VACCINE UPDATE:
FOCUS ON NEWLY APPROVED/RECOMMENDED VACCINES (COVID 2023-2024, RSV, MPOX, PCV 15&20, ENHANCED INFLUENZA)

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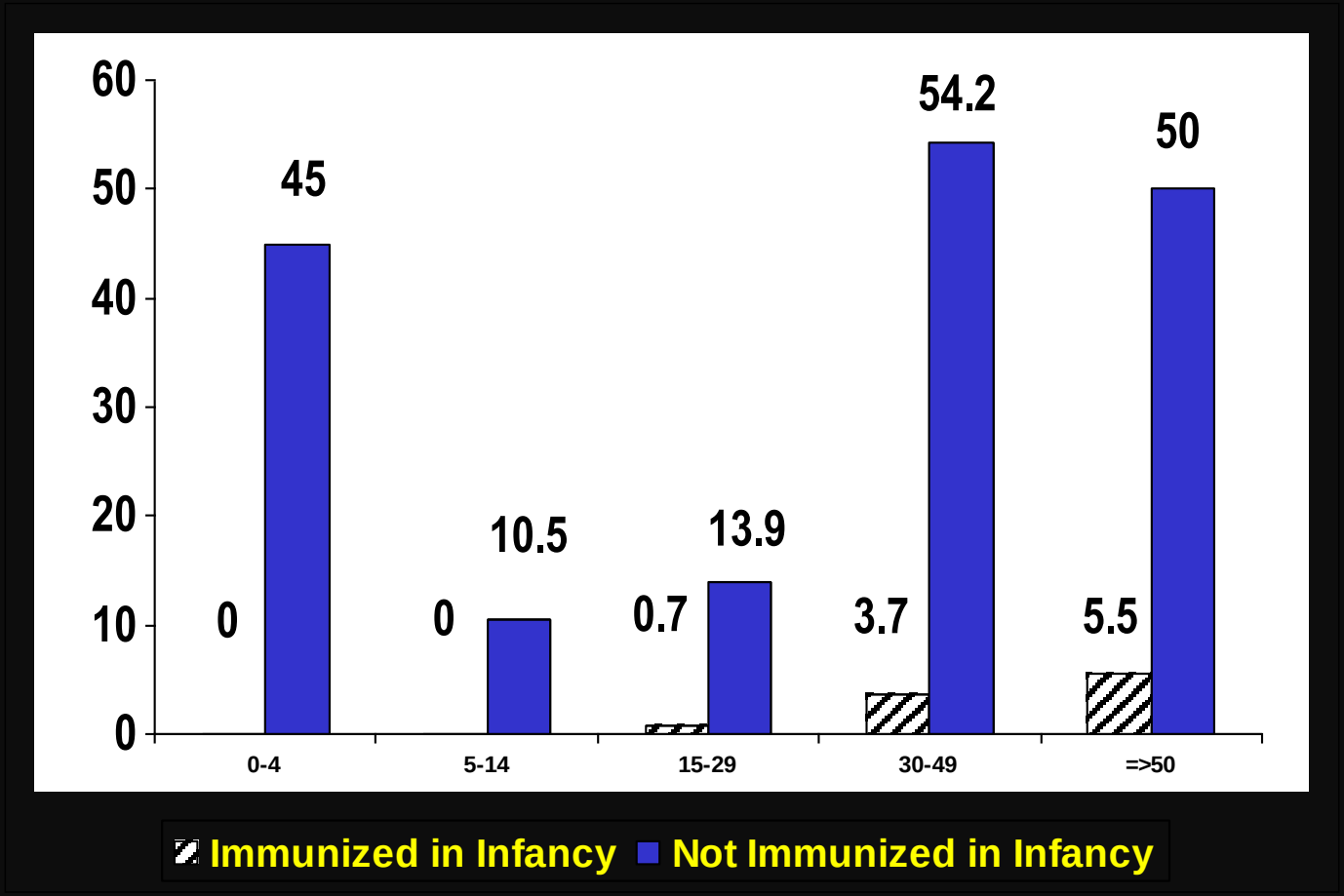
Disclosures: Consultancy; Pfizer, PDI, BD, Germitec, GAMA
All drugs/vaccines issues discussed consistent with FDA approvals or authorizations
Thanks to Sonya McElmeel for slides

Constant Joseph Desbordes (1761-1827), *Baron Jean Louis Aliibert (1768-1837) Performing the vaccination against smallpox in the Chateau of Liancourt.* C. 1820

PROTECTIVE EFFECT OF INFANT IMMUNIZATION AGAINST MORTALITY BY AGE OF INFECTION



Hanna, W. 1913, Studies in smallpox and Vaccination. Bristol, Wright.

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Recent Developments in Vaccine Design: From Live Vaccines to Recombinant Toxin Vaccines

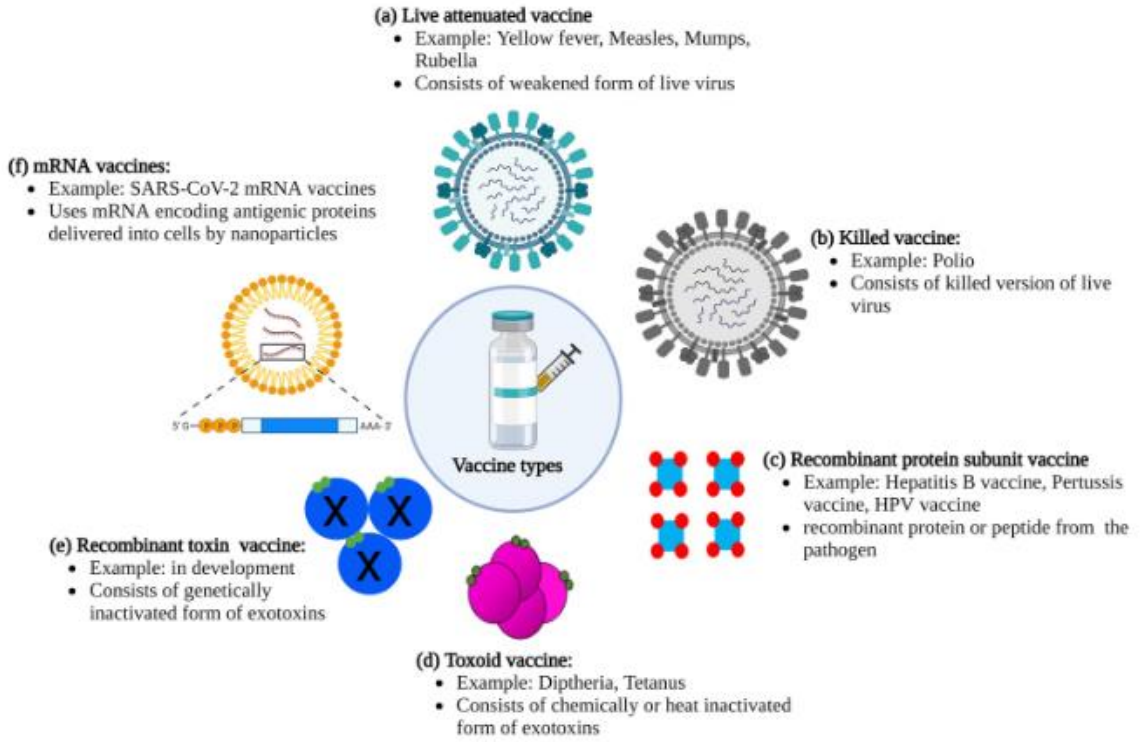

Figure 1. Description of different types of vaccine: (**a**) live attenuated vaccine; (**b**) killed vaccine; (**c**) recombinant protein subunit vaccine; (**d**) toxoid vaccine; (**e**) recombinant toxin vaccine; (**f**) mRNA vaccine. Image created with BioRender.com (accessed on 1 August 2023).

Gupta S, Pellett S. Toxins 2023:8 September

Table 1. Advantages and disadvantages corresponding to different vaccine types.

Vaccine Type	Advantages	Disadvantages
Live vaccines (attenuated)	▪ Elicit humoral as well as cellular immune responses. ▪ Long-lasting protection ▪ Single dose is normally sufficient.	▪ Risk of reversion to pathogenic strain. ▪ Complex attenuation process required. ▪ Vaccine composition not well defined.
Killed vaccines	▪ The vaccine strain does not revert back to pathogenic strain. ▪ Usually only mild side effects such as fever and nausea observed. ▪ Inexpensive to produce at mass level.	▪ Multiple boosters required. ▪ Addition of adjuvants required. ▪ Vaccine elicits primarily humoral responses. ▪ Vaccine composition not well defined. ▪ Large amounts of live pathogens must be cultured to produce vaccine antigens.
Toxoids	▪ Toxicity inactivated. ▪ Low incidence of mild adverse events such as soreness or swelling, fever, nausea. ▪ Good stability. ▪ Doesn't require cold storage.	▪ Multiple doses required to achieve immune memory. ▪ Addition of adjuvants required. ▪ Local reactions to residual formaldehyde used for inactivation. ▪ Requires large-scale production of active toxins. ▪ Immune epitopes after inactivation procedure not well defined.
Subunit vaccines	▪ Composition well defined. ▪ Can be formulated with various vaccine delivery systems such as adjuvant, viral vector, nanoparticles, etc. ▪ Live pathogen is not used to produce the antigen. ▪ The vaccine strain cannot revert back to pathogenic strain.	▪ Multiple doses or boosters required for immune memory. ▪ Antibody response restricted to subunit present in vaccine. ▪ Addition of adjuvants required. ▪ Live pathogens may be cultured to purify the vaccine antigen.
Recombinant toxin vaccines	▪ Can utilize atoxic toxin sub-domains. ▪ Can inactivate toxicity by specific mutations without altering immunogenic surface epitopes. ▪ Safe to produce as no active toxin is involved.	▪ Multiple doses or boosters required. ▪ Addition of adjuvants required. ▪ More expensive and complex to develop compared to other vaccine types.
mRNA vaccines	▪ Can be quickly designed, tested, and mass produced. ▪ Do not consist of live pathogens. ▪ Large number of uses during COVID pandemic indicates good safety and effectiveness.	▪ Requires storage in extreme cold conditions. ▪ Multiple doses or boosters required. ▪ More data on safety are required. ▪ Potential of adverse side effects caused by produced antigen.

VACCINE PREVENTABLE DISEASES

- **Anthrax***
- **Cervical cancer (vulvar, vaginal; HPV)**
- **COVID-19**
- **Diphtheria***
- **Ebola**
- **Genital warts (HPV)**
- **Hepatitis A***
- **Hepatitis B***
- **Hepatitis D (HBV vaccine)**
- ***H. influenza* type b**
- **Human papillomavirus**
- **Influenza A and B (quadrivalent)**
- **Japanese encephalitis**
- **Lyme disease (no longer available)**
- **Malaria (not FDA approved)**
- **Measles***
- **Meningococcal ACWY**
- **Meningococcal B**
- **Meningococcal ACWYB (pentavalent)**
- **Mpox (JYNNEOS)***
- **Mumps**
- **Pertussis**
- **Pneumococcal**
- **Poliomyelitis**
- **Rabies***
- **Rotavirus**
- **RSV**
- **Rubella**
- **Shingles**
- **Smallpox***
- **Tetanus**
- **Tuberculosis**
- **Typhoid fever**
- **Varicella***
- **Yellow fever**
- **Zoster***

*May be used to post-exposure prophylaxis

GREATEST PUBLIC HEALTH ACHIEVEMENTS IN THE US, CDC

1900-1998

- Vaccination
- Motor vehicle safety
- Safer workplaces
- Control of infectious diseases
- Decline in deaths from coronary artery disease and stroke
- Safer and healthier foods
- Healthier mothers and babies
- Family planning
- Fluoridation of drinking water
- Recognition of tobacco use as a health hazard

CDC. MMWR 1999;48:241-243

2001-2010

- Vaccination
- Prevention and control of communicable diseases
- Tobacco control
- Maternal and infant health
- Motor vehicle safety
- Cardiovascular disease prevention
- Occupational safety
- Cancer prevention
- Childhood lead poisoning prevention
- Public health preparedness and response

CDC. MMWR 2011;60:619-623

IMPACT OF VACCINES, US

Disease	Max. Cases (Year)	# 2018	% Reduction
Diphtheria	206,939 (1921)	1	99.99%
Invasive Hib (<5 yrs)	20,000 (1984)	38	99.81%
Measles^	894,135 (1941)	375	98.34%
Mumps	152,209 (1968)	2,515	99.13%
Meningococcal ACWY*	330 (2008)	100	69.70%
Pertussis	265,269 (1934)	15,609	94.12%
Polio	21,269 (1952)	0	100.00%
Rubella	57,686 (1969)	4	99.99%
Rubella (congenital)	20,000 (1964-65)	0	100.00%
Tetanus	601 (1948)	23	96.17%

^indigenous 296, imported 79; CDC, https://wonder.cdc.gov/nndss/nndss_annual_tables_menu.asp

ENHANSING IMMUNIZATION EFFECTIVENESS:
ANTIBODIES FOR PREVENTION AND TREATMENT OF INFECTIOUS DISEASES

- Anthrax (Raxibacumab, Anthrax Immune Globulin Intravenous {AIGIV}): PEP
- COVID-19 (multiple monoclonal antibodies available early in pandemic; none currently available due to reduced activity against Omicron variants): Initially used for PrEP and Rx (no longer available)
- Ebola (Inmazeb {atoltivimab, maftivimab and odesivimab-ebgn}, Ebanga): Rx (only tested for *Zaire ebolavirus* efficacy)
- Hepatitis A (GamaSTAND; IG): PreP, PEP
- Hepatitis B (HerpaGram B, HyperHEP B, Habi-HB; IG): PEP
- Measles (Ig): PEP
- Rabies (Human Rabies Immune Globulin; HRIG): PEP
- RSV (Nirsevimab): PrEP for all infants in their 1st year and high-risk infants in their 2nd year
- Smallpox/mpox (Vaccinia Immune Globulin {VIGIV}): Rx, PEP (mpox, vaccine contra-indicated)
- Varicella (VariZIG): PEP

Advantages of antibodies for PrEP, PEP and/or Rx: Immediately active (often used simultaneous with vaccines to provide protection until vaccine induced immunity develops), safe in pregnancy, generally well tolerated

Disadvantages: Passive therapy (i.e., limited duration), costly, limited availability worldwide, resistance may develop

See CDC for doses, routes of administration, timing

PrEP, pre-exposure prophylaxis; PEP, post-exposure prophylaxis; Rx, treatment

POSSIBLE GOALS OF VACCINATION

- Prevent colonization
  - Conjugate *H. influenzae*, meningococcal, and pneumococcal (PCV) vaccines
- Prevention infection (pre-exposure)
  - Live-attenuated polio vaccine
  - Inhaled influenza vaccine
- Prevent disease (pre-exposure)
  - Hepatitis A and B, tetanus, measles, mumps, rabies, rubella, Ebola, COVID-19, RSV
- Prevent disease (post-exposure)
  - Measles, varicella, smallpox, hepatitis A & B, tetanus, rabies
- Reduce severity
  - Influenza, pneumococcal, varicella, COVID-19
- Prevent reactivation
  - Zoster

POSSIBLE GOALS OF VACCINATION

- Provide herd (community) protection
  - Measles, mumps, rubella, varicella, smallpox, polio, meningococcal, pneumococcal
- Protect the infant (maternal immunization)
  - Pertussis (Tdap), COVID-19, RSV, hepatitis B
- Disease elimination (Incidence of 0 in a selected area)
  - Polio (Americas), measles (US)
- Disease eradication (Worldwide eradication)
  - Smallpox
  - Polio type 2 (eradicated 1999)
  - Polio type 3 (eradicated 2012)
- Reduce incidence of infections due to MDR pathogens
  - Influenza, pneumococcal, varicella/zoster
- Prevent cancer
  - Hepatitis B (liver), HPV (cervical, vaginal, vulvar, oral?)

CURRENT STATE OF US VACCINES

- Improved vaccines
  - COVID-19: XBB monovalent vaccines (2023-24 COVID-19 vaccine)
  - Influenza: Vaccines for persons ≥65 years of age; higher dose or adjuvanted influenza vaccines (HD-IIV4, RIV4, aIIV4)
  - Pneumococcal: Improved spectrum; PCV15 and PCV20
- New vaccines or indications
  - JYNNEOS: Mpox; pre- and post-exposure prophylaxis (ID or SC)
  - RSV: Indicated for older adults (≥60 years of age) and pregnant persons
  - Ebola (EBOV; species *Zaire ebolavirus*)
  - Dengue: Dengvazia (FDA approved 2019, ACIP statement 2021); Takeda (withdrawn from FDA review, July 2023)
  - Pentavalent meningococcal (A,B,C,W,Y)
- Forthcoming vaccines, 2023/2024 (FDA approval plus CDC recommendations)
  - Chikungunya fever (FDA approval expected in November 2023)
  - PCV21 (FDA approval expected first half of 2024)
  - Combined influenza plus COVID-19 (likely 2024-25)

ADULT IMMUNIZATION SCHEDULE, CDC, 2024

Recommended Adult Immunization Schedule
for ages 19 years or older

UNITED STATES 2024

Vaccines in the Adult Immunization Schedule*

Vaccine	Abbreviation(s)	Trade name(s)
COVID-19 vaccine	1vCOV-mRNA	Comirnaty®/Pfizer-BioNTech COVID-19 Vaccine SPIKEVAX®/Moderna COVID-19 Vaccine
	1vCOV-aPS	Novavax COVID-19 Vaccine
Haemophilus influenzae type b vaccine	Hib	ActHIB® Hiberix® PedvaxHIB®
Hepatitis A vaccine	HepA	Havrix® Vaqta®
Hepatitis A and hepatitis B vaccine	HepA-HepB	Twinrix®
Hepatitis B vaccine	HepB	Engerix-B® Heplisav-B® PreHevbrio® Recombivax HB®
Human papillomavirus vaccine	HPV	Gardasil 9®
Influenza vaccine (inactivated)	IIV4	Many brands
Influenza vaccine (live, attenuated)	LAIV4	FluMist® Quadrivalent
Influenza vaccine (recombinant)	RIV4	Flublok® Quadrivalent
Measles, mumps, and rubella vaccine	MMR	M-M-R II® Priorix®
Meningococcal serogroups A, C, W, Y vaccine	MenACWY-CRM MenACWY-TT	Menveo® MenQuadfi®
Meningococcal serogroup B vaccine	MenB-4C MenB-FHbp	Bexsero® Trumenba®
Meningococcal serogroup A, B, C, W, Y vaccine	MenACWY-TT/ MenB-FHbp	Penbraya™
Mpox vaccine	Mpox	Jynneos®
Pneumococcal conjugate vaccine	PCV15 PCV20	Vaxneuvance™ Prevnar 20™
Pneumococcal polysaccharide vaccine	PPSV23	Pneumovax 23®
Poliovirus vaccine	IPV	IPOL®
Respiratory syncytial virus vaccine	RSV	Arexvy® ABRYSVO™
Tetanus and diphtheria toxoids	Td	Tenivac® Tdvax™
Tetanus and diphtheria toxoids and acellular pertussis vaccine	Tdap	Adacel® Boostrix®
Varicella vaccine	VAR	Varivax®
Zoster vaccine, recombinant	RZV	Shingrix

*Administer recommended vaccines if vaccination history is incomplete or unknown. Do not restart or add doses to vaccine series if there are extended intervals between doses. The use of trade names is for identification purposes only and does not imply endorsement by the ACIP or CDC.

How to use the adult immunization schedule

1 Determine recommended vaccinations by age **(Table 1)**
2 Assess need for additional recommended vaccinations by medical condition or other indication **(Table 2)**
3 Review vaccine types, dosing frequencies and intervals, and considerations for special situations **(Notes)**
4 Review contraindications and precautions for vaccine types **(Appendix)**
5 Review new or updated ACIP guidance **(Addendum)**

Recommended by the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/acip) and approved by the Centers for Disease Control and Prevention (www.cdc.gov), American College of Physicians (www.acponline.org), American Academy of Family Physicians (www.aafp.org), American College of Obstetricians and Gynecologists (www.acog.org), American College of Nurse-Midwives (www.midwife.org), American Academy of Physician Associates (www.aapa.org), American Pharmacists Association (www.pharmacist.com), and Society for Healthcare Epidemiology of America (www.shea-online.org).

Report
- Suspected cases of reportable vaccine-preventable diseases or outbreaks to the local or state health department
- Clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System at www.vaers.hhs.gov or 800-822-7967

Questions or comments
Contact www.cdc.gov/cdc-info or 800-CDC-INFO (800-232-4636), in English or Spanish, 8 a.m.–8 p.m. ET, Monday through Friday, excluding holidays.

Download the CDC Vaccine Schedules app for providers at www.cdc.gov/vaccines/schedules/hcp/schedule-app.html.

