Advances in Vaccination
Lessons Learned, Moving Forward

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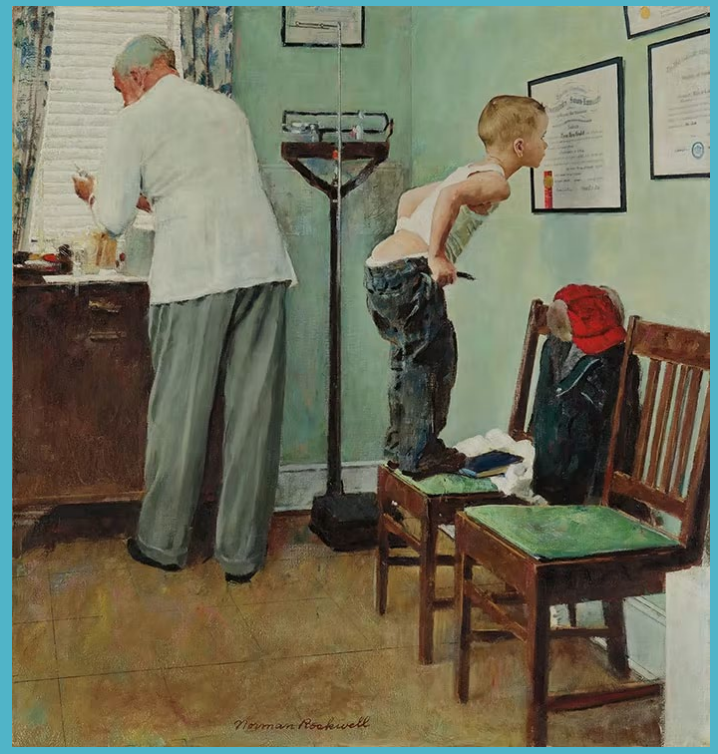


Disclosure

Recent research work with the following Companies

1. EMD Serono (Grants, clinical studies and consulting)
2. Merck (Consulting)
3. Gilead (Clinical Studies)
4. GSK (Clinical Studies)

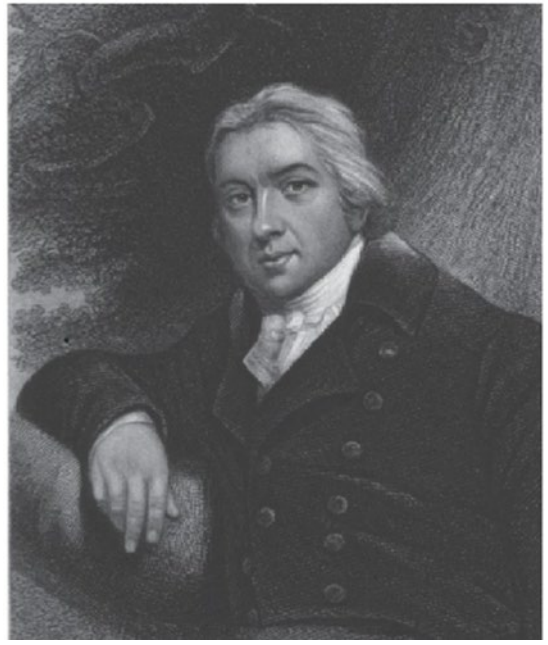
Prior and current work on Moderna, Johnson & Johnson,
Bavarian Nordic, and GSK vaccine studies

Clinical recommendations are evidence-based and free of commercial bias

Thank you

To Dr. Kathleen Maksimowicz-McKinnon, for her contributions to this presentation

Edward Jenner



Objectives

1. Vaccination history (brief)
2. Difficulties in the field- vaccine hesitancy
3. Current and Upcoming vaccines

Early Vaccination History

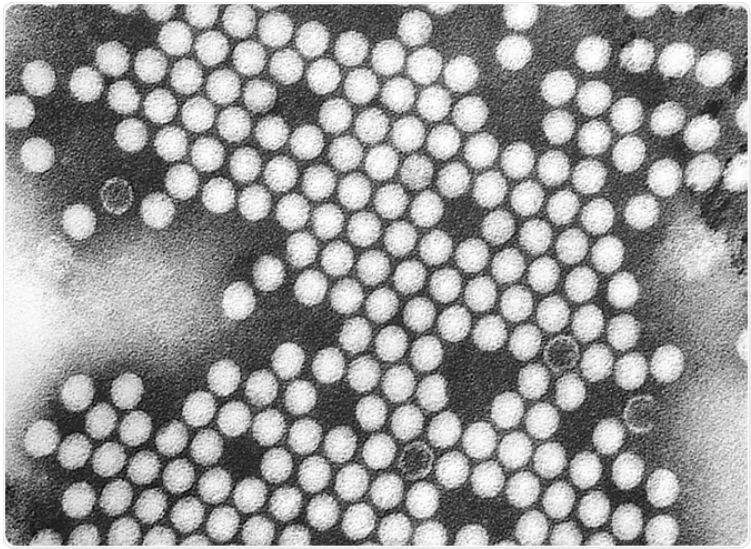
- 1000 years ago, in India and China, the practice of variolization (mechanical attenuation and intentional low dose infection) was used to reduce the virulence of subsequent smallpox infection
- 1721, Variolation was introduced to Great Britain
- 1796, Edward Jenner inoculated 8-year-old James Ripps with cowpox pustule material
- 1798, Jenner's work was published, coined the word "vaccine" as Latin for cow (vacca) and process of vaccination
- The cowpox virus was propagated and eventually developed the Vaccinia virus as a distinct vaccine strain
- 1880's- Louis Pasteur and his team discovered that drying rabies-infected tissue at room temperature attenuated the virus and serial inoculation of dogs with the tissue provided protection against rabies
- 1902- Biologic Control Act is enacted in which included regulations of vaccine and antitoxin producers and required both licensing and inspection of manufacturers
- 1944- Public Health Services Act
- 1955- Polio Vaccination Assistance Act was enacted by Congress, the first federal involvement in immunization activities
- 1962- Vaccination Assistance Act is signed into law. It allow the CDC to support mass immunization campaigns and initiate maintenance programs
- 1966- World Health Assembly called for global smallpox eradication and CDC announced the first national measles eradication campaign
- 1971- CDC recommended the discontinuation of routine Smallpox vaccination due to successful vaccination and reduced risk for disease

Recent vaccination history

- 1997- FDA Modernization Act (FDAMA) modernize the regulation of food, medical products and cosmetics
- 2012- Vaccine Error Reporting Program is launched
- 2017- new Vaccine Adverse Event Reporting System (VAERS) website is launched
- 2020- Operation Warp Speed was initiated in May by US government and supported 7 initial companies to develop COVID-19 vaccines

Types of Vaccines- Live Vaccines

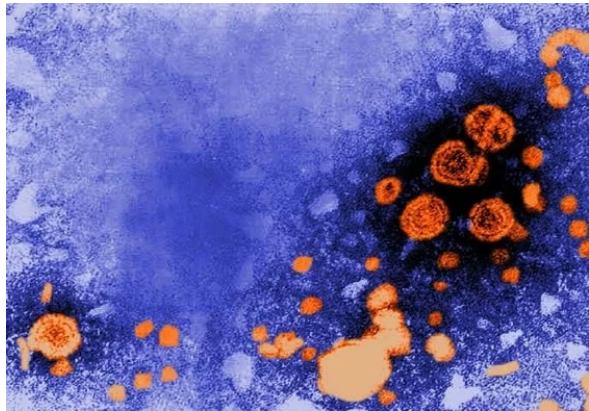
- LIVE VIRUS VACCINES
  - Vaccinia vaccine is the first example of the use of live virus vaccine with an ***attenuated virus*** *(critical step)*
    - *Other examples are polio, adenovirus, yellow fever, rubella, measles, and mumps virus vaccines*
  - *ADVANTAGES*
    - *Activation of all components of the immune system, exposure to more protective Ags*
    - *Balanced systemic and local immune responses*
    - *Broad Humoral and cell mediated response*
    - *Immunity is more durable*
- *DISADVANTAGES*
  - *Can contain adventitious agents*
  - *Can cause illness directly*
  - *Loss of attenuation, restored replication*
  - *Can spread to contacts*
  - *Can lose infectivity in storage/transport/use*
  - *Genetic instability of attenuated viruses*



Fields Virology, 2023; NIAID.nih.gov; Polio virus, electron micrograph. Dr. Shaffer. News Medical

