Vaccines in 2025: Promise and Perils



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Disclosures

I have no financial disclosures.

I love vaccines.

Key resources

- CDC ACIP adult vaccine schedules
- Immunize.org "Ask the Experts"



Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2021 27-49 years 1 dose annually or 1 dose annual dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (see no 1 dose Tdap, then Td or Tdap booster every 10 years Measles, mumps, rubella 1 or 2 doses depending on indication 2 doses 2 doses (if born in 1980 or later) 2 doses 2 or 3 doses depending on age at 1 or 2 doses depending on indication 1 dose 2 or 3 doses depending on vaccine 2 or 3 doses depending on vaccine 19 through 23 years

Meet the Experts from the Immunization Action Coalition



Kelly L. Moore, MD, MPH President and Chief Executive Officer



Carolyn B. Bridges, MD, FACP; Director for Adult Immunization



Iyabode Beysolow, MD, MPH, FAAP; Physician Consultant

The Immunization Action
Coalition acknowledges with
gratitude Deborah L. Wexler,
MD, executive director
emerita, who established
"Ask the Experts" more than
25 years ago, and William
L. Atkinson, MD, MPH, who
contributed his expertise
to this popular feature over
many years while he was
at the Centers for Disease
Control and Prevention and
later at IAC.

Learning Objectives

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

- Advise patients regarding new vaccine recommendations
- Explain the reasoning behind changes
- Evaluate data behind recent changes in vaccine guidelines
- Assess areas of controversy



FDA approves first vaccine for RSV, a moment six decades in the making

By Brenda Goodman, CNN Updated 3:56 PM EDT, Wed May 3, 2023



WHO recommends R21/Matrix-M vaccine for malaria prevention in updated advice on immunization

2 October 2023 | News release | Geneva | Reading time: 5 min (1351 words)

The Updated COVID Vaccines Are Here: 10 Things to Know

BY KATHY KATELLA OCTOBER 4, 2023

Pfizer and Valneva Initiate Phase 3 Study of Lyme Disease Vaccine Candidate VLA15

Monday, August 08, 2022 - 04:45pm

NEWS 02 October 2023

Pioneers of mRNA COVID vaccines win medicine Nobel

Katalin Karikó and Drew Weissman laid the groundwork for immunizations that were rolled out during the pandemic at record-breaking speed.

Ewen Callaway & Miryam Naddaf









Drew Weissman (left) and Katalin Karikó (right). Credit: PixelPro/Alamy



much as I do

Not everyone

loves vaccines as

"I'm right there in the room, and no one even acknowledges me."





Measles

- Vaccine implemented in 1957
- Two-dose series implemented in response to outbreak in 1989
- Eliminated in the United States in 2000!

We all know how that story goes...

- 2019: 1,282 measles cases United States
- 2025: >700 cases (through April 15), active outbreaks in 6 states

Measles cases surge worldwide, infecting 10.3 million people in 2023

RELEASE

For immediate release: November 14, 2024

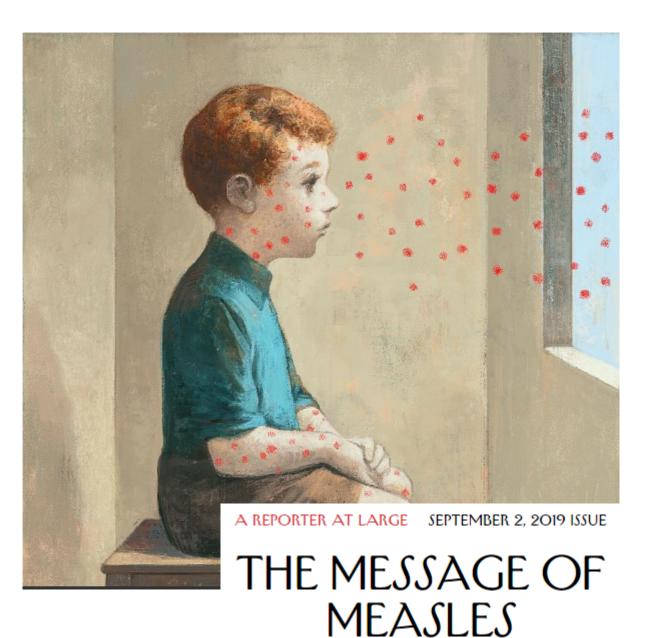
CDC Media Relations

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https://www.cdc.gov/media/



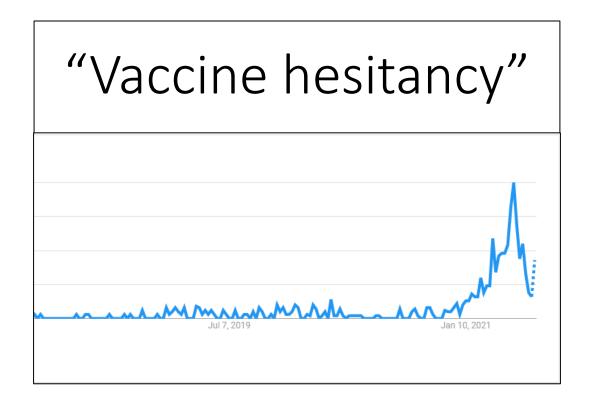




"Vaccination has been the victim of its own success. Eradication has afforded [us] the luxury of equivocation."

"The virus we are fighting isn't so much measles as it is vaccine hesitancy and refusal."

