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Recommended Vaccines for Immunocompetent Older Adults: A Work Group Report of the AAAAI Asthma, Allergic & Immunologic Diseases in Older Adults Committee

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ABSTRACT: Adults 65 years or older are more susceptible to infectious diseases, representing a significant public health concern worldwide. Although newer vaccines have been developed for older adults, confusion over frequently changing guidelines often contributes to vaccine hesitancy and low vaccination rates. An American Academy of Allergy, Asthma & Immunology work group was convened to provide a clearer summary of these guidelines from the Advisory Committee on Immunization Practices and the Centers for Disease Control and Prevention. This article reviews the epidemiology and pathology of key infectious diseases in older adults, the mechanism of action of the vaccines targeting these diseases, commercially available vaccines, their potential side effects, and current vaccination recommendations for adults 65 years or

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Abbreviations used
ACIP- Advisory Committee on Immunization Practices
CDC- Centers for Disease Control and Prevention
COVID-19- coronavirus disease 2019
RSV- respiratory syncytial virus
VZV- varicella zoster virus

older. The primary focus of this work is on adults 65 years or older; however, when possible, newer vaccination recommendations that begin at age 50 years have also been included. The diseases covered in this review include coronavirus disease 2019, pneumococcal pneumonia, respiratory syncytial virus, influenza, shingles, and tetanus. A summary table of vaccination guidelines is also included in Table III. **(J Allergy Clin Immunol Pract 2026;14:791-801)**

INTRODUCTION

Older adults (age ≥65 years) are more susceptible to many infectious diseases compared with younger adults and children, primarily due to a decline in immune function (immunosenescence).[1] Likewise, older adults are more likely to have diseases associated with age, such as type 2 diabetes mellitus, cardiovascular diseases, and chronic obstructive pulmonary disease, which increase the risk for and severity of an infection.[2] Vaccination plays a crucial role to prevent and mitigate infectious diseases and is of particular importance for this age group. The recommended guidelines for older adults are complex and confusing for patients, physicians, and other health care professionals, contributing to vaccine hesitancy and lower immunization rates in this population.[3] Frequently changing guidelines and the emergence of new vaccines can make conversations and counseling challenging for both clinicians and patients alike. Racial disparities in vaccination also are exacerbated by these problems.[4]

In this American Academy of Allergy, Asthma & Immunology Work Report, key elements regarding the immunization of older adults (≥65 years) for coronavirus disease 2019 (COVID-19), pneumococcal pneumonia, respiratory syncytial virus (RSV), influenza, shingles, and tetanus are reviewed. Nonroutine vaccinations are outside the scope of this review. For each condition, 3 main topics are covered, when information permits:

A. Disease
   1. Epidemiology (including incidence, morbidity/mortality, and health care costs)
   2. Pathobiology of infectious agent
B. Immunization
   1. Available vaccines and respective mechanism of action
   2. Evidence supporting vaccination
   3. Adverse effects of vaccination
C. Vaccine schedule recommendations

Different schedules may exist for immunocompromised individuals.

Note: Although this report summarizes recommended vaccine schedules for this age group, physicians and other health care professionals should independently verify vaccine recommendation schedules using official guidelines.

Immunosenescence

Immunosenescence, that is, the gradual decline in immune function with age, is a major factor predisposing older adults to infectious diseases. This process occurs through several mechanisms, summarized as follows:

A. *Loss of T-cell population number and diversity*: With advanced age, the T-cell repertoire undergoes a significant contraction due to several factors, including deteriorating thymic function.[5-7] This decline in T-cell diversity also manifests through a reduced T-cell receptor repertoire, further impairing the immune system's ability to mount T-cell responses against new antigens.[8]
B. *Functional defects in intact T cells*: Additional functional defects limit the immune response in other ways. Defects in apoptotic pathways of naive CD4 T cells of older adults lead to reduced expression of CD28, an essential costimulatory molecule, with one study estimating that up to 50% of the naive T-cell compartment in older adults can be composed of cells lacking CD28, termed $CD4^{+}CD28^{(null)}$.[9] Without CD28, there is reduced production of cytokines such as IL-2, leading to impaired expansion and differentiation into effector T cells.[10] Furthermore, loss of CD28 is thought to inhibit the interactions with CD40L, leading to a decreased ability of $CD4^{+}$ cells to respond to dendritic cells.[11]
C. *Loss of B-cell receptor diversity despite maintenance of B-cell population size*: Unlike naive T cells, peripheral B-cell numbers do not decline with age; however, their diversity can be significantly compromised.[12,13] Reduced B-cell diversity likely correlates with a diminished immune response because these cells can display decreased antigen responsiveness and a limited repertoire against novel antigens.[14] In addition, intrinsic defects in class-switch recombination develop, and antibody production shifts in isotype from IgG to IgM, which leads to lower affinity for novel antigens.[15]
D. *Dysregulated B-cell interactions:* Finally, B cells may also have dysregulated interactions with other immune cells, especially in germinal centers. Germinal centers play a pivotal role in the humoral immune response and are one of the main locations where follicular dendritic cells typically present antigens to B cells. Follicular dendritic cells also play other important roles, including preventing apoptosis and triggering cellular proliferation.[16] However, one study estimates that with follicular dendritic cells from older subjects, this costimulatory interaction is decreased by 70% to 80%.[17] Less effective T-cell help, due partly to the loss of CD28, further reduces antibody production.[18]

