# Adult Vaccine Update 2025: Pneumococcus, Shingles, COVID-19, and RSV



Kansas City Southwest Clinical Society January 31, 2025

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I have no relevant financial relationships to disclose.

I will not discuss off label use or investigational use in my presentation.

# Adult Vaccine Update 2025

- Types of vaccines
- Pneumococcus
- Herpes Zoster (Shingles)
- RSV
- COVID-19
- Vaccine Benefits/Myths



- Burden of disease
- Vaccine
  - Efficacy
  - Recommendations
    - General population
    - Special populations
  - Adverse effects

# Vaccines Types

- Live-attenuated
  - use a weakened (or attenuated) form of the virus
  - similar to natural infection, create a strong and long-lasting immune response
- Inactivated vaccines
  - use a killed version of the virus
  - usually don't provide immunity that's as strong as live vaccines
- Subunit and polysaccharide vaccines
  - use specific pieces of the virus/bacterium protein, sugar, or capsid
  - generate strong immune response that's targeted to key parts of the germ
  - <u>Conjugate vaccines</u> link antigens or toxoids from another microbe to the polysaccharides, enhancing the immune response
  - <u>Recombinant vaccines</u> are produced with recombinant DNA technology, insert DNA encoding an antigen (e.g. bacterial surface protein) into bacterial or mammalian cells *in vitro*, expressing the antigen in these cells and then purifying it from them
- Toxoid vaccines
  - use a toxin made by the germ that causes a disease
  - create immunity to the parts of the germ that cause a disease instead of the germ itself

sles mumps rul

Examples

Measles, mumps, rubella Rotavirus Chickenpox Yellow Fever

Hepatitis A Influenza (classic) Rabies

> Haemophilus influenzae type b Whooping cough Pneumococcal disease Meningococcal disease Hepatitis B HPV (Human papillomavirus) Shingles RSV

Diphtheria Tetanus

HHS.gov

# Newer Vaccine Types



Nature Rev Immunol 21, 83–100 (2021)

Lancet 2024; 403: 1879–92

lshtm.ac.uk

# Streptococcus pneumoniae "Pneumococcus"

- First isolated by Pasteur in 1881
- More than 80 serotypes described by 1940 (92 by 2011, now >100)
  - Most serotypes can cause serious disease but the top 10 cause 62% (historically)
- The leading cause of respiratory tract infections
  - ~400,000 hospitalizations/year in U.S. for pneumococcal pneumonia, mortality 5-7%
  - 25-30% have bacteremia (overall mortality 20%, up to 60% in the elderly)
  - ~3,000 to 6,000 cases of pneumococcal meningitis per year (child mortality 8%, adult 22%)
- IPD: Invasive Pneumococcal Disease (infection of normally sterile sites) occurs in approximately 25% of cases
  - Risk Factors: Decreased immune function (including hematologic cancer and HIV infection), asplenia (functional or anatomic), chronic heart, pulmonary (including asthma in adults), liver or renal disease, cigarette smoking, cerebrospinal fluid (CSF) leak, and cochlear implant

N Engl J Med 2015; 372(12):1114 - 25 CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases 14th ed, 2021



Impact vaccine

recommendations



## Pneumococcal Vaccines

PPSV = pneumococcal polysaccharide vaccine PCV = pneumococcal conjugate vaccine

### • Polysaccharide vaccine

- against 14 serotypes first licensed in 1977 (Pneumovax 14, PPSV14)
- expanded to 23 serotypes in 1983 (Pneumovax 23, PPSV23)
- <u>Conjugated</u> vaccine
  - against 7 serotypes licensed in 2000 (Prevnar 7, PCV7)
    - conjugated to a nontoxic variant of diphtheria toxin
    - elicits a more robust immune response
  - expanded to 13 serotypes in 2010 (Prevnar 13, PCV13)



### MORE TO FOLLOW



# Polysaccharide Pneumococcal Vaccine (*Pneumovax*, PPSV23) Efficacy

- Antibody response is poor in children <2 and adults with chronic illnesses and immunocompromise
- Efficacy results varied in multiple studies
- Overall 60%–70% effective in preventing <u>invasive disease</u> caused by serotypes included in the vaccine but not effective in reducing rates of pneumonia





## Conjugated Pneumococcal Vaccine (Prevnar 13) Efficacy



- >90% effective against <u>invasive disease</u> caused by vaccine serotypes in children, 75% effective in adults > 65
- 45% effective against vaccine-type non-bacteremic pneumococcal pneumonia in adults older than 65



# Impact of PCV13 (Prevnar-13)

- 2010 Recommended for children <5
- 2012 Recommended for high-risk adults >19
- 2014 Recommended for all adults >65



IPD rates among children < 5 years old, July 2007 - June 2016

# Impact of PCV13 (Prevnar-13)

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- 2012 Recommended for high-risk adults >19
- 2014 Recommended for all adults >65







IPD rates among children < 5 years old, July 2007 - June 2016

IPD rates among adults >65 years old, July 2007 - June 2016



"Herd Immunity"

### Rate of IPD by Serotype: Vaccine types



Post-PCV

Δ

Country

-- Australia -- Finland -- France -- Norway

Vaccine responses are heterogeneous and can vary by serotype and by location

USA



Pre-PCV10/13

Nature Sci Rep 10, 18977 (2020)

PCV era

#### Rate of IPD by Serotype: Non-Vaccine types



As IPD from serotypes in the vaccine has waned, IPD from other serotypes has increased