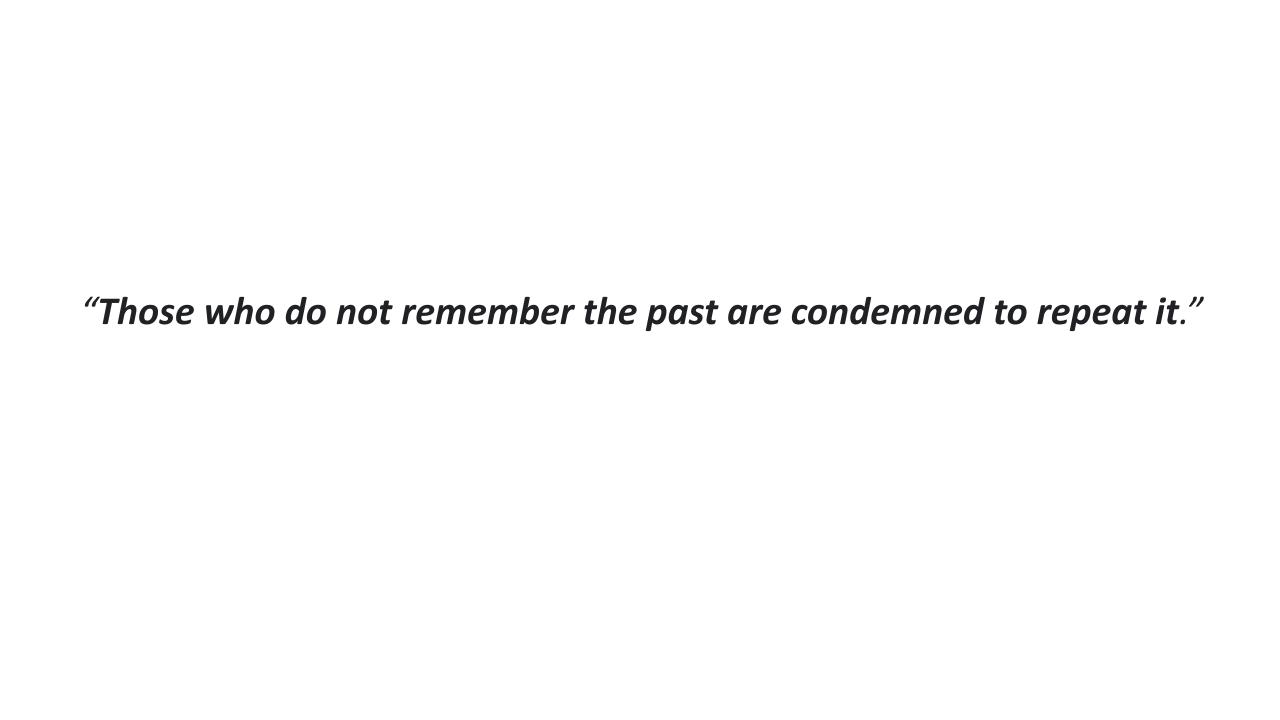
By Nick Paumgarten August 26, 2019



Survey reveals low trust in US public health agency information amid pandemic

Mary Van Beusekom, MS, March 7, 2023

Topics: COVID-19



- June 2022: Immunocompetent un-vaccinated young adult presents with fever, neck stiffness, back and abdominal pain, and flaccid weakness
- Stool specimen revealed poliovirus, confirmed by CDC
- First case of poliomyelitis in US since 2013
- Rockland County has reported overall low vaccine coverage for over 20 years
- In summer 2022, 60% of children under 2 years of age had received 3 doses of IPV
 - Zip code level as low as 37%)



Vaccines in 2025: Promise and Perils

- Vaccine development is happening at the fastest pace in history
- Vaccines continue to be the most impactful tool for disease prevention worldwide

- Trust in public health agencies is tenuous
- The anti-vaccine and anti-science movement in the United States is stronger than ever

Roadmap

- MMR
- RSV
- Pneumococcus
- COVID-19



Case

My patient was born in 1986. He is going to a new graduate program, so I checked a measles titer which was negative. His immunization record shows that he had one dose of MMR in childhood. What do you advise?

- A. Give booster MMR
- B. Give booster MMR then recheck titer 1-2 months later
- C. Documentation of 1 vaccine supersedes negative titers, no need for another shot

What counts as presumptive immunity?

ANY of the following

- Birth before 1957
- Laboratory confirmation of measles (verbal history does not count)
- Laboratory evidence of immunity
- Written documentation of adequate vaccination*



https://www.medinaction.com/your-immune-system-vaccines-and-traveling/

Adults – One Dose or Two?

• 1957-1989: one dose

• 1989: changed to two dose series

Number of doses	Seroprotection			
1	93%			
2	97%			

One dose is considered sufficient, except for:

- Healthcare personnel
- International travelers
- Persons attending college or other post-high school institution

E-consult

My patient was born in 1986. He is going to a new graduate program, so I checked a measles titer which was negative. His immunization record shows that he had one dose of MMR in childhood. What do you advise?

- A. Give booster MMR
- B. Give booster MMR then recheck titer 1-2 months later
- C. Documentation of 1 vaccine supersedes negative titers, no need for

another sh

Camille Nelson Kotton @KottonNelson · Mar 8

Time to consider getting a second dose of MMR if you were born between 1957 and approximately 1980 and never had a second dose of measles vaccine. Not for moderate to severely Immunocompromised as it's a live viral vaccine.

What to do with negative serologies?