Newer research suggests that age-associated epigenetic factors and dysregulation of the immune system also contribute to immunosenescence. Epigenetic aspects affect gene expression, and include age-related changes in DNA methylation patterns, histone modifications/variants, and micro RNA interactions.[19] Increased release of proinflammatory cytokines and chronic underlying inflammation also lead to delayed healing and increased susceptibility to disease, especially neurological and cardiovascular diseases.[20]

In summary, immunosenescence occurs through several pathways, including T cells, B cells, epigenetics, and dysregulation of the immune system. These factors play a pivotal role in the increased vulnerability of older adults to infectious diseases.

COVID-19: SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 COVID-19

Epidemiology. There are approximately 778 million confirmed cases of COVID-19, with an estimate of more than 7 million deaths globally as of August 2025, according to the World Health Organization.[21] As of 2020, approximately 81% of all US deaths due to COVID-19 (a total of ~282,836) occurred among older adults. The age-adjusted death rate among individuals 65 years or older was approximately 533.5 per 100,000 (~0.5%).[22] Older age is also a significant risk factor for inpatient mortality.[23] For example, one study found that the odds of death for patients hospitalized for COVID-19 were approximately 16 times higher among adults 80 years or older versus 18 to 34 years old.[24] Complications, such as sepsis, acute kidney failure, hyperkalemia, acidosis, acute liver damage, and neurological disorder, are more common in this age group and are also associated with increased fatalities.[24] COVID-19—related morbidity and mortality among those 65 years or older is 3 times higher among Black versus White older subjects.[25] The burden on the health care system and overall financial cost continue to worsen in turn. The average cost of an inpatient stay due to COVID-19 increased from $10,394 to $13,072 from March 2020 to March 2022. The cost for patients requiring in-hospital extracorporeal membrane oxygenation almost tripled to approximately $36,484.[26] In total, this suggests an extrapolated cost from 2020 to 2023 of approximately US $70 billion, solely for inpatient COVID-19—associated admissions.[26]

Pathobiology of infectious agent. Severe acute respiratory syndrome coronavirus 2 is a member of the betacoronavirus genus and is mainly spread through respiratory droplets. The outer surface of the virus contains a spike (S) glycoprotein that is processed into 2 subunits (S1 and S2).[27] S1 is involved in binding to a host receptor, whereas S2 helps to mediate membrane fusion.[28] Severe acute respiratory syndrome coronavirus 2 infection of the lower respiratory tract can cause diffuse alveolar damage, which is the predominant mechanism of lung injury, leading to increased rates of acute respiratory distress syndrome.[27] Disruption of the alveolar epithelium also may contribute to dysregulation of the coagulation system. Therefore, use of prophylactic anticoagulation has been correlated with prevention of death in hospitalized patients.

COVID-19 immunization

Available vaccinations and respective mechanism of action. The 4 2025-2026 COVID-19 vaccinations currently available are offered by Moderna (Spikevax and mNEXSPIKE), Pfizer-BioNTech (COMIRNATY), and Novavax (Nuvaxovid), which all target the extracellular domain of the spike glycoprotein. See Table I for all vaccine names and acronyms discussed. The Moderna vaccines (SpikeVAX and mNEXSPIKE) and the Pfizer-BioNTech (COMIRNATY) vaccine are modified mRNA vaccines encoding a stabilized version of the viral S protein; the mRNA is encapsulated into a lipid nanoparticle for delivery of the mRNA into cells.[29] The Novavax (Nuvaxovid) vaccine is an adjuvanted nanoparticle constructed from stabilized S protein, and was approved by the Food and Drug Administration in May 2025, after having been under Emergency Use Authorization since 2022.[30] The mRNA vaccines require translation by cellular machinery to produce the S glycoprotein antigen, whereas the adjuvanted nanoparticle vaccine consists of preformed antigen. Both types of vaccines produce robust antigen-specific T- and B-cell responses.[29,31,32]

TABLE I. Acronyms/abbreviations and vaccination names (bolded)