USA

PCV era o Pre-PCV ■ Pre-PCV10/13 △ Po

PCV Country - Australia - Finland - France - Norway

Nature Sci Rep 10, 18977 (2020)

### Pneumococcal Vaccines

- <u>Polysaccharide</u> vaccine
  - against 14 serotypes first licensed in 1977 (Pneumovax 14, PPSV14)
  - expanded to 23 serotypes in 1983 (Pneumovax 23, PPSV23)
- <u>Conjugated</u> vaccine
  - against 7 serotypes licensed in 2000 (Prevnar 7, PCV7)
    - conjugated to a nontoxic variant of diphtheria toxin
    - elicits a more robust immune response
  - expanded to 13 serotypes in 2010 (Prevnar 13, PCV13)
- Expanded to 15 serotypes in 2021 (adults), 2022 (children) (Prevnar 15, PCV15)

PPSV = pneumococcal polysaccharide vaccine

PCV = pneumococcal conjugate vaccine

- Expanded to 20 serotypes in 2021 (adults), 2023 (children) (Prevnar 20, PCV20)
- Expanded to 21 serotypes in 2024 (adults)



Overal

(Prevnar 21, PCV21)



CDC.gov

# Serotypes Included in Pneumococcal Vaccines

#### FIGURE. Serotypes\*<sup>,†</sup> included in pneumococcal vaccines currently recommended for adults — United States, 2024



Abbreviations: PCV = pneumococcal conjugate vaccine; PCV15 = 15-valent PCV; PCV20 = 20-valent PCV; PCV21 = 21-valent PCV; PPSV23 = 23-valent pneumococcal polysaccharide vaccine.

MMWR Morb Mortal Wkly Rep 2024;73:793–798

Risk or age group	Vaccine received previously	Options for vaccination
Adults aged ≥65 years	None or PCV7 only at any age	A single dose of PCV21, PCV20, or PCV15. If PCV15 is administered, a single dose of PPSV23* should be administered ≥1 year after the PCV15 dose. A minimum interval of 8 weeks can be considered if PCV15 is used in adults with an immunocompromising condition, <sup>†</sup> cochlear implant, or CSF leak.
	PPSV23 only	A single dose of PCV21, PCV20, or PCV15 ≥1 year after the last PPSV23 dose.
	PCV13 only	A single dose of PCV21, PCV20, or PPSV23≥1 year after the PCV13 dose. When PPSV23 is used for adults with an immunocompromising condition, <sup>†</sup> cochlear implant, or CSF leak, administer PPSV23 ≥8 weeks after the PCV13 dose.
	PCV13 at any age and PPSV23 at age <65 years	A single dose of PCV21, PCV20, or PPSV23. If PCV21 or PCV20 is used, it should be administered ≥5 years after the last pneumococcal vaccine dose. If PPSV23 is used, it should be administered ≥1 year after the PCV13 dose (or ≥8 weeks since the PCV13 dose for adults with an immunocompromising condition, <sup>†</sup> cochlear implant, or CSF leak) and ≥5 years after the previous PPSV23 dose.
	PCV13 at any age and PPSV23 at age ≥65 years	Shared clinical decision-making is recommended regarding administration of either a single dose of PCV21 or PCV20 for any adult aged ≥65 years who has completed the recommended vaccination series with both PCV13 and PPSV23 (i.e., PPSV23 administered at age ≥65 years) but PCV21, PCV20 or PCV15 not yet received. If a decision to administer PCV21 or PCV20 is made, a single dose is recommended ≥5 years after the last pneumococcal vaccine dose.
Adults aged 19–64 years with an immunocompromising condition,† a CSF leak, or a cochlear implant	None or PCV7 only at any age	A single dose of PCV21, PCV20, or PCV15. If PCV15 is used, administer a single dose of PPSV23* ≥8 weeks after the PCV15 dose.
	PPSV23 only	A single dose of PCV21, PCV20, or PCV15 ≥1 year after the last PPSV23 dose.
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	PCV13 and 1 dose of PPSV23	A single dose of PCV21 or PCV20, or $\geq 1$ dose of PPSV23. If PCV21 or PCV20 is used, it should be administered $\geq 5$ years after the last pneumococcal vaccine dose. When a second PPSV23 dose is used instead of PCV21 or PCV20, it should be administered $\geq 8$ weeks after the PCV13 dose and $\geq 5$ years after the first PPSV23 dose. The pneumococcal vaccination recommendations should be reviewed again when the person reaches age 65 years. If PCV21 or PCV20 is used in place of any dose of PPSV23, the series is complete, and it need not be followed by additional pneumococcal vaccine doses.
	PCV13 and 2 doses of PPSV23	The pneumococcal vaccination recommendations should be reviewed again when the person turns age 65 years. Alternatively, a single dose of either PCV21 or PCV20 should be administered ≥5 years after the last pneumococcal vaccine dose. If PCV21 or PCV20 is used, the series is complete, and it need not be followed by additional pneumococcal vaccine doses.
Adults aged 19–64 years with chronic medical conditions <sup>§</sup>	None or PCV7 only at any age	A single dose of PCV21, PCV20, or PCV15. If PCV15 is administered, a single dose of PPSV23* should be administered ≥1 year after the PCV15 dose.
	PPSV23 only	A single dose of PCV21, PCV20, or PCV15 ≥1 year after the last PPSV23 dose.
	PCV13 only	A single dose of PCV21, PCV20, or PPSV23 ≥1 year after the PCV13 dose.
	PCV13 and 1 dose of PPSV23	The pneumococcal vaccination recommendations should be reviewed again when the person reaches age 65 years.

