Vaccinations in Older Adults

Megan Burke, MD[a,*], Theresa Rowe, DO, MS[b]

KEYWORDS

• Vaccinations • Immunizations • Older adults • Immune senescence
• Pneumococcal • Influenza • Herpes zoster

KEY POINTS

- Older adults are at increased risk for vaccine-preventable infections. Rates of immunizations among older adults remain lower than goal despite guidelines, leaving room for intervention and improvement.
- Most of the morbidity and mortality related to vaccine-preventable illnesses in older adults in the United States is related to influenza and pneumococcal disease.
- There is a high-dose influenza vaccination specifically targeted for older adults; however, the Advisory Committee on Immunization Practices does not express preference for either high-dose or standard-dose influenza vaccine use in this population.
- Cost of immunizations influence vaccination rates in older adults.

INTRODUCTION

Vaccines are important for preventing infections in older adults aged ≥65 years. It is estimated that more than 40,000 older adults die each year in the United States from vaccine-preventable infections, with influenza being the largest contributor.[1] Increasing the rate of vaccinations among older adults is a priority of the US government addressed in the Healthy People 2020 initiative.[2] Older adults are at increased risk for serious complications from vaccine-preventable illnesses due to age-associated changes in immune function, and chronic medical comorbidities, which place them at both higher risk for infection and for having an infection with a protracted course.[3] Although practice guidelines are well established by the Advisory Committee on Immunization Practices (ACIP), and endorsed by most professional societies, vaccination rates for older adults remain low, with approximately 74.0% of

Disclosure Statement: No disclosures.
[a] Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Johns Hopkins Bayview Medical Center, 5200 Eastern Avenue, MFL Center Tower, Suite 2200, Baltimore, MD 21224, USA; [b] General Internal Medicine and Geriatrics, Northwestern Feinberg School of Medicine, 750 North Lakeshore Drive, 10th Floor, Chicago, IL 60611, USA
* Corresponding author.
E-mail address: mburke31@jhmi.edu

Clin Geriatr Med ■ (2017) ■–■
https://doi.org/10.1016/j.cger.2017.08.006
0749-0690/17/

older adults receiving the influenza vaccination during the 2015 influenza season, 64.0% of older adults receiving any pneumococcal vaccination as of 2015, and only 27.9% of eligible older adults reported receiving the herpes zoster vaccine in 2014.[4] This article focuses on the following vaccines recommended for older adults: (1) influenza; (2) pneumococcal; (3) herpes zoster; (4) tetanus, diphtheria, pertussis; and (5) hepatitis, and how cost and public misconceptions influence vaccination rates in this population.

INFLUENZA VACCINATION

Adults aged ≥65 years are at greater risk for serious complications from influenza compared with younger adults because of age-associated changes in immune function.[3] The Centers for Disease Control and Prevention (CDC) estimated that more than 50% of influenza-associated hospitalizations and 64% of deaths during the 2015 to 2016 influenza season were in adults aged ≥65 years.[5] Although vaccination is the best way to protect against influenza and is recommended by the ACIP annually in older adults,[6] studies evaluating the efficacy of vaccination in this population have produced conflicting results.[7–9] A Cochrane review from 2010 concluded that available evidence to support the efficacy of influenza vaccination in adults aged ≥65 years was of poor quality.[10] A systematic review and meta-analysis from 2012 also concluded that evidence to assess the efficacy and effectiveness of influenza vaccination in adults aged 65 and older was inadequate.[9] A meta-analysis using test-negative design case-control studies from 2014 did find, however, that among community-dwelling older adults aged ≥60, the influenza vaccine was effective against laboratory-confirmed influenza during epidemic seasons when the vaccine was matched (odds ratio [OR] 0.69, 95% confidence interval [CI] 0.48–0.99). Additionally, vaccination was significantly effective during regional (match: OR 0.42, 95% CI 0.30–0.60; mismatch: OR 0.57, 95% CI 0.41–0.79) and widespread (match: 0.54, 95% CI 0.46–0.62; mismatch: OR 0.72, 95% CI 0.60–0.85) outbreaks.[11] A 2006 Cochrane review concluded that influenza vaccination was more effective in decreasing severity of disease, hospitalization, and mortality in adults aged ≥65 residing in long-term care compared with those living in the community.[12]