Helpful Information
- Complete Advisory Committee on Immunization Practices (ACIP) recommendations: www.cdc.gov/vaccines/hcp/acip-recs/index.html
- ACIP Shared Clinical Decision-Making Recommendations: www.cdc.gov/vaccines/acip/acip-scdm-faqs.html
- *General Best Practice Guidelines for Immunization* www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
- Vaccine information statements: www.cdc.gov/vaccines/hcp/vis/index.html
- Manual for the Surveillance of Vaccine-Preventable Diseases (including case identification and outbreak response): www.cdc.gov/vaccines/pubs/surv-manual

Scan QR code for access to online schedule

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CS310321-D

Recommended Adult Immunization Schedule
for ages 19 years or older

UNITED STATES 2024

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Vaccines in the Adult Immunization Schedule*

Vaccine	Abbreviation(s)	Trade name(s)
COVID-19 vaccine†	1vCOV-mRNA	Comirnaty®/Pfizer-BioNTech COVID-19 Vaccine ~~SPIKEVAX®/Moderna COVID-19 Vaccine~~
	2vCOV-mRNA	~~Pfizer-BioNTech COVID-19 Vaccine, Bivalent~~ ~~Moderna COVID-19 Vaccine, Bivalent~~
	1vCOV-aPS	Novavax COVID-19 Vaccine
Haemophilus influenzae type b vaccine	Hib	ActHIB® Hiberix® PedvaxHIB®
Hepatitis A vaccine	HepA	Havrix® Vaqta®
Hepatitis A and hepatitis B vaccine	HepA-HepB	Twinrix®
Hepatitis B vaccine	HepB	Engerix-B® Heplisav-B® PreHevbrio® Recombivax HB®
Human papillomavirus vaccine	HPV	Gardasil 9®
Influenza vaccine (inactivated)†	IIV4	Many brands
Influenza vaccine (live, attenuated)†	LAIV4	FluMist® Quadrivalent
Influenza vaccine (recombinant)†	RIV4	Flublok® Quadrivalent
Measles, mumps, and rubella vaccine	MMR	M-M-R II® Priorix®
Meningococcal serogroups A, C, W, Y vaccine	MenACWY-D MenACWY-CRM MenACWY-TT	Menactra® Menveo® MenQuadfi®
Meningococcal serogroup B vaccine	MenB-4C MenB-FHbp	Bexsero® Trumenba®
Pneumococcal conjugate vaccine	PCV15 PCV20	Vaxneuvance™ Prevnar 20™
Pneumococcal polysaccharide vaccine	PPSV23	Pneumovax 23®
Poliovirus vaccine†	IPV	IPOL®
Tetanus and diphtheria toxoids	Td	Tenivac® Tdvax™
Tetanus and diphtheria toxoids and acellular pertussis vaccine	Tdap	Adacel® Boostrix®
Varicella vaccine	VAR	Varivax®
Zoster vaccine, recombinant	RZV	Shingrix
New vaccines added to the Schedule since February 2023 *(See Addendum)*		
Respiratory Syncytial Virus vaccine	RSV	Arexvy® ABRYSVO™

*Administer recommended vaccines if vaccination history is incomplete or unknown. Do not restart or add doses to vaccine series if there are extended intervals between doses. The use of trade names is for identification purposes only and does not imply endorsement by the ACIP or CDC.
† COVID-19, Poliovirus, and Influenza vaccines have new or updated ACIP recommendations. Please see Addendum for more details.

Recommended by the Advisory Committee on Immunization Practices (www.cdc.gov/vaccines/acip) and approved by the Centers for Disease Control and Prevention (www.cdc.gov), American College of Physicians (www.acponline.org), American Academy of Family Physicians (www.aafp.org), American College of Obstetricians and Gynecologists (www.acog.org), American College of Nurse-Midwives (www.midwife.org), American Academy of Physician Associates (www.aapa.org), American Pharmacists Association (www.pharmacist.com), and Society for Healthcare Epidemiology of America (www.shea-online.org).

Report
- Suspected cases of reportable vaccine-preventable diseases or outbreaks to the local or state health department
- Clinically significant postvaccination reactions to the Vaccine Adverse Event Reporting System at www.vaers.hhs.gov or 800-822-7967

Injury claims
All vaccines included in the adult immunization schedule except PPSV23, RZV, and COVID-19 vaccines are covered by the National Vaccine Injury Compensation Program (VICP). COVID-19 vaccines that are authorized or approved by the FDA are covered by the Countermeasures Injury Compensation Program (CICP). For more information, see www.hrsa.gov/vaccinecompensation or www.hrsa.gov/dcp.

Questions or comments
Contact www.cdc.gov/cdc-info or 800-CDC-INFO (800-232-4636), in English or Spanish, 8 a.m.–8 p.m. ET, Monday through Friday, excluding holidays.

Download the CDC Vaccine Schedules app for providers at www.cdc.gov/vaccines/schedules/hcp/schedule-app.html.

Helpful Information
- Complete Advisory Committee on Immunization Practices (ACIP) recommendations: www.cdc.gov/vaccines/hcp/acip-recs/index.html
- *General Best Practice Guidelines for Immunization* (including contraindications and precautions): www.cdc.gov/vaccines/hcp/acip-recs/general-recs/index.html
- Vaccine information statements: www.cdc.gov/vaccines/hcp/vis/index.html
- Manual for the Surveillance of Vaccine-Preventable Diseases (including case identification and outbreak response): www.cdc.gov/vaccines/pubs/surv-manual
- Travel vaccine recommendations: www.cdc.gov/travel
- Recommended Child and Adolescent Immunization Schedule, United States, 2023: www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html
- ACIP Shared Clinical Decision-Making Recommendations: www.cdc.gov/vaccines/acip/acip-scdm-faqs.html

Scan QR code for access to online schedule

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CS310321-C

Changes to notes: COVID-19, Influenza, Meningococcal, Mpox, Polio, RSV
Changes to Appendix: Mpox, COVID-19, RSV

CDC, ACIP, 25-25 Oct., 2023

Table 1 Recommended Adult Immunization Schedule by Age Group, United States, 2024

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
COVID-19	1 or more doses of updated (2023-2024 Formula) vaccine (See Notes)			
Influenza inactivated (IIV4) or Influenza recombinant (RIV4)	1 dose annually			
or	**or**			
Influenza live, attenuated (LAIV4)	1 dose annually			
Respiratory Syncytial Virus (RSV)	Seasonal administration during pregnancy. See Notes.			≥60 years
Tetanus, diphtheria, pertussis (Tdap or Td)	1 dose Tdap each pregnancy; 1 dose Td/Tdap for wound management (see notes)			
	1 dose Tdap, then Td or Tdap booster every 10 years			
Measles, mumps, rubella (MMR)	1 or 2 doses depending on indication (if born in 1957 or later)			For healthcare personnel, see notes
Varicella (VAR)	2 doses (if born in 1980 or later)		2 doses	
Zoster recombinant (RZV)	2 doses for immunocompromising conditions (see notes)		2 doses	
Human papillomavirus (HPV)	2 or 3 doses depending on age at initial vaccination or condition	27 through 45 years		
Pneumococcal (PCV15, PCV20, PPSV23)				See Notes
				See Notes
Hepatitis A (HepA)	2, 3, or 4 doses depending on vaccine			
Hepatitis B (HepB)	2, 3, or 4 doses depending on vaccine or condition			
Meningococcal A, C, W, Y (MenACWY)	1 or 2 doses depending on indication, see notes for booster recommendations			
Meningococcal B (MenB)	19 through 23 years	2 or 3 doses depending on vaccine and indication, see notes for booster recommendations		
Haemophilus influenzae type b (Hib)	1 or 3 doses depending on indication			
Mpox				

Recommended vaccination for adults who meet age requirement, lack documentation of vaccination, or lack evidence of past infection

Recommended vaccination for adults with an additional risk factor or another indication

Recommended vaccination based on shared clinical decision-making

No recommendation/ Not applicable

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2024

Always use this table in conjunction with Table 1 and the Notes that follow. Medical conditions or indications are often not mutually exclusive. If multiple conditions/indications are present, refer to guidance in all relevant columns. See Notes for medical conditions or indications not listed.

VACCINE	Pregnancy	Immunocompromised (excluding HIV infection)	HIV infection CD4 percentage and count		Men who have sex with men	Asplenia, complement deficiency	Heart or lung disease	Kidney failure, End-stage renal disease or on dialysis	Chronic liver disease; alcoholism[a]	Diabetes	Healthcare Personnel[b]
			<15% or <200mm	≥15% and ≥200mm							
COVID-19		See Notes									
IIV4 or RIV4	1 dose annually										
LAIV4					1 dose annually if age 19 - 49 years		1 dose annually if age 19 - 49 years				
RSV	Seasonal administration. See Notes	See Notes				See Notes					
Tdap or Td	Tdap: 1 dose each pregnancy	1 dose Tdap, then Td or Tdap booster every 10 years									
MMR	*										
VAR	*			See Notes							
RZV		See Notes									
HPV	*	3 dose series if indicated									
Pneumococcal											
HepA											
Hep B	See Notes									Age ≥ 60 years	
MenACWY											
MenB											
Hib		HSCT: 3 doses[c]				Asplenia: 1 dose					
Mpox	See Notes				See Notes						See Notes

- Recommended for all adults who lack documentation of vaccination, **OR** lack evidence of past infection
- Not recommended for all adults, but is recommended for some adults based on either age **OR** increased risk for or severe outcomes from disease
- Recommended based on shared clinical decision-making
- Recommended for all adults, and additional doses may be necessary based on medical condition or other indications. See Notes.
- Precaution: Might be indicated if benefit of protection outweighs risk of adverse reaction
- Contraindicated or not recommended *Vaccinate after pregnancy, if indicated
- No Guidance/ Not Applicable

a. Precaution for LAIV4 does not apply to alcoholism.

b. See notes for influenza; hepatitis B; measles, mumps, and rubella; and varicella vaccinations.

c. Hematopoietic stem cell transplant.

COVID-19 VACCINES

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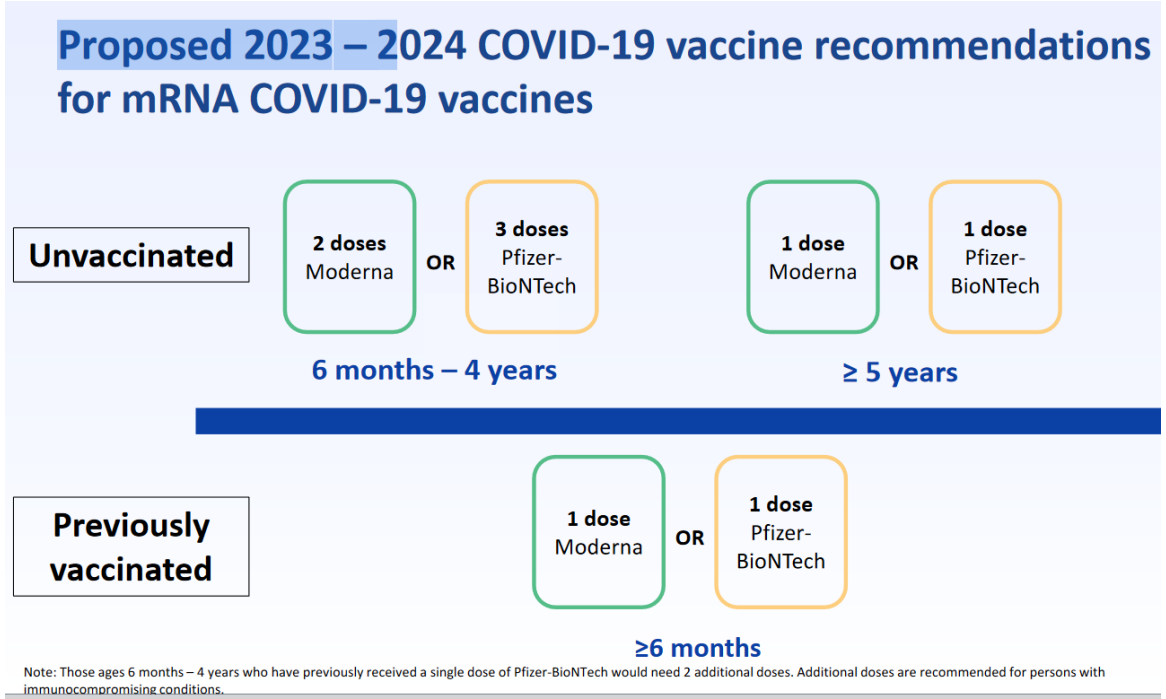
Recommendations for use of the 2023–2024 formulations of Moderna COVID-19 Vaccine and Pfizer-BioNTech COVID-19 Vaccine, CDC

- Everyone ages 5 years and older is recommended to receive 1 dose of updated (2023–2024 Formula) mRNA COVID-19 vaccine
- Children ages 6 months–4 years
  - Initial vaccination: should receive either 2 doses of updated (2023–2024 Formula) Moderna or 3 doses of updated (2023–2024 Formula) Pfizer-BioNTech COVID-19 vaccine
  - Received previous mRNA doses: need 1 or 2 doses of updated (2023–2024 Formula) Moderna or updated (2023–2024 Formula) Pfizer-BioNTech COVID-19 vaccine, depending on the number of prior doses
- People who are moderately or severely immunocompromised
  - Initial vaccination: should receive a 3-dose series of updated (2023–2024 Formula) Moderna or updated (2023–2024 Formula) Pfizer-BioNTech COVID-19 vaccine
  - Received previous mRNA doses: need 1 or 2 doses of updated (2023–2024 Formula) Moderna or updated (2023–2024 Formula) Pfizer-BioNTech COVID-19 vaccine, depending on the number of prior doses
  - May receive 1 or more additional updated (2023–2024 Formula) mRNA COVID-19 vaccine doses



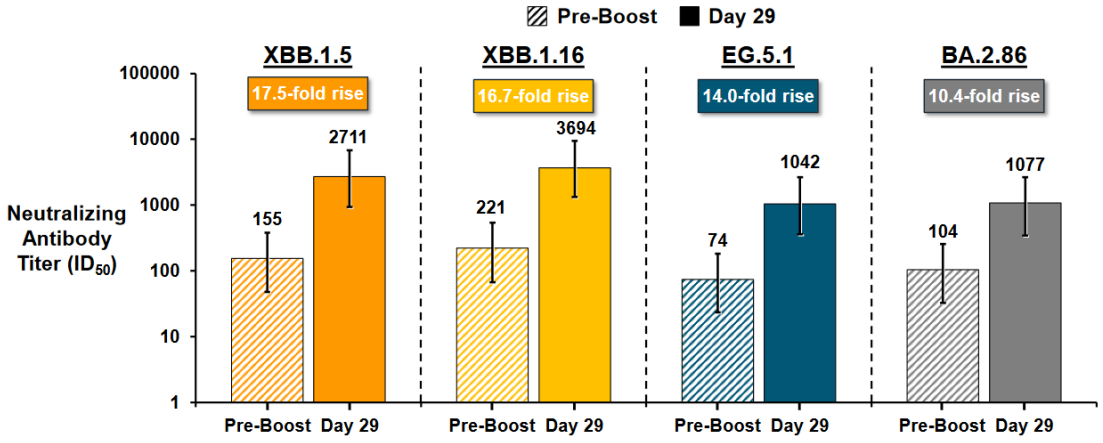
No specific recommendation by CDC for HCP to receive COVID-19 immunization or the 2023-24 vaccine
Timing: Recent COVID-19, wait 3 months; Recent COVID-19 vaccine primary series/booster, wait 2 months

CDC: https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html
Wallace M, et al. ACIP 9/12/23

Safety and Immunogenicity of Moderna COVID-19 Vaccine (2023-2024 Formula)

Cross Neutralization Results (Day 29) After XBB.1.5 Vaccine in Adults – *Duke Assay*

Study 205J, Per-Protocol Immunogenicity Set - All Participants

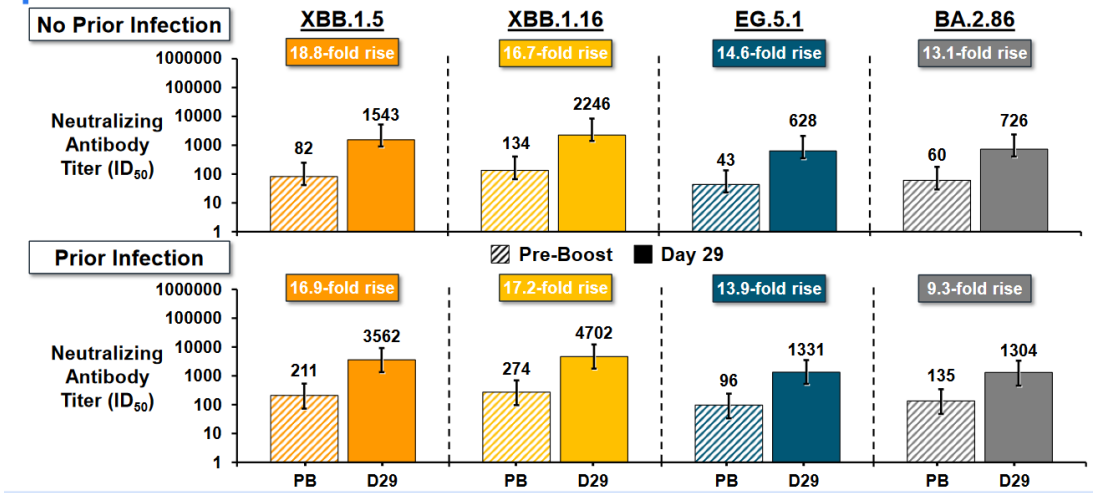


Substantial fold rise demonstrated across newer variants

Priddy F. ACIP, 9/12/2023

Cross Neutralization Results (Day 29) After XBB.1.5 Vaccine in Adults by Baseline SARS-CoV-2 Serostatus - *Duke Assay*

Study 205J, Per-Protocol Immunogenicity Set

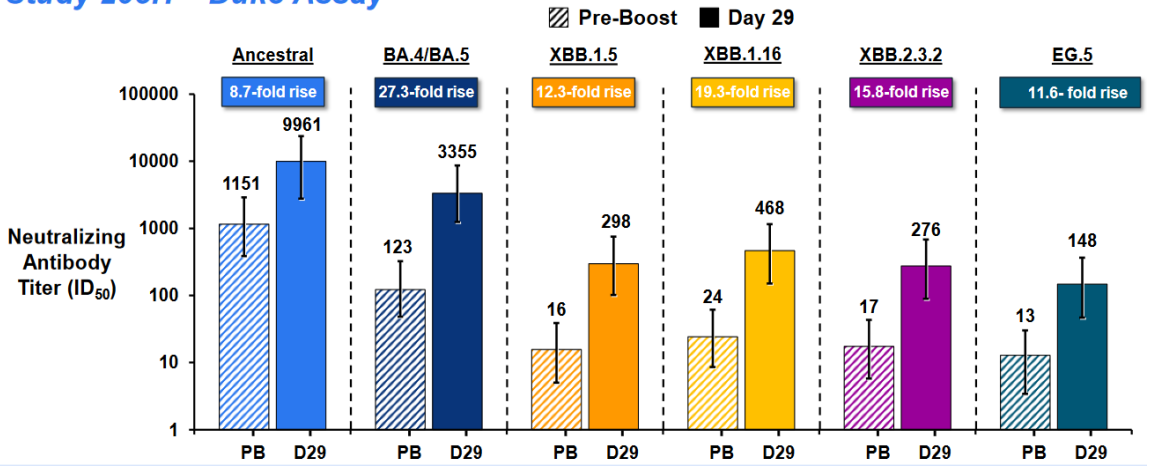


Cross neutralization demonstrated regardless of prior SARS-CoV-2 infection

Pseudovirus neutralization assay

Cross Neutralization Results (Day 29) in Adults after Bivalent BA.4/BA.5 Vaccine

Study 205H – Duke Assay

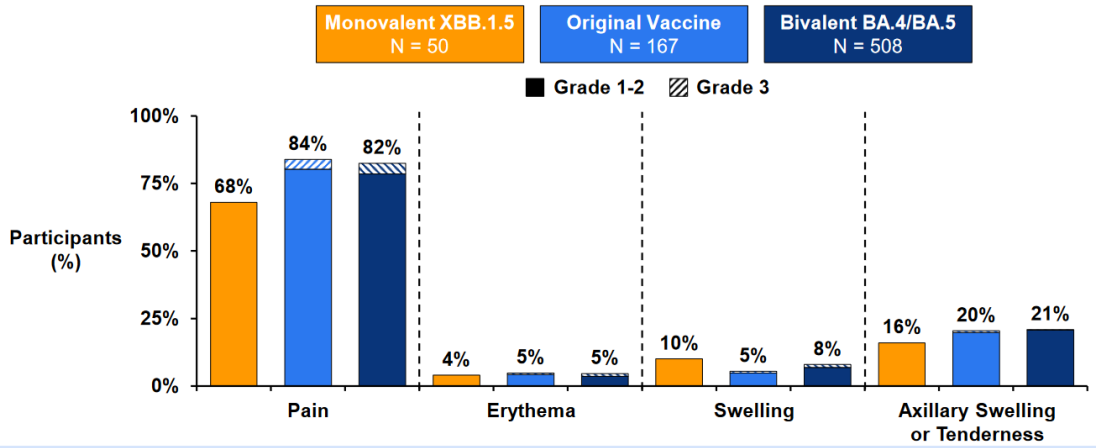


Limited cross neutralization to newer variants after previously authorized BA.4/BA.5 bivalent vaccine

Safety and Immunogenicity of Moderna COVID-19 Vaccine (2023-2024 Formula)

Local Reactions Following Booster Doses in Adults

Study 205J and Study 205H, Solicited Safety Set

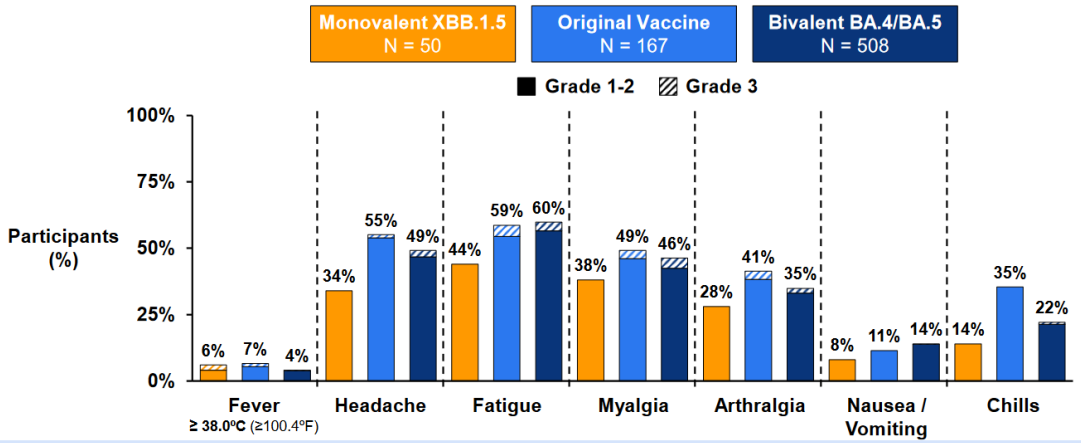


Local reactions similar or lower than previously authorized Moderna COVID-19 vaccines

Within 7 days of injection; No Grade 4 events reported
Chalkias et al., *medRxiv,* 2022, Chu et al, *Nat Med* 28:1041, 2022

Systemic Reactions Following Booster Doses in Adults

Study 205J and Study 205H, Solicited Safety Set



Systemic reactions similar or lower than previously authorized Moderna COVID-19 vaccines

Within 7 days of injection; No Grade 4 events reported
Chalkias et al., *medRxiv,* 2022, Chu et al, *Nat Med* 28:1041, 2022

Priddy F. ACIP, 9/12/2023

Estimates of SARS-CoV-2 Seroprevalence and Incidence of Primary SARS-CoV-2 Infections Among Blood Donors, by COVID-19 Vaccination Status, US, April 2021–September 2022

Summary

What is already known about this topic?