- Sensitivity of serology only ~80%
- Probably less sensitive to detect vaccineinduced immunity
- Age-appropriate documented vaccination, trumps post-vaccination titers

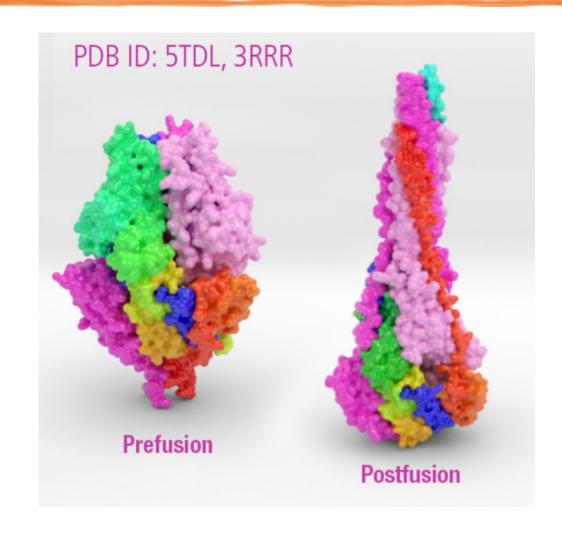
Case



For which of the following patients would you recommend the RSV vaccine?

- A. 71-year-old with no medical problems, exercises 7 days/week
- B. 81-year-old with no medical problems, exercises 7 days/week
- C. 65-year-old with history of ESRD s/p renal transplant on tacrolimus, MMF, prednisone
- D. 58-year-old with DM2, COPD and CHF
- E. 32-year-old pregnant woman with no medical problems at 33 weeks gestation
- F. 38-year-old pregnant woman with SLE on prednisone at 14 weeks gestation

RSV F-protein



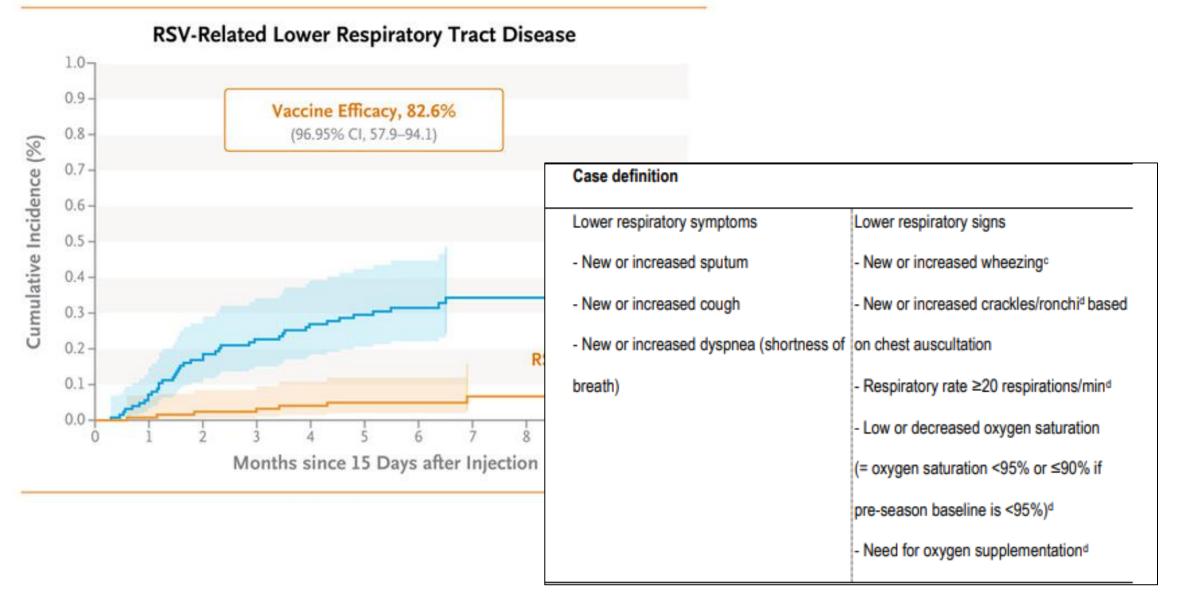
Respiratory Syncytial Virus Prefusion F Protein Vaccine in Older Adults

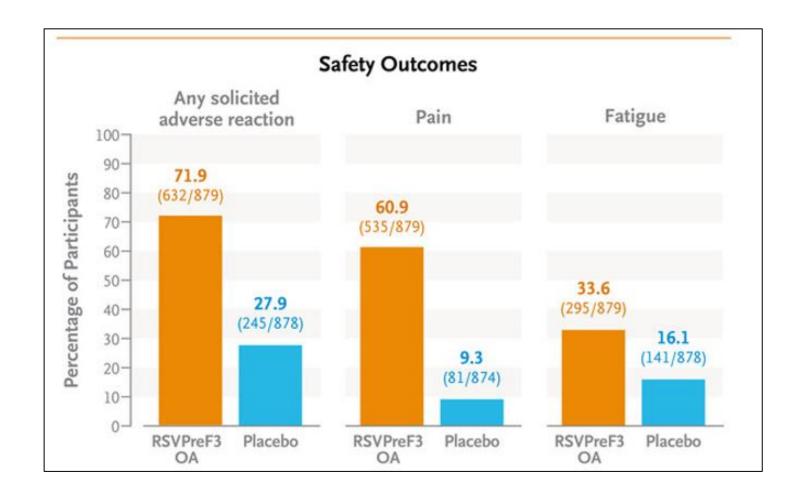
Alberto Papi, M.D., Michael G. Ison, M.D., Joanne M. Langley, M.D., Dong-Gun Lee, M.D., Ph.D., Isabel Leroux-Roels, M.D., Ph.D., Federico Martinon-Torres, M.D., Ph.D., Tino F. Schwarz, M.D., Ph.D., Richard N. van Zyl-Smit, M.D., Ph.D., Laura Campora, M.D., Nancy Dezutter, Ph.D., Nathalie de Schrevel, Ph.D., Laurence Fissette, M.S., et al., for the AReSVi-006 Study Group*