High-Dose Influenza Vaccination

Several studies have shown that adults aged ≥65 years respond less robustly to influenza vaccination (ie, produce fewer antibodies) compared with younger adults, likely a result of age-related immunosenescence.[13,14] To improve the efficacy of the influenza vaccine in older adults, a high-dose vaccine containing 4 times the amount of antigen (60 μg of hemagglutinin) compared with the standard-dose vaccine (15 μg of hemagglutinin) was developed and shown to stimulate more antibody production in this population.[13] The high-dose vaccine was approved by the Food and Drug Administration (FDA) in 2009 and was available for use in the 2010 to 2011 influenza season. A randomized controlled trial published in 2014 demonstrated that vaccination with the high-dose vaccine was 24.2% (95% CI 9.7–36.5) more effective in preventing laboratory-confirmed influenza in adults aged ≥65 years living in the United States compared with the standard-dose vaccination.[14] However, a subsequent large retrospective study in community-dwelling adults aged ≥65 in the United States did not find the high-dose vaccine to be more effective than the standard-dose vaccine for protecting against hospitalization for influenza or pneumonia (risk ratio 0.98; CI 0.68–1.40), except in a subgroup analysis of adults aged ≥85 years.[15] A more recent

systematic review and meta-analysis that included 7 studies aimed to compare the efficacy and safety of the high-dose influenza vaccine with the standard-dose influenza vaccine in adults aged >65, found that adults receiving the high-dose vaccine had significantly less risk of developing laboratory-confirmed influenza infections (relative risk 0.76, 95% CI 0.65–0.90) compared with those receiving the standard-dose vaccine.[16]

The safety profile of the high-dose vaccine is similar to the standard-dose vaccine, although one study found that injection site pain (36% vs 24%) and fever ≥38°C (1.1% vs 0.3%) were higher in older adults receiving the high-dose vaccine.[13] The ACIP does not express a preference for either the high-dose or standard-dose influenza vaccination, as it is still unknown if the high-dose vaccine results in greater protection against influenza illness on a population level.[17] More studies regarding the efficacy and effectiveness of both the standard and high-dose influenza vaccinations and their cost-effectiveness are needed.

PNEUMOCOCCUS VACCINE

Pneumococcal disease causes a variety of infections in adults aged ≥65 years, including otitis media, pneumonia, meningitis, and sepsis, and is associated with significant morbidity and mortality in this age group.[18] The incidence of pneumococcal disease and pneumococcal pneumonia disproportionally affects adults aged ≥65 years, particularly in those with chronic medical comorbidities.[19] Pneumococcal cases account for more than 240,000 hospitalizations and approximately 16,000 deaths in older adults in the United States annually.[18] Pneumonia is the most common pneumococcal infection in older adults for which 80% of cases require hospitalization.[18] With the aging of the population, pneumococcal pneumonia hospitalizations are expected to increase to more than 750,000 by 2040, with an estimated cost of $2.5 billion annually.[20] There are currently 2 pneumococcal vaccines licensed for use in older adults in the United States, the 13-valent pneumococcal conjugate vaccine (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23).[21]

Pneumococcal Polysaccharide Vaccine

A vaccine against *Streptococcus pneumonia* was first developed in 1977 protecting against 14 types of pneumococcal bacteria, and then later expanded in 1983 to protect against 23 types of pneumococcal bacteria, known today as the 23-valent polysaccharide vaccine (PPSV23).[22] The ACIP currently recommends that adults aged ≥65 years receive PPSV23 at least once.[21] Additionally, ACIP recommends that adults who received PPSV23 before the age of 65 (recommended for other chronic medical conditions in younger adults) should receive another dose at age 65 or older if at least 5 years have passed since their previous dose.[21] These recommendations are based on few studies that have demonstrated efficacy of the PPSV23 against invasive pneumococcal diseases in older adults.[23,24] However, few studies evaluating the efficacy of the PPSV23 in older adults have revealed conflicting results, particularly in preventing pneumococcal pneumonia.[25] A 2013 systematic review and meta-analysis by Moberley and colleagues[24] assessed the efficacy of PPSV23 for preventing invasive pneumococcal disease, all-cause pneumonia, and all-cause mortality in adults. The investigators found that PPSV23 reduced the risk of invasive pneumococcal disease (OR 0.26, 95% CI 0.14–0.45) in the general adult population, including the subgroup of otherwise healthy individuals in high-income countries (OR 0.20, 95% CI 0.10–0.39), which included a

large proportion of older adults. In this subgroup, however, there was no difference in all-cause pneumonia or mortality.[24] A more recent study published in 2017 sought to identify the serotype-specific effectiveness of the PPSV23 against pneumococcal pneumonia in adults 65 years and older. The investigators found that PPSV23 had low to moderate effectiveness against all pneumococcal pneumonia (27.4%) and against PPSV23-specific serotypes (33.5%).[26] Although not statistically significant, they found that protection was greater in adults aged <75 years.[26]