SARS-CoV-2 hybrid immunity (immunity derived from both previous infection and vaccination) has been reported to provide better protection than that from infection or vaccination alone.

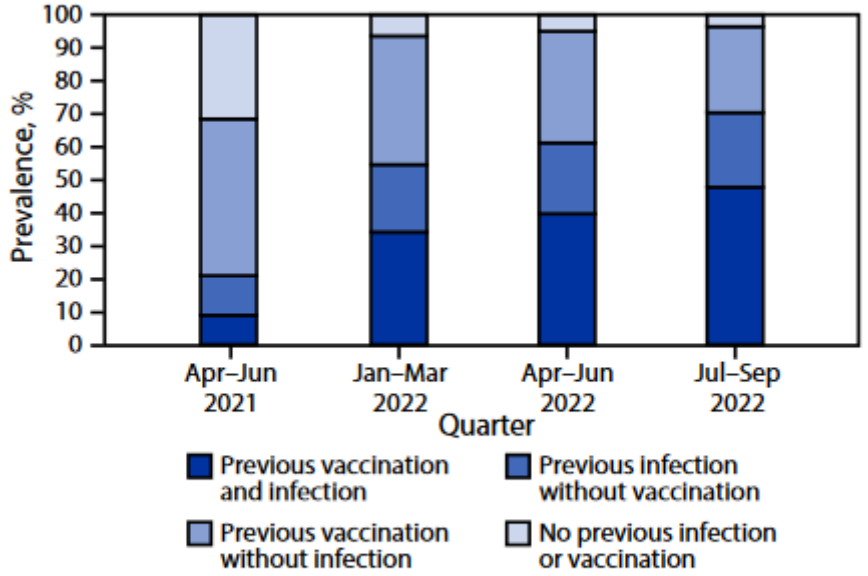
What is added by this report?

By the third quarter of 2022, an estimated 96.4% of persons aged ≥16 years in a longitudinal blood donor cohort had SARS-CoV-2 antibodies from previous infection or vaccination, including 22.6% from infection alone and 26.1% from vaccination alone; 47.7% had hybrid immunity. Hybrid immunity prevalence was lowest among adults aged ≥65 years.

What are the implications for public health practice?

Low prevalence of infection-induced and hybrid immunity among older adults, who are at increased risk for severe disease if infected, reflects the success of public health infection prevention efforts while also highlighting the importance of this group staying up to date with recommended COVID-19 vaccination, including at least 1 bivalent dose.

FIGURE 1. Prevalences of vaccine-induced, infection-induced, and hybrid* immunity† against SARS-CoV-2 among blood donors aged ≥16 years — United States, April 2021–September 2022



* Immunity derived from a combination of vaccination and infection.
† Ascertained by the presence of anti-spike antibodies (present in both COVID-19–vaccinated and SARS-CoV-2–infected persons) and anti-nucleocapsid antibodies (present only in previously infected persons) and self-reported history of vaccination.

Jones JM, et al. MMWR 2023;72:601 (June 2)

mRNA-1273 bivalent (original and Omicron) COVID-19 vaccine effectiveness against COVID-19 outcomes in the US

The bivalent (original and Omicron BA.4/BA.5) mRNA-1273 COVID-19 vaccine was authorized to offer broader protection against COVID-19. We conducted a matched cohort study to evaluate the effectiveness of the bivalent vaccine in preventing hospitalization for COVID-19 (primary outcome) and medically attended SARS-CoV-2 infection and hospital death (secondary outcomes). Compared to individuals who did not receive bivalent mRNA vaccination but received ≥2 doses of any monovalent mRNA vaccine, the relative vaccine effectiveness (rVE) against hospitalization for COVID-19 was **70.3%** (95% confidence interval, 64.0%–75.4%). rVE was consistent across subgroups and not modified by time since last monovalent dose or number of monovalent doses received. Protection was durable ≥3 months after the bivalent booster. rVE against SARS-CoV-2 infection requiring emergency department/urgent care and against COVID-19 hospital death was **55.0%** (50.8%–58.8%) and **82.7%** (63.7%–91.7%), respectively. The mRNA-1273 bivalent booster provides additional protection against hospitalization for COVID-19, medically attended SARS-CoV-2 infection, and COVID-19 hospital death.

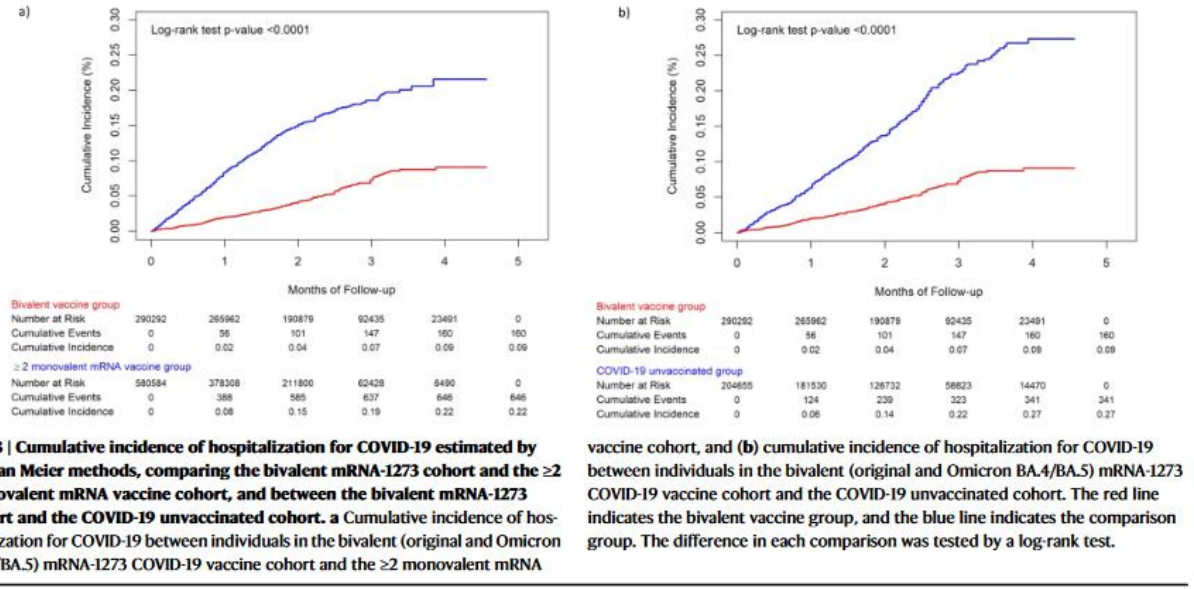


Fig. 3 | Cumulative incidence of hospitalization for COVID-19 estimated by Kaplan Meier methods, comparing the bivalent mRNA-1273 cohort and the ≥2 monovalent mRNA vaccine cohort, and between the bivalent mRNA-1273 cohort and the COVID-19 unvaccinated cohort. a Cumulative incidence of hospitalization for COVID-19 between individuals in the bivalent (original and Omicron BA.4/BA.5) mRNA-1273 COVID-19 vaccine cohort and the ≥2 monovalent mRNA vaccine cohort, and **(b)** cumulative incidence of hospitalization for COVID-19 between individuals in the bivalent (original and Omicron BA.4/BA.5) mRNA-1273 COVID-19 vaccine cohort and the COVID-19 unvaccinated cohort. The red line indicates the bivalent vaccine group, and the blue line indicates the comparison group. The difference in each comparison was tested by a log-rank test.

Tseung HF, et al. Nature 2023;14:5851 (20 Sept)

BNT162b2 Against COVID-19-Associated ED and Urgent Care Visits Among Children 5–11 Years of Age: A Test Negative Design

In a 1:1 matched test-negative design among 5- to 11-year-olds in the Kaiser Permanente Southern California health system (n = 3984), BNT162b2 effectiveness against the omicron-related emergency department or urgent care encounters was 60%[95%CI: 47−69] <3 months post-dose-two and 28% [8−43] after ≥3 months. A booster improved protection to 77% [53−88].

Tartof SY, et al. J Ped Infect Dis Soc 2023;12:177

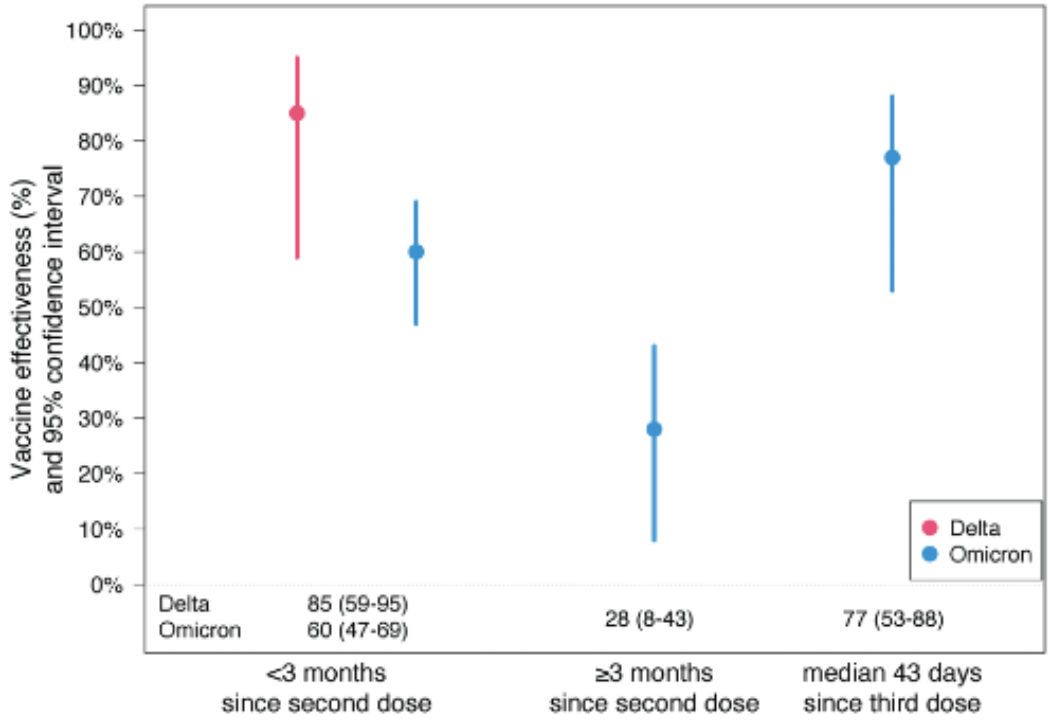
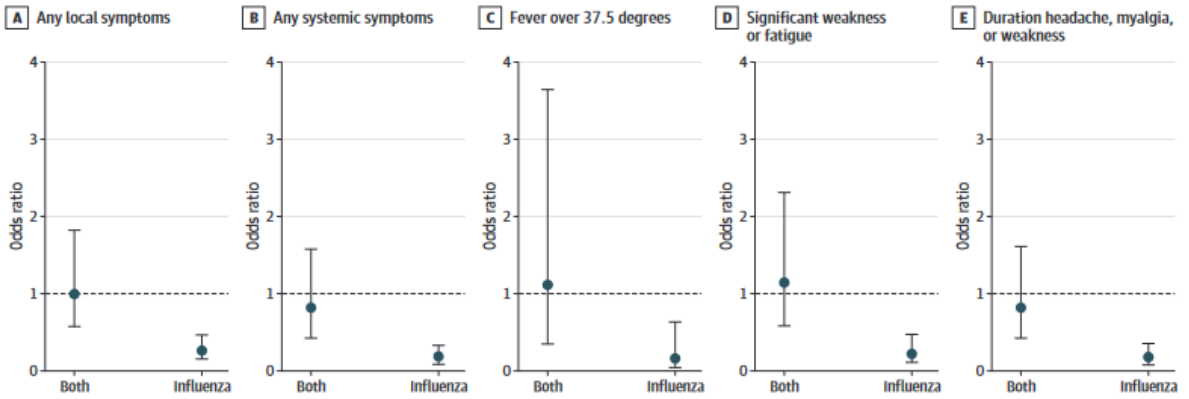


Figure 1. BNT162b2 vaccine effectiveness by variant, number of doses, and time since receipt of last dose.

Immunogenicity and Reactogenicity of Coadministration of COVID-19 and Influenza Vaccines

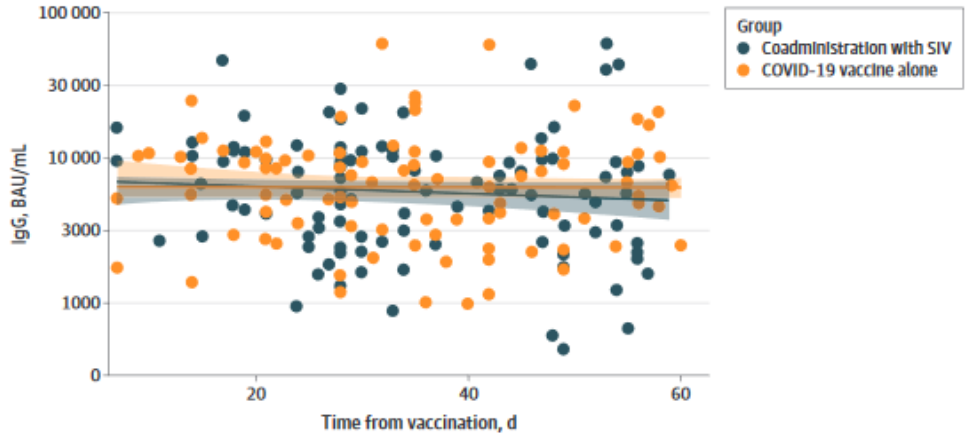
- Prospective cohort study that assessed reactogenicity and immunogenicity of COVID-19 (bivalent) and seasonal influenza vaccines (SIV). Compared with COVID-19 vaccination alone, the risk of systemic symptoms was similar in the coadministration group (odds ratio, 0.82; 95% CI, 0.43-1.56). Geometric mean titers in the coadministration group were estimated to be 0.84 (95% CI, 0.69-1.04) times lower than in the COVID-19 vaccine–alone group. In this cohort study of HCP who received a COVID-19 vaccine, an influenza vaccine, or both, coadministration was not associated with substantially inferior immune response or to more frequent adverse events compared with COVID-19 vaccine administration alone, supporting the coadministration of these vaccines.

Figure 2. Estimated Odds of Adverse Events in the Coadministration Group (COVID-19 Vaccine and Seasonal Influenza Vaccine [SIV]) and SIV Group Compared With the COVID-19 Vaccine–Alone Group



Logistic regression was used for binary outcomes, while an ordered logit model was used for the ordinal outcome. The model was adjusted for age, sex, and number of comorbidities. Missing data in number of comorbidities were multiply imputed 5 times, with the estimates from each complete data set pooled using Rubin rules.

Figure 3. Postvaccination Anti-Spike IgG Geometric Mean Titers Plotted as a Function of Time Elapsed From Vaccination, COVID-19 Vaccine–Alone Compared With the Coadministration of COVID-19 With Seasonal Influenza Vaccine (SIV)



Gonen T, et al. JAMA Network Open 2023;6:e2332813

UNC SCHOOL OF MEDICINE

RSV VACCINES

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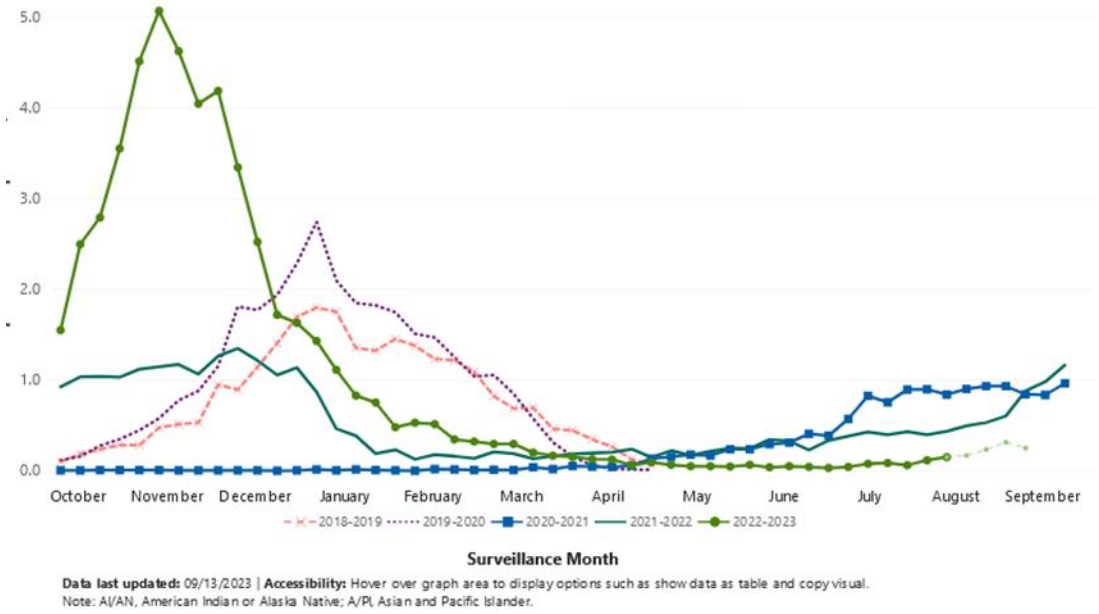
Respiratory Syncytial Virus–Associated Hospitalizations Among Young Children: 2015–2016



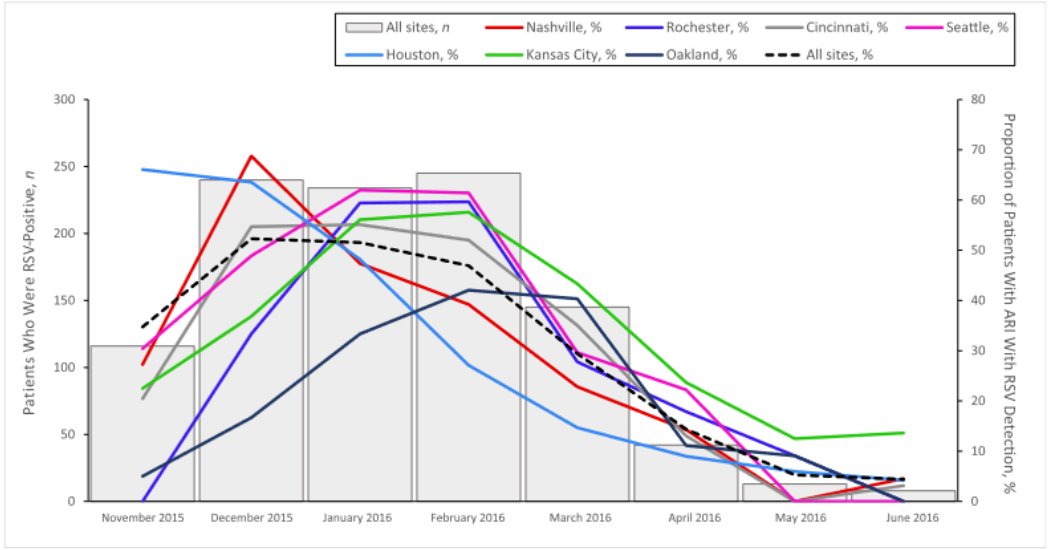


FIGURE 2
RSV-associated hospitalized children <5 years of age by enrollment date and site.