- Monovalent vaccine (GSK)
- Uses same adjuvant as RZV (Shingrix), but lower dose
- Adults ≥ 60
- 25,000 participants from 17 countries
- Randomized to vaccine vs placebo before RSV season
- Immunocompromised patients excluded

Age range	% participants
60-69	56
70-79	36
>/=80	8

Frailty status	% participants
Fit	60
Pre-frail	38
Frail	1.5





3 Inflammatory neurologic events

- 1 case of GBS
- 2 cases of ADEM

RENOIR: **R**SV vaccine **E**fficacy study i**N O**lder adults **I**mmunized against **R**SV disease

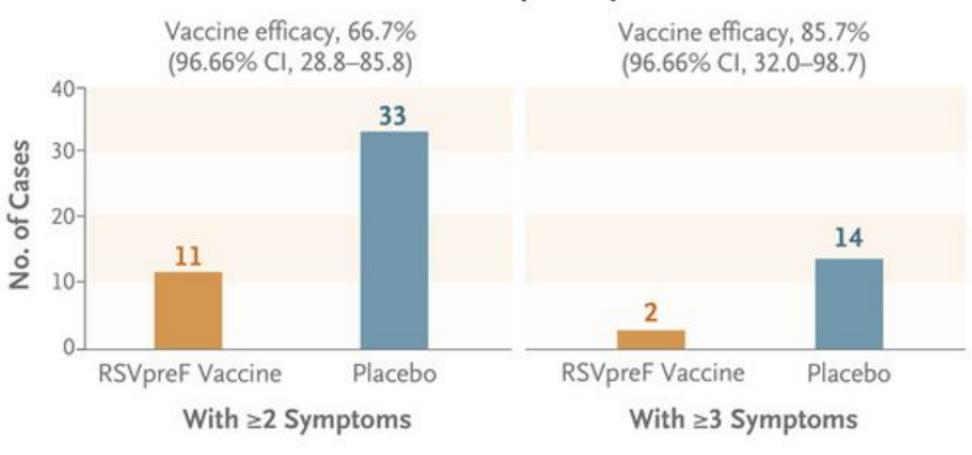


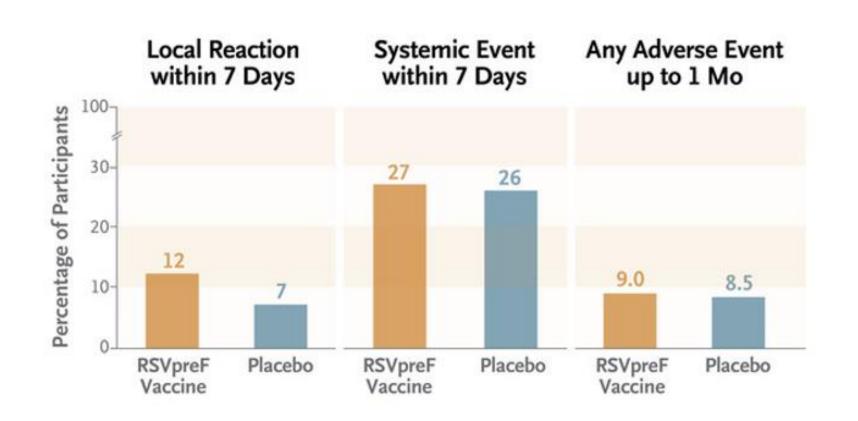
- Bivalent vaccine (Pfizer)
- No adjuvant
- Individuals 60 years and older
- ~34,000 participants
- Randomized to vaccine vs placebo before RSV season
- Immunocompromised patients excluded

Age range	% participants
60-69	62
70-79	32
>/=80	6

≥1 High risk condition	% participants
Yes	51.5
No	48.5

RSV-Associated Lower Respiratory Tract Illness





3 Inflammatory neurologic events

- 1 case of GBS
- 1 case of Miller-Fisher syndrome
- 1 case of undifferentiated lower motor neuron disease

May 3, 2023



FDA approves first vaccine for RSV, a moment six decades in the making

By Brenda Goodman, CNN Updated 3:56 PM EDT, Wed May 3, 2023



June, 2023



ACIP Advisory panel vote:

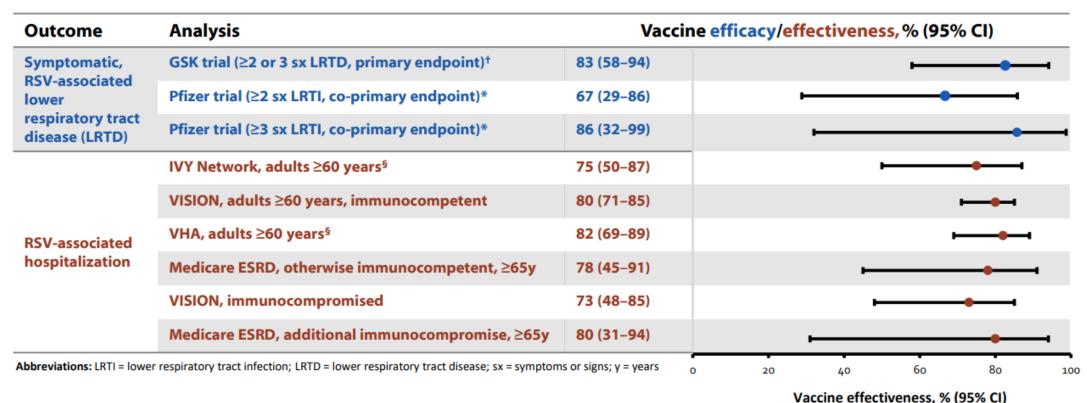
• Shared decision making for anyone ≥ 60