Pneumococcal Conjugate Vaccine

In September 2014, the ACIP released new recommendations that all adults aged ≥65 years receive the pneumococcal conjugate vaccine (PCV13), previously recommended only for use in younger children and those with high-risk medical conditions (eg, asplenia).[21] The rationale behind its use is that the conjugated protein vaccine might elicit a stronger immune response compared with the nonconjugated vaccine (PPSV23) in older adults.[27] The new guidelines are mostly based on results from a large randomized controlled trial published in 2015, concluding that among adults aged ≥65 years, PCV13 was found to be effective in preventing (1) vaccine-type community-acquired pneumonia (vaccine efficacy 45.6%, 95% CI 21.8%–62.5%), (2) confirmed nonbacteremic and noninvasive community-acquired pneumonia (vaccine efficacy 45%, 95% CI 14.2%–65.3%), and (3) invasive pneumococcal disease (vaccine efficacy 75%, CI 41.4%–90,8%).[28] There was no difference in all-cause mortality. However, this study was done in older adults living in the Netherlands who had not received the PPSV23. As opposed to the United States, the PPSV23 was not routinely administered to adults aged ≥65 years in the Netherlands during the trial period. Thus, the efficacy of PCV13 to older adults already vaccinated with PPSV23 is unknown. Additionally, widespread vaccination of younger children with PCV13 has likely reduced the burden of pneumococcal disease in older adults through herd immunity.[29] Although currently recommended in the United States, many developed countries do not recommend the routine use of PCV13 in adults aged ≥65 without high-risk comorbidities.[30] See **Fig. 1** for the recommended pneumococcal vaccination schedule in older adults.

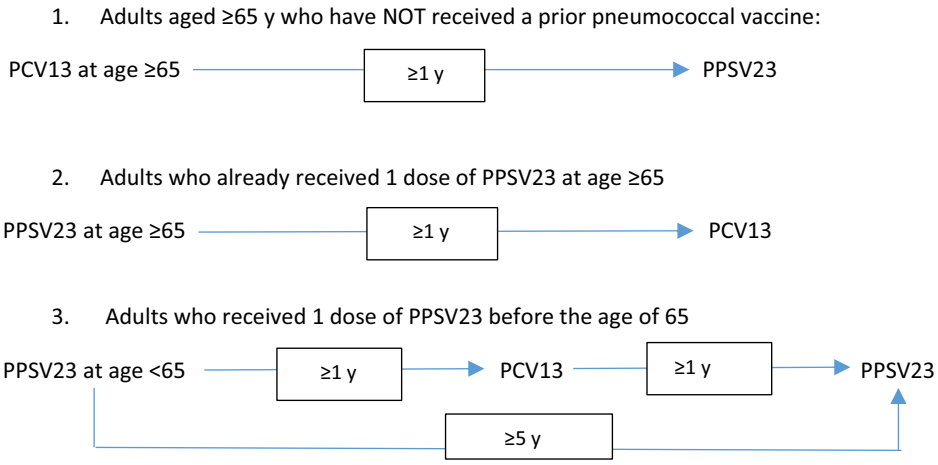

Fig. 1. Recommended pneumococcal vaccination schedule in adults aged ≥65. (*Adapted from* Kobayashi M, Bennett NM, Gierke R, et al. Intervals between PCV13 and PPSV23 vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2015;64(34):944–7.)

VARICELLA-ZOSTER VIRUS VACCINE

Older adults are at increased risk of varicella virus reactivation (ie, herpes zoster or shingles) and for greater disease severity because of age-associated changes in cell-mediated immunity.[31,32] Herpes zoster vaccination has been shown to decrease the risk of developing herpes zoster and postherpetic neuralgia by boosting cell-mediated immunity to the varicella virus.[32,33] A randomized placebo-controlled trial comparing the efficacy of herpes zoster vaccination with placebo in adults aged ≥60 described the following results[34]:

- Efficacy of herpes zoster vaccine in prevention of zoster was 51.3% over 3 years compared with placebo (1.6% vs 3.3%, $P<.001$).
- Mean duration of pain and discomfort was shorter in the vaccinated group compared with placebo (21 days vs 24 days, $P = .03$).
- Efficacy for prevention of postherpetic neuralgia was overall 66.5% (0.46 cases vs 1.38 cases per 1000 person-years).