Types of Vaccines- Inactivated Vaccines

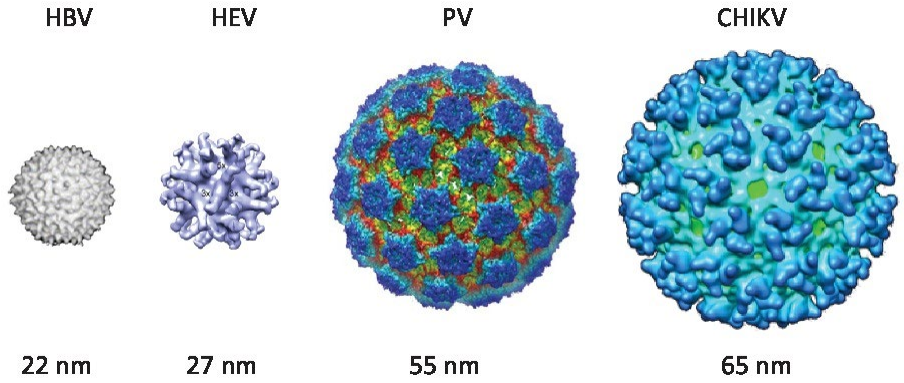
- INACTIVATED VIRUS VACCINES
  - Influenza A and B vaccines have been the prototypical inactivated vaccines
    - *Other examples are inactivated polio, JEV, rabies, HAV.*
    - *Can be either whole inactivated virus or virus like particles (VLPs; HBV, HPV)*
    - *VLPs are produced in yeast, human, bacterial or insect cells*
  - *ADVANTAGES*
    - *Immunization with the entire antigenic content of the virus*
    - *Little to no risk of infection*
    - *VLPs can carry key antigens/epitopes for immune protection without viral genomes*
  - *DISADVANTAGES*
    - *Can contain adventitious agents or active virus*
    - *Loss of immunity with time*
    - *Potential for atypical disease and severe presentations (Measles, 1960's RSV)*
    - *Antibody-dependent enhancement of disease (ADE)*
    - *Mucosal protection is less than live vaccines*
    - *VLPs do not lead to ongoing production of Ags, immune response maybe lower*



Fields Virology, 2023 ; NIAID.nih.gov; HBV virus (Dane particles), electron micrograph. CDC.gov.

Types of Vaccines- Virus-like Particle Vaccines

- VLP VACCINES
  - Two approved US VLP vaccines include HBV and HPV vaccines
    - *Hepatitis E vaccine is available in China*
    - *VLPs are self-assembling viral proteins that can mimic the particle structure of virions*
    - *No viral genomes are present*
    - *VLPs are produced in yeast, human, bacterial or insect cells*
  - *ADVANTAGES*
    - *Immunization with the entire antigenic content of the virus*
    - *Broad immune response, better immunogens*
    - *VLPs can carry key antigens/epitopes for immune protection without viral genomes*
    - *First anticancer vaccines*
    - *No genetic material present, Little to no risk of infection*
    - *Stable particles*
  - *DISADVANTAGES*
    - *Cost and complexity of production*
    - *VLPs do not lead to ongoing production of Ags, immune response maybe lower compared to live vaccines*
    - *Can require adjuvants to enhance immunogenicity*
  - Other Points
    - *The VLPs may be made non-enveloped (parvovirus B-1, norovirus candidates) or enveloped (HIV candidates)*



Variations on VLP particle size and structure

Fields Virology, 2023 ; NIAID.nih.gov.

Types of Vaccines- Other Vaccines

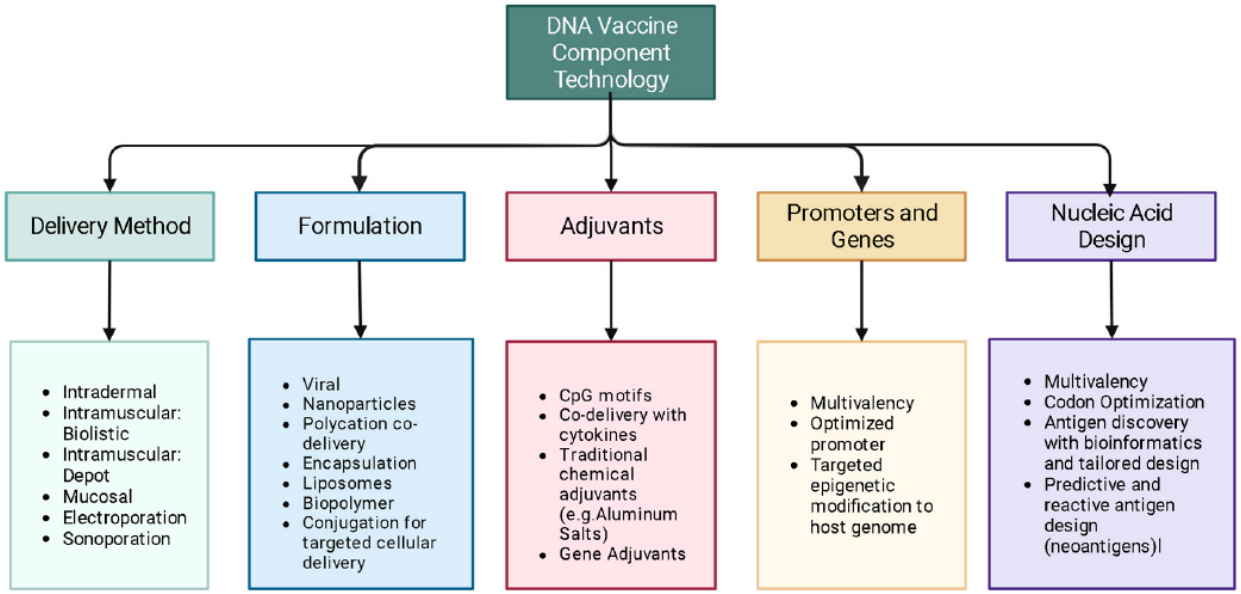
- **Subunit (Peptide, Polysaccharide) and Conjugated vaccines**
  - Use selected antigens instead of whole viruses
  - Tries to use the most relevant protective antigenic sites
  - Diminishes risk of contamination by unrecognized pathogens
  - First one introduced was Pertussis vaccines in 1940s
  - Conjugated vaccines were developed to improve immune responses
- **Toxoid Vaccines**
  - *Inactivated bacterial toxins*
  - *Laboratory derived from inactivated toxins to eliminate the biological toxicity but preserve the specific immune response*
  - *No live organisms are present*
  - *May require adjuvants*
  - *Diphtheria and tetanus vaccines are the classic examples (DTP, Tdap)*

Fields Virology, 2023 ; NIAID.nih.gov; Kozak M, Hu J, 2024; Montero DA, 2023

Types of Vaccines- Nucleic Acid Vaccines
DNA Vaccines

- ***Vaccination by Gene Delivery***
  - *Genes are modified to be non-functional, improve expression and maintain antigenicity*
  - *New technology allows for combination of antigens from multiple strains or different pathogens – simplifying vaccination regimens*
  - *Vectors use can be either replication competent (eg, Adenovirus) or replication defective (eg, Poxvirus)*

- ***DNA Vaccines***
  - *First DNA vaccine in phase I trials was an HIV-1 vaccine 1990*
  - *First approved DNA vaccine is the Indian ZyCovD vaccine against SARS-CoV-2 in 2021*

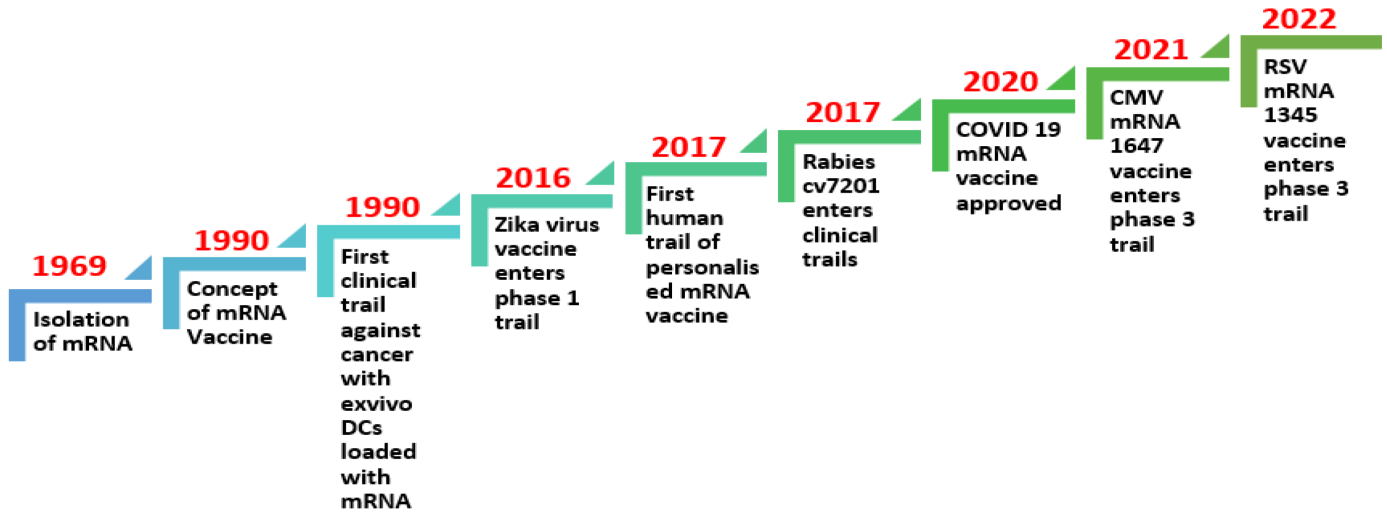


Fields Virology, 2023 ; NIAID.nih.gov; Kozak M, Hu J, 2024

Types of Vaccines- Nucleic Acid Vaccines mRNA Vaccines

- **These are lipid nanoparticle (LNP)-encapsulated nucleoside-modified mRNA**
  - Developed by Drs. K. Kariko and D. Weissman, who received 2023 Nobel prize for their work
  - Lipid nanoparticles are used to protect the mRNA
  - COVID-19 Pandemic spurred the rapid development of these vaccines
  - First two vaccines were
    - *mRNA vaccine BNT162b2*
    - *mRNA-1273*