Term	Definition
ABRYVSO	Vaccine against RSV (produced by Pfizer)
ACIP	Advisory Committee on Immunization Practices
ADEM	Acute disseminated encephalomyelitis
ARDS	Acute respiratory distress syndrome
AREXVY	Vaccine against RSV (produced by GSK)
CAP	Community-acquired pneumonia
CDC	Centers for Disease Control and Prevention
CHF	Congestive heart failure
COMIRNATY	Vaccine against COVID-19 (mRNA vaccine; produced by Pfizer)
COPD	Chronic obstructive pulmonary disease
COVID-19	SARS-CoV-2; coronavirus disease 2019
CPS	Capsular polysaccharide
DAD	Diffuse alveolar damage
ECMO	Extracorporeal membrane oxygenation
Fluad	Vaccine against influenza (produced by Seqirus)
Flublok	Vaccine against influenza (produced by Sanofi Pasteur)
Fluzone	Vaccine against influenza (produced by Sanofi Pasteur)
GSK	GlaxoSmithKline; pharmaceutical company
mNEXSPIKE	mRNA-based vaccine against COVID-19 (Moderna)
mResvia	mRNA-based vaccine against RSV (Moderna)
SpikeVAX	mRNA-based vaccine against COVID-19 (Moderna)
Nuvaxovid	Vaccine against COVID-19; protein-subunit vaccine (Novavax)
PCV15	Vaccine against Pneumoccal pneumonia (also called ***Vaxneuvance***), no longer widely used
PCV20	Vaccine against Pneumococcal pneumonia (also called ***Prevnar 20***)
PCV21	Vaccine against Pneumococcal pneumonia (also called ***Capvaxive***)
PHN	Postherpetic neuralgia; complication of shingles
PPSV23	Vaccine against Pneumococcal pneumonia (also called ***Pneumovax***)
RSV	Respiratory syncytial virus
RT-PCR	Reverse transcription, polymerase chain reaction
rVE	Relative vaccine effectiveness
Shingrix	Vaccination against shingles (also called *HV/su*)
Td	Vaccination against tetanus & diphtheria (***TENIVAC***, ***TDVAX***)
Tdap	Vaccination against tetanus, diphtheria, and acellular pertussis (***Adacel***, ***Boostrix***)
VZV	Varicella zoster virus
WHO	World Health Organization
Zostavax	Previous shingles vaccine; no longer available in the United States

Evidence supporting vaccination. A meta-analysis of COVID-19 vaccination efforts worldwide indicate a pooled

effectiveness between 67% and 74% with 1 dose of the vaccine, with increase up to 89% to 93% after the second dose.[33] Between December 2020 and September 2021, it is estimated that in the United States alone, COVID-19 vaccination attenuated the infectious process, likely preventing 27 million infections, 1.6 million hospitalizations, and 235,000 deaths.[34] There is further evidence to suggest that vaccination also prevents against development of long COVID.[35] A more recent observational study, published in October 2025, in US veterans found that COVID-19 vaccination was estimated to be approximately 29% effective against preventing emergency department visits and 64% effective at preventing COVID-19 deaths.[36]

Adverse reactions to vaccination. One survey found that approximately 65% of patients experience side effects of the vaccine; however, approximately 95% are self-limited and only 5% required medical attention or hospitalization, the latter extremely rare.[37] Rates of the following side effects are described in cases per million vaccinations: myocarditis (4.94), thrombosis (8.36), tachycardia (12.45), and hypertension (13.70).[37] Vaccine-associated myocarditis appears to be more common in young males/adolescents who receive an mRNA COVID-19 vaccine, rather than older adults.[38] A separate study found that risk of myocarditis due to COVID-19 among non-vaccinated individuals is higher, estimated at approximately 0.21/1000 or approximately 210 per 1 million infected patients.[38] There are case reports of other adverse effects, such as leukocytoclastic vasculitis, renal complications, and acute disseminated encephalomyelitis, although the incidence of these is unclear.[37]

COVID-19 vaccine schedule recommendations

When first produced, the initial regimen for vaccinations involved a 2-shot series. Advisory Committee on Immunization Practices (ACIP) recommendations from October 2024 recommended that adults 65 years and older, if immunocompetent, should receive 2 doses of any 2024-2025 COVID-19 vaccine, with an interval of 6 months in between, regardless of previous vaccination status.[39,40]

More recently, as of November 2025, the Centers for Disease Control and Prevention (CDC) has issued interim guidance to instead recommend shared decision making for those 65 years and older. These recommendations are under review by ACIP and are likely to continue to change.[41]

Current CDC Regimen (2025-2026): Shared Decision Making. One Proposed Schedule Below

- Regardless of previous vaccination status: 2 doses of 2025-2026 vaccines, with general interval of 6 months after first shot.

Of note, this change in guidelines from recommendation to shared decision making is controversial because the reasoning behind it has not been clearly outlined. This has prompted concern that these recommendations are not based on the evidence surrounding COVID-19 and vaccination. Multiple health organizations, including the American Academy of Pediatrics, the American College of Physicians, the American Public Health Association, the Infectious Diseases Society of America, Massachusetts Public Health Alliance, and the Society for Maternal-Fetal Medicine, have filed suit in Massachusetts against the US Department of Health and Human Services and Secretary Kennedy in regard to this recommendation.[42]