#### TABLE. Clinical guidance for implementing pneumococcal vaccine recommendations for adults aged ≥19 years — United States, 2024

MMWR <u>September 12, 2024</u> / 73(36);793–798

Risk or age group	Vaccine received previously	Options for vaccination	
Adults aged ≥65 years	None or PCV7 only at any age	A single dose of PCV21, PCV20, or PCV15. If PCV15 is administered, a single dose of PPSV23* should be administered ≥1 year after the PCV15 dose. A minimum interval of 8 weeks can be considered if PCV15 is used in adults with an immunocompromising condition, <sup>†</sup> cochlear implant, or CSF leak.	ך
	PPSV23 only	A single dose of PCV21, PCV20, or PCV15 ≥1 year after the last PPSV23 dose.	
	PCV13 only	A single dose of PCV21, PCV20, or PPSV23 $\geq$ 1 year after the PCV13 dose. When PPSV23 is used for adults with an immunocompromising condition, <sup>†</sup> cochlear implant, or CSF leak, administer PPSV23 $\geq$ 8 weeks after the PCV13 dose.	
	PCV13 at any age and PPSV23 at age <65 years	A single dose of PCV21, PCV20, or PPSV23. If PCV21 or PCV20 is used, it should be administered $\geq$ 5 years after the last pneumococcal vaccine dose. If PPSV23 is used, it should be administered $\geq$ 1 year after the PCV13 dose (or $\geq$ 8 weeks since the PCV13 dose for adults with an immunocompromising condition, <sup>†</sup> cochlear implant, or CSF leak) and $\geq$ 5 years after the previous PPSV23 dose.	
	PCV13 at any age and PPSV23 at age ≥65 years	Shared clinical decision-making is recommended regarding administration of either a single dose of PCV21 or PCV20 for any adult aged ≥65 years who has completed the recommended vaccination series with both PCV13 and PPSV23 (i.e., PPSV23 administered at age ≥65 years) but PCV21, PCV20 or PCV15 not yet received. If a decision to administer PCV21 or PCV20 is made, a single dose is recommended ≥5 years after the last pneumococcal vaccine dose.	
Adults aged 19–64 years with an immunocompromising condition,†	None or PCV7 only at any age	A single dose of PCV21, PCV20, or PCV15. If PCV15 is used, administer a single dose of PPSV23* ≥8 weeks after the PCV15 dose.	
a CSF leak, or a cochlear implant	PPSV23 only	A single dose of PCV21, PCV20, or PCV15 ≥1 year after the last PPSV23 dose.	
	PCV13 only	A single dose of PCV21, PCV20, or PPSV23. If PCV21 or PCV20 is used, it should be administered ≥1 year after the PCV13 dose. If PPSV23 is used, administer PPSV23 ≥8 weeks after the PCV13 dose. When PPSV23 is used instead of PCV21 or PCV20 for these adults, a single dose of PCV21, PCV20 or PPSV23 dose is recommended ≥5 years after the first PPSV23 dose.	
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	PCV13 and 1 dose of PPSV23	The pneumococcal vaccination recommendations should be reviewed again when the person reaches age 65 years.	MMWR <u>Septe</u>

#### TABLE. Clinical guidance for implementing pneumococcal vaccine recommendations for adults aged ≥19 years — United States, 2024

Now very complicated

Complicated is not good

MMWR <u>September 12, 2024</u> / 73(36);793–798



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PCV21																																
PPSV23			Μ																													
PCV20																																
PCV15																																

 In certain adult populations in the western United States, high percentages (i.e.,  $\geq 30\%$ ) of IPD caused by serotype 4 have occurred. The available IPD serotype data from CDC's Active Bacterial Core surveillance, as well as similar surveillance from Alaska and the Navajo Nation, indicate that these high percentages are particularly prevalent in Alaska, Colorado, the Navajo Nation, New Mexico, and Oregon. Typically, persons living within these geographic areas who develop serotype 4 IPD are adults aged <65 years with specific underlying conditions or risk factors, such as alcoholism, chronic lung disease, cigarette smoking, homelessness, and injection drug use. Importantly, these persons usually have not received a pneumococcal conjugate vaccine containing serotype 4. In such populations, other recommended pneumococcal vaccines (e.g., PCV20 alone or both PCV15 and PPSV23) are expected to provide broader serotype coverage against locally circulating strains compared with PCV21.

MMWR September 12, 2024 / 73(36);793-798

### Also:

## CDC Recommends Lowering the Age for Pneumococcal Vaccination from 65 to 50 Years Old



Committee on Immunization Practices' (ACIP) recommendation for lowering the age for pneumococcal vaccination from 65 to 50 years old.

RELATED PAGES



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#### PneumoRecs VaxAd...