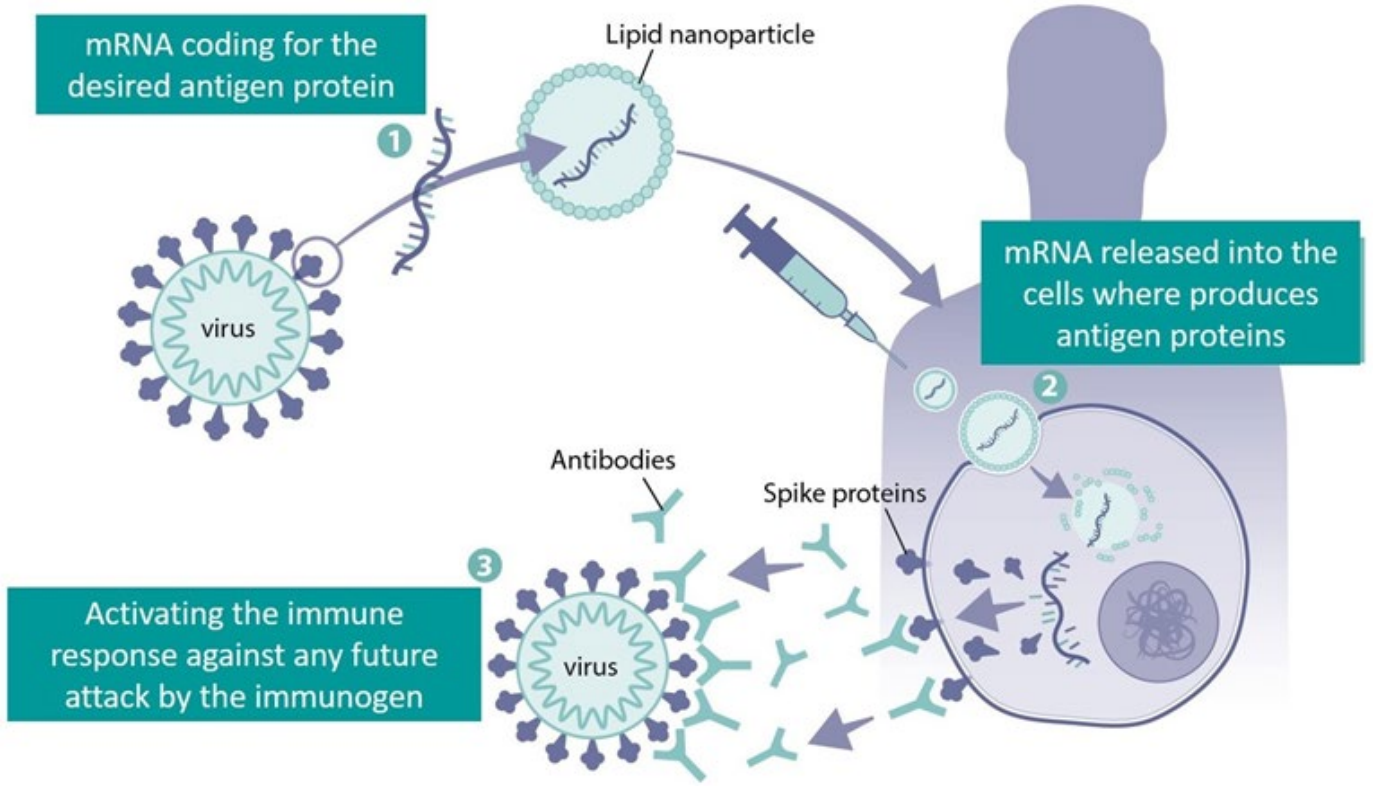
- **mRNA Vaccine Advantages**
  - *No integration of mRNA into host DNA*
  - *Non-infectious*
  - *Scalable, rapid and cost-effective production*
  - *Can code for multiple antigens in one vaccine*



Fields Virology, 2023; Venkata L, et al. 2024; Gote V, et al, 2023

Types of Vaccines- Nucleic Acid Vaccines
mRNA Vaccines

- mRNA vaccines are easily & rapidly adaptable to cover new strains of virus
  - 2021 Vax- Wuhan SARS-CoV-2 strain
  - 2022 Vax- Wuhan SARS-CoV-2 strain and BA.4/BA.5 Omicron subvariants
  - 2023 Vax- BA.4/BA.5 Omicron subvariants only
  - 2023 Vax- XBB.1.5 Omicron variant
  - 2024 Vax- KP.2 Omicron variant (descendant of JN.1)



Fields Virology, 2023; Venkata L, et al. 2024; Gote V, et al, 2023

Other vaccine buzzwords

- **Vectors**
  - *Can be used to deliver genes or antigens*
    - *Live Live-Modified (viruses)*
    - *Killed viruses*
    - *Recombinant viral vectors*
    - *DNA*
    - *Plant Cell Produced (paramyxovirus)*
- **Adjuvants**
  - *Inactivated virus vaccines, purified viral proteins, or peptide Ags by themselves have relatively weak immunogenicity in a host*
  - *Help produce a stronger immune response to vaccine antigens*
- **Vaccine delivery vehicles**
  - Refers to the approaches of transporting a vaccine antigen to particular location (host)
    - *Synthetic peptides (microparticles)*
    - *Conjugates (conjugated proteins)*
    - *Mechanical devices (needles, inhalers)*
    - *Lipid based carriers*
    - *Cell based carriers (dendritic cells)*

Fields Virology, 2023; Venkata L, et al. 2024; Gote V, et al, 2023; Montero DA, et al, 2023

Type of vaccine	Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)	Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism	Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid	Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)	Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle	Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle	Group B meningococcal	1987 (group B meningococcal)
Protein–polysaccharide conjugate	*Haemophilus influenzae* type B, pneumococcal, meningococcal, typhoid	1987 (*H. influenzae* type b)
Viral vectored	Ebola	2019 (Ebola)
Nucleic acid vaccine	SARS-CoV-2	2020 (SARS-CoV-2)
Bacterial vectored	Experimental	–
Antigen-presenting cell	Experimental	–