PNEUMOCOCCAL: *STREPTOCOCCUS PNEUMONIAE*

Pneumococcal disease

Epidemiology. Pneumonia is defined as an infection affecting 1 or both lungs, frequently causing alveoli to fill with fluid and can be caused by bacterial, viral, or fungal pathogens. Regardless of etiology, pneumonia is a common and sometimes fatal disease, especially in older adults. The estimated rate of all-cause pneumonia in older adults in the United States is 6930 per 100,000 adults.[43] In those with at least 1 chronic medical condition, the rate ratio increases to 3.2 compared with a healthy adult of the same age.[43] Among older adults, mortality rates from pneumococcal pneumonia are significantly higher among Black versus White individuals.[44] This disparity may reflect differing vaccination rates: the CDC notes that in 2021, 70.1% of White individuals age 65 years or older received at least 1 pneumococcal vaccine, compared with 54.8% of Black individuals from the same age range.[45] In many cases, no definitive organism is identified. Some references estimate that the etiology of community-acquired pneumonia is identified in only about 60% of cases.[46] *Streptococcus pneumoniae* is often cited as a common infectious culprit, although estimates vary regarding the burden of disease attributable to *S pneumoniae* worldwide, with estimates ranging from 19% to 35%.[47] In the United States, it is estimated that pneumococcal pneumonia causes approximately 150,000 annual hospitalizations among all age groups, with a case-fatality rate ranging from 5% to 7%. Pneumococcal disease can significantly impact the health care system: one 2010 study estimated an annual cost of US $3.7 billion, although this included all manifestations of pneumococcal disease (including pneumonia, bacteremia, and meningitis).[48]

Pathobiology of infectious agent. *Streptococcus pneumoniae* is a gram-positive diplococcus, with multiple virulence factors. One of the difficulties in creating a vaccination against this bacteria is the presence of a wide variety of capsular polysaccharides.[49,50] Almost 100 variations exist, although 23 serotypes account for about 80% to 90% of all invasive pneumococcal disease.[49] Pneumococcal vaccines promote the generation of antibodies against these capsular polysaccharides,[51] although with varying levels of efficacy. One of the inherent difficulties lies in the nature of the disease: when specific serotypes are targeted, the prevalence of other serotypes may rise, reducing the overall effectiveness of the current vaccine, a process known as serotype replacement.[49]

Pneumococcal immunization

Available vaccinations and respective mechanism of action. Two types of pneumococcal vaccines are approved: (1) isolated polysaccharide vaccinations (PPSV23) and (2) conjugate vaccinations (PCV15, PCV20, PCV13, PCV21). PPSV23 (Pneumovax) is a 23-valent polysaccharide vaccine approved for adults 65 years or older. In contrast, PCV15 (Vaxneuvance, 15-valent), PCV20 (Prevnar20, 20-valent), and PCV21 (Capvaxive, 21-valent) are conjugate vaccines with the polysaccharides conjugated to modified, nontoxic diphtheria

TABLE II. Pneumococcal vaccination recommendations (age 50 y or older)

Group	Recommendation	Notes
Without previous vaccination, received only PCV7 or PPSV23, or unknown vaccination history	Single dose of PCV15, PCV20, or PCV21	If PCV15 is used, a single dose of PPSV23 should be administered 1 y later. Shorter intervals can be considered in certain populations (those who are immunocompromised, have a cochlear implant, or a cerebrospinal fluid leak)
PCV13 only	Single dose of PCV20 or PCV21	Should be administered at least 1 y after PCV13 dose
PCV13 at any age and PPSV23 at age <65 y	Single dose of PCV20 or PCV21	Should be administered at least 5 y after the last pneumococcal vaccine dose
PCV13 at any age and PPSV23 at age ≥65 y	Shared decision making for additional dose of PCV20 or PCV21	If administering additional dose, should be administered at least 5 y after the last pneumococcal vaccine dose
Received either PCV20 or PCV21	No further vaccinations needed	

protein. PCV13 (13-valent) is an older version of these conjugate vaccines, particularly PCV20. Conjugate vaccines are believed to stimulate a more robust and enduring immune response than polysaccharide vaccines, particularly in children. The newest pneumococcal vaccines are both conjugate vaccines: PCV20 (approved April 2021), PCV15 (approved June 2022), and PCV21 (approved June 2024).

Evidence supporting vaccination. The CDC estimates the clinical effectiveness of PPSV23 in preventing invasive disease at 60% to 70%.[52] Among individual trials globally, there is a wide range in reported efficacy. A meta-analysis, published in 2023, estimated that the PPSV23 vaccine is 45% effective against invasive pneumococcal disease, and 18% against pneumococcal pneumonia.[53] When comparing PCV20 to PCV13 or PPSV23, one study found that in adults 60 years or older, PCV20 elicited noninferior immune responses to all 13 serotypes covered in PCV13, and 6 of the 7 additional serotypes included in PCV20 were noninferior to those covered by PPSV23.[54] In the safety, tolerability, and immunogenecity of an adult pneumococcal conjugate vaccine, V116 (STRIDE-3) trial, which compared the efficacy of PCV20 against PCV21 in adults 50 years and older, PCV21 was found to induce noninferior responses to 10 serotypes shared among both vaccinations and superior responses with regard to 10 of 11 serotypes only found in PCV21.[55]

Adverse reactions to vaccination. In adults older than 60 years, the most common reported adverse reactions to PCV20 include pain at the injection site (>50%), muscle pain and fatigue (>30%), headache (>20%), and arthralgia (>10%).[51] There is one report of a serum-sickness–like reaction after PCV13; however, 1 month postdiagnosis, the patient had no further sequelae.[56] There are no current reports of any long-term complications due to PCV20.