Medical

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			neumoRecs VaxAdvi	or		
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		Age Age: 22 years				
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CSF leak or cochlear implant	Select	PPSV23				
Cerebrospinal fluid (CSF) leak  Cochlear implant		PCV13	or doe of			
Immunocompromising conditions	Select	Recommend	dation			
Chronic renal failure  Congenital or acquired asplenia  Congenital or acquired immunodefici  Generalized malignancy  HiV infection  Hodgkin disease  latrogenic immunosuppression <sup>4</sup> Leukemia  Lymphoreal  Multiple myeloma  Neiphore syndrome	iencies <sup>3</sup>	Give one dose PCV13. Give a years after the final dose of P years as long i since the seco	of PPSV23 at least a second dose of PP first PPSV23 dose. PSV23 is not indicat as at least 5 years h nd dose of PPSV23.	8 weeks after SV23 at least 5 A third and ed until age 65 we passed		
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Home Disclaimer	() About	<b>R</b> Home	 Disclaimer	() About		
	Which of the following risk fac your patient have? CSF leak or cochlear implant - Cerebrospinal fluid (CSF) leak - Cochlear implant Immunocompromising conditions - Chronic renal failure - Congenital or acquired asplenia - Congenital or acquired immunodefic - Generalized malignancy - HW infection - HW infection - Information - Leukemia - Lymphoma - Leukemia - Lymphoma - Solid organ transplant Foremer: - Continue - Solid organ transplant - Solid organ transplant	Which of the following risk factors does your patient have?      CSF leak or cochlear implant    Select      • Cerebrospinal fluid (CSF) leak    Cochlear implant      • Cordenar implant    Select      • Cordenar implant    Select      • Cordenar implant    Select      • Concentration of the select    Select      • Chronic renal failure    Select      • Congenital or acquired asplenia    Select      • Congenital or acquired immunodeficiencies <sup>3</sup> Select      • Bodgin disease    Istrogenic immunosuppression <sup>4</sup> • Leukemia    Lymphoma      • Multipe myelona    Solid organ transplant      • Solid organ transplant    Forewere      Former    O About	Which of the following risk factors does your patient have?    Age: 22 years      CSF leak or cochlear implant    Select      CSF leak or cochlear implant    Select      C Creebrospinal fluid (CSF) leak    PSV23      Cochlear implant    Select      Immunocompromising conditions    Select      Chronic renal failure    Coogenital or acquired asplenia      Coogenital or acquired asplenia    Give one dose PCV13. Give a years after the final dose of P years after the final dose of P years as long;      HV Infection    Select      Leukemia    Lymphoma      Leukemia    Solid organ transplant      Former    Continue      More coll disease and other hemoglobinopathies      Solid organ transplant    Continue      Former    Disclaimer    About	Age      Age:      Conspendant malant      Congenital or acquired aplenia      Congenital or acquired inmunodeficiencies <sup>3</sup> Comernalized malignancy      HW infection      Autrophoma      Autrophoma      Autrophoma      Autrophoma      Solid organ transplant      Freemers      Continue      About		

# Pneumococcal Vaccine Adverse Events

	Polysaccharide	Conjugate
Local Reactions	30-50%	5-49%
Fever, Myalgia	<1%	24-35%
Febrile Seizures in children		1.2-13.7/100,000 4-44.9/100,000 with TIV—

After evaluating the data on febrile seizures and taking into consideration benefits and risks of vaccination, ACIP made no change in its recommendations for use of TIV or PCV13.

CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases 13th ed, 2015

# Herpes Zoster (Shingles)

- "Shingles" from the Latin word cingulum, for belt or girdle
- Reactivation of varicella zoster virus (VZV)
  - More than 99% of Americans born before 1980 have had varicella, even if they don't remember it
- 500,000 to 1 million episodes per year (U.S.)
- Lifetime risk of zoster estimated to be 32%
  - Risk increases with age
  - 50% of (unvaccinated) persons living until age 85 years will develop zoster

MMWR 2008; 57(05);1-30

CDC. Epidemiology and Prevention of Vaccine-Preventable Diseases 13th ed, 2015





## Zoster Vaccines

- First herpes zoster vaccine (*Zostavax*) approved by FDA in 2006 for use in persons 60 years of age and older
  - In 2011, approved for persons 50-59 years of age
  - A live-attenuated viral vaccine
  - Contains the same varicella zoster virus used in varicella vaccine but at a much higher titer
- Vaccine recipients 60-80 years of age had 51% fewer episodes of zoster
  - reduced the risk of postherpetic neuralgia by 66.5%





N Engl J Med 2005; 352:2271-2284

## Zostavax Caveats

• Efficacy declines with increasing age



- Not recommended for people:
  - with HIV/AIDS or another disease that affects the immune system
  - on treatment with drugs that affect the immune system, such as steroids
  - with cancer treatment such as radiation or chemotherapy
  - with leukemia or lymphoma
  - who are or might be pregnant

N Engl J Med 2015;372:2087-96

## Zoster Vaccines

- Second zoster vaccine (Shingrix) approved October, 2017
- Recombinant, adjuvanted zoster vaccine against Varicella surface glycoprotein E (<u>not a live virus</u>)
- >90% reduction in zoster and PHN
  - no reduced efficacy with age

Protection stays above 85% for at least four years, 82% at 11 years<sup>2</sup>

Zostavax was discontinued in 2020 Shingrix is "The Shingles Vaccine"

#### N Engl J Med 2015;372:2087-96

<sup>2</sup>Diez-Domingo J, et al. Abstract presented at European Society of Clinical Microbiology and Infectious Diseases (ESCMID); 27–30 April 2024, Barcelona, Spain