RSV vaccine: limitations

- Immunocompromised patients not included in studies
- Did not include many participants >75 (group at highest risk)
- Safety:
 - What to make of the inflammatory neurologic events in each study?
- Protection drops in the second season
 - A second shot booster did not seem to help
 - Boosters after 2 years under investigation

Real-world RSV vaccine effectiveness

Observational VE studies show RSV vaccines protect against severe RSV disease, similar to results from trials, although endpoints differ



RSV vaccine efficacy

		RSV Vaccination (GSK or Pfizer)				No Vaccination			
	N	No. of Events	Follow-up, person- years	Incidence Rate (events/ 1000 person- years)	No. of Events	Follow- up, person- years	Incidence Rate (events/ 1000 person- years)	Vaccine Effectiveness, % (95% CI)	
Age group									
60-69 years	28,247	17	7,494	2.3 (1.3–3.6)	74.9	7,474	10.0 (7.9–12.4)	78 (63–86)	
70-79 years	82,734	47	22,251	2.1 (1.6–2.8)	204.8	22,168	9.2 (8.0–10.6)	77 (69–83)	
≥80 years	35,691	26	9,601	2.7 (1.8–4.0)	93.5	9,500	9.8 (8.0–12.0)	72 (59–81)	
Immunocompromised*									
No	135,936	71	36554	1.9 (1.5–2.5)	325.5	36,354	9.0 (8.0–10.0)	78 (72–83)	
Yes	10,639	16	2753	5.8 (3.3–9.4)	54.2	2,730	19.9 (15.2–25.8)	71 (52–83)	

Limitations of observational VE studies

- RSV vaccine uptake in study populations was 5-10%
 - Early adopters of new vaccines may have different healthcare-seeking behaviors than gen population which could bias VE estimates upwards
- Definitions of immunocompromise varied across studies and studies were not powered to assess VE for specific types of immunosuppression
- Insufficient follow-up time to determine duration of RSV vaccine effectiveness beyond 1 season

- Results from two different types of analyses are mixed and highly uncertain
- These analyses do not provide clear, conclusive evidence of an elevated risk of GBS, but elevated risk cannot be ruled out at this time
- FDA is conductive medical chart review on individual cases



ACIP Advisory panel vote:

- 1. One dose RECOMMENDED for anyone age 75 and older
- 2. One dose RECOMMENDED for 60-74 who are at high risk for severe RSV disease
- 3. For people 60-74 who are NOT at risk for severe RSV disease, RSV vaccine is NOT RECOMMENDED.

RSV vaccination will have the most benefit if given in late summer or early fall.

Adults who have already received a dose of RSV vaccine DO NOT need to receive another dose this year.

Late Breaker!!!



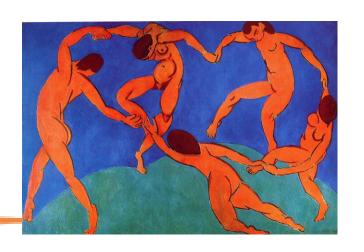
News > FDA

Pfizer Wins FDA Approval of RSV Vaccine for Broader Adult Population

October 23, 2024 | 2 min read | Tristan Manalac

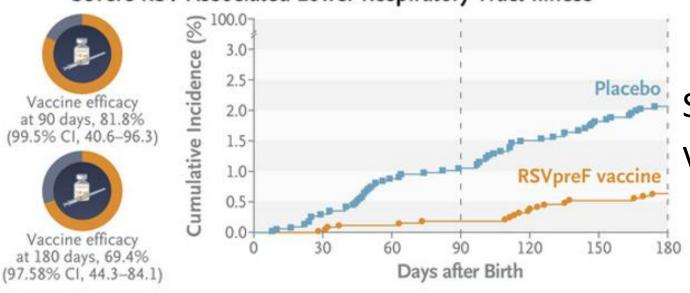
- Abrysvo approved by FDA for use in adults 18-59 years old at increased risk for lower respiratory tract disease
- ACIP has not weighed in on this recommendation yet

MATISSE: MATernal Immunization Study for Safety and Efficacy



- Same Bivalent vaccine candidate (Pfizer)
- Maternal immunization at 24-36 weeks gestation → passive immunity to infants
- Primary outcome: RSV in infants
- 7392 participants
- Healthy, uncomplicated, singleton pregnancies
- Women with high-risk pregnancies were excluded

Severe RSV-Associated Lower Respiratory Tract Illness

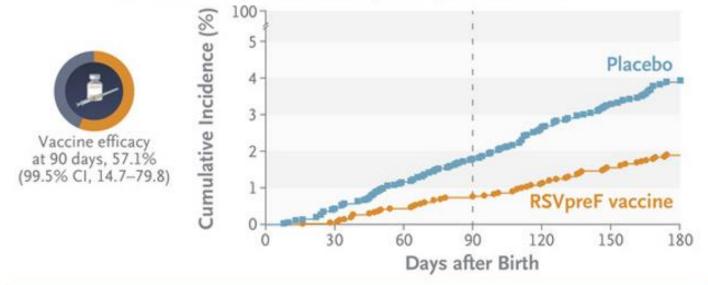


Severe disease:

Vaccine efficacy 82%

No safety signal in maternal participants or in newborns/toddlers up to 24 months after birth

RSV-Associated Lower Respiratory Tract Illness



Any LRTI:

Vaccine efficacy 57.1%



For pregnant women, <u>CDC</u> and <u>ACOG</u> recommend:

Seasonal administration of one dose of RSV vaccine for pregnant people during weeks 32 through 36 of pregnancy between September to January.