Pneumococcal vaccine schedule recommendations

Previously, the vaccination schedule recommended for most adults involved PCV13 or PCV15, and PPSV23 after age 65 years. PPSV23 covered a greater number of serotypes than PCV13; however, PCV13 can induce greater immunologic responses and memory.[57] ACIP Guidelines from October 2024 were updated to include PCV20, PCV15, and PCV21, and the recommendation has also been changed to include adults starting at age 50 years (Table II).[58]

In summary, most immunocompetent individuals should receive a single dose of pneumococcal vaccine (PCV20 or PCV21), at age 50 years.[59]

RESPIRATORY SYNCYTIAL VIRUS

RSV disease

Epidemiology. RSV is acknowledged as the most common viral etiology of pediatric bronchiolitis; however, it also causes infection in older adults. Estimates of RSV burden among adults vary, and evidence suggests that RSV is still comparatively more frequent among children. One estimate from Poland suggests that, based on the detection of RSV-positive RT-PCR (RSV genome), RSV frequency among children from 2008 to 2009 was 53%; in contrast, among adults, it was approximately 25%. These numbers vary with regard to the detection mechanism used; the authors noted that the RSV genome was better for detecting infection in children (many of whom were hospitalized) but that the RSV antigen was better for detecting infection in adults (many of whom were sampled as an outpatient).[60] Regardless, RSV exerts a significant burden among older US adults. One estimate from 2022 suggests that RSV contributes to approximately 159,000 annual hospitalizations among this population, with an estimated 9500 to 12,700 associated deaths.[61] Risk factors for RSV infection, greater infection severity, and hospitalization include increased age and comorbid medical conditions, such as congestive heart failure, chronic obstructive pulmonary disease, and others. A CDC study of 12 states from July 2022 to June 2023, using a random sample of 1600 older adult patients with RSV-associated hospitalization, noted that more than half (54.1%) were aged at least 75 years.[62] Furthermore, adults 65 years and older living in assisted living or skilled nursing facilities have at least a 3 times greater risk of hospitalization due to RSV than do adults living in the community.[63] It is thought that the financial burden of RSV in the United States among all age groups is approximately US $6.6 billion, with more than 90% of costs attributed to the less than 5% of RSV cases necessitating hospitalization.[64]

Pathobiology of infectious agent. RSV is a member of the orthopneumovirus genus. It is typically classified into 2 antigenic subgroups (A and B), defined by the epitopes

presented on the fusion protein (F) and the attachment protein (G) on the virion surface.[65] The F protein contains conserved epitope across the A and B subgroups.[66]

RSV immunization

Vaccinations available and respective mechanism of action. There are several RSV vaccines available, all of which work by eliciting immunity to the RSV F protein.[67] These vaccines include recombinant protein-based vaccines, namely, AREXVY (GlaxoSmithKline) and ABRYSVO (Pfizer), and an mRNA-based vaccine called mResvia (Moderna).

- *Protein-based vaccines*: AREXVY is a monovalent (subgroup A) stabilized prefusion F protein vaccine adjuvanted with $ASO1_E$, which is a proprietary suspension component containing MPL (3-O-desacyl-4\'-monophosphoryl lipid A) and QS-21, a saponin fraction extracted from *Quillaja saponaria.*[68] ABRYSVO is an unadjuvanted bivalent (subgroups A and B) stabilized prefusion F protein vaccine.
- *mRNA-based vaccine*: mResvia is a lipid nanoparticle-encapsulated mRNA that encodes a stabilized prefusion form of the RSV F glycoprotein, which when delivered to human cells instructs the cell to produce the viral protein.[69]

Evidence supporting vaccination. Based on a phase-3 clinical trial, including approximately 25,000 immunocompetent patients, the efficacy of 1 dose of AREXVY (GlaxoSmithKline) to prevent lower respiratory tract disease over 2 seasons was approximately 74.5%; however, this study was not powered to determine efficacy against hospitalization or severe illness needing respiratory intervention.[70] The efficacy of the ABRYSVO (Pfizer) vaccine, over a different phase-3 clinical trial involving approximately 36,000 patients, was approximately 84.4% of preventing lower respiratory tract disease over 2 seasons.[70] A new study published in 2024 examined approximately 28,000 hospitalizations for RSV infection in 8 US states from October 2023 to March 2024. It found that vaccination with either AREXVY or ABRYVSO was 80% effective against RSV-associated hospitalizations and 81% effective against RSV-associated deaths in immunocompetent adults older than 60 years.[71] The ConquerRSV trial examined the efficacy of mResvia among approximately 35,000 adults and found that the vaccine was approximately 68% effective against RSV-associated respiratory disease.[69] A study compared the efficacy of these 3 RSV vaccines, and reported that a single dose of mResvia was nearly 50% effective against RSV lower respiratory tract disease (over 18 months) compared with approximately 67% with AREXVY (over 23.3 months) and approximately 81% with ABRYVSO (over 16.4 months).[69] Initial research suggests that 1 dose of RSV vaccination (with adjuvanted $ASOE_1$ prefusion F protein—based vaccination) is effective for at least 3 seasons against RSV lower respiratory tract disease, and that a second dose 1 year after the first dose did not significantly improve outcomes.[72] Newer research suggests that in adults older than 60 years, vaccination with RSV prefusion vaccine (compared with no vaccination) conveyed a significant decrease in all-cause cardiorespiratory hospitalizations.[73] Furthermore, when compared with no vaccine, the RSV prefusion vaccine additionally decreases RSV-related respiratory hospitalizations.[74]