## Recombinant Zoster Vaccine (RZV) Recommendations

- Healthy adults >=50 years old and adults >= 19 years old who are or will be immunosuppressed should get two doses of RZV (Shingrix), 2 to 6 months apart
  - If pt waits more than 6 months, give the second dose but don't restart the series
- People should get RZV even if they:
  - had shingles in the past
  - received Zostavax
  - are unsure if had chickenpox
  - received varicella (chickenpox) vaccine
- Do not give Shingrix if:
  - tested negative for immunity to varicella zoster virus (should get chickenpox vaccine)
  - currently have shingles (no benefit)
  - moderate or severe acute illness (risk of poor response to vaccine)
- Pregnancy
  - No ACIP recommendation for RZV use in pregnancy
  - Providers should consider delaying RZV until after pregnancy (risk of poor response to vaccine)
  - There is no recommendation for pregnancy testing prior to vaccination
- Breastfeeding no known risk for mothers who are breastfeeding or their infants



CDC.gov

# Shingrix Adverse Effects

- Sore arm with mild or moderate pain (80%)
- Redness and swelling at injection site (~30%)
- Fatigue, myalgia, headache, fever, stomach pain, nausea (20-40%)
- About 15% experience side effects that prevent them from doing regular activities
- Symptoms resolve in about 2 to 3 days
- Side effects more common in younger people



### COVID-19





Daily Trends in Number of COVID-19 Cases in The United States Reported to CDC

CDC.gov

#### Cumulative confirmed COVID-19 deaths by world region

Due to varying protocols and challenges in the attribution of the cause of death, the number of confirmed deaths may not accurately represent the true number of deaths caused by COVID-19.



Our World in Data

#### ourworldindata.org

### COVID-19 Hospitalizations and Deaths

From October 2023 – April 2024

- Adults aged ≥65 years accounted for 70% of all COVID-19–associated hospitalizations among adults
- Most hospitalized adults had multiple underlying medical conditions
- Only 12% had received the recommended COVID-19 2023–2024 formula vaccine (88% had not)



#### Est. 46,582 deaths in the U.S. in 2024

In at least 66% of these deaths, COVID-19 was listed as the underlying cause of death. For the remaining deaths, COVID-19 was listed as a contributing cause of death.

#### Est. 28,000 deaths from Influenza 2023 – 2024



MMWR October 3, 2024 / 73(39);869-875

Provisional COVID-19 Deaths, by Week, in The United States, Reported to CDC



### SARS-CoV-2 Continues to Evolve



Weighted Estimates: Variant proportions based on reported genomic sequencing results



Nowcast\*\*: Model-based projected estimates of variant proportions



Collection date, two-week period ending

MMWR October 24, 2024 / 73(42);938–945

CDC.gov

## COVID-19 Vaccines

Currently available in the U.S.

#### Pfizer and Moderna mRNA vaccines



Novavax adjuvanted recombinant vaccine with nanoparticle technology



Science 27 Nov 2020: Vol. 370, Issue 6520, pp. 1022 DOI: 10.1126/science.370.6520.1022

novavax.com

## COVID-19 mRNA Vaccine Basics



- mRNA vaccines inject cells with instructions to generate the SARS-CoV-2 spike protein
- The protein made in response to the vaccine elicits an immune response. Later, if the person is exposed to the virus, their immune system will recognize and respond to it
- mRNA vaccines are safe and cannot alter your DNA, and you cannot get COVID-19 from the vaccine
- mRNA vaccines may seem to have arrived quickly, but this technology is built on decades of scientific research

genome.gov

### **COVID-19 Vaccine Efficacy**

#### Pfizer



NEJM 383;27 December 31, 2020



NEJM 384;5 February 4, 2021





JAMA Netw Open. 2023 Apr 3;6(4):e239135

## **COVID-19** Vaccines

- Estimated to have prevented<sup>1</sup>
  - 27 million infections
  - 1.6 million hospitalizations
  - 235,000 deaths

from 12/1/2020 to 9/30/2021 in the U.S.



- IF all adults 18 and older in the U.S. had received the vaccine<sup>2</sup> from 1/1/2021 to 4/30/2022
  - estimated additional 320,000 deaths would have been averted

<sup>1</sup>JAMA Network Open 2022;5(7):e2220385

<sup>2</sup>Journal of Pharmacy and Pharmacology Research 7 (2023): 163-167

# COVID-19 Vaccine Adverse Effects

### **Common Side Effects**

- Pain, soreness, redness at injection site
- Fatigue
- Headache
- Muscle pain
- Joint pain
- Chills
- Fever
- Nausea/vomiting (Moderna)
- Less common with successive doses

Rare Side Effects

- Anaphylaxis occurs at a rate of approximately 5 cases per one million vaccine doses administered
- Myocarditis and pericarditis after COVID-19 vaccination are rare
  - Most people with myocarditis or pericarditis after COVID-19 vaccination respond well to treatment and rest and feel better quickly
  - Myocarditis has been most frequently seen in adolescent and young adult males within 7 days of their second mRNA COVID-19 vaccine dose. (Cases have also been observed in females, in other age groups, and after other vaccine doses.)