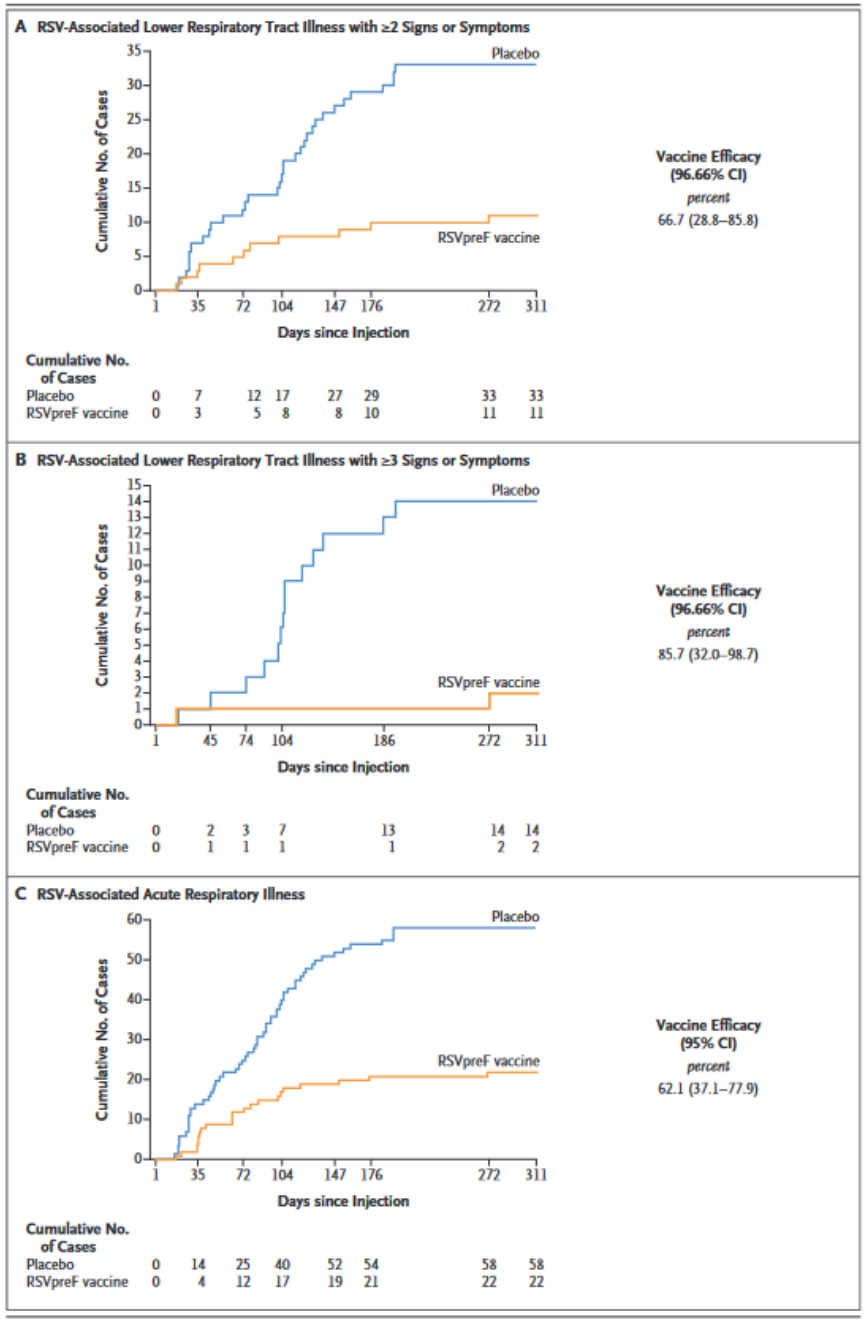
Rha B, et al. Pediatr 2020;146:1

Efficacy and Safety of a Bivalent RSV Prefusion F Vaccine in Older Adults

Methods: In this ongoing, phase 3 trial, we randomly assigned, in a 1:1 ratio, adults (≥60 years of age) to receive a single intramuscular injection of RSVpreF vaccine at a dose of 120 µg (RSV subgroups A and B, 60 µg each) or placebo.

Results: At the interim analysis (data-cutoff date, July 14, 2022), 34,284 participants had received RSVpreF vaccine (17,215 participants) or placebo (17,069 participants). RSV-associated lower respiratory tract illness with at least two signs or symptoms occurred in 11 participants in the vaccine group (1.19 cases per 1000 person-years of observation) and 33 participants in the placebo group (3.58 cases per 1000 person-years of observation) (vaccine efficacy, 66.7%; 96.66% confidence interval [CI], 28.8 to 85.8); 2 cases (0.22 cases per 1000 person-years of observation) and 14 cases (1.52 cases per 1000 person-years of observation), respectively, occurred with at least three signs or symptoms (vaccine efficacy, 85.7%; 96.66% CI, 32.0 to 98.7). RSV-associated acute respiratory illness occurred in 22 participants in the vaccine group (2.38 cases per 1000 person-years of observation) and 58 participants in the placebo group (6.30 cases per 1000 person-years of observation) (vaccine efficacy, 62.1%; 95% CI, 37.1 to 77.9).

Conclusions: RSVpreF vaccine prevented RSV-associated lower respiratory tract illness and RSV-associated acute respiratory illness in adults (≥60 years of age), without evident safety concerns.



Walsh EE, et al. NEJM 2023;388:1465

Use of RSV Vaccines in Older Adults: Recommendations of the ACIP, US, 2023

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

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

Abbreviations: LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus.

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

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

TABLE 3. Efficacy of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023

Efficacy evaluation period	Vaccine efficacy against outcome, % (95% CI)*	
	RSV-associated LRTD†	RSV-associated medically attended LRTD§
Season 1¶	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)§§	84.4 (59.6–95.2)	81.0 (43.5–95.2)

Abbreviations: LRTD = lower respiratory tract disease; LRTI = lower respiratory tract illness; RSV = respiratory syncytial virus.

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

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

Abbreviations: AE = adverse events; GBS = Guillain-Barré syndrome.

Melgar M, et al. MMWR2023;72:793

Use of RSV Vaccines in Older Adults: Recommendations of the ACIP, US, 2023

CDC Recommendations

- On June 21, 2023, ACIP recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making
- For RSV vaccination, the decision to vaccinate a patient should be based on a discussion between the health care provider and the patient, which might be guided by the patient's risk for disease and their characteristics, values, and preferences; the provider's clinical discretion; and the characteristics of the vaccine. As part of this discussion, providers and patients should consider the patient's risk for severe RSV-associated disease. Epidemiologic evidence indicates that persons aged ≥60 years who are at highest risk for severe RSV disease and who might be most likely to benefit from vaccination include those listed in Box.

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†
- Advanced age§
- 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

Abbreviation: RSV = respiratory syncytial virus.

Melgar M, et al. MMWR2023;72:793

VACCINES RECOMMENDED FOR PREGNANT PERSONS

COVID-19

Influenza (IIV4 or RIV4){each year}

Tdap {each pregnancy to protect the infant}

RSV {seasonal}

Hepatitis B (Heplisav-B and PreHevbria are not recommended)

Contraindicated or not recommended: LAIV4, MMR, VAR, HPV
Precautions: MenB
Vaccine protects the pregnant person AND the infant

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An Update on COVID-19 Vaccination and Pregnancy

Main Benefits of COVID-19 Vaccination in Pregnancy	Main Risks of COVID-19 Vaccination in Pregnancy
Reduction in the risk of SARS-CoV-2 infection [10,25,38–45]	Injection site pain [24,25]
Reduction in the risk of severe SARS-CoV-2 infection [25,38–44,46,47]	Fever [24,25]
Reduction in the risk of COVID-19-related hospitalization [10,25,38–45,47]	Rash [24,25]
Reduction in the risk of ICU admission [25,38–44,47]	Fatigue [24,25]
Reduction in the risk of maternal mortality [25,38–44]	Arthralgia [24,25]
Decrease in stillbirth [1,38,39,48]	Myalgia [24,25]
Decrease in total preterm births [43,48,49]	Headache [24,25]
Reduction in the risk of SARS-CoV-2 infection in infants <6 months [50,51]	Nausea or vomiting [24,25]
Reduction in the risk of severe SARS-CoV-2 infection in infants, including MIS-C [3,52]	Chills [24,25]
Reduction in the risk of hospitalization for COVID-19 in infants <6 months [17,25,40,43,53,54]	Lymfadenopathy [24,25]
Reduction in the risk of ICU admission in infants <6 months [3]	Lymfadenithis [24,25]

Julia-Burches C, Marinez-Varea A.
J Personalized Med 2023;May

UNC SCHOOL OF MEDICINE

Associations of COVID-19 vaccination during pregnancy with adverse neonatal and maternal outcomes: A systematic review and meta-analysis

Forty-three observational studies were included. COVID-19 vaccination [96,384 (73.9%) BNT162b2, 30,889 (23.7%) mRNA-1273, and 3,172 (2.4%) other types] during pregnancy [23,721 (18.3%) in the first trimester, 52,778 (40.5%) in the second trimester, and 53,886 (41.2%) in the third trimester],was associated with reduced risks of stillbirth or neonatal death (OR, 0.74; 95% CI, 0.60–0.92). COVID-19 vaccination during pregnancy was not associated with congenital anomalies (OR, 0.83; 95% CI, 0.63–1.08), preterm birth (OR, 0.98; 95% CI, 0.90–1.06), NICU admission or hospitalization (OR, 0.94; 95% CI, 0.84–1.04), an Apgar score at 5 min <7 (OR, 0.93; 95% CI, 0.86–1.01), low birth weight (OR, 1.00; 95% CI, 0.88–1.14), miscarriage (OR, 0.99; 95% CI, 0.88–1.11), cesarean delivery (OR, 1.07; 95% CI, 0.96–1.19), or postpartum hemorrhage (OR, 0.91; 95% CI, 0.81–1.01).

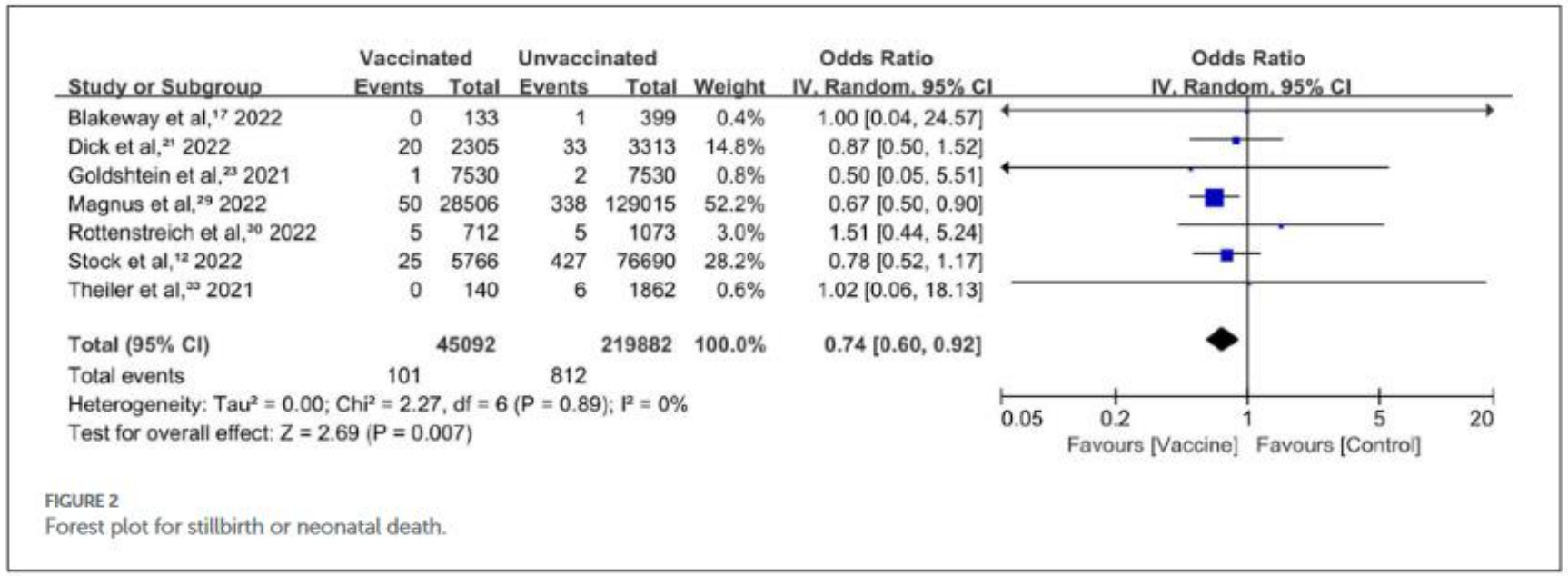


FIGURE 2
Forest plot for stillbirth or neonatal death.

Ding C, et al.
Front Public Health, 2023; Jan

UNC SCHOOL OF MEDICINE

Safety of COVID-19 vaccines during pregnancy: A systematic review and meta-analysis

Results: Among non-COVID-19 vaccines, the most frequent exposures were AS03 and aluminum-based adjuvants. A meta-analysis of studies that adjusted for potential confounders showed no association with adverse outcomes, regardless of the vaccine or the trimester of vaccination. Neither the reported rates of adverse pregnancy outcomes nor reactogenicity exceeded expected back-ground rates, which was the case for ASO3- or aluminum-adjuvanted non-COVID-19 vaccines in the proportion meta-analyses of uncontrolled studies/arms. The only exception was postpartum hemorrhage after COVID-19 vaccination (10.40%; 95% CI: 6.49–15.10%), reported by two studies; however, the comparison with non-exposed pregnant persons, available for one study, found non-statistically significant differences (adjusted OR 1.09; 95% CI 0.56–2.12). Animal studies showed consistent results with studies in pregnant persons.

Conclusion: We found no safety concerns for currently administered COVID-19 vaccines during pregnancy.

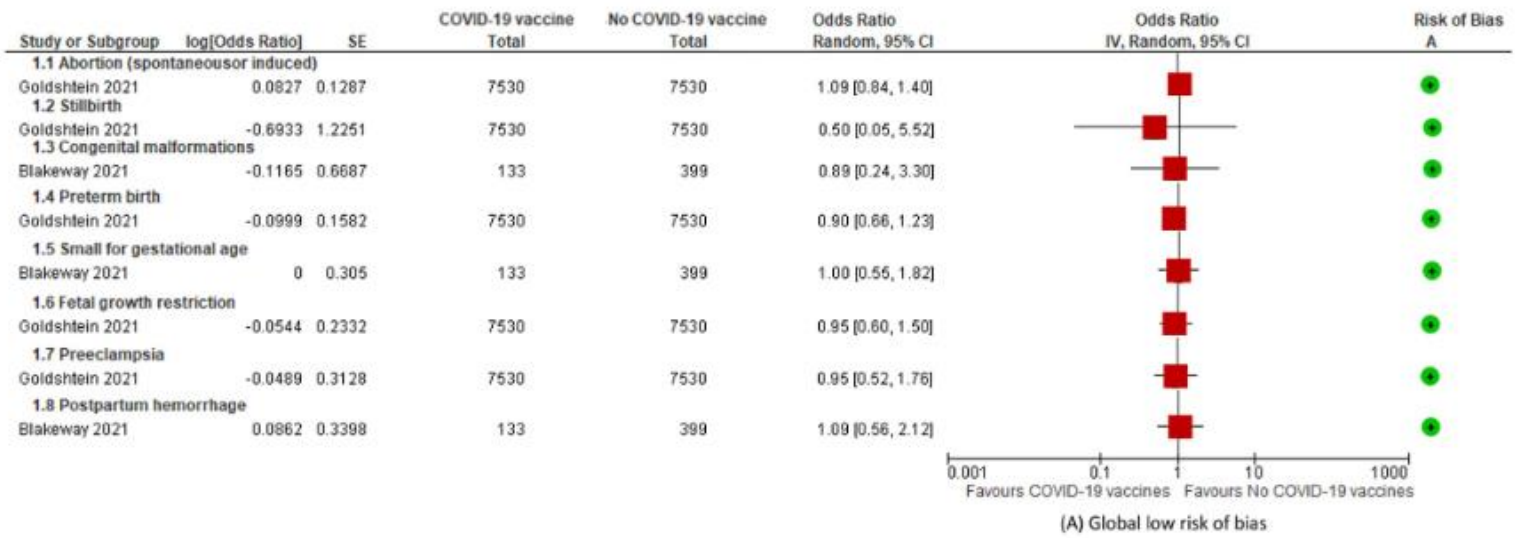
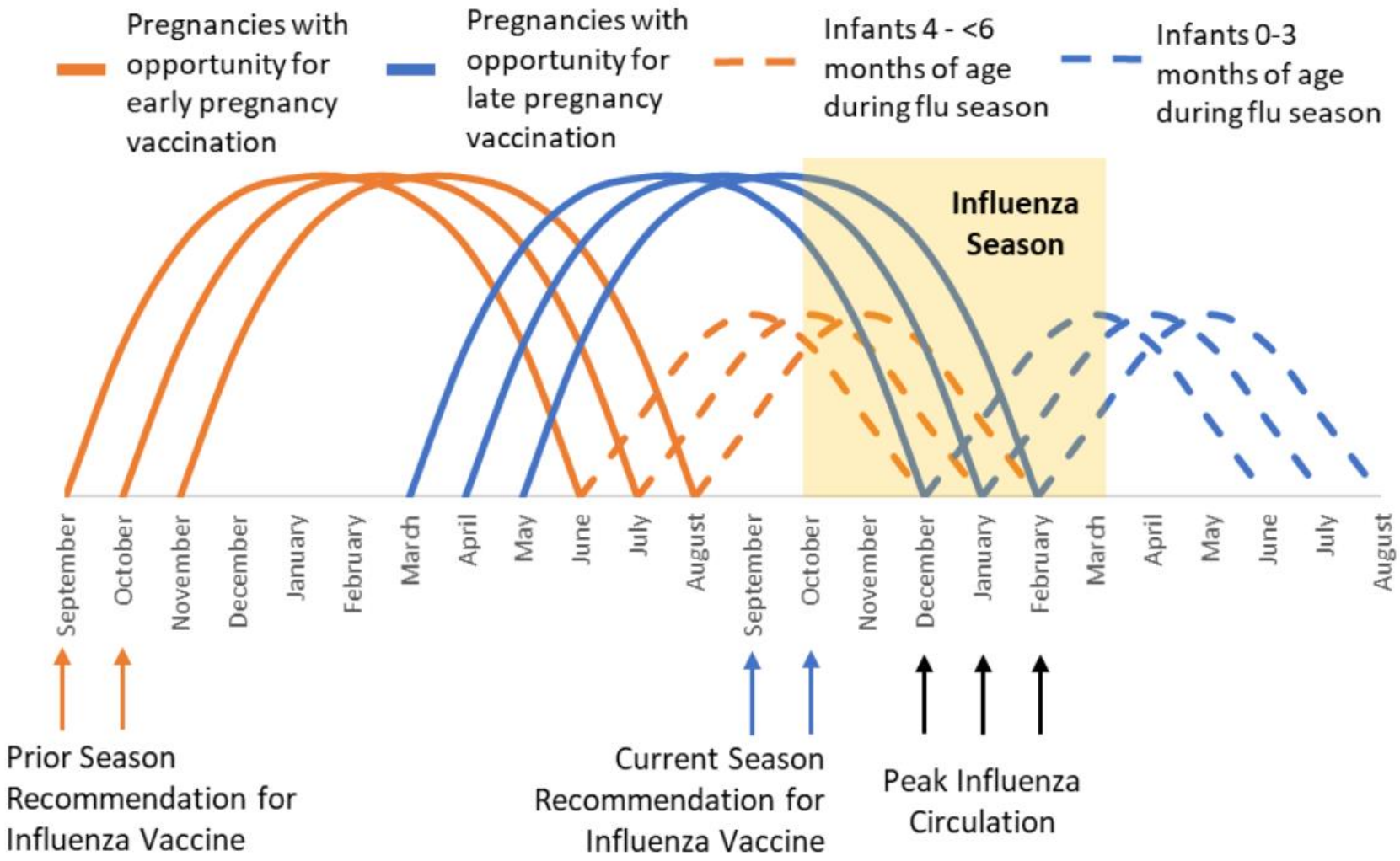


Fig. 2. Forest plots of pregnancy outcomes comparing exposure with no exposure to COVID-19 vaccines.