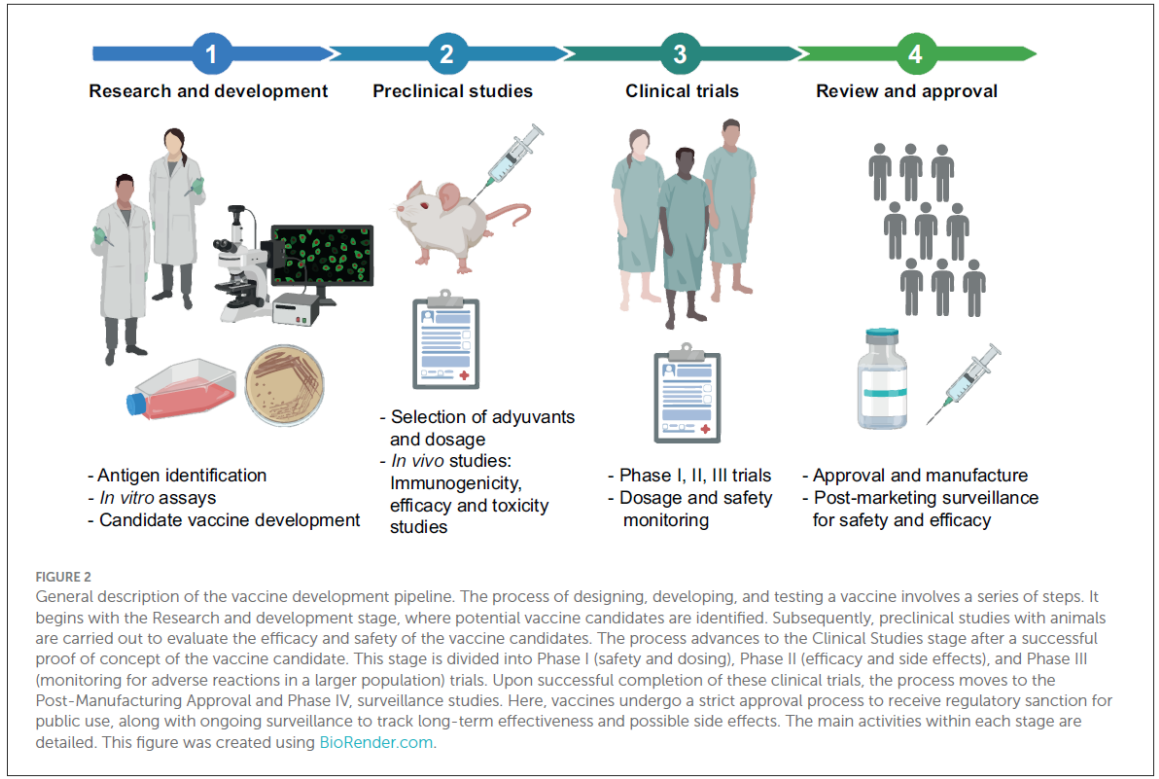


FIGURE 2
General description of the vaccine development pipeline. The process of designing, developing, and testing a vaccine involves a series of steps. It begins with the Research and development stage, where potential vaccine candidates are identified. Subsequently, preclinical studies with animals are carried out to evaluate the efficacy and safety of the vaccine candidates. The process advances to the Clinical Studies stage after a successful proof of concept of the vaccine candidate. This stage is divided into Phase I (safety and dosing), Phase II (efficacy and side effects), and Phase III (monitoring for adverse reactions in a larger population) trials. Upon successful completion of these clinical trials, the process moves to the Post-Manufacturing Approval and Phase IV, surveillance studies. Here, vaccines undergo a strict approval process to receive regulatory sanction for public use, along with ongoing surveillance to track long-term effectiveness and possible side effects. The main activities within each stage are detailed. This figure was created using BioRender.com.

Operation Warp Speed help to bring the mRNA COVID vaccine to clinical use in 8 months (April to December 2020)

Pollar AJ, Bijker EM. 2021; Montero DA, et al, 2024.

A Little Immunology

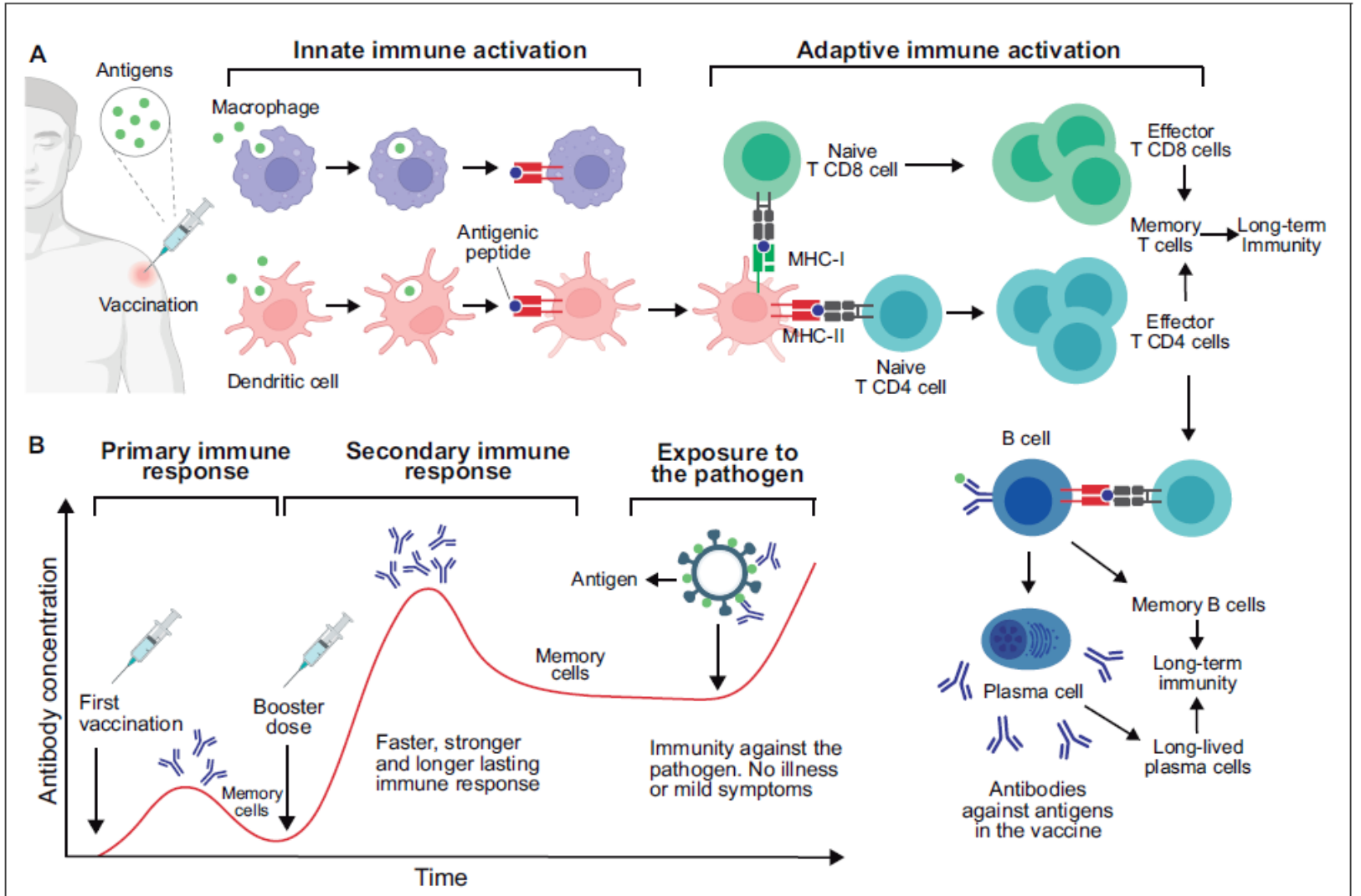


FIGURE 1

Immune response to vaccination and acquisition of immunity. **(A)** Immune response post-vaccination. This process is initiated by the activation of innate immune cells including macrophages and dendritic cells, which engulf and process antigens, leading to the presentation of antigenic peptides (epitopes) via class I or II major histocompatibility complex (MHC-I or MHC-II). These activated innate cells present antigens to CD4 and CD8 T lymphocytes, leading to their activation. Once activated, these T cells proliferate and exercise their effector functions; notably, CD4 T cells stimulate B lymphocytes specific to the antigen. These B cells proliferate and mature into plasma cells, producing antigen-specific antibodies. Of note, a number of memory T and B cells persist in the body to provide long-term immunity. Also, plasma cells can become long-lived plasma cells and secrete antibodies for months or years. **(B)** Timeline of antibody production post-vaccination. Primary and secondary immune responses are shown following the initial vaccination and subsequent booster dose, respectively. These generated antibodies and memory cells provide protective immunity against future exposure to the target pathogen. This figure was created using BioRender.com.

Montero DA, et al. 2024.

How Vaccines Work

- **Humoral Immunity (Passive or Active)**
  - *Vaccines need to mediate B cells to produce antibodies*
  - *The antibodies provide the protection against infection to the antigen included in the vaccine*
  - *Polysaccharide vaccines work only by inducing antibodies (no T cell response)*
  - *Antibodies produce can neutralize the infectious agent by*
    - **Aggregating** the pathogen (virus) particles impeding their infection of cells
    - Abs **can inhibit attachment** of the virus to the cells by binding to the attachment proteins
    - Abs can inhibit cell entry **after viral attachment**, block fusion and may even impact viral processes after entry

- **Cellular Immunity**
  - *Effective vaccines also induce T cell cellular immunity*
  - *T cell responses are induced by protein carrier for polysaccharide vaccines or to protein antigens (conjugated vaccines- PCV21)*
  - *T cells help in **the development of B cells** and antibody production*
  - *T helper cells type I are involved in IgG subclasses IgG1 & IgG3*
  - *TH17 cells are important for mucosal immunity (Gut, Lung)*
  - *T cells are also **cytotoxic cells** (CD8) to aid in killing of infected cells*
  - *T follicular helper cells help in the generation of high-affinity antibodies*

Fields Virology, 2023 ; Pollard AJ, 2021

How Vaccines Work- Correlates of Protection

- A correlate of protection is an immune function that statistically correlates with protection
  - Mechanistic- a marker that known to directly measure the immune effects that mediate protection
  - Non-mechanistic- a maker that is simply associated with protection
- The CoP will vary depending on the vaccine as the targets and pathogens differ
  - *Example- quantitative CoPs in use include a threshold of 10 mIU/mL in serum of hepatitis B antibodies detected*
- Abs that correlate with protection can vary IgA (influenza) vs IgG