Case



For which of the following patients would you recommend the RSV vaccine?

- A. 71-year-old with no medical problems, exercises 7 days/week
- B. 81-year-old with no medical problems, exercises 7 days/week
- C. 65-year-old with history of ESRD s/p renal transplant on tacrolimus, MMF, prednisone
- D. 58-year-old with history of ESRD s/p renal transplant on tacrolimus, MMF, prednisone
- E. 32-year-old pregnant woman with no medical problems at 33 weeks gestation
- F. 38-year-old pregnant woman with SLE on prednisone at 14 weeks gestation

Pneumococcal vaccine Case series

What pneumococcal series, including booster, does each patient need?

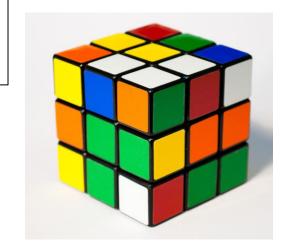
65-year-old with no medical problems.

52-year-old with no medical problems.

20-year-old with cochlear implants

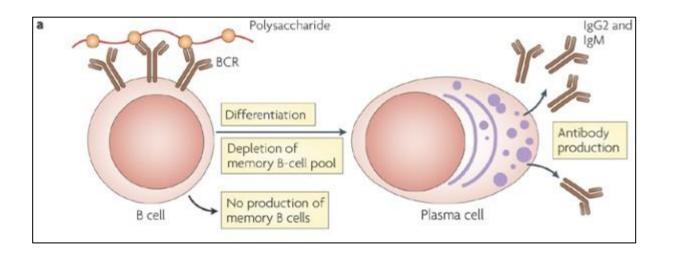
26-year-old with sickle cell disease and functional asplenia

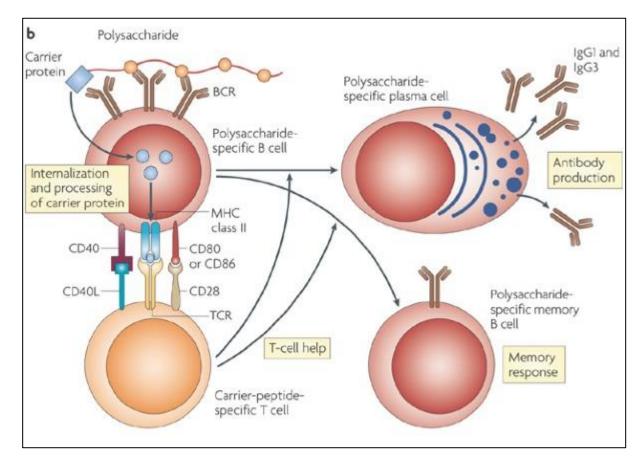
26-year-old with multiple sclerosis on ocrelizumab



Polysaccharide vaccines (eg PPSV)
composed of polysaccharides that
resemble pneumococcal
serotypes, produce Abs

Conjugated vaccines (eg PCV)
joins protein to polysaccharide
chain. Protein brings in T cell
help & leads to memory B cells





New Pneumococcal Vaccines, 2022

- Pneumococcal 15-valent conjugative vaccine (PCV15, Merck)
 - Studied as a series, followed by PPSV-23 (pneumovax)
- Pneumococcal 20-valent conjugate vaccine (PCV20, Pfizer)
 - Studied as a single, stand-alone pneumococcal vaccine

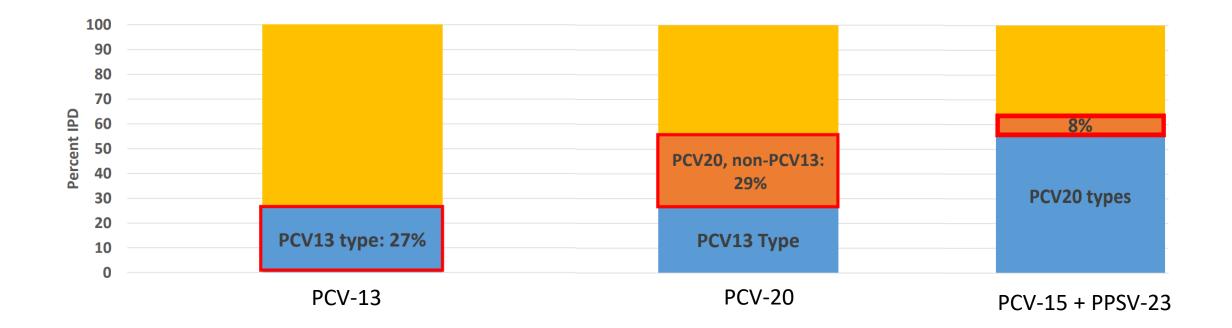
Serotypes contained in pneumococcal vaccines

	1	3	4	5	6A	6B	7 F	9V	14	18 C	19 A	19 F	23 F	22 F	33 F	8	10 A	11 A	12 F	15 B	2	9N	17 F	20
PCV13																								
PCV15																								
PCV20																								
PPSV23																								

PCV-20 vs PCV-15 + PPSV-23

Favors PCV-15 + PPSV-23

Provides broader serotype coverage



PCV-20 vs PCV-15 + PPSV-23

Favors PCV-20

- Easy! One and done.
- Expected to provide better protection than PPSV-23 for the shared serotypes