Ciapponi A, et al. Vaccine 2023;41:3688

UNC SCHOOL OF MEDICINE

Timing of maternal influenza vaccination during pregnancy in the context of infant age and influenza seasonality

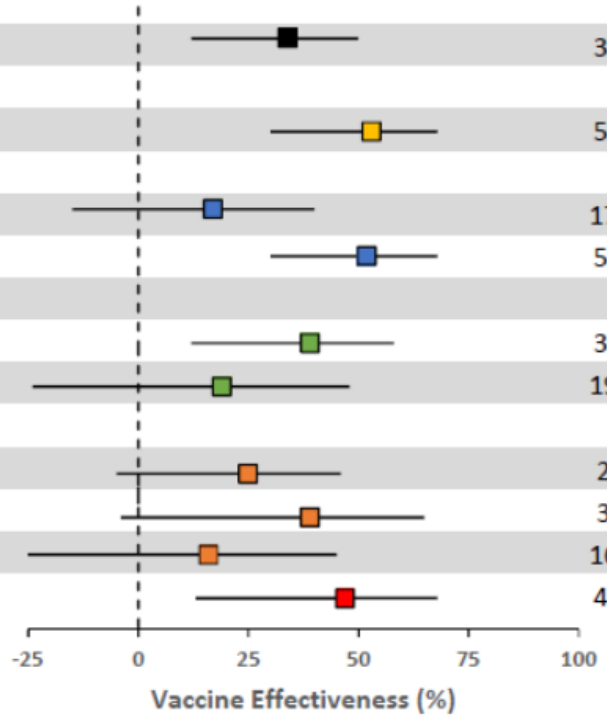


CDC, ACIP,
25-26 Oct. 2023

UNC SCHOOL OF MEDICINE

Maternal Vaccine Effectiveness against Influenza-associated Hospitalizations and ED Visits in Infants <6 months, CDC

Infants <6 months of age	No. Vaccinated Mothers /Total no. (%)		Effectiveness of Maternal Vaccination against Influenza Illness in Infants % (95% CI)
	Case-infants	Control-infants	
Overall effectiveness of maternal vaccination	94/223 (42)	1913/3541 (54)	34 (12 to 50)
Infants <3 months of age	49/106 (46)	1293/2147 (60)	53 (30 to 68)
Vaccinated during first or second trimester of pregnancy	59/188 (31)	1009/2637 (38)	17 (-15 to 40)
Vaccinated during third trimester of pregnancy	35/164 (21)	904/2532 (36)	52 (30 to 68)
Hospital Admission	55/125 (44)	1416/2541 (56)	39 (12 to 58)
ED Visit	39/98 (40)	497/1000 (50)	19 (-24 to 48)
Influenza A	70/157 (45)	1913/3541 (54)	25 (-5 to 46)
H1N1	21/53 (40)	1913/3541 (54)	39 (-4 to 65)
H3N2	42/87 (48)	1913/3541 (54)	16 (-29 to 45)
Influenza B	25/67 (37)	1913/3541 (54)	47 (13 to 68)



CDC, ACIP, 25-26 Oct. 2023

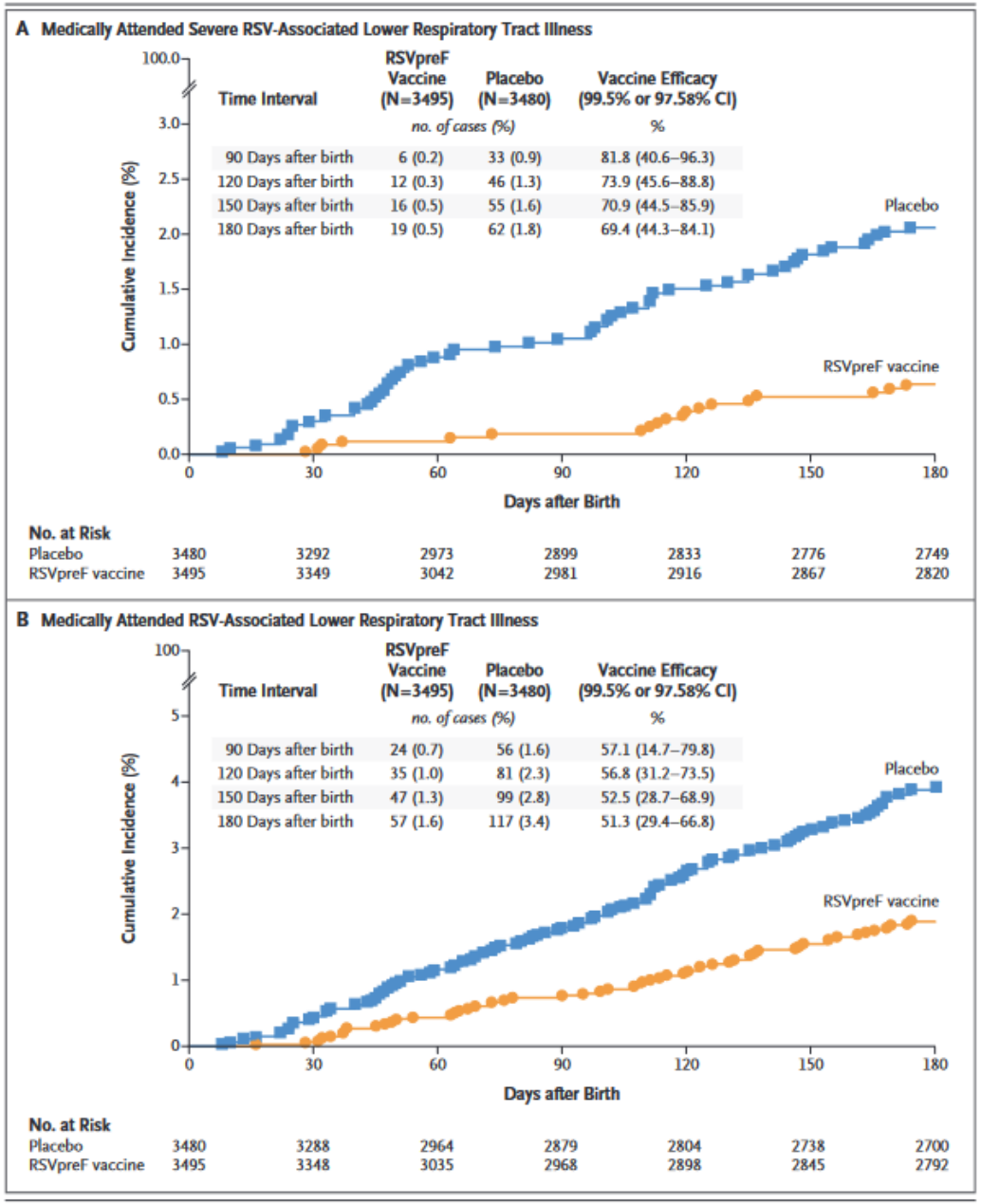
UNC SCHOOL OF MEDICINE

Bivalent Prefusion F Vaccine in Pregnancy to Prevent RSV Illness in Infants

Methods: In this phase 3, double-blind trial conducted in 18 countries, we randomly assigned, in a 1:1 ratio, pregnant women at 24 through 36 weeks' gestation to receive a single intramuscular injection of 120 µg of a bivalent RSV prefusion F protein–based (RSVpreF) vaccine or placebo.

Results: At this prespecified interim analysis, the success criterion for vaccine efficacy was met with respect to one primary end point. Medically attended severe lower respiratory tract illness occurred within 90 days after birth in 6 infants of women in the vaccine group and 33 infants of women in the placebo group (vaccine efficacy, 81.8%; 99.5% CI, 40.6 to 96.3); 19 cases and 62 cases, respectively, occurred within 180 days after birth (vaccine efficacy, 69.4%; 97.58% CI, 44.3 to 84.1). Medically attended RSV-associated lower respiratory tract illness occurred within 90 days after birth in 24 infants of women in the vaccine group and 56 infants of women in the placebo group (vaccine efficacy, 57.1%; 99.5% CI, 14.7 to 79.8); these results did not meet the statistical success criterion. No safety signals were detected in maternal participants or in infants and toddlers up to 24 months of age.

Conclusion: RSVpreF vaccine administered during pregnancy was effective against medically attended severe RSV-associated lower respiratory tract illness in infants, and no safety concerns were identified.



Kampmann B, et al. NEJM 2023;388:1451

Influenza, Tdap, and COVID-19 Vaccination Coverage and Hesitancy Among Pregnant Women, US, April 2023

Summary

What is already known about this topic?

Influenza, tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis (Tdap), and COVID-19 vaccines can reduce the risk for severe respiratory illness among pregnant women and their infants.

What is added by this report?

During the 2022–23 influenza season, 47.2% of women received influenza vaccination before or during pregnancy, 55.4% of women with a recent live birth received Tdap vaccination during pregnancy, and 27.3% of women received a COVID-19 bivalent booster vaccine before or during pregnancy. Pregnant women who received a provider recommendation for vaccination were less hesitant about influenza and Tdap vaccines.

What are the implications for public health practice?

Promotion of efforts to improve vaccination coverage among pregnant women, such as provider recommendation for vaccination and informative conversations with patients to address vaccine hesitancy, could reduce adverse maternal and infant illness and death from vaccine-preventable diseases.

Razzaghi H, et al. MMWR 2023;72:1065
29 Sept

FIGURE. Percentage of pregnant women* who were hesitant† about receiving influenza vaccine (A) and tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (B) — Internet panel survey, United States, 2019–20 through 2022–23 influenza seasons

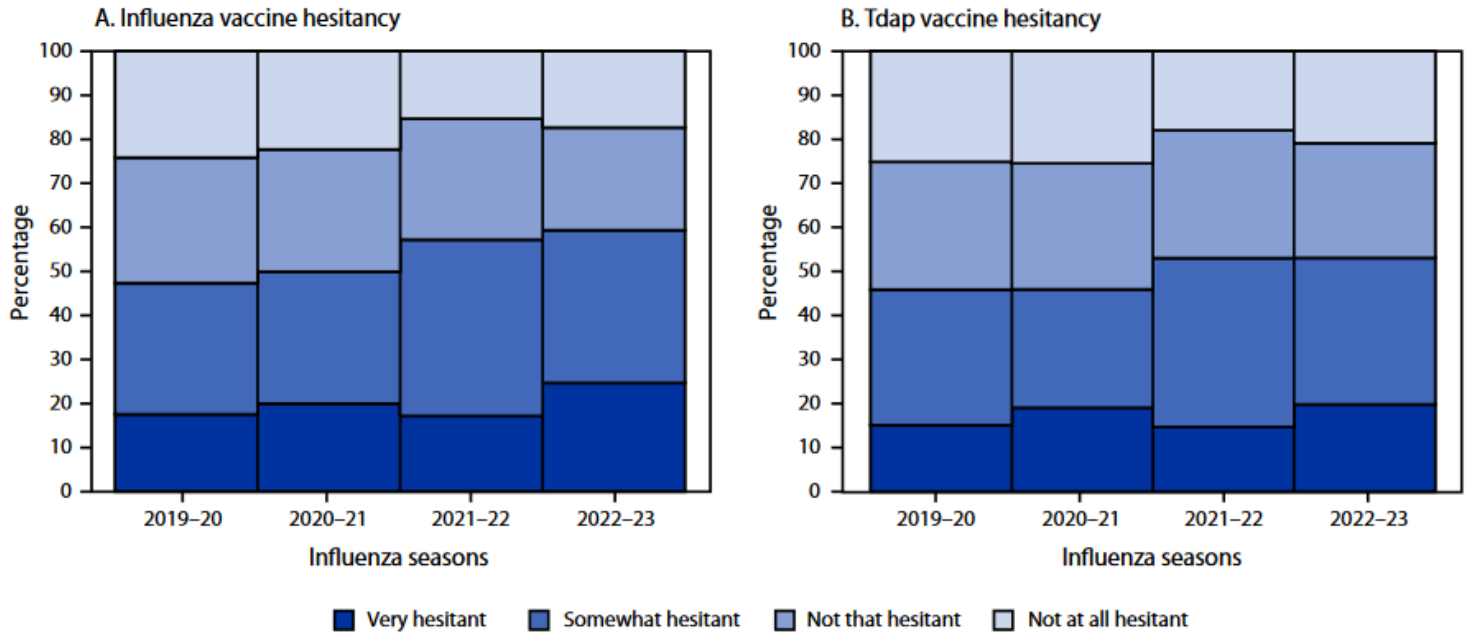


TABLE 2. COVID-19 vaccination coverage among pregnant women, by selected characteristics — Internet panel survey, United States, April 2023

Characteristic	Total no. (weighted %)†	Weighted % (95% CI)*		
		Received ≥1 COVID-19 vaccine dose§	Completed primary COVID-19 vaccination series¶	Received a COVID-19 bivalent booster dose**
Overall	1,252 (100.0)	64.9 (61.9–67.8)	58.7 (55.6–61.7)	27.3 (24.7–30.0)

PNEUMOCOCCAL VACCINES

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UNC MEDICAL CENTER PNEUMOCOCCAL VACCINE ALGORITHMS

Adults ≥65 years old		
Prior vaccines	Option A (preferred)	Option B
None or PCV7 only	PCV20	PCV15 → ≥1 year → *PPSV23
PPSV23 only (at any age)	≥1 year → PCV20	≥1 year → PCV15
PCV13 only (at any age)	≥1 year → PCV20	≥1 year → *PPSV23
PCV13 (at any age) PPSV23 at <65 years	≥5 years → PCV20	≥5 years → *PPSV23

*Consider minimum interval of 8 weeks for adults with immunocompromising condition, cochlear implant, or CSF leak

Minimum interval for PPSV23 is 8 weeks since last PCV13 dose and 5 years since last PPSV23 dose

Vaccination	Route of Administration	Dose
PCV13, Prevnar13®	IM	0.5 mL
PPSV23, Pneumovax23®	IM or SQ	0.5 mL
PCV15, Vaxneuvance®	IM	0.5 mL
PCV20, Prevnar20®	IM	0.5 mL

Gender and Weight	Needle Length	Needle Gauge	Injection Site
Intramuscular (IM)			
Female or Male, ≤59 kg (≤130 lbs)	5/8-1”**	22-25	Deltoid muscle of the arm
Female or Male, 60-69 kg (131-152 lbs)	1”		
Female, 70-90 kg (153-200 lbs)	1-1½“		
Male, 70-120 kg (153-265 lbs)	1-1½“		
Female, >90 kg (>200 lbs)	1½“		
Male, >118 kg (>260 lbs)	1½“		
Subcutaneous (SQ)			
All patients	5/8”	23-25	Fatty tissue overlying triceps muscle

**A 5/8” needle may be used in patients who weigh less than 130 lbs or less than 60 kg for IM injection in the deltoid muscle only if the skin is stretched tight, subcutaneous tissue is not bunched, and the injection is made at a 90-degree angle to the skin.

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UNC MEDICAL CENTER PNEUMOCOCCAL VACCINE ALGORITHMS

Adults 19-64 years old with specified immunocompromising conditions		
Prior vaccines	Option A (preferred)	Option B
None or PCV7 only	PCV20	PCV15 → ≥1 year → *PPSV23
PPSV23 only	≥1 year → PCV20	≥1 year → PCV15
PCV13 only	≥1 year → PCV20	≥8 weeks → PPSV23 → ≥5 years → PPSV23 Review vaccine recommendations again when patient turns 65 years old.
PCV13 PPSV23 (one dose)	≥5 years → PCV20	≥5 years → *PPSV23 Review vaccine recommendations again when patient turns 65 years old.
PCV13 PPSV23 (two doses)	≥5 years → PCV20	Review vaccine recommendations again when patient turns 65 years old.

*Consider minimum interval of 8 weeks for adults with immunocompromising condition, cochlear implant, or CSF leak

··Minimum interval for PPSV23 is 8 weeks since last PCV13 dose and 5 years since last PPSV23 dose

High Risk Conditions, Patients 19-64 Years of Age

- Chronic heart, lung, or liver disease
- Diabetes mellitus
- Alcoholism
- Cigarette smoking
- CSF leaks
- Cochlear implants
- Sickle cell disease or other hemoglobinopathies
- Congenital or acquired asplenia†
- Congenital or acquired immunodeficiencies†
- HIV infection†
- Chronic renal failure†
- Nephrotic syndrome†
- Leukemia†
- Lymphoma†
- Hodgkin disease
- Generalized malignancy†
- Iatrogenic immunosuppression (radiation and long-term steroid use) †
- Solid organ transplant†
- Multiple myeloma†

†*Immunocompromising Conditions*

UNC MEDICAL CENTER PNEUMOCOCCAL VACCINE ALGORITHMS

Adults 19-64 years old with cochlear implant or CSF leak		
Prior vaccines	Option A (preferred)	Option B
None or PCV7 only	PCV20	PCV15 → ≥8 weeks → PPSV23
PPSV23 only	≥1 year → PCV20	≥1 year → PCV15
PCV13 only	≥1 year → PCV20	≥8 weeks → PPSV23 Review vaccine recommendations again when patient turns 65 years old.
PCV13 PPSV23 (one dose)	≥5 years → PCV20	Review vaccine recommendations again when patient turns 65 years old.

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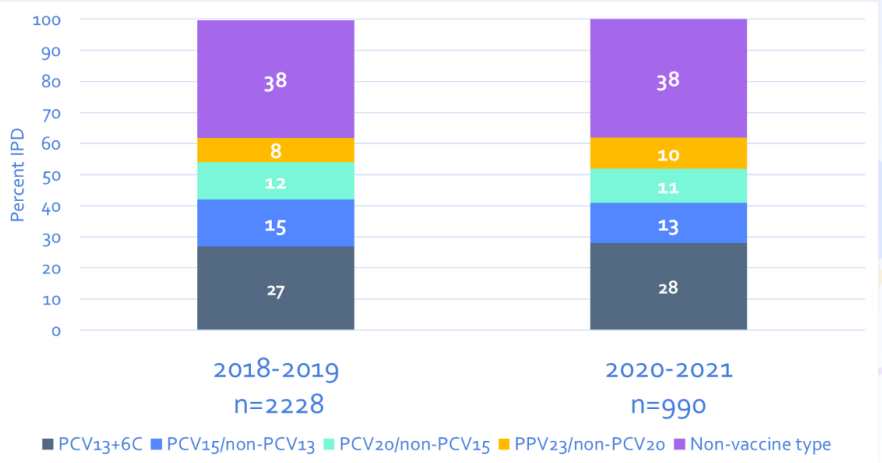
PNEUMOCOCCAL SEROTYPES CAUSING DISEASES AND IN VACCINES

Approximately 40% of IPD cases in adults aged ≥65 years were caused by serotypes not contained in currently recommended vaccines



New Adult Pneumococcal Vaccines in Advanced Stages of Development

	1	3	4	5	6A	6B	7F	9V	14	18C	19A	19F	23F	22F	33F	8	10A	11A	12F	15B	2	9N	17F	20	15A	15C	16F	23A	23B	24F	31	35B
PCV15																																
PCV20																																
PPSV23																																
Pn-MAPS24v																								20B								
VAX-24																								20B								
V116																								20A								

24-valent pneumococcal vaccines

- Completed phase 1/2 study for adults[1] — **Pn-MAPS24v, GSK**
- Completed phase 1/2 studies for adults, undergoing phase 2 studies in infants[2] — **VAX-24, Vaxcyte**

21-valent pneumococcal conjugate vaccine — **V116, Merck**

- Completed phase 1/2 study for adults[3]
- Phase 3 studies in adults are currently ongoing

1. Chichili et al. Vaccine 2022; 2.ClinicalTrials.gov ID: NCT05266456, NCT05297578, and NCT05844423; 3. Platt et al. Lancet ID 2022.

CDC, ACIP, 25-25 Oct. 2023

UNC SCHOOL OF MEDICINE

Safety, tolerability, and immunogenicity of a 21-valent pneumococcal conjugate vaccine, V116 (PCCV21), in healthy adults: phase 1/2, randomized, double-blind, active comparator-controlled, multicenter, US-based trial

Methods: We did a phase 1/2, randomized, double-blind, active comparator-controlled, multicenter, non-inferiority and superiority trial

Results: V116 was well tolerated with a safety profile generally similar to PPSV23; consistent with licensed pneumococcal conjugate vaccines. Functional OPA antibodies were induced to all V116 vaccine serotypes. The vaccine was non-inferior to PPSV23 for the 12 serotypes common to both vaccines and superior to PPSV23 for the nine unique serotypes in V116. Our findings support the development of V116 for prevention of pneumococcal disease in adults.

Serotypes: 3, 6A, 7F, 8, 9V, 9N, 10A, 11A, 12F, 15A,15B, 16F, 17F, 19A, 20, 22F, 23A, 23B, 24F, 31, 33F, 35B

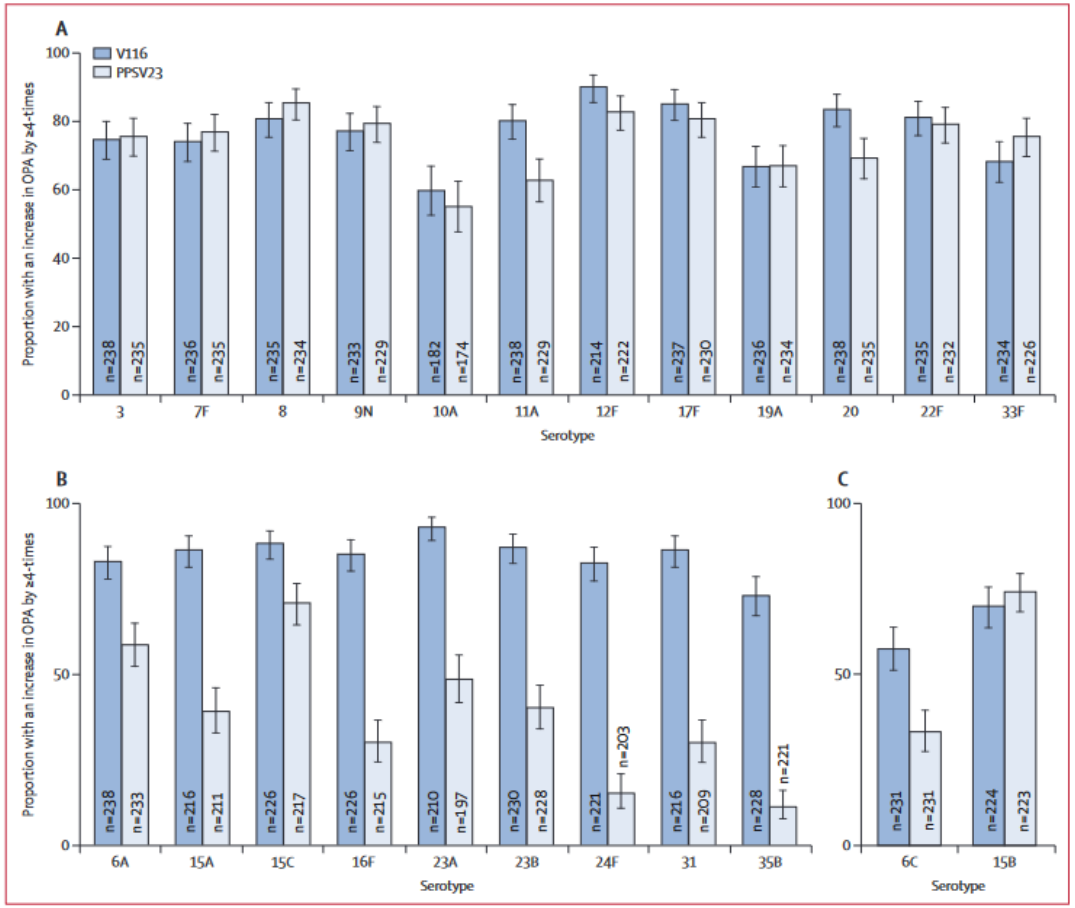


Figure 4: **Proportion of participants with an increase in OPA titre by four-times or more 30 days after vaccination**
The proportion of participants with an increase in OPA titre by four-times compared with baseline or more 30 days after vaccination for common serotypes (A) and unique serotypes to V116 (B). Cross reactivity serotypes 6C and 15B assessment (C). Error bars are 95% CI. GMT=geometric mean titre. OPA=opsonophagocytic antibody.