Adverse reactions to vaccination. The most common side effects to ABRYSVO in adults aged 60 years and older include fatigue (15.5%), headache (12.8%), pain at injection site (10.5%), and muscle pain (10.1%).[75] It is important to note that many of these side effects, including significant adverse events, also had similar rates among placebo populations.[75] The most common adverse effects to mResvia included injection-site pain (~55%), axillary swelling/tenderness (15%), fatigue, headache, myalgia, and urticaria.[69] A postmarketing observational study indicated that individuals vaccinated with either AREXVY or ABRYVSO may have an increased risk of Guillain-Barre syndrome, with a rate of approximately 9 excess cases of Guillain-Barre syndrome per million doses of ABRYVSO (~0.0009%) and with a rate of approximately 7 excess cases of Guillain-Barre syndrome per million doses of AREXVY (~0.0007%)[76] but was not able to demonstrate definitive causality.[76]

RSV vaccine schedule recommendations

Vaccine schedule recommendations have changed in recent years. The CDC had initially recommended that individuals 60 years and older should engage in shared clinical decision making with their physician or health care professional if they should receive a single dose of the vaccine. Persons at highest risk who were considered to benefit from vaccination include residents of nursing homes and long-term care facilities and those with chronic medical conditions, including but not limited to diabetes, congestive heart failure, chronic obstructive pulmonary disease, and kidney or liver disorders.[70] In June 2024, the CDC strengthened its recommendation, stating that in addition to at-risk individuals aged 60 years and older, everyone aged 75 years and older should receive the RSV vaccine.[77]

Guidelines have currently been shifting to incorporate those 50 years and older at increased risk. All 3 vaccines (AREXVY, ABRYVSO, and mResvia) have been approved for those 50 years and older.[78-80] In April 2025, the ACIP indicated that it was planning to change the recommendation to start at age 50 years for those at increased risk.[81] In July 2025, the CDC followed suit, recommending the vaccine for all adults 75 years and older, and for adults aged 50 to 74 years who are at increased risk.[82]

In summary, for RSV vaccinations:

- 75 years or older: One dose is recommended for all.
- 50 to 74 years: One dose recommended in patients with risk factors, including diabetes, congestive heart failure, chronic obstructive pulmonary disease, and kidney or liver disorders.

INFLUENZA: HIGH-DOSE INFLUENZA

Influenza disease

Epidemiology. There are an estimated annual 1 billion cases of influenza globally in the general population, exerting a significant toll on public health. Adults 65 years and older comprise a disproportionate number of those seriously affected: accounting for approximately 50% to 70% of flu-related hospitalizations and 75% to 80% of flu-related deaths in the United States.[83,84] Therefore, older adults likely account for most of influenza-related annual direct health care costs, estimated at approximately US $3.2 billion.[85] Other estimates suggest a much higher annual cost of approximately US $10 billion.[86] Similar to pneumococcal pneumonia, deaths from influenza are significantly higher among Black versus White individuals; however, lower immunization rates among Black individuals may also contribute to this.[44] The CDC estimates that during the 2021-2022 season, approximately 54% of White adults were

vaccinated while 42% of Black adults were, although this statistic does not stratify further on the basis of age group.[87]

Pathobiology of infectious agent. Influenza is an enveloped negative single-stranded RNA virus, which typically replicates in both the upper and the lower respiratory tracts. Typical symptoms involve cough, high fever, and shortness of breath, which can persist for 7 to 10 days. It is often associated with secondary bacterial pneumonia. The virus is known for a high mutation frequency, partly due to its replication complex's lack of proofreading capacity for completed segments.[88] The composition of the influenza vaccines is adjusted each year to match the circulating influenza strains. The original influenza vaccine composition was trivalent, representing H1N1, H3N2, and influenza B. An additional influenza B strain was added in 2012, resulting in a quadrivalent vaccine. For the 2024-2025 season, the influenza vaccine will return to a trivalent formulation.

Influenza immunization

Vaccinations available and respective mechanism of action. Vaccinations available include the following:

A. Fluzone high-dose vaccine (Sanofi Pasteur; HD-IIV3); *high-dose, inactivated*
B. Flublok recombinant vaccine (Sanofi Pasteur; RIV3); *recombinant*
C. Fluad flu vaccine, adjuvanted (Seqirus; aIIV3); *adjuvanted, inactivated*

The CDC recommends 1 of 3 different vaccines for people 65 years or older: (a) a high-dose inactivated vaccine, (b) a recombinant vaccine, or (c) an adjuvanted (MF59) inactivated vaccine.[89] The inactivated vaccines are derived from influenza viruses propagated in eggs, whereas the recombinant vaccine contains protein produced in insect cells. The influenza vaccines recommended for older adults contain either increased antigen levels (Fluzone, Flublok) or an adjuvant to prompt patients to have a stronger immunologic response (Fluad).[84]