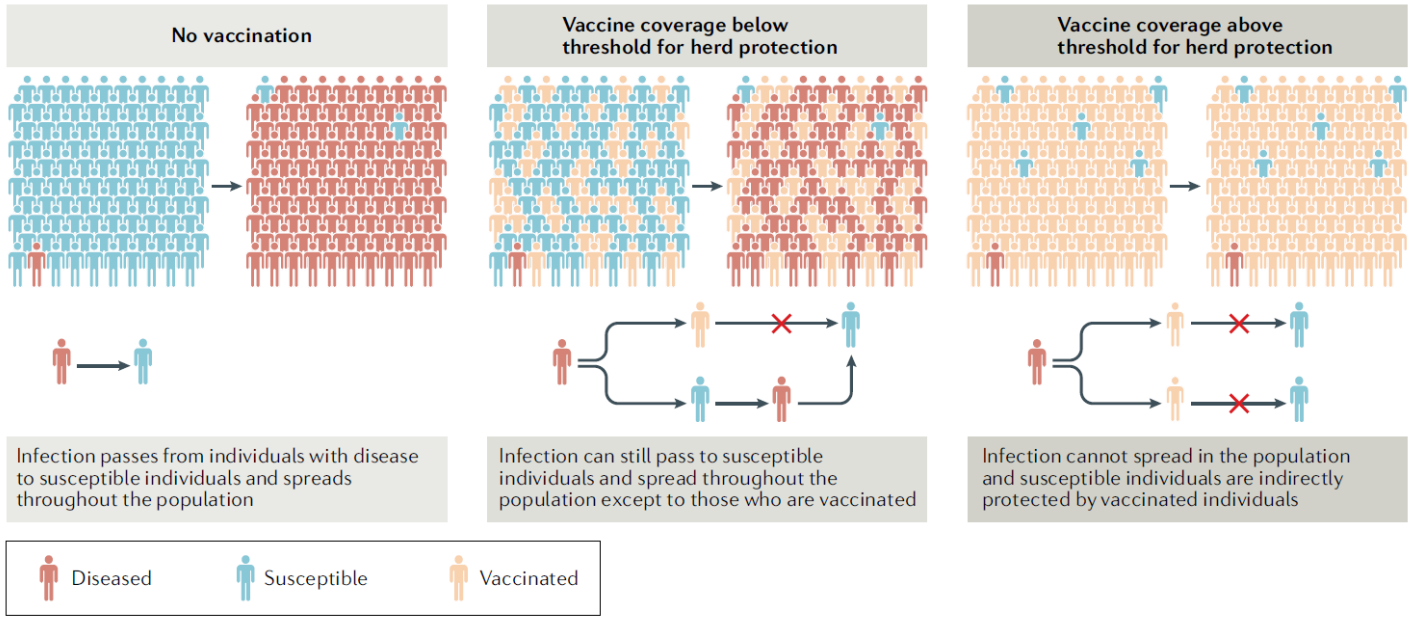
Term	Synonyms	Definition
CoP (correlate of protection)	Predictor of protection	An immune marker statistically correlated with vaccine efficacy (equivalently predictive of vaccine efficacy) that may or may not be a mechanistic causal agent of protection[a]
mCoP (mechanistic correlate of protection)	Causal agent of protection; protective immune function	A CoP that is mechanistically and causally responsible for protection
nCoP (nonmechanistic correlate of protection)	Correlate of protection not causal; predictor of protection not causal	A CoP that is not a mechanistic causal agent of protection

[a] A correlate of protection can be used to accurately predict the level of vaccine efficacy conferred to vaccine recipients (individuals or subgroups defined by the immune marker level).

Fields Virology, 2023; Goodman & Gilmans, 2023; Plotkin SA, 2011.

Herd or Community Immunity

- Occurs when a large enough number/percentage of the population is immunized(vaccine/natural) so that non-immunized individual is protected
- To achieve it, the vaccine must prevent transmission of the viruses as well as prevent disease
- Example- oral polio vaccine through IgA production
  - Killed polio vaccine does not prevent transmission



Levinson's Review of Medical Microbiology & Immunology, 2024; Pollar AJ, Bijker EM. 2021.

Licensed Vaccines in the US

1885 & 1980 Rabies

1914, 1994 Typhoid and Rabies

1915 Pertussis vaccine

1923 Diphtheroid toxoid, 1927 BCG

1945, 1960s, 1978, 2003, 2011, 2013+ Influenza

1944, 1965, 2007, 2010 Smallpox

1948, 1967, 1971, 2005 Mumps/MMVR

1949 DTP, 1953, 1991 tetanus and diphtheria toxoids

1955, 1963, 1987, 1990 Polio

1956, 1980 Adenovirus

1963, 1968, 1971, 2005 Measles, MMVR

1969+ Rubella

1977, 1983, 2010+ Pneumococcal

1978 Yellow Fever

1981, 1986, 2001+ HBV

1985, 1988, 1989, 1993 Hib vaccines

1992, 2009 Japanese Encephalitis

1995, 2001 HAV

1998 Rotavirus, 1999, 2002+ DTaP

1998, 2006, 2008 Rotavirus

2001 HAV/HBV

2005+ Meningococcal

2006, 2009+ HPV

2019, 2023 Ebola

2023 RSV

1995, 2005, 2006, 2017 Varicella & VZV

2019, 2022 MPox

2020, 2021+ COVID-19

2021 Dengue

2023 CHIKV

1900 1920 1940 1960 1980 2000 2020

CDC.gov; FDA.gov; Immunize.org;
Rodrigues CM, Plotkin SA, 2020

HIV Vaccines- Moved science forward, but no vaccine yet!

- **1987 First HIV Vaccine trial with gp160 subunit**
- 1988 NIAID AIDS Vaccine Evaluation Group is formed
- 1992 First phase 2 HIV vaccine trial launced
- 1998 First large scale trial, AIDSVAX (VAX004) is launched in the US and the Netherlands, 5400 patients
- 1999 First NIAID HIV vaccine trial in Africa (Uganda); AIDSVAX (VAX003) opened in Thailand
- 2000 HIV Vaccine Trials Network (HVTN) formed in NIAID
- 2003 RV144 HIV vaccine strategy trial- “prime-boost” was started in US and Thailand
- 2004 Both VaxGen candidates failed
- 2009 Phase 2 HVTN 505 study was initiated to evaluate “Prime-Boost” vaccine regimen
- **2009 RV144 trial- only large trial to demonstrate efficacy for an investigational vaccine**

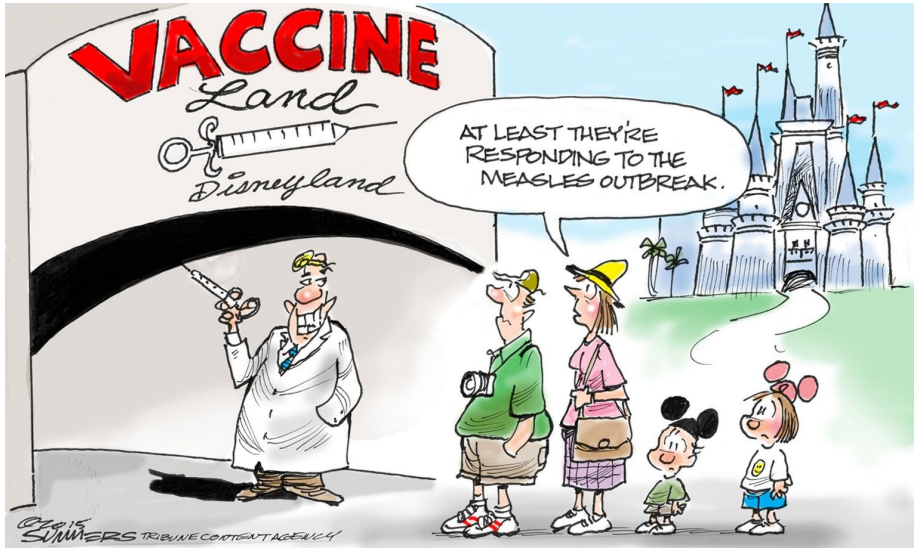
niaid.nih.gov; iavi.org/iavi-report/40-years-aids-vaccine-research/;