A retrospective cohort study in 2011 in community-dwelling adults aged ≥60 years living in the United States also found that the incidence of herpes zoster was lower in vaccinated adults (hazard ratio 0.45; 95% CI 0.42–0.48) compared with unvaccinated adults. The number of herpes zoster cases among vaccinated individuals was 6.4 per 1000 person-years compared with 13.0 per 1000 person-years in unvaccinated adults. The vaccine was associated with lower incidence among all age groups, including those aged ≥70.[35] A systematic review and meta-analysis published in 2016 also concluded that herpes zoster vaccine was effective in preventing cases of herpes zoster, although noted that protection beyond 3 years was uncertain.[36] The Shingles Prevention Study, which followed adults aged ≥60 who received the herpes zoster vaccine, concluded that the clinical efficacy of zoster vaccination was limited beyond 5 years after vaccination. Administration of a booster vaccine may be beneficial; however, there is currently no recommendation from ACIP for booster administration.[37] A new investigational inactivated herpes zoster vaccine containing recombinant varicella-zoster virus glycoprotein E in combination with an adjuvant (ASO1B) was found to significantly reduce the risks of herpes zoster and poster herpetic neuralgia in adults aged 70 years who were followed for a mean of 3.7 years. The vaccine is promising for older adults, although not yet approved for use. This vaccine, however, requires 2 intramuscular injections, as opposed to a single injection, making adherence a potential barrier to complete vaccination.[38]

Herpes Zoster Vaccine Administration

ACIP recommends that all adults aged ≥60 receive the herpes zoster vaccine, regardless of whether they have had a prior episode of herpes zoster.[39,40] For patients with a known history of herpes zoster (ie, shingles), administration of the herpes zoster vaccine should be delayed at least a year to provide optimal immune response.[40] Vaccination should be given to all adults even if history of primary varicella virus infection (ie, chicken pox) is unknown, and there is no need to perform serologic testing to determine varicella immunity.[39,41] ACIP considers that adults born in the United States before 1980 are immune to varicella. If serologic evidence demonstrating that adults are not immune to varicella becomes available, older adults should be offered varicella vaccine and not the zoster vaccine. The herpes zoster vaccine can be given to older adults with comorbidities; however, because it contains live virus, should be avoided in patients with moderate to severe immunosuppression due to theoretic risk of potential disseminated herpes zoster infection.[39,41]

TETANUS, DIPHTHERIA, PERTUSSIS VACCINATION

Tetanus and Diphtheria

Tetanus and diphtheria are now rare diseases in the United States, although the incidence of both tetanus and diphtheria are highest in older adults.[42] Tetanus is an infection caused by *Clostridium tetani* and because the most common cause of infection is unpredictable acute injuries, vaccination remains the best way to prevent infection.[42] Although the tetanus vaccine has been available and recommended since 1940 in the United States, data show that fewer than 30% of adults aged ≥70 in the United States have protective levels of tetanus antibody.[43] The CDC estimates that only 40% to 60% of adults aged ≥65 received any form of the tetanus vaccine within the past 10 years.[4,44] Similar to tetanus, a cross-sectional survey found that only 30% of adults aged ≥60 living in the United States had protective levels of diphtheria antibody, likely a result of low vaccination rates.[45]

Pertussis

Pertussis is an acute, infectious cough illness that remains endemic in the United States despite longstanding routine childhood vaccination.[46] Immunity to pertussis wanes approximately 5 to 10 years after completion of childhood vaccination, leaving adolescents and adults susceptible to pertussis. The National Disease Surveillance System reported that among adults aged ≥65 years old there have been an average 318 cases of documented pertussis in the United States annually from 2000 to 2012 (range of 71–719 cases per year). Because older adults often present with pertussis atypically, the burden of disease actually may be higher.[46]

Recommended Vaccination Schedule

Although previously recommended only to adults aged ≥65 years old if in close contact with infants, the FDA approved the tetanus diphtheria acellular pertussis vaccine (Tdap) for use in older adults in 2011 and the ACIP began recommending the Tdap vaccination for all adults ≥65 years old in 2012.[46]

HEPATITIS VACCINATIONS

There are 2 vaccinations against hepatitis infections available for older adults: hepatitis A vaccine and hepatitis B vaccine. Recommendations for hepatitis vaccination in older adults are similar to younger adults, and are guided by specific risk factors and not age alone.[6] As many older adults are living longer, healthier lives, it is important for clinicians to ask about risk factors, including sexual activity and travel history.

Hepatitis A

ACIP recommends hepatitis A vaccination in the following situations:

1. Travel outside of the United States
2. Men who have sex with men
3. Illicit drug users (both injection and noninjection)
4. Individuals with chronic liver disease (especially those with chronic hepatitis B and/or hepatitis C infection)
5. Individuals with clotting factor disorders

Hepatitis B

ACIP recommends consideration of hepatitis B vaccination in the following situations:

1. Multiple sexual partners
2. History of a sexually transmitted disease

3. Men who have sex with men
4. Illicit drug users (both injection and noninjection)
5. Living with someone who has chronic hepatitis B
6. On hemodialysis
7. Travel to countries with moderate to high rates of hepatitis B
8. Exposure to blood at work

See **Table 1** for the recommended vaccination schedule for vaccines discussed previously.