Platt H, et al. Lancet ID 2023;23:233-46

CURRENT AND FUTURE CHALLENGES AND SOLUTIONS

New Methodologies for Assessing Vaccine Efficacy: Test Negative Design

Disappearance of Influenza B/Yamagata Lineage

Combined mRNA Influenza and COVID-19 Vaccine

Vaccines to Combate Bacterial Resistance

Reduced Vaccine Coverage During The Pandemic

Aging Population (immune senescence)

Big Three (failure to develop effective vaccines): HIV, TB, Malaria

Increase in Vaccine Hesitancy

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Methodologic Considerations for Different Vaccine Study Designs

Design	Methodological considerations
Outbreak investigation	VE is anticipated to be lower during outbreak than non-outbreak periods under the leaky, exposure threshold or waning immunity models. During outbreaks, cases and controls may be more likely to have similar opportunities for exposure to infection, and detection of milder cases may be better because of enhanced public awareness and decreased provider and patient bias against testing vaccinated cases. This may explain why lower, and arguably more accurate, VE estimates are found than in non-outbreak periods.
Unmatched case control study with population based controls	Case-control VE studies usually yield similar results to cohort studies [60]. However, for appropriate comparability cases and controls both need to have equal chance of exposure to infection, the same likelihood of disease detection, and unbiased record of vaccination status. VE can be over-estimated in non-epidemic periods. For example, a matched case-control study in Japan during a non-epidemic period found pertussis VE ranged between 96.9 and 95.9% [61], while during an outbreak, VE was substantially lower (78%) [62].
Matched case control study	If disease attack rates are high in vaccinated, VE may be overestimated [63].
Indirect cohort design	In the indirect cohort design ("Broome" method) [64,65] the control group consists of individuals identified through the same system as the cases and with the same disease but who have a non-vaccine type of infection, such as a non-vaccine serogroup of pneumococcal disease or a non-vaccine HPV strain.
Test negative case control study	Test-negative designs (TND) [66] have been most frequently conducted for influenza VE studies [67], for which they have been validated [67–70]. Cited strengths are that controls are comparable for healthcare seeking behaviour and disease exposure. However, test-negative controls risk not being representative of cases, and false-negative cases may appear amongst controls, both of which are conservative selection biases in the direction of under-estimating VE. Test-negative influenza VE studies are also vulnerable to "collider bias", where test negative individuals could differ from cases because they are selected on the basis of being tested, but testing is also linked to likelihood of having influenza, of being vaccinated, and other confounding factors [71,72]. TND studies of pertussis have a few advantages over influenza studies in that almost everyone has been vaccinated and fewer alternative pertussis-like-illnesses exist [73,74]. Although older cases may present for care later, have milder disease and have a negative culture or PCR result [75], misclassification bias analysis has supported using TND for pertussis [19].VE may be lower in a TND versus population-based controls because of: (1) adjustment for healthcare seeking behaviour (2) more comparable exposure to disease (3) conservative bias (if over-matching)

Crowcroft NS, Klein NP. Vaccine 2018;36:7286-7293

Bacterial Vaccines In The Fight Against Antimicrobial Resistance: An Analysis Of The Preclinical and Clinical Development Pipeline

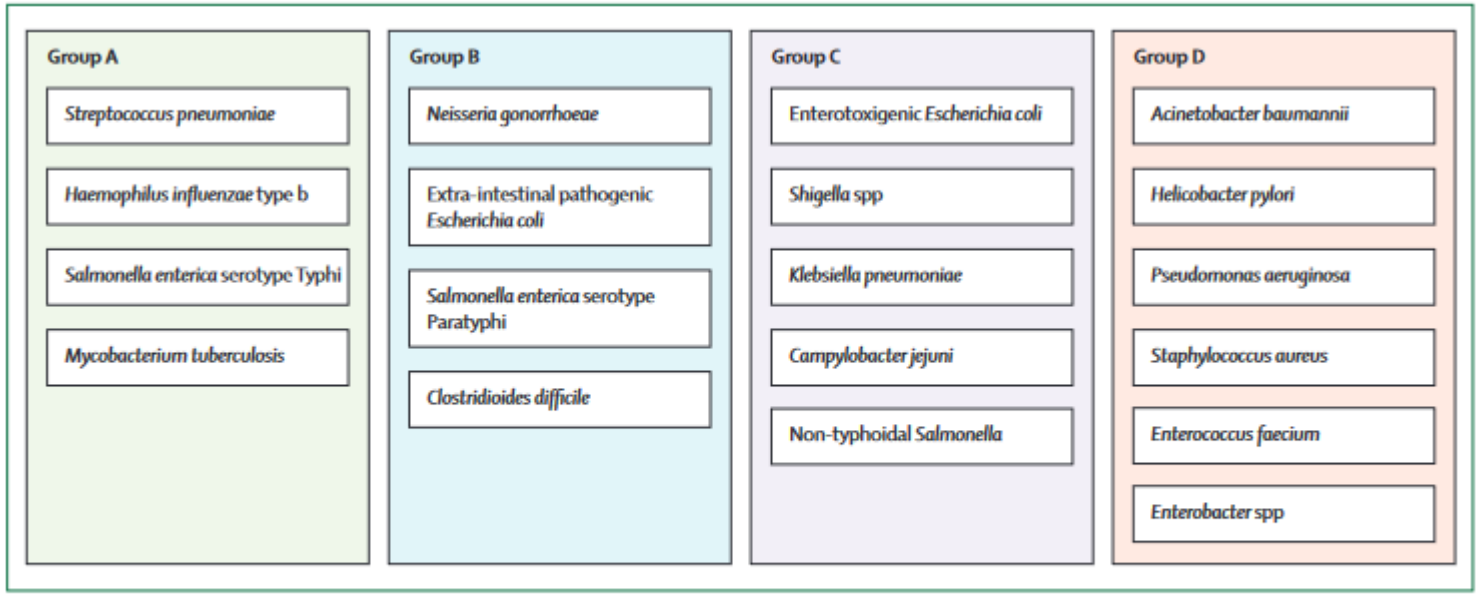


Figure 5: **Categorisation of priority pathogens as targets for vaccination**
Group A contains pathogens with vaccines that are already licensed. Group B contains pathogens with vaccines in late-stage clinical trials with high development feasibility. Group C contains pathogens with vaccine candidates either in early clinical trials or with moderate to high feasibility of vaccine development. Group D contains pathogens with a small number or no vaccine candidates in the pipeline and low vaccine development feasibility in the near future.

Panel 1: Challenges of developing vaccines against pathogens causing hospital-acquired infections

Many of the WHO bacterial priority pathogens cause hospital-acquired infections, in particular *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Staphylococcus aureus*, extra-intestinal pathogenic *Escherichia coli*, *Clostridioides difficile*, *Enterococcus faecium*, and *Enterobacter* spp. There are multiple challenges[35] for the clinical development of vaccines against these pathogens:

- The relatively low incidence of infections in the vaccine target population makes efficacy trials prohibitively large in terms of trial sites and patient numbers, and expensive[3]
- Potential target populations tend to be critically ill, with multiple comorbidities and severely compromised immune systems, making clinical endpoints hard to establish[36,37]
- Identification of populations at risk of hospital-acquired infections at intensive care unit admission is impracticable, due to the little time available to mount an effective immune response[38]
- At present there is no regulatory or policy precedent for a vaccine against hospital-acquired infections

Despite these limitations, it could be possible to identify patients at high risk, such as those scheduled for elective surgery or hospital treatment, which would allow enough time for their immune systems to respond to vaccine administration. Given these challenges, regulators could explore the use of correlates of protection in phase 3 trials followed by the collection of post-licensure effectiveness data and real-world evidence. However, correlates of protection are currently absent for these pathogens. Combination vaccines might require fewer participants in clinical trials than single-target vaccines as multiple causes of disease are being targeted and incidence will be higher, which could help facilitate trials.

Frost I, et al. Lancet Microbe 2023:4:e113-25

COMBINED INFLUENZA & COVID-19 VACCINE, MODERNA, OCTOBER 4, 2023

- The ongoing Phase 1/2 clinical trial (ClinicalTrials.gov Identifier: NCT05827926) is a randomized, observer blind study evaluating the safety and immunogenicity of mRNA-1083 compared to a standard dose influenza vaccine, Fluarix, in adults 50-64 years of age and against an enhanced influenza vaccine, Fluzone HD, in adults 65-79 years of age. For both age groups, mRNA-1083 was compared against Spikevax booster.
- in the Phase 1/2 study. mRNA-1083 resulted in geometric mean titer (GMT) ratios >1.0 relative to Fluarix in adults 50-64 years of age, for all four influenza vaccine strains. GMT ratios for mRNA-1083 relative to Fluzone HD in adults 65-79 were also >1.0, for all four influenza vaccine strains. The GMT ratios of mRNA-1083 relative to Spikevax bivalent were >0.9 in adults 50 to 64 years of age and > 1.0 in adults 65 to 79 years of age, relative to Spikevax.
- Reported rates of solicited local and systemic adverse reactions after mRNA-1083 administration were similar to the standalone COVID-19 vaccine group in the trial. The majority of solicited adverse reactions were grade 1 or 2 in severity. Grade 3 solicited local or solicited systemic reactions were reported in less than 4% of participants ages 50 and above. No new safety concerns were identified for mRNA-1083 compared to the standalone vaccines.
- The Company plans to begin a Phase 3 trial of mRNA-1083 in 2023 and is targeting potential regulatory approval for the combination vaccine in 2025.

https://investors.modernatx.com/news/news-details/2023/Moderna-Announces-Positive-Phase-12-Data-from-mRNA-1083-the-Companys-Combination-Vaccine-Against-Influenza-and-COVID-19/default.aspx

Impact of the COVID-19 pandemic on vaccination uptake in the US

The COVID-19 pandemic disrupted routine healthcare delivery, causing declines in CDC-recommended vaccination rates across the life-course in the United States (US). While vaccination rates stagnated or declined across some populations pre-pandemic, the review indicated there were further VCR declines in 2020 and 2021 compared to 2019 across numerous CDC-recommended vaccines, ages, and geographies, with some vaccines and sub-populations disproportionally impacted. The review additionally identified declines in patient healthcare visit frequency and increases in morbidity and mortality associated with vaccine-preventable disease (VPD) complications.

A collection of state-level recovery strategies found six primary recovery intervention themes: 1) increased communication from providers and states to the general public to convey the importance of routine vaccination, 2) authorization of more vaccinators (e.g., through expanded scope of practice), 3) utilization of digital tools, 4) expanded school vaccination requirements and enforcement, 5) vaccine education and awareness campaigns, and 6) comprehensive funding for catch-up efforts for all adults and children.

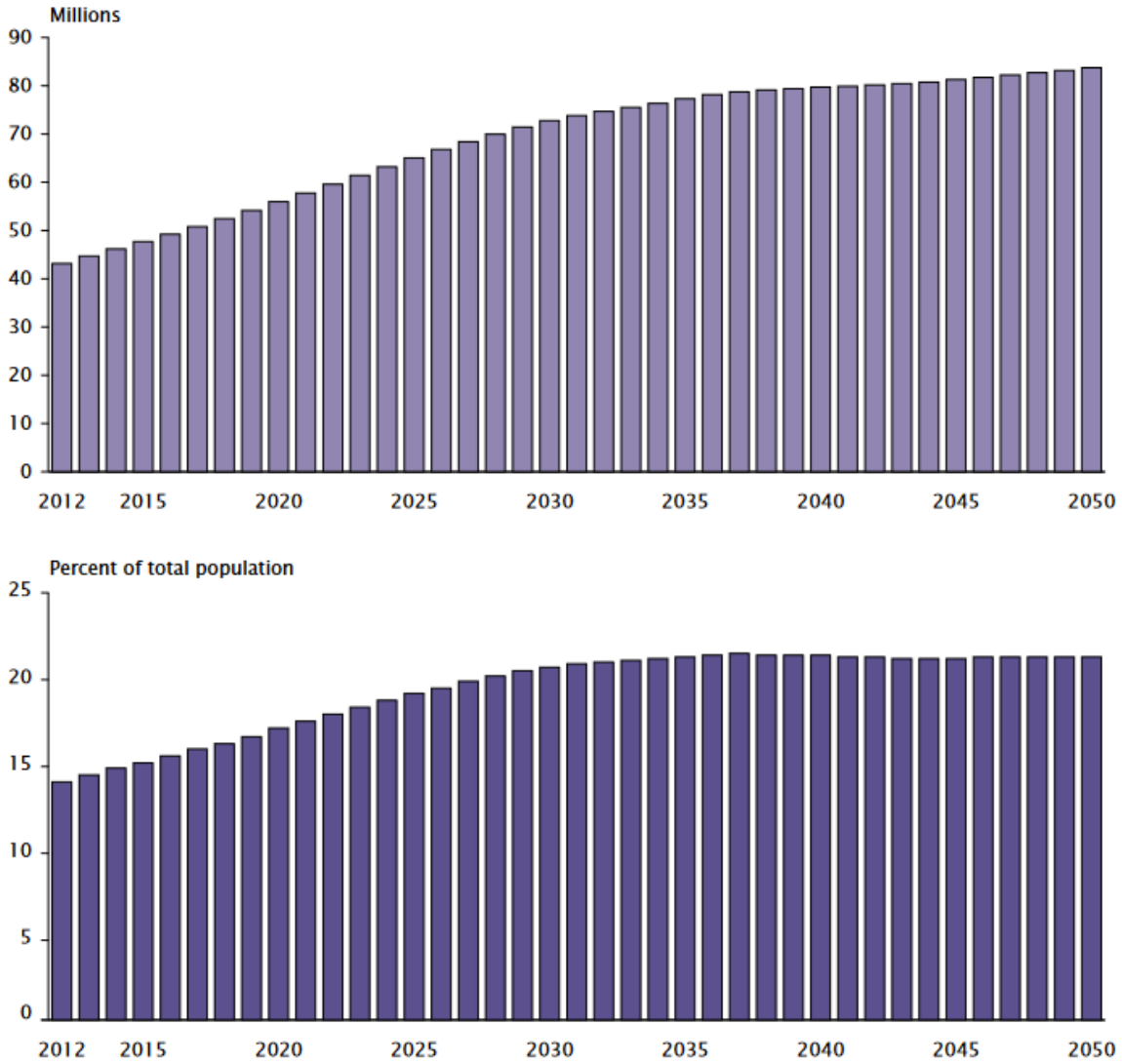
Also suggested: 1) the use of personalized communication from providers with individuals not up-to-date on routine vaccinations, 2) liaising with trusted community-based messengers to build vaccine confidence through direct outreach and education, and 3) changes to the Vaccines for Children (VFC) program.

Cunniff L, et al. Human Vaccines & Immunotherapies 2023;19:2246502

Table 2. Summary of literature findings.

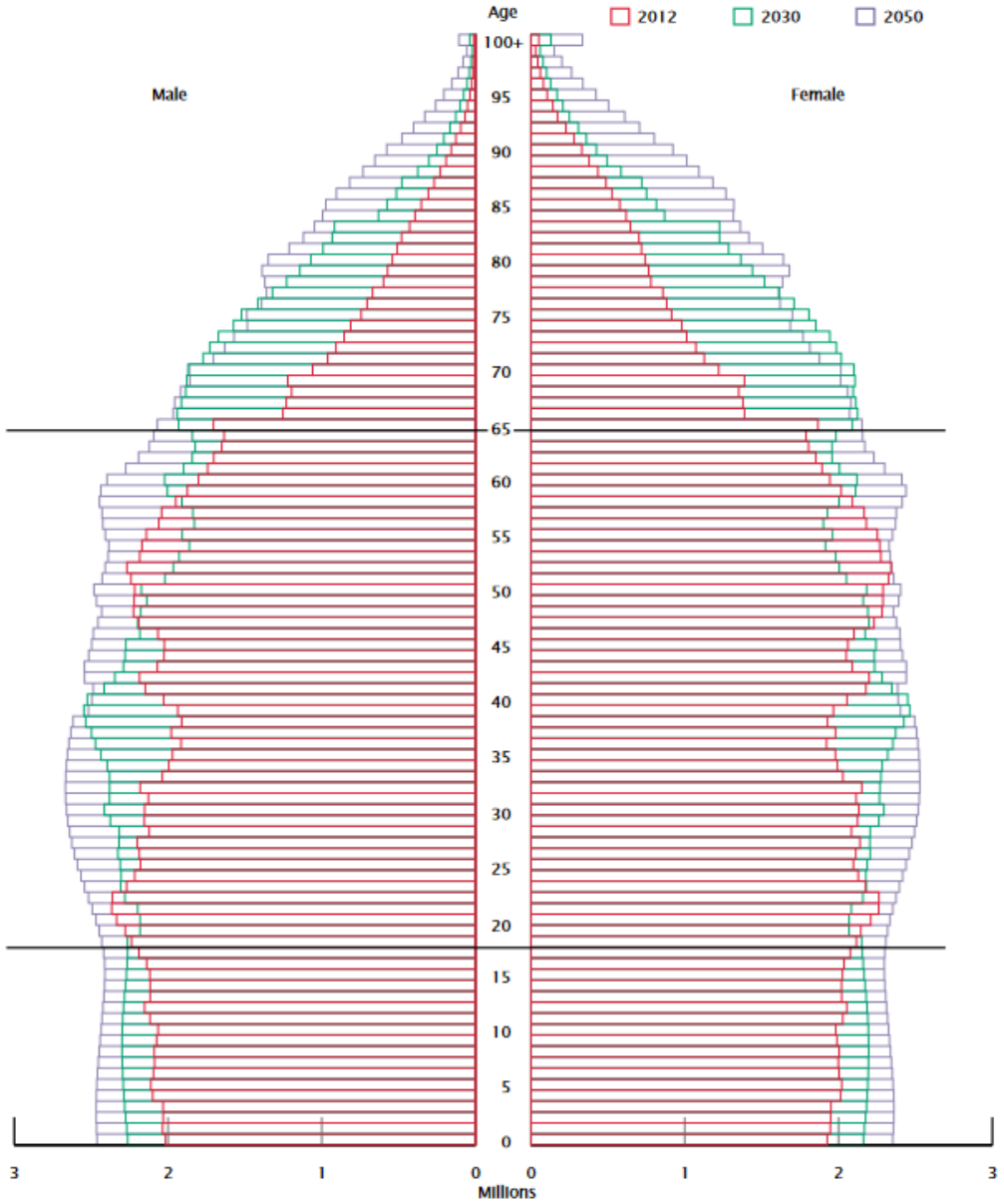
Literature Themes	Key Findings
Observed Declines in VCRs or Vaccine Administration	• Adult and pediatric vaccine administration and VCRs decreased across CDC-recommended routine vaccines; some vaccines had higher rates of decline, including HPV.[10–14] • Vaccine coverage disparities were more pronounced among Black and Hispanic children compared to White and Asian children.[4,5] • Larger disparities were observed among Medicaid-enrolled children, who were less likely to receive recommended vaccines than those privately insured.[4] • Among states with diverse population distributions, rural regions generally reported lower vaccine administration compared to urban regions.[2]
Impacts Due to COVID-19	• Deficits in VCRs are predicted to increase disease burden, including excess and preventable HPV, herpes zoster, and oropharyngeal cancer (OPC)-related morbidity and mortality.[13,15,16] • Well-child visits decreased, leading to fewer, in-person routine vaccine administration opportunities.[3,17–20] • Decrease in pro-vaccine attitudes and intention to receive routine vaccinations.[21]
Potential Recovery Strategies	• Multisectoral interventions provide opportunities to facilitate routine vaccination recovery.[22–24] • Interventions include increased outreach to individuals lagging on their vaccinations,[1,14,18,22–24] expanding pharmacist authority as vaccinators,[22,25] allowing patients to access their vaccination status records through patient portals,[22,26–29] and use of widespread vaccine education and awareness campaigns[14,23,30]

Figure 1.
Population Aged 65 and Over for the United States: 2012 to 2050



Source: U.S. Census Bureau, 2012 Population Estimates and 2012 National Projections.

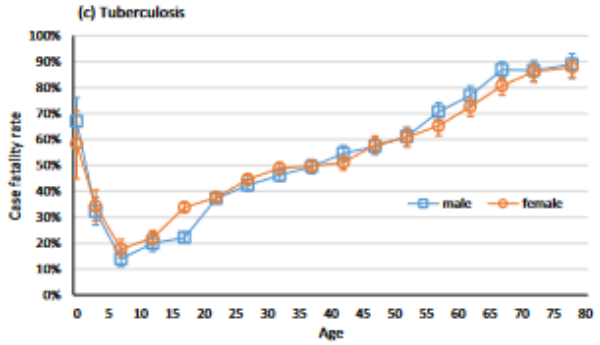
Figure 2.
Age and Sex Structure of the Population for the United States: 2012, 2030, and 2050

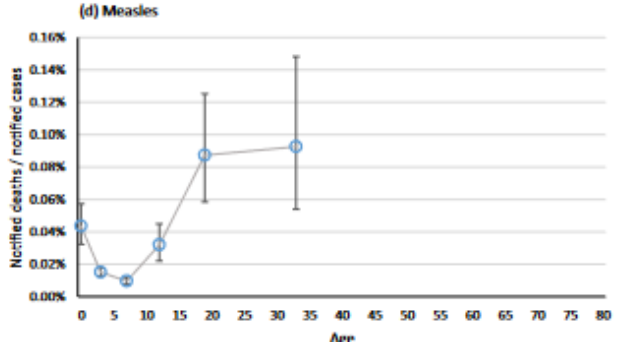


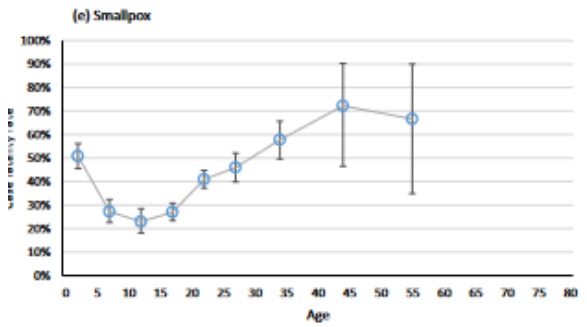
Source: U.S. Census Bureau, 2012 Population Estimates and 2012 National Projections.