- **2012 additional analyses of RV144 provided insight on the types of immune responses needed for an effective vaccine**
- 2013 HVTN 505 stopped due to lack of efficacy
- 2016 HVTN 702 launched to test whether a new version of the RV144 HIV vaccine candidate
- 2017 HVTN 705/HPX2008, a Phase 2b, “mosaic” vaccine
- 2019 The Mosaico or HVTN 706/HPX3002 Phase III trial begins in North and South America and Europe testing the efficacy of an Ad26-based mosaic HIV vaccine candidate
- 2020 The PrEPVacc trial begins enrollment. This African-led Phase IIb/III clinical trial is evaluating two experimental HIV vaccine regimens compared to placebo, as well as a new PrEP combination pill known as Descovy
- 2021 Following the results of the Uhambo trial, more and more researchers in the field converge on the idea that an effective vaccine will need to induce so-called Broadly Neutralizing Antibodies (bnAbs)
- 2021/2023 both Imboko and Mosaico trials were stopped because of no statistically significant efficacy
- **2024 and beyond- new vaccine strategies and combinations are being evaluated with more basic science studies ongoing**

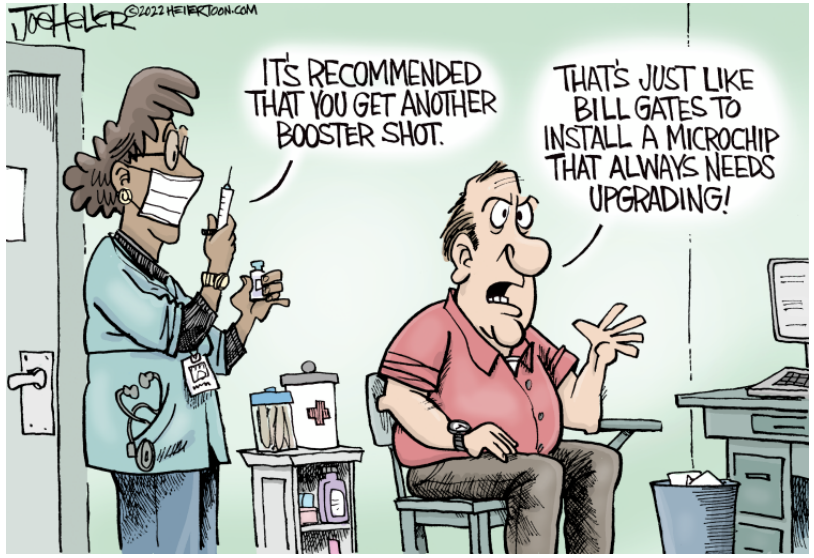
Vaccine Hesitancy and Vaccine Missteps

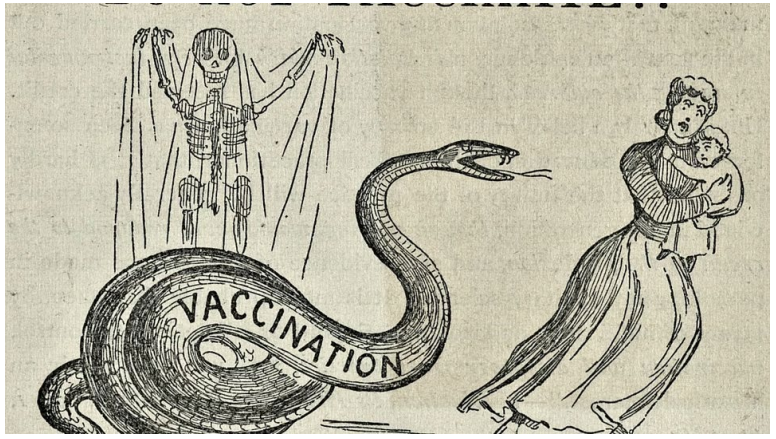
Primum Non Nocere

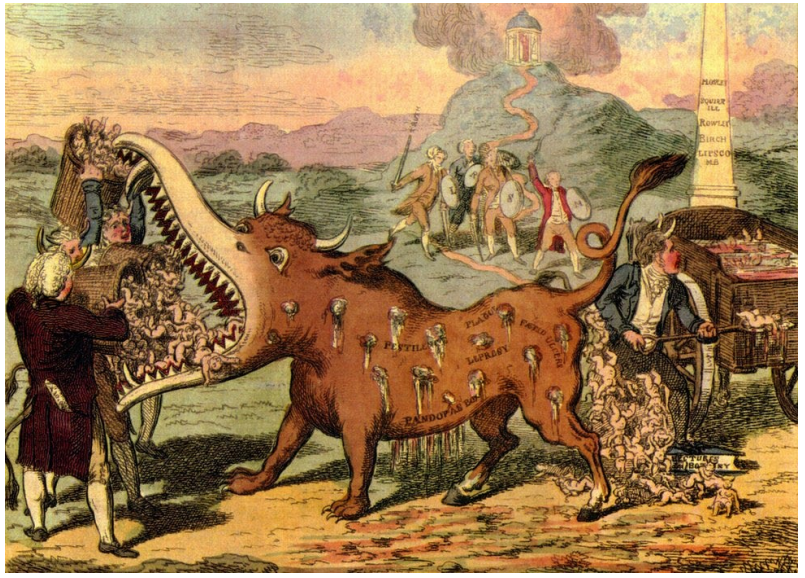

The Cow Pock — or — the Wonderful Effects of the New Inoculation!


VACCINE
Land
Disneyland
AT LEAST THEY'RE RESPONDING TO THE MEASLES OUTBREAK.
©2015 SUMMERS TRIBUNE CONTENT AGENCY

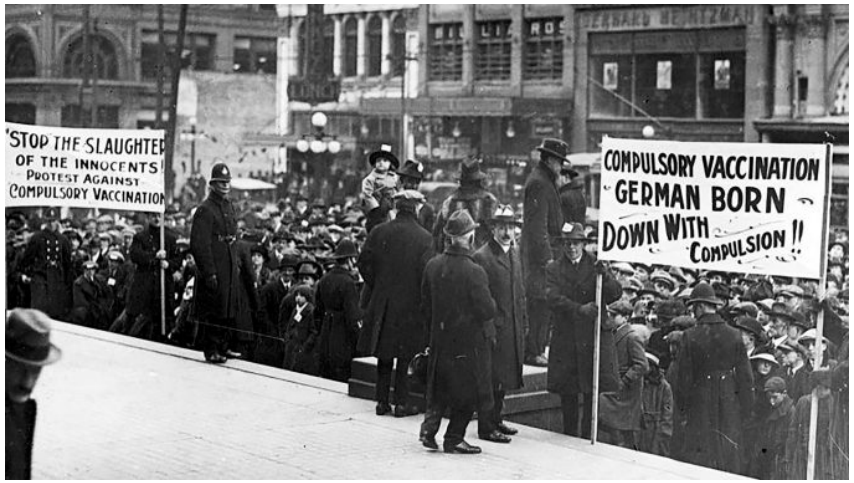

We found the vaccine for covid-19 !
But you didn't test it on humans?
He is human, those are side effects.


JOE HELLER ©2022 HELLERTOON.COM
IT'S RECOMMENDED THAT YOU GET ANOTHER BOOSTER SHOT.
THAT'S JUST LIKE BILL GATES TO INSTALL A MICROCHIP THAT ALWAYS NEEDS UPGRADING!


VACCINATION



Vaccine Setbacks



- 1901, 13 children died of ***tetanus-contaminated*** diphtheria antitoxin in St. Louis and 9 children in NJ died from tainted smallpox vaccine.
- 1955, Cutter Laboratories ***polio vaccine*** spread polio due to lack of inactivation of the live polio virus in the vaccine
- 1976 Guillain-Barre syndrome was associated with the widespread use of inactivated A H1N1 (swine) virus vaccine (1976-1977)
  - *Rate 1 per 100K with H1N1, as compared to 1 per 1 million vaccinated with Influenza*
  - *Cause never confirmed*
- 1998 Lancet MMR autism fraud paper by Wakefield A.
- Vaccine mandates or Compulsory vaccination has never been popular from Victorian times to now (Government vs. Personal Freedom)

Vaccine Hesitancy

- Definition:

  "Delay in acceptance or refusal of vaccines despite availability of vaccination services"

- 1968 to 2019, there are only 768 publications about vaccine hesitancy listed in Pubmed; *>7,470 since 2020!*

- 2015 WHO published "Recommendations on Vaccine Hesitancy" in a special issue of the journal Vaccine.