The risk of myocarditis was more than seven-fold higher in persons who were infected with the SARS-CoV-2 than in those who received the vaccine

Front Cardiovasc Med. 2022 Aug 29;9:951314

CDC.gov

## **COVID-19 Vaccine Recommendations**

#### Everyone age 6 months and older should get a 2024–2025 COVID-19 vaccine

#### People ages 12-64 years

- You are up to date when you have received:
  - 1 dose of the 2024–2025 Moderna COVID-19 vaccine OR
  - 1 dose of the 2024–2025 Pfizer-BioNTech COVID-19 vaccine OR
  - 1 dose of the 2024–2025 Novavax vaccine unless you are receiving a COVID-19 vaccine for the very first time. If you have never received any COVID-19 vaccine and get Novavax, you need 2 doses of 2024–2025 Novavax COVID-19 vaccine to be up to date.

#### People ages 65 years and older

You are up to date when you have received:

Nev 2 doses of any 2024–2025 COVID-19 vaccine 6 months apart.

 While it is the *recommended* to get 2024-2025 COVID-19 vaccine doses 6 months apart, the *minimum* time is 2 months apart, which allows flexibility to get the second dose prior to typical COVID-19 surges, travel, life events, and healthcare visits Vaccine recommendations for people who are moderately or severely immunocompromised

#### Already completed initial series

 People ages 12 years and older: Get 2 doses of 2024–2025 COVID-19 vaccine from any brand (Moderna, Pfizer-BioNTech, or Novavax) spaced 6 months apart.\*

#### Never received a COVID-19 vaccine

 People ages 12 years and older: Get initial series of 2024–2025 COVID-19 vaccines from the same brand (Moderna, Pfizer-BioNTech, or Novavax), followed by 1 dose from any brand 6 months later.\*

#### CDC.gov

# **Respiratory Syncytial Virus**

- In children:
  - RSV is the most common cause of bronchiolitis and pneumonia in children under 12 months of age
  - In the U.S. there are between 75,000 and 125,000 children hospitalized each year due to complications of RSV infection
  - Est. globally there are 64 million cases of RSV annually that result in 253,500 deaths
  - Almost all children will have had an RSV infection by their second birthday
- In adults:
  - RSV is associated with up to 12% of medically attended acute respiratory illnesses
  - <1% require hospitalization
  - RSV is the third most commonly identified virus in adults hospitalized with pneumonia (pre-COVID-19 pandemic) after Rhinovirus and Influenza
- In adults >65 with moderate-to-severe ILI\* episodes, those with RSV are about twice as likely to be hospitalized than those with any other virus (19.5% vs. 8.6%) and 5-fold more likely than Influenza A (3.8%)

\*Influenza-Like Illness with pneumonia, hospitalization, or maximum daily influenza symptom severity score (ISS) >2

*Influenza Other Resp Viruses* 2022;16:1133–1140 *J Virology* July 2014 88(13): 7602–7617 CDC.gov PLoS ONE 2017 12(8): e0182321 *J Infectious Diseases* 2014 Jun 15; 209(12): 1873–1881



#### Most adult RSV hospitalizations occur in older adults

est 60,000 - 160,000 hospitalizations and 6,000 - 10,000 deaths annually among adults aged  $\geq 65$  years (U.S.)

Mean Estimated Influenza and RSV Hospitalization Rates per 100,000 person-years, United States 1993 - 2008 2500 2000 309.1 1500 Influenza 86.1 ~28% RSV of 309.1 1000 Range 136.9-508.5 53.7-124.5 Aged >65 Y 500 The overall rate of hospitalization for RSV is lower than for Influenza because of the lower rate of infection Aged >65 Y Aged <1 y Aged 1-4 y Aged 5-49 y Aged 50-64 y

data from *Clinical Infectious Diseases* 2012;54(10):1427–36

#### Morbidity and Mortality in Older Adults (aged ≥60 years) ple of ized with Hospitalized with RSV

Characteristics of a random sample of patients aged ≥60 years hospitalized with laboratory-confirmed RSV infection (N = 1,634), RSV–Associated Hospitalization Surveillance Network, 12 states, October 2022–April 2023

_	Overall						
Characteristic	No.	Weighted % (95% CI)					
Underlying medical condition							
≥1 underlying medical condition***	1,584	95.5 (93.2-97.2)					
Chronic lung disease	813	49.2 (45.7-52.7)					
COPD	552	33.7 (30.5-37.0)					
Asthma	332	19.1 (16.6-21.8)					
Otherttt	72	5.4 (3.8-7.3)					
Cardiovascular disease	1,108	67.1 (63.7-70.5)					
CHF555	545	33.2 (30.0-36.5)					
CAD	435	26.4 (23.5-29.5)					
CVA****	253	13.7 (11.7-15.9)					
Immunocompromising condition	292	18.6 (16.0-21.4)					
Diabetes mellitus	553	32.6 (29.5-35.8)					
Neurologic condition	439	27.3 (24.3-30.5)					
Dementia <sup>††††</sup>	183	12.4 (10.1-15.0)					
Other	256	14.9 (12.6-17.4)					
Kidney disorder	477	29.3 (26.3-32.5)					
Obesity	572	37.8 (34.3-41.4)					

Hospitalization outcome <sup>§§</sup>		%
Hospital stay, days, median (IQR)	4.1 (2.2-7.6)	_
BiPAP/CPAP	339	19.8 (17.3-22.6)
High-flow nasal cannula	80	4.3 (3.2-5.7)
≥1 severe outcome <sup>¶¶</sup>	332	18.5 (15.9-21.2)
ICU admission	297	17.0 (14.5–19.7)
Invasive mechanical ventilation	94	4.8 (3.5-6.3)
In-hospital death	98	4.7 (3.6-6.1)

