when available.
- Provide pneumococcal polysaccharide vaccine (Pneumovax) to all adults aged ≥ 65 years.
- Offer pneumococcal conjugate vaccine (Prevnar) to immunocompromised adults and those with chronic conditions (given prior to Pneumovax).
- Prevent shingles and postherpetic neuralgia with the recombinant zoster vaccine (Shingrix).
- Boost tetanus protection with either Tdap or Td every 10 years.

Table 7 summarizes the main 2020 ACIP immunization dosing recommendations for adults who are not immunocompromised.

Table 7: Immunization recommendations for older adults who are not immunocompromised* [53]

	50-64 years	≥65 years
Influenza (inactivated or recombinant)	**1 dose annually**	
Pneumococcal pneumonia: **Pneumovax** (pneumococcal polysaccharide, PPSV 23)	**Yes, if risk factors**	**1 dose** (if dose was given <65, wait 5 years before the next)
Prevnar (pneumococcal conjugate, PCV 13)	**Yes, if risk factors**	**1 dose** (optional)
Shingles (zoster, recombinant [Shingrix])	**2 doses, 2-6 months apart**	
Tetanus, diphtheria, pertussis (Tdap or Td)	**1 dose of Tdap, then Td or Tdap booster every 10 years**	

*Full adult vaccine schedule is at cdc.gov/vaccines/schedules. Travel related vaccine recommendations are at cdc.gov/travel.

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