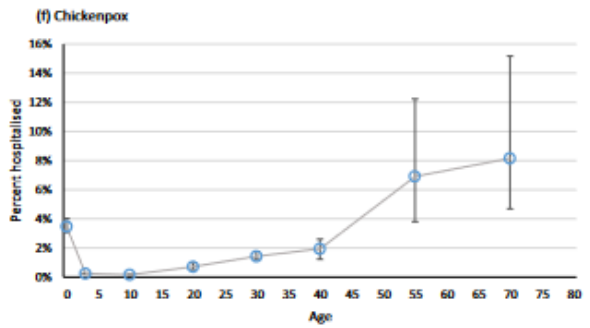
An Aging Nation: The Older Population in the United States - https://www.census.gov/content/dam/Census/library/publications/2014/demo/p25-1140.pdf

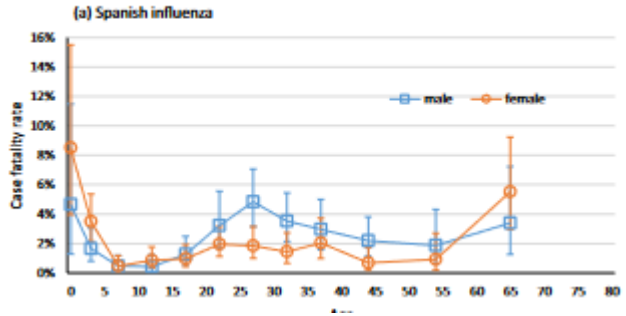
Systematic Analysis of Infectious Disease Outcomes by Age Shows Lowest Severity in School-Age Children

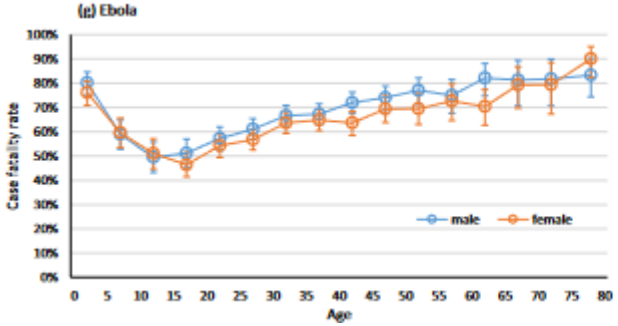


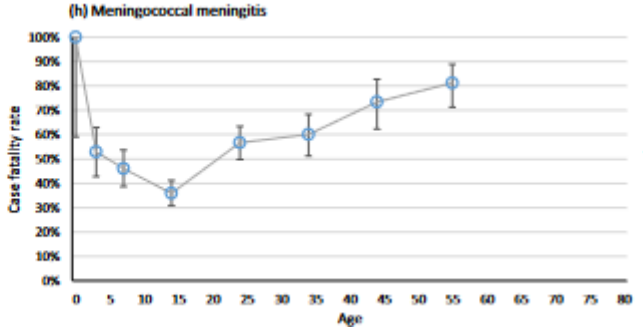


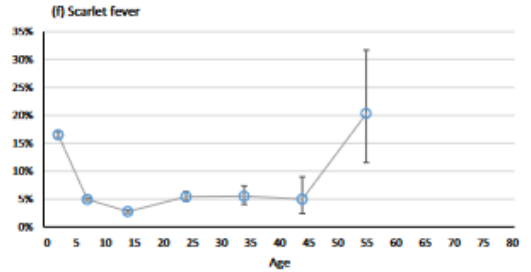


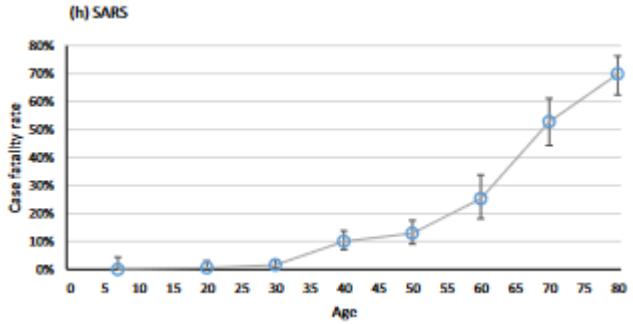


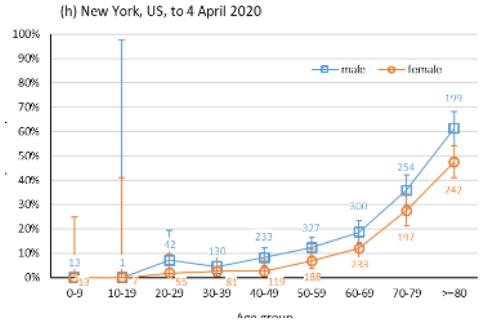


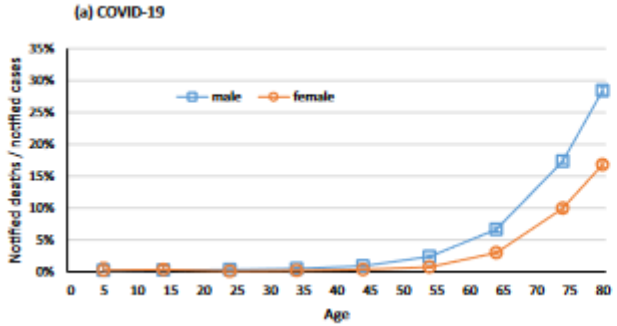


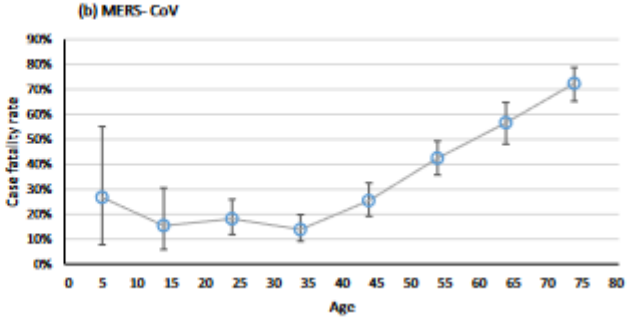












Glynn JR, Moss PAH. Sci Data 2020;15:e41597-020-00668-y

Efficacy and Safety of Vaccinations in Geriatric Patients

Importance of Vaccination in Older Adults

Factors affecting vaccines response in the Elderly	
Individual factors	*General factors*
Stimulate the immune system	Combat antibiotic resistance
Reducing the likelihood of infection	Reduce antibiotics overuse.
Reducing the sequelae of infection	Decrease Vaccine-Preventable Infections
Ameliorate quality of life	Contribute to herd immunity

Resistance to Vaccine Response in Older Adults

Factors affecting vaccines response in the elderly	
Related Timic involution	*Related to immunity factors*
Increase memory cells	Increase T cells senescence
Increase effectors T cells	Diminution T cells functions
Diminution of naive T cells	Diminution antigen recognition
Diminution of B cells response	

Ciarambino T, et al. Vaccines 2023;11:1414

Efficacy and Safety of Vaccinations in Geriatric Patients: Take Home Messages

- Vaccination is an important preventive measure to protect the health and well-being of older adults. It not only reduces the risk of severe infections but also decreases mortality rates associated with vaccine-preventable diseases;
- Many vaccine-preventable infections, such as pneumonia, meningitis, and certain respiratory and bloodstream infections, are commonly associated with antibiotic use. By vaccinating older adults against these diseases, the incidence of infections can be reduced, thereby potentially decreasing the need for antibiotics and reducing the selection pressure for antibiotic-resistant bacteria;
- The safety of vaccines in the elderly has been extensively studied and vaccines are generally considered safe for older adults. Vaccination plays a crucial role in protecting older individuals from vaccine-preventable diseases and their associated complications;
- Vaccines can significantly reduce the risk of infections and related complications. The efficacy of vaccines can be influenced by factors such as age, underlying health conditions, immune status, and the specific vaccine's characteristics;
- Promoting the integration of various institutions and professionals in the field of health care should be considered to maintain successful national immunization programs;
- Promote a massive information campaign on the part of the scientific world, state health authorities, and various health operators which makes vaccination perceived as a healthy element of life, using high-quality forms of vaccination advice and thus further contributing to the increase in immunization rates in the elderly population and their caregivers.

Major Scientific Hurdles in HIV Vaccine Development: Historical Perspective and Future Directions

TABLE 1 | Illustration of completed and documented HIV vaccine trials.

Vaccine Trial	Year	Site	Target group	Vaccine	Immune response	Result	Reference
VaxSyn	1987	Canada (Clade B)	72 adults	Recombinant envelope glycoprotein subunit (rgp160) of HIV	Neutralizing antibodies were detected	No vaccine efficacy	(37)
HIVAC-1e	1988	USA (Clade B)	35 male adults	Recombinant vaccinia virus designed to express HIV gp160	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(38)
Vax004	1998–2002	North America (Clade B)	5,417 MSM and 300 women	AIDSVAX B/B gp120 with alum	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(39, 40)
Vax003	1999–2003	Thailand (Clade B/E)	2,545 men and women IDUs	AIDSVAX B/E gp120 with alum	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(39, 40)
HVTN 505	2009–2013	United States (Clade B)	2,504 men or transgender women who have sex with men	Three vaccinations with DNA encoding HIV clade B *gag*, *pol* and *nef* as well as *env* from HIV clades A, B and C followed by an Ad5 vector-based vaccine encoding clade B *gag* and *pol* as well as *env* from clades A, B and C	Vaccine was unable to prevent infection or decrease viral load in vaccinated volunteers	No vaccine efficacy	(41, 42)
STEP/HVTN 502 trial	2004–2007	North America the Caribbean South America, and Australia (Clade B),,	3,000 MSM and heterosexual men and women	MRKAd5 HIV-1 *gag/pol/nef* trivalent vaccine	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(43, 44)
Phambili/ HVTN 503 trial	2003–2007	South Africa (Clade C)	801 adults	rAd5 (*gag/pol/nef*)	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(24)
RV144	2003–2009	Thailand (Clade B)	16,402 community-risk men and women	ALVAC-HIV (vCP1521) and AIDSVAX B/E vaccines	IgG antibody avidity for Env in vaccine recipients with low IgA	31.2% vaccine efficacy at 42 months	(45, 46)
HVTN 305	2012–2017	Thailand (Clade B/E)	162 women and men	ALVAC-HIV and AIDSVAX B/E		No vaccine efficacy	(47)
HVTN 306	2013–2020	Thailand (Clade B/E)	360 men and women aged 20–40 years	ALVAC-HIV and AIDSVAX B/E	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(48)
HVTN 097	2012–2013	South Africa (Clade B/E)	100 black Africans (men and women) aged 18–40 years	ALVAC-HIV (vCP1521) and AIDSVAX B/E	Induction of $CD4^+$ T cells directed to HIV-1 Env	No vaccine efficacy	(49)
HVTN 100	2015–2018	South Africa (Clade C)	252 men and women	ALVAC-HIV (vCP2438) and bivalent subtype C gp120/MF59	$CD4^+$ T-cell responses and gp120 binding antibody responses	No vaccine efficacy	(50)
HVTN 702	2016–2020	South Africa (702Clade C)	5,400 men and women	ALVAC-HIV (vCP2438) and bivalent subtype C gp120/MF59	Vaccine was unable to confer protection against HIV	No vaccine efficacy	(51)

MSM, men who have sex with men; IDUs, IV drug users.

Ng'uni T, et al; Front Immunol 2020;11:590780

Table 1 | Factors associated with immune dysfunction other than destruction of $CD4^+$ T cells

Cell type	Immunopathological effects
$CD8^+$ cytotoxic T lymphocytes	Above the normal range during acute phase (normal $CD8^+$ T cell range: 150–1,000 cells/mm^3)
	Decline at later stages
Natural killer cells	Impaired numbers
	Impaired function
Monocytes and macrophages	Defects in chemotaxis
	Inability to promote T cell proliferation (normal $CD4^+$ T cell range: 460–1,600 cells/mm^3)
	Defects in Fc receptor function, which is an important requirement for monocytes and macrophages to recognize and eliminate antibody bound to a foreign antigen
B cells	Increased production of IgG and IgA
	Antibody responses to multiple pathogens, after either prior infection or vaccination, are low compared with people without HIV infection

Bekker L-G, et al
Natur Rev Disease Primer
2023;42

UNC SCHOOL OF MEDICINE

Tuberculosis Vaccine: A Journey from BCG to Present

Tuberculosis (TB) is the leading cause of death worldwide due to an infectious disease, causing around 1.6 million deaths each year. This situation has become more complicated by the emergence of drug-resistant Mycobacterium tuberculosis (M.tb) and HIV-TB co-infection, which has significantly worsened TB prognosis and treatment. Despite years of intensive research, Bacille Calmette-Guerin (BCG) remains the only licensed vaccine and has variable efficacy. It provides protection against childhood TB but is not effective in adult pulmonary TB. As a result of intense research in understanding TB vaccinology, there are many new vaccine candidates in clinical development and many more in pre-clinical trials which aim either to replace or boost BCG vaccine.

TABLE 1 SWOT (strengths, weaknesses, opportunities and threats) analysis: creation of a Tuberculosis (TB) Vaccine Accelerator Council (TB VAC)

Strengths
TB VAC will address and proactively tackle the adverse impact of COVID-19 on TB services
TB VAC encourages global collaboration among funders, global health agencies, the private sector and governments
TB VAC is getting high-level support from eminent global health leaders, such as Dr Tedros Adhanom Ghebreyesus, the Director-General of the World Health Organization
Weaknesses
TB VAC will need to find solutions for the complex scientific and technical challenges related to vaccine efficacy, safety and immunological responses
TB VAC requires huge resources and adequate funding for successful establishment and day-to-day operation
Navigating the time-consuming and challenging regulatory and approval processes for vaccine development can be difficult
Achieving sufficient manufacturing capacity and a robust supply chain for TB vaccines can be challenging
Inadequate skilled researchers, laboratories and infrastructure may impact progress
Access to target populations: the logistics of reaching and vaccinating affected populations, particularly in low-income and middle-income countries could be enormous
Opportunities
Improved TB prevention: development of effective vaccines to reduce global TB cases including drug-resistant cases and deaths
Global health impact: potential to significantly impact global health by accelerating TB vaccine development
Threats
Insufficient funding: inadequate financial resources could impede the successful establishment and operation of the TB VAC
Scientific challenges: overcoming scientific bottlenecks related to vaccine efficacy, safety, and immunological responses

Adepoju VA, Onyezue OI. Breathe 2003;19:230036

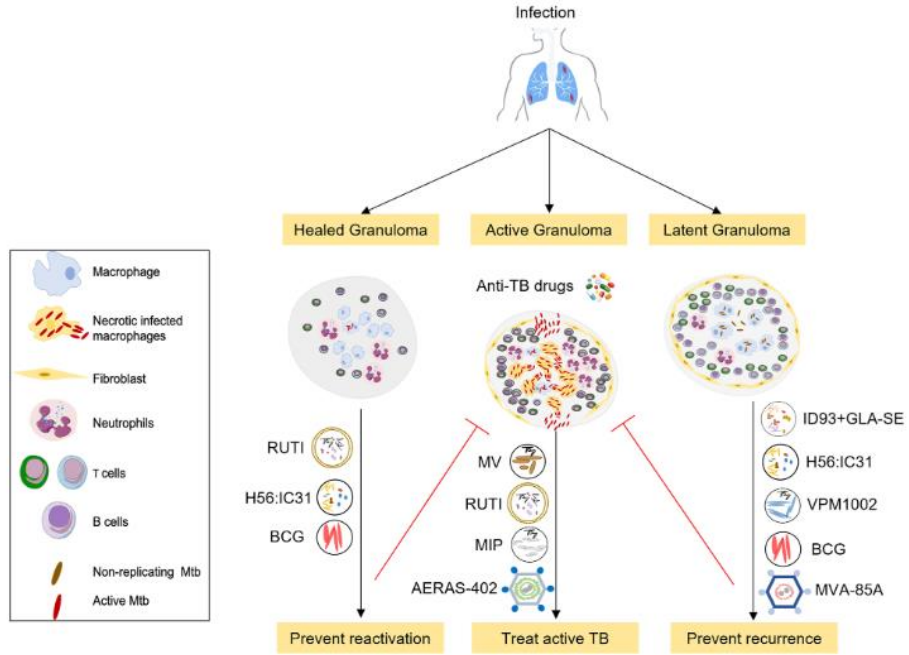


FIGURE 1 | Overview of selected therapeutic TB vaccines in the clinical pipeline. The initial stages of TB infection involve inhalation of Mtb bacilli into the lung and phagocytosis by resident alveolar macrophages. The human immune system can contain or eliminate Mtb infection in the majority of cases, only a small proportion of exposed individuals go on to develop active tuberculosis. Therapeutic TB vaccines serve as immunotherapeutic adjuncts to chemotherapy and act through modulating host anti-TB immunity. These vaccines are either administrated to potentiate treatment during treatment of active disease (middle) or to prevent recurrence or relapse after standard treatment (right), or to prevent reactivation of latent tuberculosis to active tuberculosis (left). Vaccines that are being developed to improve treatment outcomes in active TB comprise *M. vaccae*, RUTI, MIP and AERAS-402. Vaccines that prevent relapse and reinfection include H56:IC31 and ID: GLA-SE subunit vaccines, RUTI, BCG, the recombinant BCG vaccine VPM1002 as well as MVA-85A. These candidates are currently in phase 2 or 3 clinical trials in TB patients during or after completion of treatment.

Bourzeyen R, Javid B. Frontier Immunol 2022;June

WHO RECOMMENDED MALARIA VACCINES: RTS,S/AS01 & R21 Matrix-M

Recommended for children >5 mo

	Phase 3 trial*—children aged 5–17 months at 20 months of follow-up[10]	Phase 3 trial*—children aged 5–17 months at 4 years of follow-up[1,4]	MVIP†—children aged 7–9 months at average 1 year of follow-up (range 1–22 months)[3,13]
Vaccinated to unvaccinated mortality ratio			
Total	1·12 (0·75–1·69)	1·22 (0·87–1·71)‡	0·93 (0·84–1·03)
Females	1·70 (0·94–3·08)	2·00 (1·18–3·39)‡	0·98 (0·86–1·10)
Males	0·70 (0·39–1·26)	0·77 (0·48–1·22)‡	0·90 (0·78–1·04)
Female to male mortality ratio			
Vaccinated	1·75 (1·09–2·80)	1·50 (1·03–2·18)‡	--
Unvaccinated	0·72 (0·36–1·43)	0·57 (0·32–1·04)‡	--
Vaccinated adjusted for ratio in unvaccinated§	2·43 (1·05–5·61)	2·63 (1·31–5·29)‡	1·08 (0·92–1·28)

Data are mortality ratio (95% CI) **from the phase 3 trial and the MVIP.** MVIP=malaria vaccine implementation programme. *The phase 3 trial was conducted in seven countries (Kenya, Malawi, Ghana, Tanzania, Mozambique, Gabon, and Burkina Faso) in 5948 RTS,S vaccinated children compared with 2974 receiving a placebo; age at enrolment and first dose of the RTS,S vaccine was 5–17 months.[1,4,10] †The MVIP was conducted in three countries (Kenya, Malawi, and Ghana) in 494 745 children eligible to have received the three doses of the RTS,S vaccine (120 795, 173 152, and 200 398 children, respectively) and compared with children of the same age in non-vaccine areas; age at third dose was 7–9 months.[13,14] ‡Calculated from table 1 in Klein et al.[4] §The mortality ratio is defined as the ratio of the mortality rate between vaccine recipients and controls for girls, relative to that for boys.