BARRIERS TO VACCINATION IN OLDER ADULTS

Cost of Vaccinations

Most vaccinations are covered by Medicare. More than 90% of Medicare beneficiaries have Medicare Part B, which covers seasonal influenza vaccinations, pneumococcal vaccinations, and hepatitis B vaccinations. Other vaccinations, including herpes zoster and Tdap, are covered by Medicare Part D and are subject to deductibles and copays for each vaccine.[47] Approximately 71% of older adults are enrolled in Medicare Part D. Although routine vaccinations are covered by Medicare, cost has been found to be a significant barrier to vaccine administration in

Table 1
Recommended vaccination schedule of selected vaccines in older adults as recommended by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices

Vaccine	Recommended Dose/Schedule
Flu (*Influenza*)	High-dose or standard inactivated influenza vaccine yearly
Pneumococcal conjugated (PCV13)	One dose before receiving PPSV23 in adults aged ≥65 y or ≥1 y after adults aged ≥65 y receiving PPSV23[a]
Pneumococcal polysaccharide (PPSV23)	One dose in adults aged ≥65 or 5 y after previous dose if given before age 65
Shingles (*Zoster*)	One dose in adults ≥60 y, even if prior history of shingles[b]
Hepatitis A	Two doses based on risk factors[c]
Hepatitis B	Three doses based on risk factors[d]
Td (*Tetanus, diphtheria*)/Tdap (*Tetanus, diphtheria, pertussis*)	Tdap once with Td booster every 10 y

For complete list visit: https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf.

Abbreviation: Tdap, tetanus diphtheria acellular pertussis vaccine.

[a] See **Fig. 1** for dosing schedule if already received PPSV23.

[b] Should not be given to older adults with severe acquired or primary immunodeficiency.

[c] Risk factors include men who have sex with men, persons who use illicit drugs, persons with chronic liver disease or who receive clotting factor concentrates, or international travelers.

[d] Risk factors include sexually active persons not in a monogamous relationship, injection drug users, men who have sex with men, those being evaluated for a sexually transmitted infection, diabetic patients, those potentially exposed to blood or body fluids (eg, health care workers), persons with end-stage renal disease (including those on hemodialysis), human immunodeficiency virus infection, persons with chronic liver disease, household contacts and sex partners of hepatitis B–positive persons, international travelers, all adults in institutions and nonresidential daycare facilities, or persons with developmental disabilities.

older adults.[48] This is particularly true for the herpes zoster vaccine, for which only 20% to 30% of older adults actually receive.[4] In a study by Hurley and colleagues[49] in 2010, assessing barriers to herpes zoster vaccination in primary care, the most frequently reported barrier to vaccination was financial. Only 45% of primary care physicians (PCPs) were aware that the herpes zoster vaccine was reimbursed through Medicare Part D. Additionally, 12% of PCPs reported that they stopped administering herpes zoster vaccine in their office because of cost and reimbursement issues.

Another study by Hurley and colleagues[50] in 2017, exploring financial barriers to PCPs recommending vaccinations to their adult patients, found that a significant proportion of PCPs did not recommend vaccines because they thought that (1) a patient's insurance would not cover it (35%) or (2) the patient could be vaccinated more affordably elsewhere (38%). PCPs also reported that patients were less likely to decline vaccines for which no copay was required (eg, vaccines covered by Medicare Part B) and more likely to refuse vaccines covered by Medicare Part D (eg, herpes zoster and Tdap) because of the additional copay.[48,49] There were also concerns from PCPs about inadequate reimbursement for vaccinations, which influenced their willingness to recommend them.[48]

Similar financial issues were a known barrier to pediatric immunizations in the United States. The development of Vaccines for Children (VFC), a program designed to ensure that cost did not prohibit children from receiving vaccinations, has been successful in improving and sustaining a high vaccination rate in this population.[51] A similar program specifically for older adults also may be beneficial in increasing the vaccination rate; however, no such program has yet been developed.

Racial and Ethnic Barriers

There continues to be significant racial/ethnic gaps in coverage for all vaccinations recommended for older adults, with white individuals having the highest vaccination rates. For the pneumococcal vaccine, coverage among white individuals aged $\geq$65 was approximately 65%, compared with black individuals at approximately 50%, Hispanic individuals 45%, and Asian individuals 48%.[4] In a cross-sectional survey of patients with Medicare in the United States, white patients had significantly higher odds of vaccination than did black patients (OR 1.52, 95% CI 1.35–1.71), after adjusting for patient, physician, health system, and area-level characteristics.[52] Further studies and programs addressing racial and ethnic barriers to vaccinations are needed.