Evidence supporting vaccination. High-dose flu vaccines are considered more effective than standard dose flu vaccine. One systematic review found that relative vaccine effectiveness for high-dose flu vaccinations was 15.9% against influenza-like illnesses and 8.4% against all-cause hospital admissions.[90,91] Relative vaccine effectiveness measures the incremental improvement in the efficacy of the measured vaccination (high-dose flu) against standard dose vaccination. However, it is important to recognize that relative vaccine effectiveness varies compared with the absolute vaccine effectiveness of the initial vaccination, which in turn can vary depending on the season and circulating strains, making comparisons difficult.[92]

Adverse reactions to vaccination. Side effects can be more common among higher-dose versus standard-dose vaccines; however, most of these are mild and/or self-limiting. For example, for Fluzone, these include headache (~20%), pain (~40%), and redness at the injection site (~6%).[93,94]

Influenza vaccination schedule recommendations

A major and consistent hallmark of immunosenescence is the significant alteration in both quantity and quality of the T-cell compartment. Therefore, vaccines with more potent and durable immune response are required for adults 65 years and older. The CDC preferentially recommends high-dose (inactivated or recombinant) or adjuvanted inactivated influenza vaccines for people 65 years and older (ie, Fluzone high-dose at 60 μg/strain) to induce stronger immunologic responses.[84] The ACIP recommends that adults 65 years and older receive 1 high-dose (inactivated or recombinant) or adjuvanted inactivated vaccine annually.[95] If high-dose or adjuvanted vaccines are unavailable, clinicians can consider other age-appropriate vaccine.

SHINGLES: HERPES ZOSTER

Shingles: Herpes zoster disease

Epidemiology. Shingles is a disease triggered by reactivation of varicella zoster virus (VZV). Approximately 1 in 3 people develop shingles over the course of their life, with an estimated 1 million cases annually.[96] Rates of disease and severity are greater in older adults.[97] One of the most devastating aspects of shingles is postherpetic neuralgia, which can cause persistent pain even after disappearance of the rash. Other complications include herpes zoster ophthalmicus, which can cause vision loss. Because of its prolonged systemic effects, herpes zoster is associated with loss of more than 60,000 quality-of-life years, which accounts for secondary infections, incidence of postherpetic neuralgia, and ophthalmic complications.[97,98] Furthermore, there are significant financial costs associated with shingles estimated at US $2.4 billion annually in the United States alone. By 2030, shingles in adults 65 years and older is projected to cost US $4.74 billion.[96]

Pathobiology of infectious agent. VZV is a double-stranded DNA virus, which typically infects children as varicella, causing chickenpox. Reactivation of latent VZV later in life leads to the development of shingles. The virus typically lies dormant in the dorsal root ganglia and can activate spontaneously or from stress.[99] The virus is composed of various glycoproteins, which play different roles in its pathogenesis and are targets for vaccine development.

Shingles: Herpes zoster immunizations

Vaccinations available and respective mechanism of action. The previous VZV vaccine, Zostavax (ZVL), was a live-attenuated vaccine that is no longer recommended for older adults and was discontinued in the United States by 2020. In contrast, the currently available VZV vaccine (Shingrix, HZ/su, RZV; GlaxoSmithKline) is a recombinant protein. Shingrix is an adjuvanted ($AS01_B$) protein vaccine consisting of recombinant VZV glycoprotein E, an essential viral surface/envelope antigen.[96]

Evidence supporting vaccination. The Shingrix vaccine was studied in 2 phase 3 trials (ZOE-50 and ZOE-70). Vaccine efficacy in ZOE-70 was 89.8% at preventing herpes zoster, per 1000 adults, with an incidence of disease of 0.9/1000 in vaccinated adults versus 9.2/1000 in the placebo group.[96] The CDC summarizes the data and reports that in immunocompetent adults 50 to 69 years old, Shingrix is 97% effective at preventing shingles, which falls to 91% in adults 70 years and older.[100] Regarding postherpetic neuralgia, the CDC reports that Shingrix is 91% effective in preventing it in adults 50 years and older and 89% effective in adults 70 years and older.[100]

TABLE III. Summary of routine immunization recommendations for immunocompetent adults

Age	Disease	Vaccines available	General guidelines
All adults	Tetanus	Tdap; Td	1 booster dose of Tdap or Td every 10 y
≥50 y	Herpes zoster (shingles)	Shingrix (GSK; HV/su)	2 doses, separated by a period of 2-6 mo
	Pneumococcal (*Streptococcus pneumoniae*)	Prevnar20 (PCV20) PCV21 (Capvaxive) PCV15 PPSV23 (Pneumovax)	1 single dose of PCV20 or PCV21
	RSV	AREXVY (GSK) ABRYVSO (Pfizer) mResvia (Moderna)	For those with at-risk conditions, recommend single dose
≥65 y	Flu (influenza)	Fluzone (Sanofi Pasteur) Flublok (Sanofi Pasteur) Fluad (Seqirus)	Annual single dose of high-dose vaccine
	COVID-19	SpikeVAX, mNEXSPIKE (Moderna, mRNA) COMIRNATY (Pfizer, mRNA) Nuvaxovid (Novavax, protein subunit)	~October 2024 (ACIP): Recommend 2 doses of vaccine ~November 2025 (CDC Interim Guidance): Shared Decision Making. Consider 2 doses of updated 2025-2026 vaccine, 6 mo apart
≥75 y	RSV	AREXVY (GSK) ABRYVSO (Pfizer) mResvia (Moderna)	Everyone should receive 1 single dose, if have not previously received

Please see text for details.