Table 1: **Mortality ratios for RTS,S vaccinated versus unvaccinated children and for females versus males**

We conclude that the claimed impact of the MVIP on mortality is not based on enough scientific evidence and that the MVIP findings do not rule out the possibility of increased mortality among vaccinated girls compared with vaccinated boys, as observed in the phase 3 studies.
Bijorkman A, et al. Lancet ID 2023;23:e318

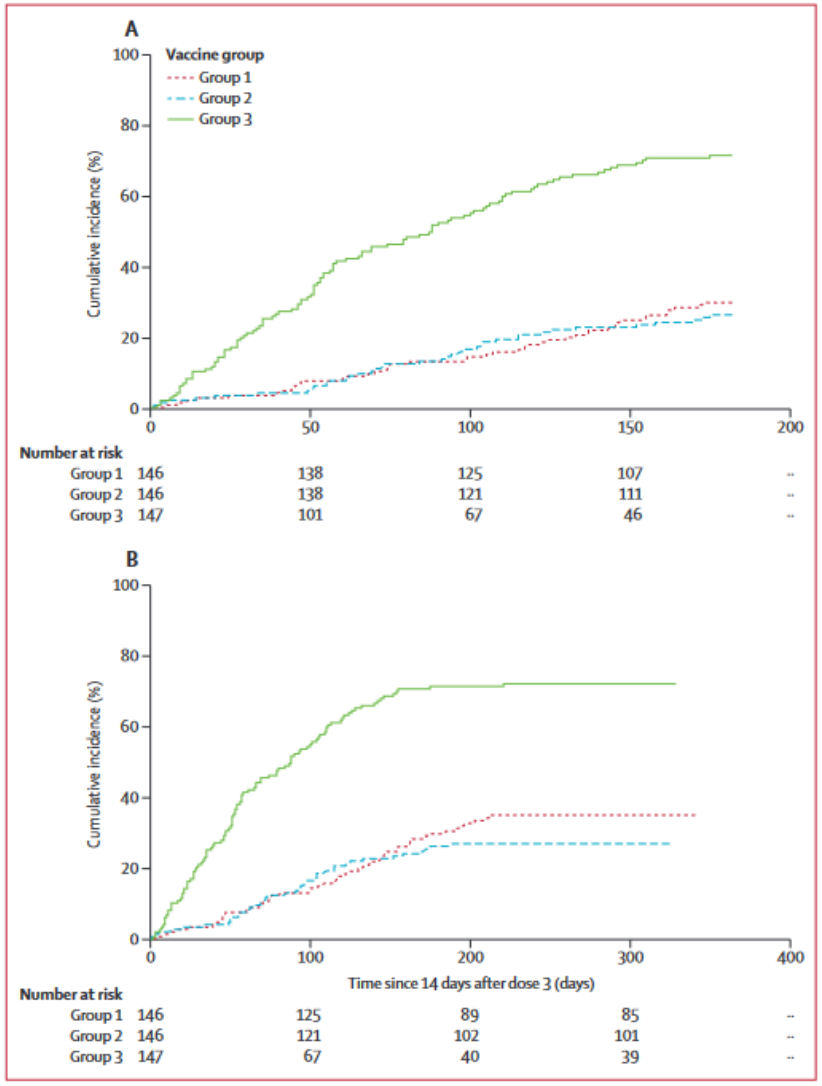


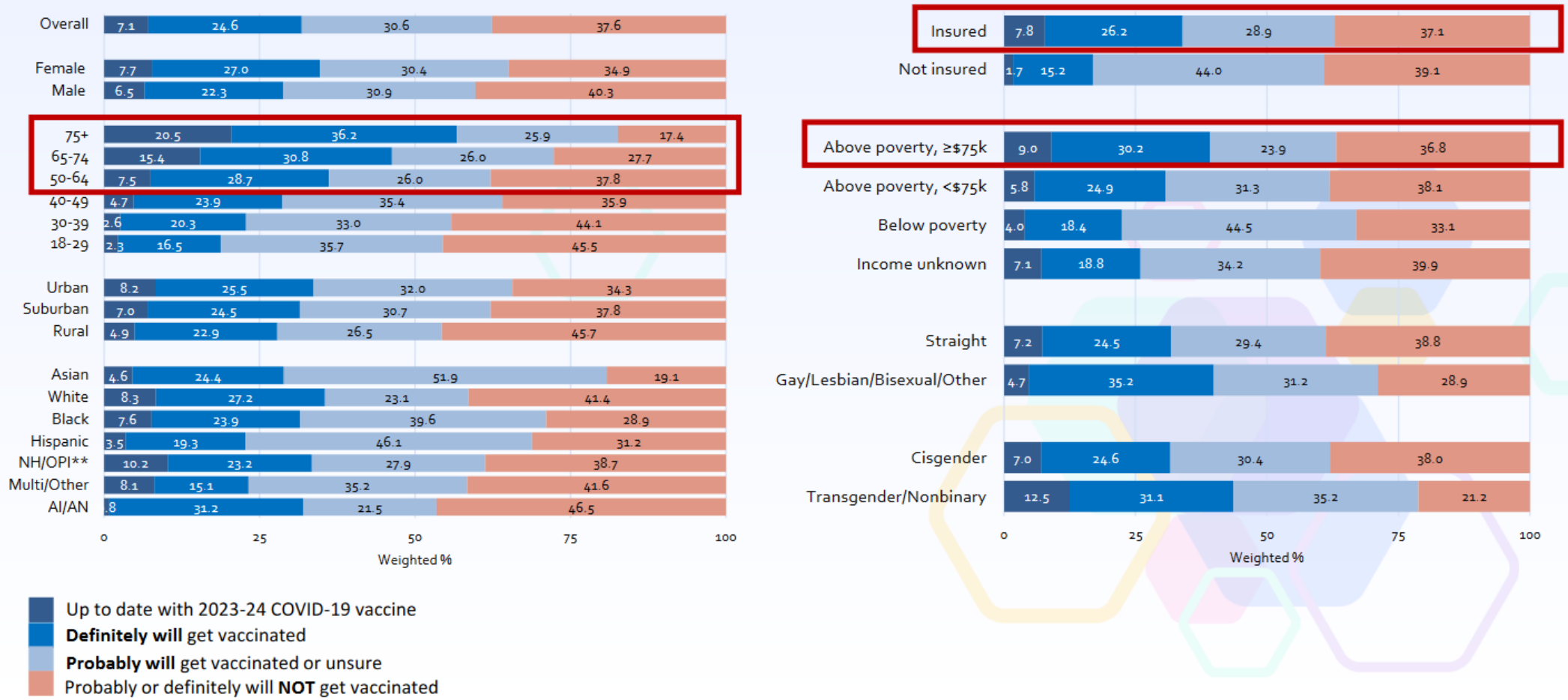
Figure 2: **Kaplan-Meier estimates of the time to first episode of clinical malaria**
The primary analysis was based on a modified intention-to-treat population. Group 1 received 5 µg R21/25 µg MM, group 2 received 5 µg R21/50 µg MM, and group 3, the control group, received rabies vaccinations (Rabivax-S). (A) Data beginning from 14 days to 6 months after third vaccination. (B) Data beginning from 14 days to 12 months after third vaccination. MM=Matrix-M.

1 year, vaccine efficacy remained high, at 77% (67–84) in group 1.

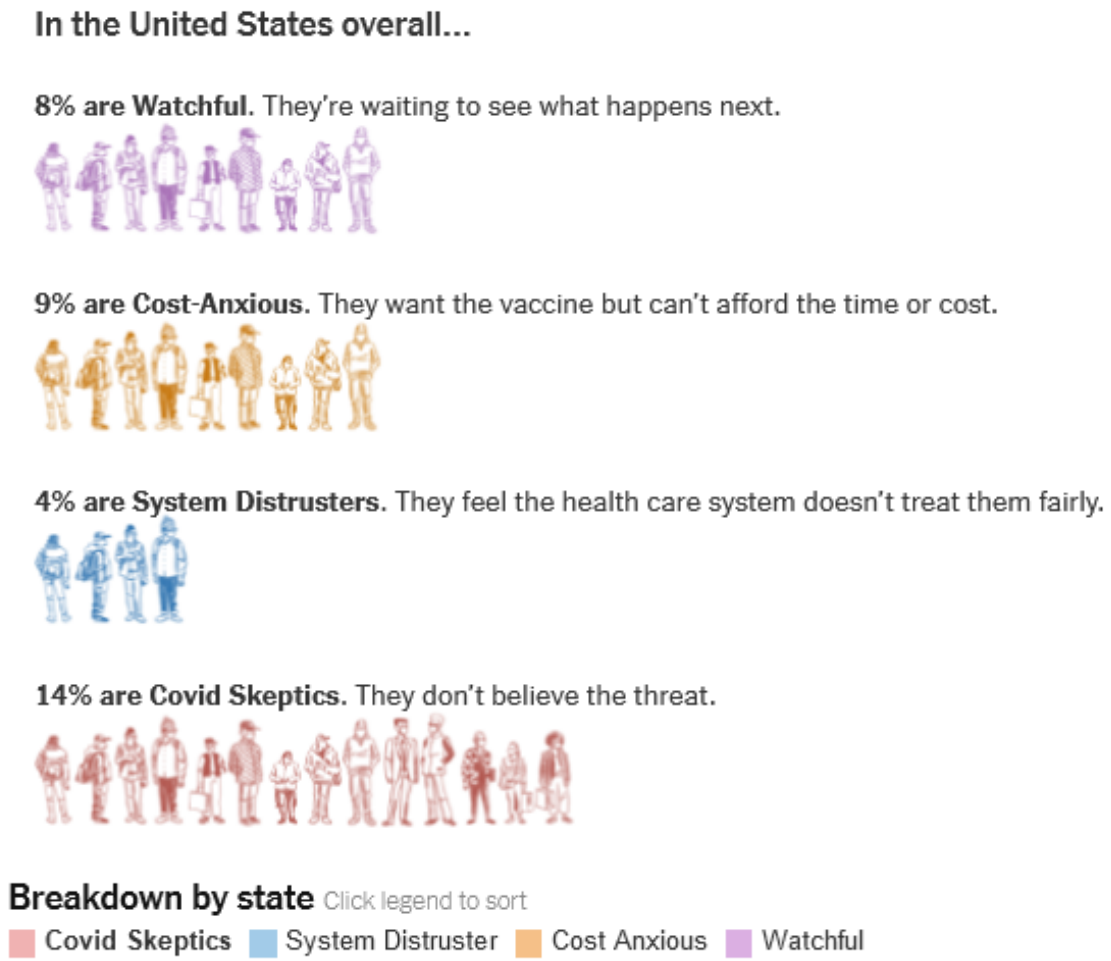
Datoo M, et al
Lancet2 2021;397:1809

Receipt of a COVID-19 vaccine was more frequently reported among adults who were older, insured, and with higher incomes.

COVID-19 Vaccination Status and Intent Among Adults Age ≥18 Years by Demographics,
National Immunization Survey-Adult COVID Module, October 8–14, 2023



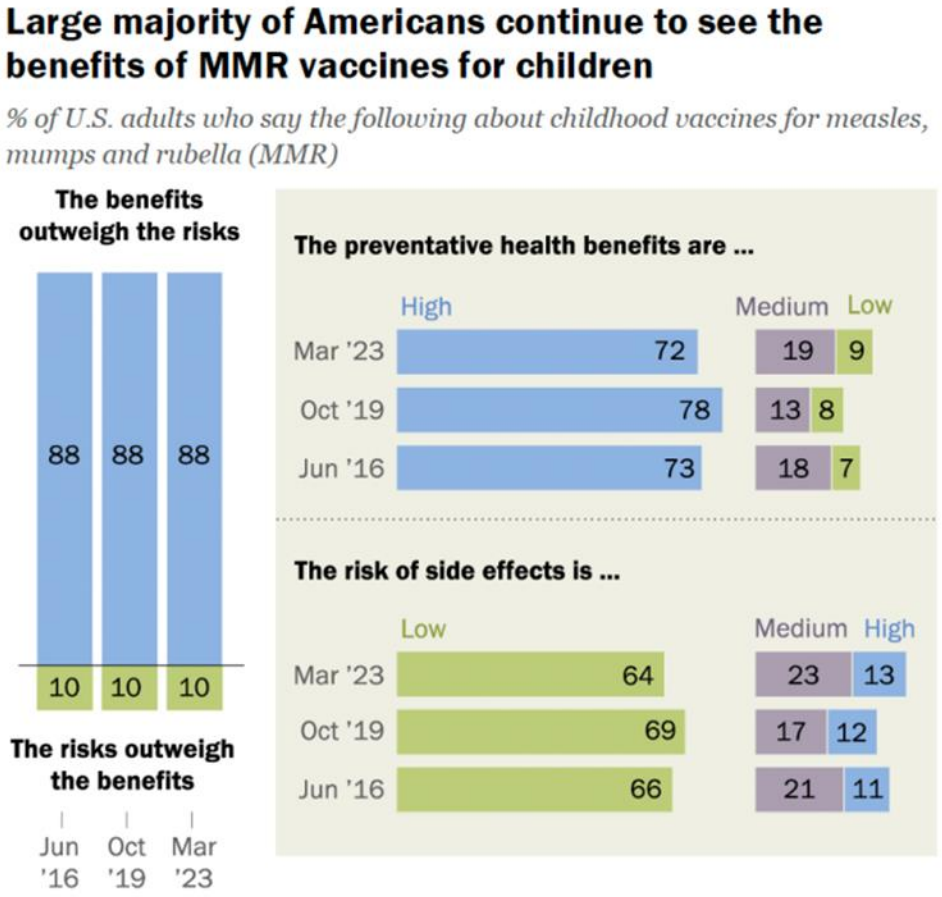
Reasons for Vaccine Hesitancy

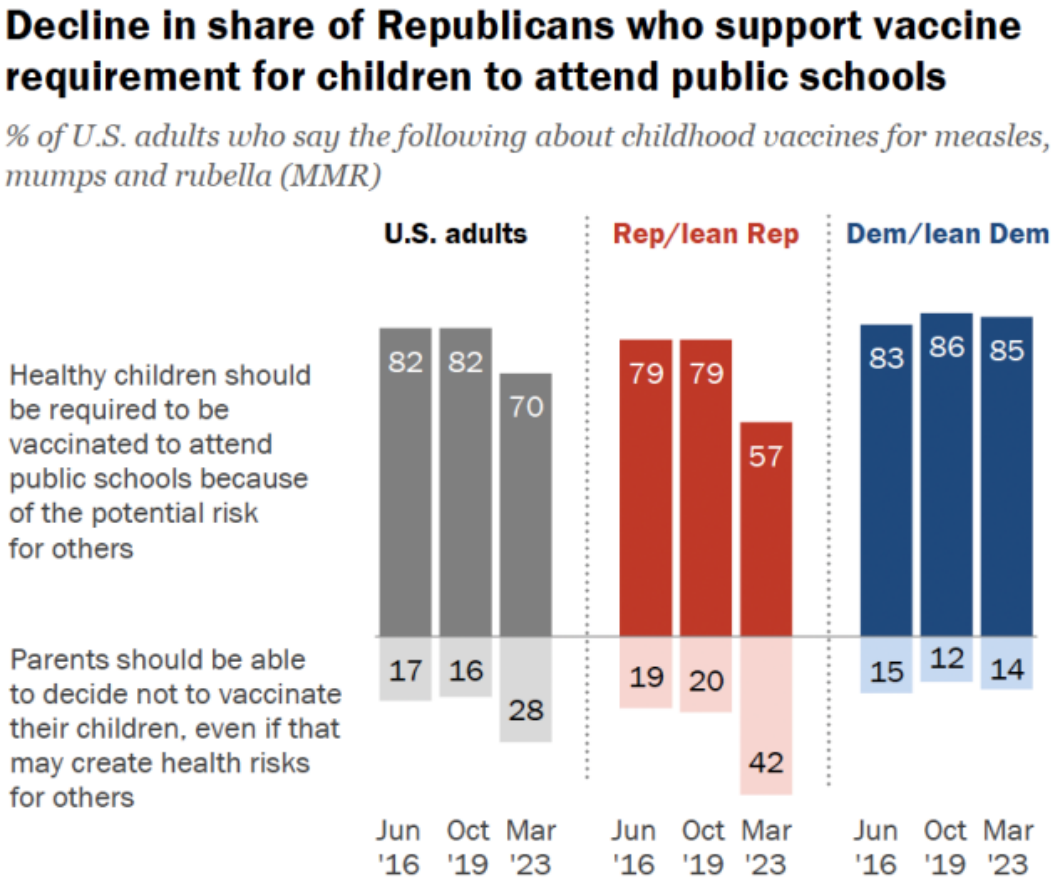


- The **Watchful** are holding out to see what kind of experience their friends or neighbors have with the vaccine before committing themselves. Solution=Allow for a "vaccinate later" option
- The **Cost-Anxious** worry about the time and potential expense of getting vaccinated (even if it is actually free). Solution=stress that vaccine is free and encourage businesses to provide paid time off for both vaccines
- The **System Distrusters** believe that the health care system doesn't treat them fairly. Most, but not all, members of this group are people of color. Solution=engage trusted member of their own communities to air concerns and be transparent
- **Covid Skeptics** are at the far end of the spectrum as the least likely to get vaccinated. The primary barrier for people in this group are their specific, deeply held beliefs about Covid-19. Everyone in this group believes at least one conspiracy theory related to the pandemic. Solution=avoid trying to debunk person's beliefs; listen to concerns and emphasize that vaccination is their own personal choice – and it protects friends and family members

https://www.nytimes.com/interactive/2021/05/18/opinion/covid-19-vaccine-hesitancy.html

VACCINE HESITANCY: A GROWING PUBLIC HEALTH CONCERN





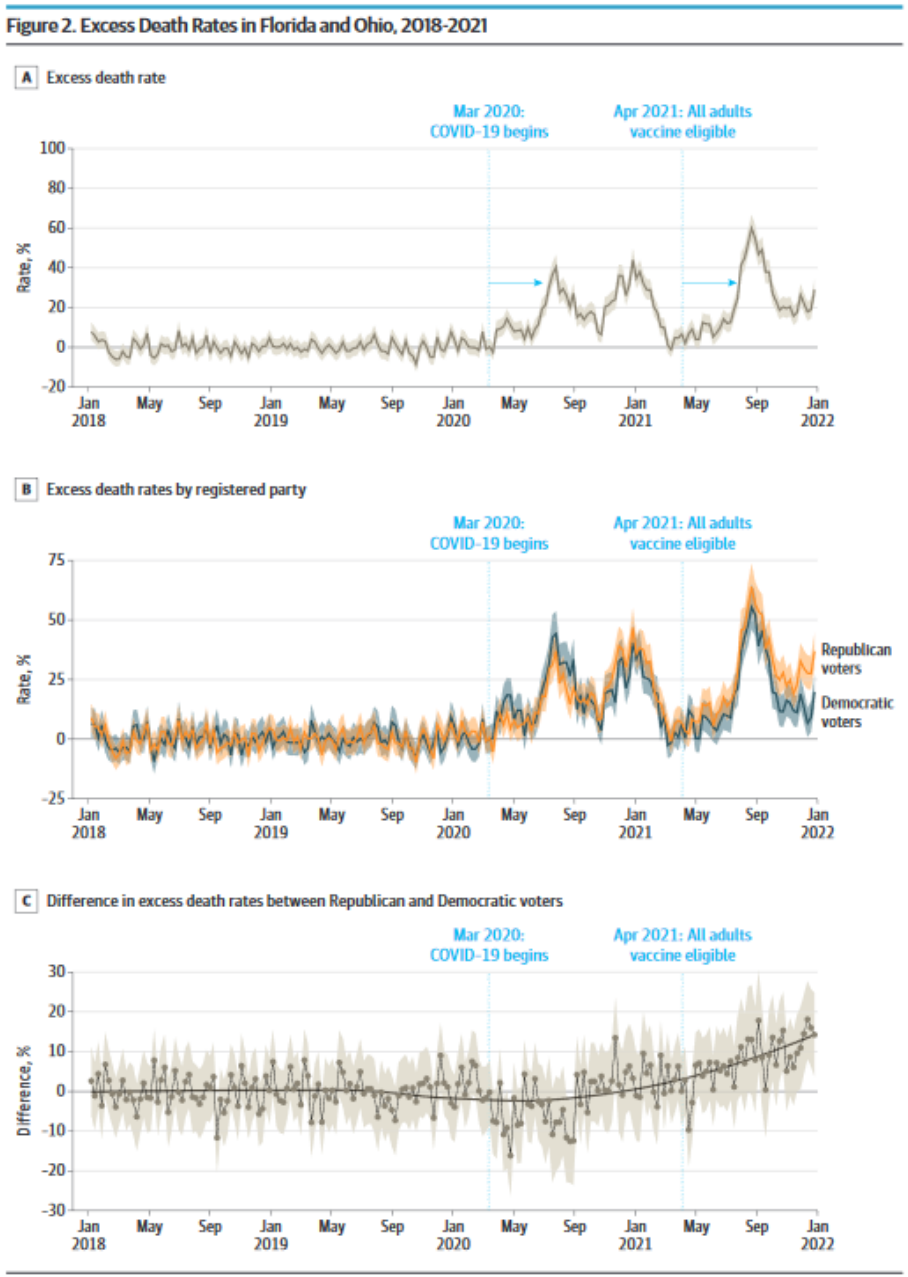
Pew Research Center: https://www.pewresearch.org/science/2023/05/16/americans-largely-positive-views-of-childhood-vaccines-hold-steady/ps_2023-05-16_vaccines_00-02/

Excess Death Rates for Republican and Democratic Registered Voters in Florida and Ohio During the COVID-19 Pandemic

Design: A cross-sectional comparison of excess mortality between registered Republican and Democratic voters between March 2020 and December 2021 adjusted for age and state of voter registration was conducted.

Results: Between January 1, 2018, and December 31, 2021, there were 538 159 individuals inOhio and Florida who died at age 25 years or older in the study sample. Overall, the excess death rate for Republican voters was 2.8 percentage points, or 15%, higher than the excess death rate for Democratic voters (95% prediction interval [PI], 1.6-3.7 percentage points). After May 1, 2021, when vaccines were available to all adults, the excess death rate gap between Republican and Democratic voters widened from −0.9 percentage point (95% PI, −2.5 to 0.3 percentage points) to 7.7 percentage points (95% PI, 6.0-9.3 percentage points) in the adjusted analysis; the excess death rate among Republican voters was 43% higher than the excess death rate among Democratic voters. The gap in excess death rates between Republican and Democratic voters was larger in counties with lower vaccination rates and was primarily noted in voters residing in Ohio.

Wallace J, et al. JAMA Intern Med 2023;24 July



Constant Joseph Desbordes (1761-1827), *Baron Jean Louis Aliibert (1768-1837) Performing the vaccination against smallpox in the Chateau of Liancourt.* C. 1820