Misconceptions

Other common barriers to vaccinations in older adults are associated with misconceptions about vaccinations and include (1) beliefs that vaccines cause illness, (2) beliefs that vaccines are generally ineffective, and (3) belief that older adults are at little risk for vaccine-preventable illnesses.[53] In 2011, the National Vaccine Advisory Committee developed a guidance document with a summary of recommendations to address barriers to vaccination in adults.[1] It is important to highlight that health care professionals can significantly influence vaccination rates. Several studies have found that physician counseling and recommendations significantly improve vaccination uptake in older adults.[50,53] **Fig. 2** reviews the percentage of older adults receiving appropriate vaccinations compared with all adults for which each vaccine is recommended.

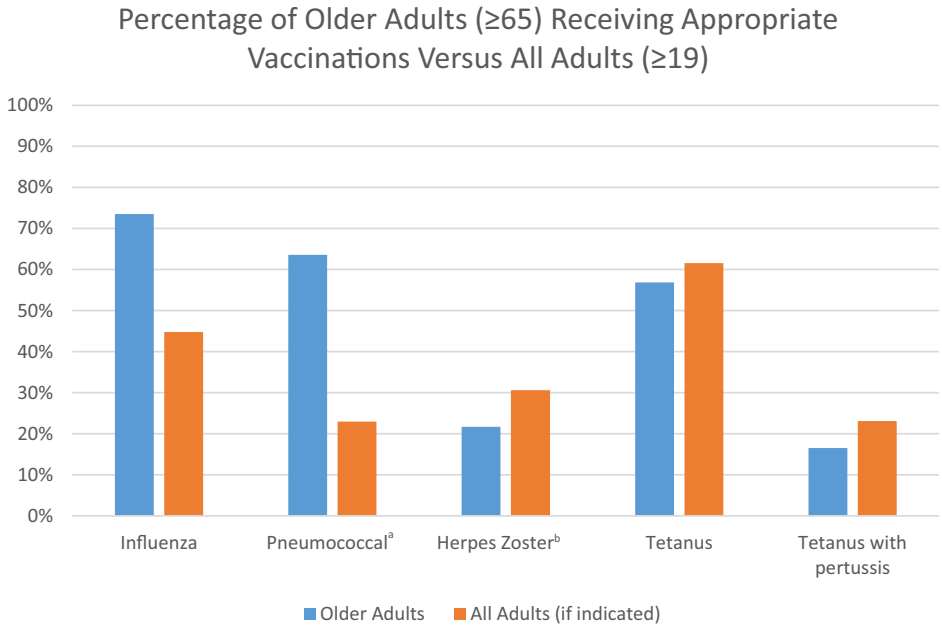

Fig. 2. Vaccination coverage in older adults. [a] Pneumococcal vaccine is indicated in adults younger than 65 years at increased risk. [b] Herpes zoster rates are compared in this chart between adults ≥65 years and ≥60 years. (*Data from* Williams WW, Lu PJ, O'Halloran A, et al. Surveillance of vaccination coverage among adult populations—United States, 2015. MMWR Surveill Summ 2017;66(11):1–28.)

SUMMARY

Vaccines are crucial to improving the health of older adults. Although older adults have a blunted immune response to vaccines, they remain one of the most important prevention strategies for several devastating illnesses that most commonly affect this population. Despite national campaigns highlighting the benefits of vaccinations, overall vaccination rates in this age group remain low, especially among minorities.[4] Clinician recommendations largely influence whether or not patients receive vaccinations and are an important target for improving vaccination coverage. Further studies exploring costs and other barriers to vaccination specifically in older adults are needed.

REFERENCES

1. National Vaccine Advisory Committee. A pathway to leadership for adult immunization: recommendations of the National Vaccine Advisory Committee: approved by the National Vaccine Advisory Committee on June 14, 2011. Public Health Rep 2012;127(Suppl 1):1–42.
2. Healthy people 2020. Available at: https://www.healthypeople.gov/2020/topics-objectives/topic/immunization-and-infectious-diseases. Accessed May 17, 2017.
3. Castle SC, Uyemura K, Fulop T, et al. Host resistance and immune responses in advanced age. Clin Geriatr Med 2007;23(3):463–79, v.
4. Williams WW, Lu PJ, O'Halloran A, et al. Surveillance of vaccination coverage among adult populations—United States, 2015. MMWR Surveill Summ 2017;66(11):1–28.
5. Rolfes MA, Foppa IM, Garg S, et al. Estimated influenza illnesses, medical visits, hospitalizations, and deaths averted by vaccination in the United States. 2016;