TABLE IV. Commonly encountered barriers to vaccine administration among older adults and recommendations for addressing them

Barriers	Recommendations
False beliefs about vaccine side effects	Explore current beliefs and why they are held and offer reassurance based on data
Limited means of transportation to facilities that can administer vaccines	Offer vaccines if available in clinic; strategize with patients where and how to get vaccines, eg, local pharmacies
Limited access to vaccines at skilled nursing facility	Communicate with staff at nursing facility about the specific vaccines that the patient needs; coordinate with visiting clinicians about vaccine delivery
Mechanical limitations	If patient gets medications delivered at home, coordinate with home medication administration service about the specific vaccines that the patient needs
Concerns about vaccine contraindications with comorbidities	Explore current concerns and offer reassurance based on data if appropriate
Physicians caring for adults rarely provide vaccinations for their patients in their clinics	Cost-effective methods for physicians to give these vaccines in their clinics are needed

Adverse reaction to vaccination. The most common adverse reactions include sore arm (78%), redness (38%), and swelling (26%); in general, adverse reactions are more common among younger individuals. Side effects usually self-resolved within 2 to 3 days.[100,101]

Shingles—Vaccine schedule recommendations

Shingrix is recommended for adults 50 years and older in 2 doses, administered 2 to 6 months apart. Vaccination is recommended regardless of a previous shingles episode, Zostavax, or chickenpox vaccine administration.[100]

TETANUS: *CLOSTRIDIUM TETANI*

Tetanus disease

Epidemiology. Tetanus is most common in rural and agricultural areas, especially in countries with low vaccination rates. In 2020, the CDC estimates that there were more than 11,750 tetanus cases worldwide, with most cases reported in Southeast Asia and Africa.[102] This number likely does not account for neonatal tetanus, and in 2021, the World Health Organization estimated that there were 24,000 newborn deaths from tetanus.[103] In the United States, the incidence of tetanus is much lower. There were only 264 total cases from 2009 to 2017 in the United States; of these, only 25% had received 3 or more doses of tetanus toxoid vaccine. Twenty-three percent of cases occurred in adults 65 years or older.[104] Across this same period, there were 19 deaths from tetanus, all of which occurred in adults 50 years or older.[104] Approximately 30 cases of tetanus occur every year in the United States.

Pathobiology of infectious agent. Tetanus is caused by an anaerobic gram-positive bacteria, *Clostridium tetani*, which resides in the soil and can form spores. The bacteria is transmitted to humans through contaminated metal puncture wounds. Some spores can contain a plasmid encoding the gene for a neurotoxin, called tetanus neurotoxin, which is made up of

a polypeptide chain. The toxin can migrate in retrograde fashion to the spinal cord and block inhibitory interneurons from releasing neurotransmitters. Thus, once the organism infects an individual, the toxin from *C tetani* leads to contraction (and failure of relaxation) of skeletal muscles, giving rise to the clinical signs of opisthotonus and lockjaw.[105]

Tetanus immunization

Available vaccinations and respective mechanism of action. There are 2 main tetanus vaccinations for adults: Tdap and Td. Tdap (Adacel, Boostrix) contains tetanus, diphtheria, and acellular pertussis, whereas Td (TENIVAC and TDVAX) solely prevents against tetanus and diphtheria. In each vaccine, the tetanus component is a small dose of tetanus toxoid.

Evidence supporting vaccination. The tetanus vaccination is very effective, estimated to elicit nearly 100% response in individuals (measured as antitetanus levels $>$ 0.1 IU/mL).[106] This is further supported by anecdotal evidence that most tetanus cases occur in those not completely vaccinated.

Adverse reactions to vaccination. The most common adverse effects include pain, redness, or swelling at the site of injection. Some patients can have fever, nausea, or headache.[107]

Tetanus vaccine schedule recommendations

All adults should have received at least 1 lifetime Tdap booster. The ACIP recommends that immunocompetent individuals should then receive either Td or Tdap booster doses every 10 years. Although receiving Tdap may convey additional protection against pertussis, Tdap is also more expensive, and there is insufficient evidence to support the use of Tdap over Td.[108]

Summary and conclusion

Older adults represent an age group particularly vulnerable to severe infections. Appropriate vaccination can lead to a significantly decreased burden of disease and mortality. Furthermore, preventing these diseases can decrease health care costs. An abbreviated summary of vaccination recommendations with general guidelines is included in Table III. Having concise immunization recommendations available for patients is only one piece of the puzzle to improving immunization rates among older adult patients. Addressing systemic barriers to vaccination, such as limited access to vaccines, mobility issues, as well as vaccination hesitancy and distrust of the medical profession, is also important. Some of these barriers and recommendations on how to overcome them are summarized in Table IV. The allergist/immunologist in community practice and academic settings plays a crucial role in discussing vaccines with older adult patients, in overcoming barriers, and in improving vaccination rates.

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