Serotypes Contained in Current and New Pneumococcal Vaccines

	1	3	4	5	6A	6B	7 F	9V	14	18 C	19 A	19 F	23 F	22 F	33 F	8	10 A	11 A	12 F	15 B	2	9N	17 F	20
PCV13																								
PCV15																								
PCV20																								
PPSV23																								

Outcome: PCV-20 vs PCV-15 + PPSV-23



Not enough data to state preference

October, 2021

PCV20 alone OR PCV15 + PPSV23 one year later

• All patients >65 years old

AND

 Patients 19-64 years old with underlying medical condition or risk factors*



*Conditions Alcohol use disorder Heart disease Liver disease Lung disease CKD Cigarette smoking Cochlear implant Asplenia CSF leak Diabetes Malignancy HIV Hodgkin disease **Immunodeficiency Immunosuppression** Solid organ transplant Sickle cell disease



June, 2024



ACIP recommends PCV21 as an option for adults aged ≥19 years who currently have a recommendation to receive a dose of PCV.

Wait...PCV 21???

PCV-21 is not just PCV-20 + 1

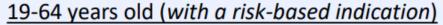
21-valent pneumococcal conjugate vaccine (CAPVAXIVE™, Merck):

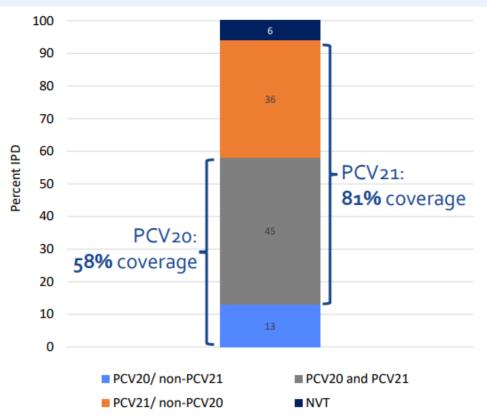
Approved by the FDA for adults aged ≥18 years on June 17, 2024¹

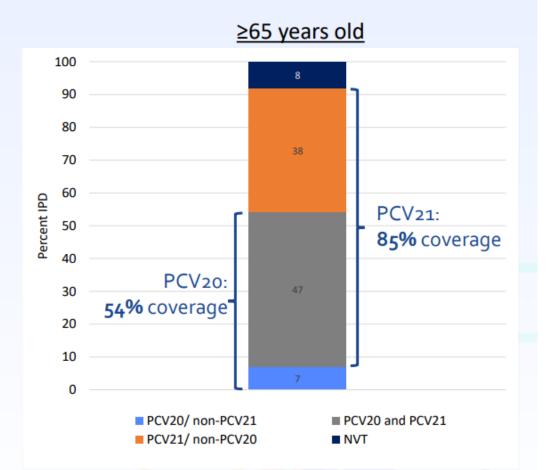
	1	3	4	5			8	9	9	3	2	3	0	1	2	5	2	N	7	0	5	5	6	3	3	4	
PCV15																											
PCV20																											
PPSV23																											
PCV21																											

PCV-21 is not just PCV-20 + 1

Proportion of IPD by vaccine-type among adults with a pneumococcal vaccine indication, 2018–2022









June, 2024



- ACIP recommends PCV21 as an option for adults aged ≥19 years who currently have a recommendation to receive a dose of PCV.
- People who have previously been vaccinated with PCV-20 do not need a dose of PCV-21

ACIP October 2024

October, 2024



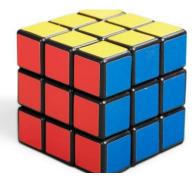
KEY POINTS

- CDC recommends pneumococcal vaccination for children younger than 5 years and adults 50 years or older.
- CDC also recommends pneumococcal vaccination for children and adults at increased risk for pneumococcal disease.
- Follow the recommended immunization schedule to ensure that your patients get the pneumococcal vaccines that they need.

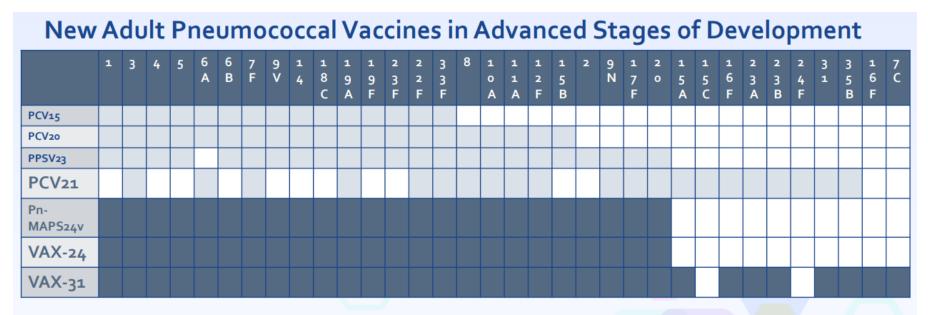
Pneumococcal vaccine Case series

What pneumococcal series, including booster, does each patient need?

PCV-20 or 21 x1*



But wait...there's more



24-valent pneumococcal vaccines:

- Pn-MAPS24v (GSK): Completed phase 1/2 study for adults; Breakthrough Therapy Designation granted and Phase 3 study in preparation; undergoing phase 2 studies in infants¹
- VAX-24 (Vaxcyte): Completed phase 1/2 studies for adults, completed enrollment for phase 2 studies in infants²

31-valent pneumococcal vaccine (VAX-31, Vaxcyte):

Completed enrollment of phase 1/2 study in adults aged ≥50 years³

My predictions...