Available at: https://www.cdc.gov/flu/about/disease/2015-16.htm. Accessed May 17, 2017.
6. Kim DK, Riley LE, Harriman KH, et al. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older—United States, 2017. MMWR Surveill Summ 2017;66(5):136–8.
7. Kwong JC, Campitelli MA, Gubbay JB, et al. Vaccine effectiveness against laboratory-confirmed influenza hospitalizations among elderly adults during the 2010-2011 season. Clin Infect Dis 2013;57(6):820–7.
8. Talbot HK, Griffin MR, Chen Q, et al. Effectiveness of seasonal vaccine in preventing confirmed influenza-associated hospitalizations in community dwelling older adults. J Infect Dis 2011;203(4):500–8.
9. Osterholm MT, Kelley NS, Sommer A, et al. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. Lancet Infect Dis 2012;12(1):36–44.
10. Jefferson T, Di Pietrantonj C, Al-Ansary LA, et al. Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev 2010;(2):CD004876.
11. Darvishian M, Bijlsma MJ, Hak E, et al. Effectiveness of seasonal influenza vaccine in community-dwelling elderly people: a meta-analysis of test-negative design case-control studies. Lancet Infect Dis 2014;14(12):1228–39.
12. Rivetti D, Jefferson T, Thomas R, et al. Vaccines for preventing influenza in the elderly. Cochrane Database Syst Rev 2006;(3):CD004876.
13. Falsey AR, Treanor JJ, Tornieporth N, et al. Randomized, double-blind controlled phase 3 trial comparing the immunogenicity of high-dose and standard-dose influenza vaccine in adults 65 years of age and older. J Infect Dis 2009;200(2):172–80.
14. DiazGranados CA, Dunning AJ, Kimmel M, et al. Efficacy of high-dose versus standard-dose influenza vaccine in older adults. New Engl J Med 2014;371(7):635–45.
15. Richardson DM, Medvedeva EL, Roberts CB, et al, Centers for Disease Control and Prevention Epicenter Program. Comparative effectiveness of high-dose versus standard-dose influenza vaccination in community-dwelling veterans. Clin Infect Dis 2015;61(2):171–6.
16. Wilkinson K, Wei Y, Szwajcer A, et al. Efficacy and safety of high-dose influenza vaccine in elderly adults: a systematic review and meta-analysis. Vaccine 2017;35(21):2775–80.
17. Centers for Disease Control and Prevention (CDC). Licensure of a high-dose inactivated influenza vaccine for persons aged >or=65 years (Fluzone High-Dose) and guidance for use—United States, 2010. MMWR Morb Mortal Wkly Rep 2010;59(16):485–6.
18. Huang SS, Johnson KM, Ray GT, et al. Healthcare utilization and cost of pneumococcal disease in the United States. Vaccine 2011;29(18):3398–412.
19. Wagenvoort GH, Knol MJ, de Melker HE, et al. Risk and outcomes of invasive pneumococcal disease in adults with underlying conditions in the post-PCV7 era, The Netherlands. Vaccine 2016;34(3):334–40.
20. Wroe PC, Finkelstein JA, Ray GT, et al. Aging population and future burden of pneumococcal pneumonia in the United States. J Infect Dis 2012;205(10):1589–92.
21. Tomczyk S, Bennett NM, Stoecker C, et al. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged >/=65 years: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2014;63(37):822–5.