Vaccine Hesitancy- Suggested Approaches by WHO Reviewers

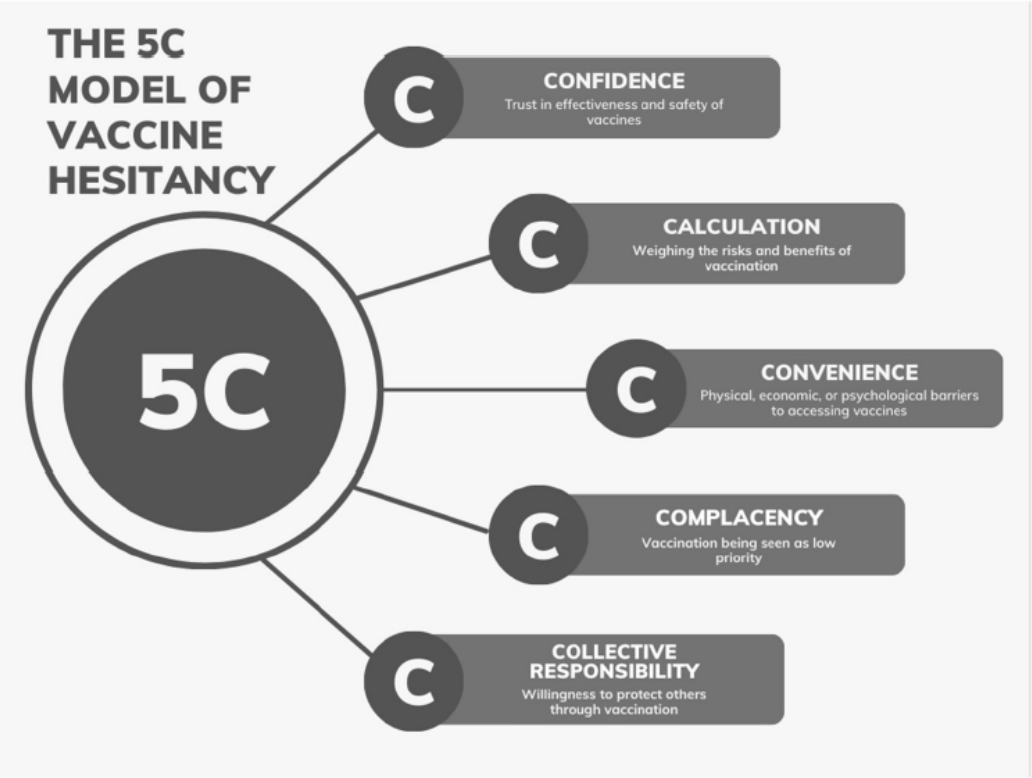
- Approaches with some benefit identified
  - *Directly targeted interventions to unvaccinated or under-vaccinated populations*
  - *Interventions aimed at improving vaccination knowledge and awareness*
  - *Improve convenience and access to vaccination*
  - *Interventions targeted to specific populations (HCW)*
  - *Mandated vaccinations or sanction against non-vaccination – very controversial!*
  - *Engaging with religious or other influential leaders to promote vaccination*

- *Tailored interventions to specific populations and their specific concerns were the most effective in the WHO review.*
- *"Interventions to increase uptake that are multi-component and/or have a focus on dialogue-based approaches tend to perform better."*

Jarrett C, et al, 2015

Vaccine Hesitancy- With COVID!

- Nwachukwu G and colleagues did a systematic review of 544 studies evaluating vaccine hesitancy with COVID-19 vaccines in the US



Variables	Category	Frequency	Percentage
Hesitancy Predictors	Health Concerns	311	20.97%
	Speed of Vaccine Development/Safety Concerns	289	19.49%
	Mistrust	206	13.89%
	Misinformation/Misperception	96	6.47%
	Systemic and Institutional Factors	91	6.14%
	Political and Ideological	76	5.12%
	Psychological Factors	69	4.65%
	Racial and Ethnic Influences	61	4.11%
	Social Influence	49	3.30%
	Demographics and Identity	44	2.97%
	Psychosocial Factors	41	2.76%
	Cultural Beliefs	31	2.09%
	Accessibility Issues	27	1.82%
	Economic Factors	26	1.75%
	Individual Experiences	19	1.28%
	Communication and Messaging	15	1.01%
	Technological Aspects	10	0.67%
	Environmental Factors	9	0.61%
	Global and Local Dynamics	5	0.34%
	Legal and Ethical Considerations	3	0.20%
	N/A	3	0.20%
	Compliance and Convenience	2	0.13%
Uptake Factors	Trust and Confidence	186	13.18%
	Community and Social Factors	133	9.43%
	Demographics and Identity	130	9.21%
	Healthcare Provider Recommendations	117	8.29%
	Health Concerns	113	8.01%
	Psychological Factors	92	6.52%
	Information Sources and Education	92	6.52%
	External Motivations and Support	81	5.74%
	Vaccination History	68	4.82%
	Previous Experiences and Behavior	65	4.61%
	Safety	60	4.25%
	Political and Social Influences	52	3.69%
	Vaccine Choice	45	3.19%
	Policy and Communication	42	2.98%
	Media and Information Influence	26	1.84%
	N/A	23	1.63%
	Ending Pandemic	24	1.70%
	Job Security	18	1.28%
	Mandate	16	1.13%
	Incentives and Rewards	14	0.99%
	Availability	12	0.85%

Nwachukwu G, et al, 2024

Vaccine Hesitancy- With COVID Vax!

- *Key factors driving vaccine **hesitancy***
  - *Health concerns (20.97%)*
  - *Vaccine characteristics (19.49%)*
  - *Mistrust (13.89%)*

- *Key factors driving vaccine **uptake***
  - *Trust and confidence (13.18%)*
  - *Community and social factors (9.43%)*
  - *Demographics and identity (9.21%)*

Table A4. Population studies with vaccination acceptance rates.

Population Studied	Acceptance Rate (Avg)
Arab	74.35%
Asian	66.7%
White	62.9%
Minority Population	60.07%
Hispanic	57.59%
Black/African-American	56.07%

Nwachukwu G, et al, 2024

Vaccine Hesitancy- in African Americans

- *Savoia and colleagues performed a systematic review of the reasons for vaccine hesitancy in AA populations*
- *30 Qualitative and quantitative studies were reviewed*
- ***Factors***
  - *Age 18-24yo less likely to get vaccinated*
  - *Education was inconsistent with some college educated populations doing worse*
  - *Higher incomes more likely to be vaccinated*
  - *More religious more likely to be vaccinated*
  - *Political party association was a non-factor*
  - *All 5 studies showed a positive association between beliefs about the **safety and effectiveness** of the vaccine and vaccine acceptance.*
  - *All 6 studies showed the impact of **Mistrust/Trust** in HS and Providers*

Savoia E, et al, 2024

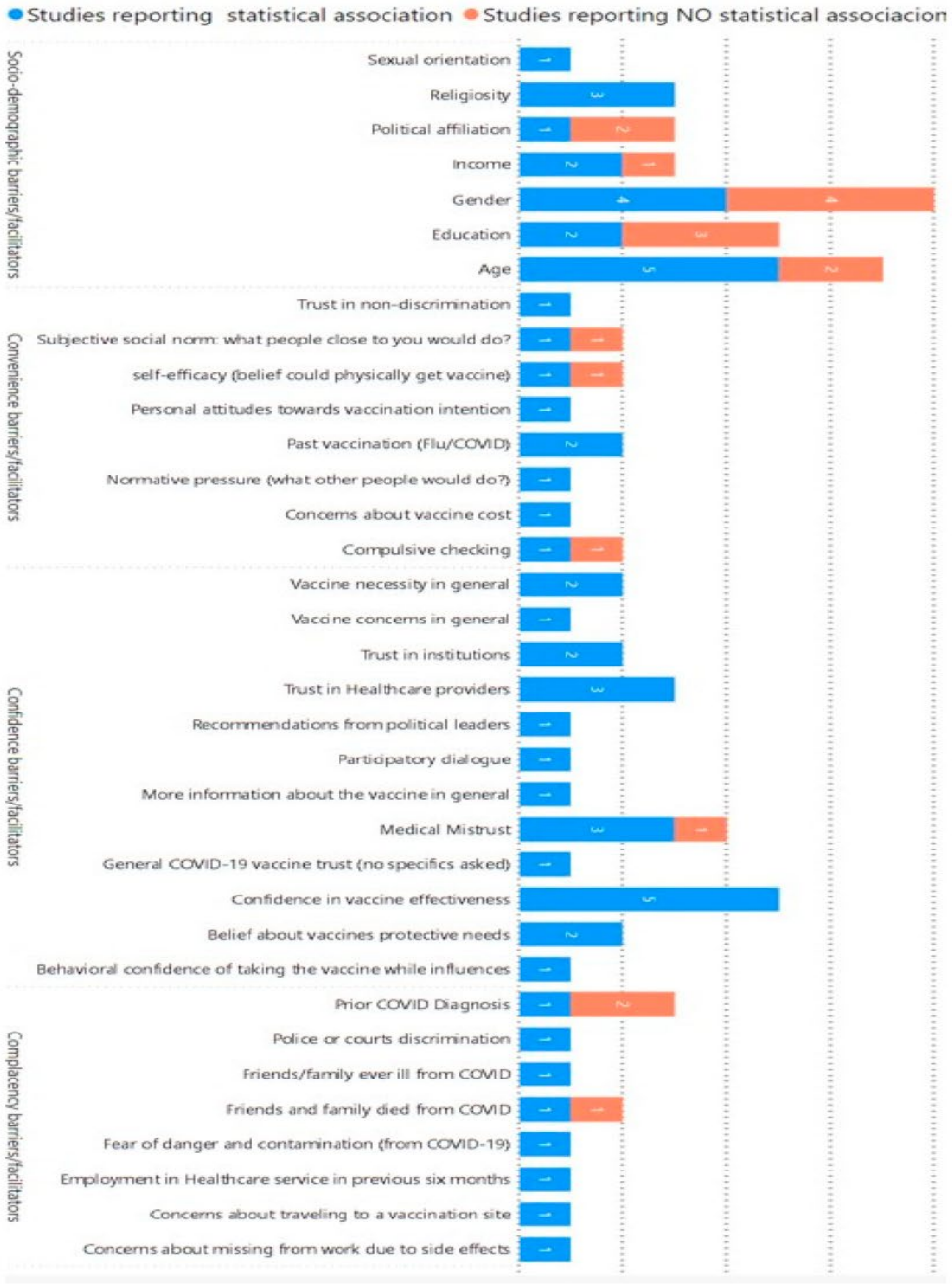


Figure 2. Distribution of variables examined by the quantitative studies (based on the 3C model [1]).