**¶¶** Severe outcome is defined as requiring ICU admission or mechanical ventilation or experiencing in-hospital death

\*\*\* Defined as one or more of the following: chronic lung disease, including asthma; chronic metabolic disease including diabetes mellitus; blood disorder or hemoglobinopathy; cardiovascular disease; neurologic disorder; immunocompromising condition; renal disease; gastrointestinal or liver disease; rheumatologic, autoimmune, or inflammatory condition; obesity; feeding tube dependency; and wheelchair dependency

MMWR October 6, 2023 Vol. 72 No. 40 pages 1075-1082



# Efficacy of RSV Vaccines

TABLE 1. Efficacy of 1 dose of <u>GSK</u> respiratory syncytial virus RSVpreF3 vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

	Vaccine efficacy against outcome*							
Efficacy evaluation period	RSV-associated LRTD <sup>†</sup>	RSV-associated medically attended LRTD <sup>§</sup>						
Season 1 <sup>¶</sup>	82.6 (57.9-94.1)**	87.5 (58.9-97.6)**						
Season 2 <sup>§§</sup>	56.1 (28.2-74.4)**	11						
Combined seasons 1 and 2 (interim)***	74.5 (60.0-84.5)***	77.5 (57.9-89.0)**						

LRTD = lower respiratory tract disease

<sup>†</sup> LRTD defined as two or more lower respiratory symptoms (new or increased sputum, cough, and dyspnea) or signs (new or increased wheezing, crackles or rhonchi detected during chest auscultation, respiratory rate ≥20 respirations per minute, low or decreased oxygen saturation [<95% or ≤90% if baseline was <95%] and need for oxygen supplementation) for ≥24 hours, including one or more lower respiratory signs, or three or more lower respiratory symptoms for ≥24 hours.</p>

N Engl J Med 2023;388:1465-77 MMWR July 21, 2023 Vol. 72 No. 29 pages 793-801 TABLE 3. Efficacy of 1 dose of <u>Pfizer</u> respiratory syncytial virus RSVpreF vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

	Vaccine efficacy against outcome, % (95% CI)						
Efficacy evaluation period	RSV-associated LRTD <sup>+</sup>	RSV-associated medically attended LRTD <sup>§</sup>					
Season 1 <sup>9</sup>	88.9 (53.6-98.7)	84.6 (32.0-98.3)					
Season 2 (interim)**	78.6 (23.2-96.1)						
Combined seasons 1 and 2 (interim) <sup>§§</sup>	84.4 (59.6-95.2)	81.0 (43.5-95.2)					

<sup>§</sup> Medically attended RSV-associated LRTD defined as LRTD plus attention at one or more inpatient or outpatient health care service. Estimates were not included in per-protocol assessments.

Neither of the two clinical trials that led to FDA approval of RSV vaccines for older adults was powered to assess protection against hospitalization, though both trials showed moderate to high efficacy of RSV vaccination against LRTD, which is in the causal pathway leading to severe disease



## **RSV Vaccine in Adults**

 On June 21, 2023, ACIP voted to recommend that adults aged ≥60 years may receive a single dose of an RSV vaccine (either GSK or Pfizer), using shared clinical decision-making. ("Talk to your doctor.")



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# Safety of RSV Vaccines

### TABLE 2. Safety\* of 1 dose of <u>GSK</u> respiratory syncytial virus RSVPreF3 vaccine in adults aged ≥60 years — multiple countries, 2021–2023

	Risk for event									
Safety event	RSVPreF3 recipients no./No. (%) <sup>†</sup>	Placebo recipients no./No. (%)§	Relative risk (95% Cl)¶							
Serious AE**	549/12,570 (4.4)	540/12,604 (4.3)	1.02 (0.91-1.15)							
Severe reactogenicity events <sup>††</sup>	37/979 (3.8)	9/976 (0.9)	4.10 (1.99-8.45)							
Inflammatory neurologic events	3 events in trials without placebo recipients <sup>¶¶</sup>		1 _11							

One case of GBS and two cases of acute disseminated encephalomyelitis in 17,922 doses given over all trials

TABLE 4. Safety\* of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine in adults aged  $\geq 60$  years — multiple countries, 2021–2023

	Risk for event									
Safety event	RSVpreF recipients no./No. (%) <sup>†</sup>	Placebo recipients no./No. (%) <sup>§</sup>	Relative risk (95% Cl)¶							
Serious AE**	792/18619 (4.3%)	749/18334 (4.1%)	1.04 (0.94-1.15)							
Severe reactogenicity events <sup>1†</sup>	36/3673 (1.0%)	24/3491 (0.7%)	1.43 (0.85–2.39)							
Inflammatory neurologic events	3/18622 (—)	0/18335 (—)	_11							

One case each of GBS, Miller Fisher syndrome (a GBS variant), and undifferentiated motor-sensory axonal polyneuropathy

#### GBS = Guillain-Barre Syndrome

Whether these events occurred due to chance, or whether RSV vaccination increases the risk for inflammatory neurologic events is currently unknown. Until additional evidence becomes available, RSV vaccination in older adults should be targeted to those who are at highest risk for severe RSV disease and therefore most likely to benefit from vaccination.