22. Centers for Disease Control and Prevention. In: Hamborsky JKA, Wolfe S, editors. Epidemology and prevention of vaccine-preventable diseases. 13th edition. Washington, DC: Public Health Foundation; 2015.
23. Jackson LA, Neuzil KM, Yu O, et al. Effectiveness of pneumococcal polysaccharide vaccine in older adults. New Engl J Med 2003;348(18):1747–55.
24. Moberley S, Holden J, Tatham DP, et al. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev 2013;(1):CD000422.
25. Huss A, Scott P, Stuck AE, et al. Efficacy of pneumococcal vaccination in adults: a meta-analysis. CMAJ 2009;180(1):48–58.
26. Suzuki M, Dhoubhadel BG, Ishifuji T, et al. Serotype-specific effectiveness of 23-valent pneumococcal polysaccharide vaccine against pneumococcal pneumonia in adults aged 65 years or older: a multicentre, prospective, test-negative design study. Lancet Infect Dis 2017;17(3):313–21.
27. French N, Gordon SB, Mwalukomo T, et al. A trial of a 7-valent pneumococcal conjugate vaccine in HIV-infected adults. N Engl J Med 2010;362(9):812–22.
28. Bonten MJ, Huijts SM, Bolkenbaas M, et al. Polysaccharide conjugate vaccine against pneumococcal pneumonia in adults. N Engl J Med 2015;372(12):1114–25.
29. Centers for Disease Control and Prevention. Epidemiology and prevention of vaccine-preventable diseases. In: Hamborsky JKA, Wolfe S, editors. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine among adults aged $\geq$ 65 years: recommendations of the Advisory Committee on Immunization Practices (ACIP). 13th edition. Washington, DC: Public Health Foundation; 2015. p. 279–94.
30. NHS. Pneumococcal vaccine. 2016. Available at: http://www.nhs.uk/Conditions/vaccinations/Pages/pneumococcal-vaccination.aspx. Accessed October 5, 2017.
31. Levin MJ, Smith JG, Kaufhold RM, et al. Decline in varicella-zoster virus (VZV)-specific cell-mediated immunity with increasing age and boosting with a high-dose VZV vaccine. J Infect Dis 2003;188(9):1336–44.
32. Weinberg A, Zhang JH, Oxman MN, et al. Varicella-zoster virus-specific immune responses to herpes zoster in elderly participants in a trial of a clinically effective zoster vaccine. J Infect Dis 2009;200(7):1068–77.
33. Levin MJ, Oxman MN, Zhang JH, et al. Varicella-zoster virus-specific immune responses in elderly recipients of a herpes zoster vaccine. J Infect Dis 2008;197(6):825–35.
34. Oxman MN, Levin MJ, Johnson GR, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. New Engl J Med 2005;352(22):2271–84.
35. Tseng HF, Smith N, Harpaz R, et al. Herpes zoster vaccine in older adults and the risk of subsequent herpes zoster disease. JAMA 2011;305(2):160–6.
36. Gagliardi AM, Andriolo BN, Torloni MR, et al. Vaccines for preventing herpes zoster in older adults. Cochrane Database Syst Rev 2016;(3):CD008858.
37. Morrison VA, Johnson GR, Schmader KE, et al. Long-term persistence of zoster vaccine efficacy. Clin Infect Dis 2015;60(6):900–9.
38. Cunningham AL, Lal H, Kovac M, et al. Efficacy of the herpes zoster subunit vaccine in adults 70 years of age or older. New Engl J Med 2016;375(11):1019–32.
39. Hales CM, Harpaz R, Ortega-Sanchez I, et al, Centers for Disease Control and Prevention (CDC). Update on recommendations for use of herpes zoster vaccine. MMWR Morb Mortal Wkly Rep 2014;63(33):729–31.
40. Morrison VA, Oxman MN, Levin MJ, et al. Safety of zoster vaccine in elderly adults following documented herpes zoster. J Infect Dis 2013;208(4):559–63.

41. Harpaz R, Ortega-Sanchez IR, Seward JF, Advisory Committee On Immunization Practices Centers for Disease Control and Prevention. Prevention of herpes zoster: recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Recommendations Rep 2008;57(RR-5):1–30 [quiz: CE32-34].
42. Centers for Disease Control and Prevention (CDC). Tetanus surveillance—United States, 2001-2008. MMWR Morb Mortal Wkly Rep 2011;60(12):365–9.
43. Gergen PJ, McQuillan GM, Kiely M, et al. A population-based serologic survey of immunity to tetanus in the United States. New Engl J Med 1995;332(12):761–6.
44. Singleton JA, Greby SM, Wooten KG, et al. Influenza, pneumococcal, and tetanus toxioid vaccination of adults–United States, 1993-7. MMWR CDC Surveill Summ 2000;49(9):39–62.
45. McQuillan GM, Kruszon-Moran D, Deforest A, et al. Serologic immunity to diphtheria and tetanus in the United States. Ann Intern Med 2002;136(9):660–6.
46. Kretsinger K, Broder KR, Cortese MM, et al. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. MMWR Recommendations Rep 2006; 55(RR-17):1–37.
47. Aging NCo. Vaccines: what Medicare pays for. 2016; Available at: https://www.ncoa.org/wp-content/uploads/medicare-vaccines.pdf. Accessed May 23, 2017.
48. Hurley LP, Bridges CB, Harpaz R, et al. U.S. physicians' perspective of adult vaccine delivery. Ann Intern Med 2014;160(3):161.
49. Hurley LP, Lindley MC, Harpaz R, et al. Barriers to the use of herpes zoster vaccine. Ann Intern Med 2010;152(9):555–60.
50. Hurley LP, Lindley MC, Allison MA, et al. Primary care physicians' perspective on financial issues and adult immunization in the era of the Affordable Care Act. Vaccine 2017;35(4):647–54.
51. Whitney CG, Zhou F, Singleton J, et al. Benefits from immunization during the vaccines for children program era—United States, 1994-2013. MMWR Morbidity Mortality Weekly Rep 2014;63(16):352–5.
52. O'Malley AS, Forrest CB. Immunization disparities in older Americans: determinants and future research needs. Am J Prev Med 2006;31(2):150–8.
53. Nagata JM, Hernandez-Ramos I, Kurup AS, et al. Social determinants of health and seasonal influenza vaccination in adults >/=65 years: a systematic review of qualitative and quantitative data. BMC Public Health 2013;13:388.