- Polysaccharide vaccine (PPSV-23) will be phased out very soon
- Rolling approval of conjugate vaccines with broader serotype coverage
- Will people previously vaccinated with PCV-20 need broader serotype boosters when available?

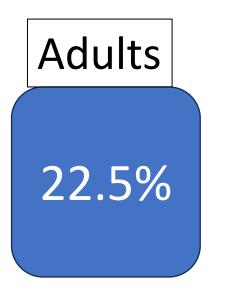
Case

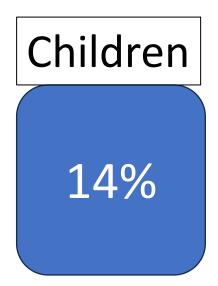


A healthy 24-year-old man presents for yearly physical. He has received 3 doses of mRNA vaccine and has had COVID twice. Last infection was 1 month ago. Courses were mild. Do you recommend the updated COVID vaccine?

- A. Yes, give it now
- B. Yes, but wait until at least 3 months from last infection
- C. No

CDC recommends yearly COVID boosters for everyone 6 months and older





Influenza and COVID-19 Vaccination Coverage Among Health Care Personnel — National Healthcare Safety Network, United States, 2023–24 Respiratory Virus Season

Weekly / October 31, 2024 / 73(43);966-972

Boosters for young healthy individuals: Considerations

- No clinical data on effectiveness inferred from neutralizing antibody response
- Antibody titers wane after 60-90 days
- Risk of severe outcome is very low in young healthy individuals who have been previously vaccinated and/or infected (hybrid immunity)
- Vaccine is very safe; low, but non-zero risk of post-vaccine myocarditis especially in young men

United States is now an outlier

- UK, Sweden, Germany, Norway, Finland recommend only for those at highest risk
- WHO: "Although additional boosters are safe for this group, we do not routinely recommend them, given the comparatively low public health returns."



Does Everyone Need a Yearly Covid Booster?

The most recent recommendation by the CDC has come under question.



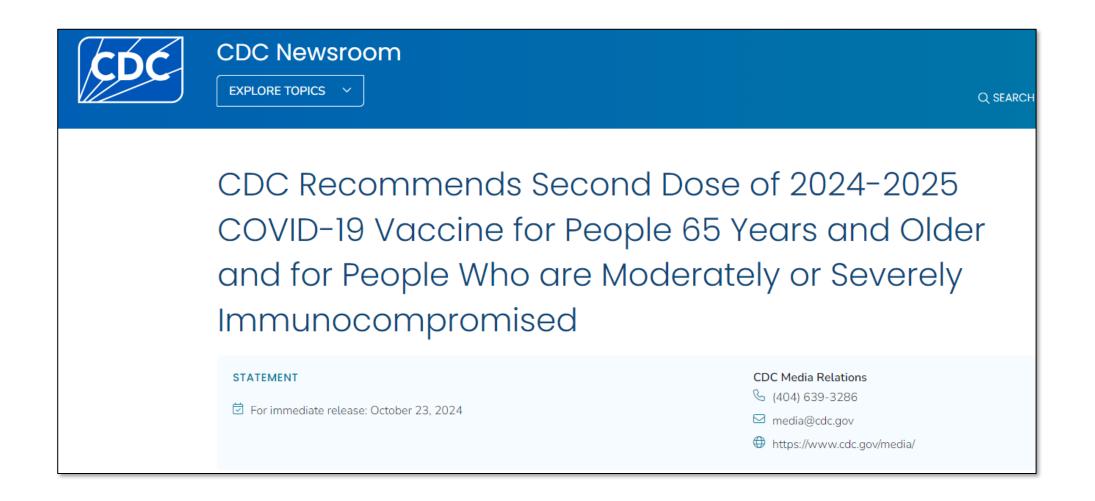
CDC recommends yearly COVID boosters for everyone 6 months and older

WHAT TO KNOW

- Everyone ages 6 months and older should get a 2024–2025 COVID-19 vaccine.
- The COVID-19 vaccine helps protect you from severe disease, hospitalization, and death.
- It is especially important to get your 2024–2025 COVID-19 vaccine if you are ages
 65 and older, are at high risk for severe COVID-19, or have never received a COVID-19 vaccine.
- Vaccine protection decreases over time, so it is important to stay up to date with your COVID-19 vaccine.



October 23, 2024



Vaccine considerations in IC patients

- Low efficacy during periods intense immunosuppression
- Vaccinate BEFORE the need for immunosuppression (when possible)
- Ideally 2 weeks before initiation or resumption of immunosuppression
- B-cell depleting therapies: aim for 4 weeks prior to the next scheduled dose
- Some data support lightening immunosuppression leads to higher efficacy
- Live viral vaccines (MMR, Varicella): suspend immunosuppression x1 month, give vaccine, wait another month, restart immunosuppression
- Make sure to vaccine household contacts

Vaccines beyond 2025

- Vaccine development is happening at the fastest pace in history
- Vaccines continue to be the most impactful tool for disease prevention worldwide

- Trust in public health agencies is tenuous
- The anti-vaccine and anti-science movement in the United States is stronger than ever

Key Points

- RSV vaccine now recommended for age >75 and high risk individuals aged 60-74
- Pneumococcal vaccine recommended for anyone 50 or older
- PCV-21 is an acceptable option for pneumococcal vaccination
- Consider twice-yearly COVID vaccines for highest risk patients (age, immunocompromise)
- Shared decision making for COVID boosters in young, healthy adults

Selected References

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