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### Moderna mRNA RSV Vaccine



N Engl J Med. 2023 Dec 14;389(24):2233-2244

Estimated RSV-Associated Outcomes<sup>1</sup> Preventable <u>over 3 RSV Seasons</u> vs. attributable risk of GBS estimated from self-controlled case series analysis through FDA-CMS partnership, 42-day risk interval<sup>2</sup>

#### Adults Aged $\geq$ 75 Years, Adults Aged 60–74 Years<sup>3</sup> at Increased **General Population Risk of Severe RSV Disease** 5,600 3,700 Hospitalizations (1,700-6,900)(3,600-8,900)850 830 **ICU Admissions** (520-1,310) (390-1,580) 320 790 Deaths (310 - 1, 450)(120–610) 9000 8000 7000 6000 5000 4000 3000 2000 1000 1000 2000 3000 4000 5000 6000 7000 8000 9000 0

Per 1 Million Persons Vaccinated with Protein Subunit RSV Vaccine:

CDC.gov ACIP Presentation 10/24/2024

0–18<sup>4</sup> attributable cases of GBS



fda.gov

## **Current RSV Vaccine Recommendation**

- As of June 26, 2024,
  - all adults aged ≥75 years and adults aged 60–74 years who are at increased risk for severe RSV disease should receive a single dose of RSV vaccine\*

For pregnant people (maternal RSV vaccine)

- FDA approved Pfizer RSV vaccine (<u>Abrysvo</u> ) in 2023. Pfizer RSV vaccine is approved for pregnant people at 32 through 36 weeks gestational age to protect their babies from LRTD caused by RSV.
- Pfizer is the only RSV vaccine approved and recommended for use in pregnant people.
  GSK (Arexvy) and Moderna (mResvia) RSV vaccines are not recommended for pregnant people.

- Chronic underlying medical conditions associated with increased risk · Lung disease (such as chronic obstructive pulmonary disease and asthma) · Cardiovascular diseases (such as congestive heart failure and coronary artery disease) Moderate or severe immune compromise\* Diabetes mellitus Neurologic or neuromuscular conditions Kidney disorders Liver disorders · Hematologic disorders · Other underlying conditions that a health care provider determines might increase the risk for severe respiratory disease Other factors associated with increased risk Frailty<sup>†</sup> Advanced age<sup>§</sup> · Residence in a nursing home or other long-term care facility · Other underlying factors that a health care provider determines might increase the risk for severe respiratory disease
- A single dose provides protection for at least two RSV seasons. The need for additional RSV vaccine doses will be evaluated by ACIP in the future; ACIP will update recommendations as needed

CDC.gov

TABLE. Estimated number of illnesses, hospitalizations, and deaths prevented by routine childhood immunization for selected vaccinepreventable diseases among children born during the Vaccines for Children era — United States, 1994–2013

	Cases prevented (in thousands)						
Vaccine-preventable disease*	Illnesses	Hospitalizations	Deaths				
Diphtheria	5,073	5,073	507.3				
Tetanus	3	3	0.5				
Pertussis	54,406	2,697	20.3				
Haemophilus influenzae type B	361	334	13.7				
Polio	1,244	530	14.8				
Measles	70,748	8,877	57.3				
Mumps	42,704	1,361	0.2				
Rubella	36,540	134	0.3				
Congenital rubella syndrome	12	17	1.3				
Hepatitis B	4,007	623	59.7				
Varicella	68,445	176	1.2				
Pneumococcus-related diseases <sup>†</sup>	26,578	903	55.0				
Rotavirus	11,968	327	0.1				
Total	322,089	21,055	731.7				

 Vaccines were considered as preventing disease for birth cohorts born in all years during 1994–2013 except for the following, which were only in use for part of the 20-year period: varicella, 1996–2013; 7-valent and 13-valent pneumococcal conjugate vaccines, 2001–2013; and rotavirus, 2007–2013.
 Includes invasive pneumococcal disease, otitis media, and pneumonia.

### Vaccine Benefits

MMWR 2014; 63(16):351-55

### Anti-vaxers

- Antivaccination protests are as old as vaccines
- Today's antivaccine movement was heavily influenced by a 1998 paper by Andrew Wakefield published in the Lancet that purported a link between autism and the MMR (measles, mumps, rubella) vaccine
- Wakefield had applied for a patent on his own measles vaccine and had received money (>\$600,000) from a lawyer trying to sue companies making the MMR vaccine
- The article was later retracted, and Wakefield's medical license was revoked by the U.K.
- Numerous studies have refuted any link between vaccines and autism or neurodevelopmental disorders

www.sciencemag.org

Dialogues Clin Neurosci 2017 Dec; 19(4): 403–407





# Vaccine Myths

- MMR causes autism
- Giving an infant multiple vaccines can overwhelm their immune system
- Thimerosal causes autism
- Spreading out vaccines can be safer for kids
- Vaccines are harmful to people who are sick
- The flu shot causes influenza
- COVID-19 vaccines contain alter your DNA, affect fertility, and/or contain microchips



## Vaccines Bottom Line

- Pneumonia vaccine for all  $\geq$  50 years
  - and high-risk  $\geq$  19 years
- Shingles vaccine for all  $\geq$  50 years
  - and immunocompromised  $\geq$  19 years
- COVID-19 for all  $\geq$  6 months
  - Two doses for immunocompromised or >=65 years
- RSV for all ≥75 years
  - and 60–74 years at increased risk for severe RSV disease

KEEP CALM AND GET YOUR FLU SHOT

# Adult Vaccine Update 2025: Pneumococcus, Shingles, COVID-19, and RSV



Kansas City Southwest Clinical Society January 31, 2025

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