Vaccination Rates

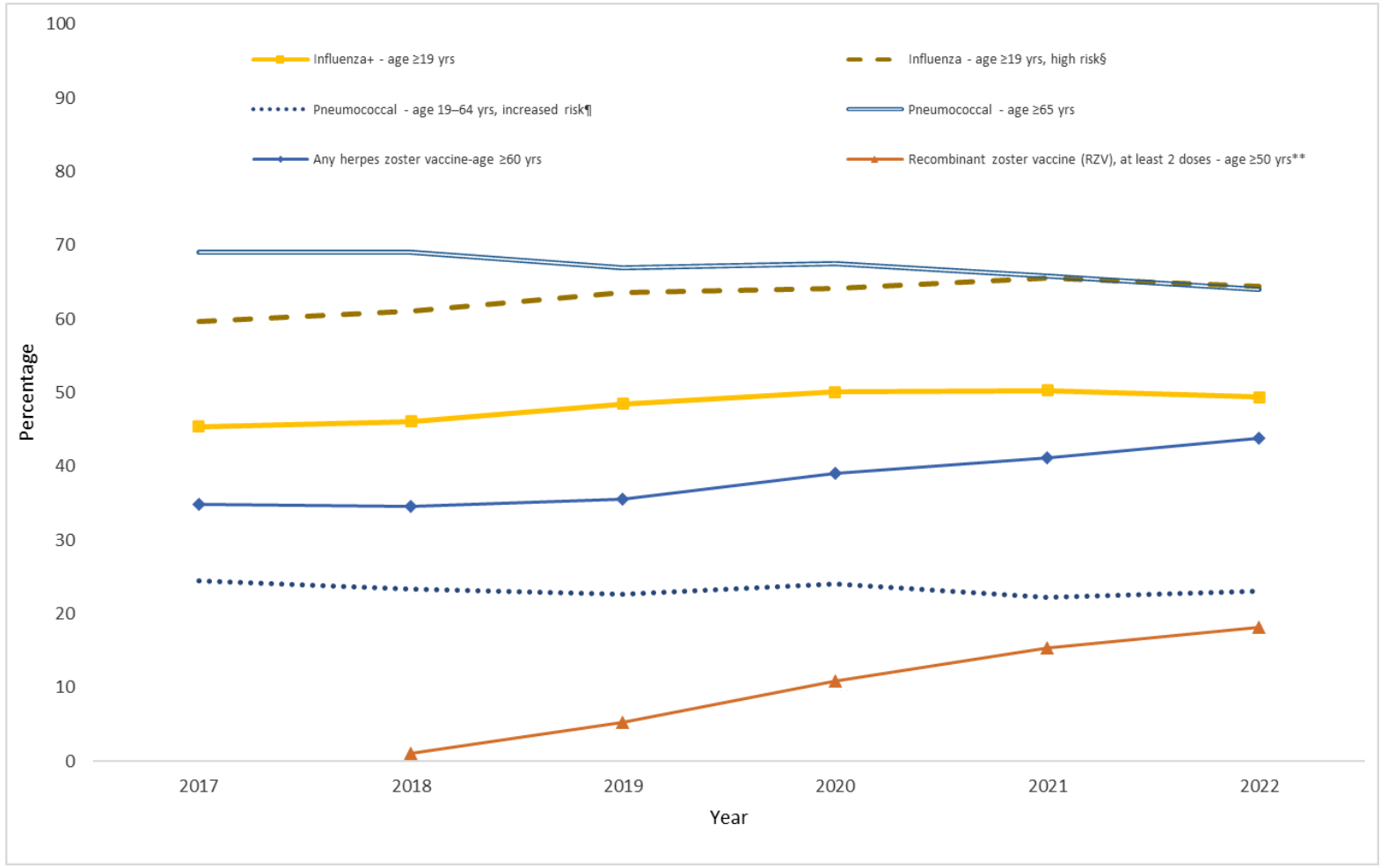
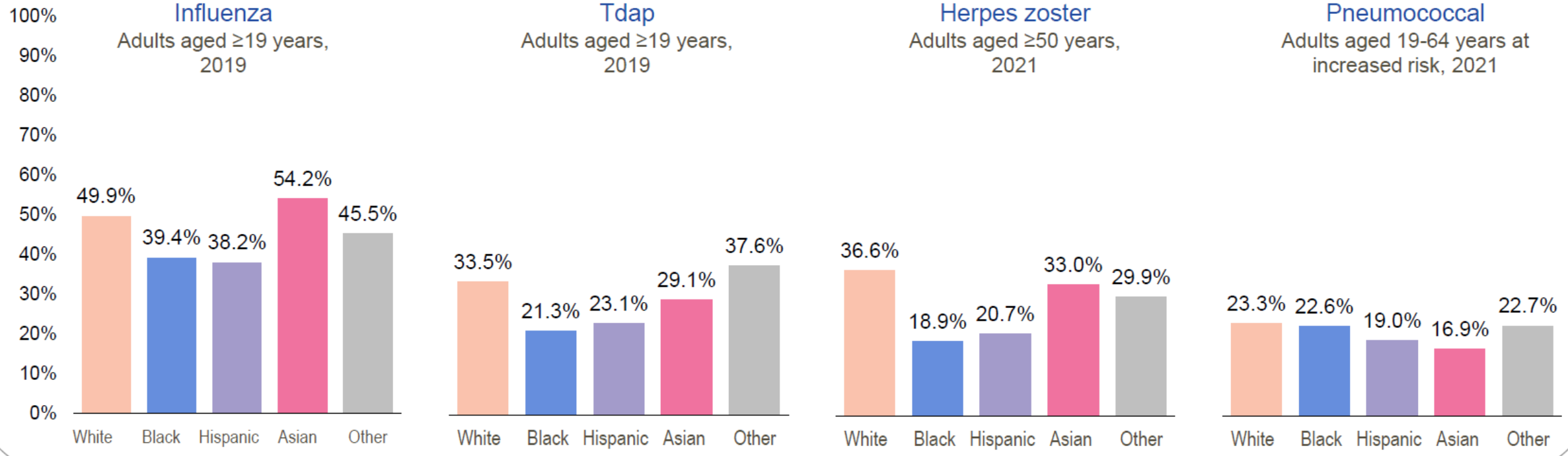


FIGURE 1. Estimated proportion of adults aged ≥19 years who received selected vaccines,* by age group and risk status — National Health Interview Survey, United States, 2017–2022

Vaccination Rates

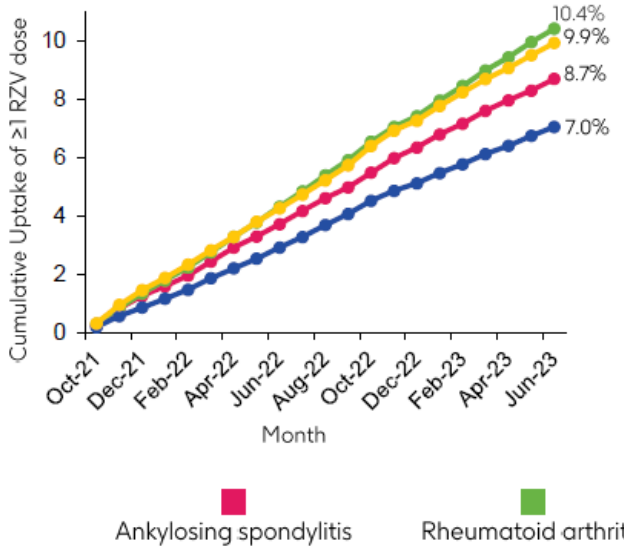


1. CDC. Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2019-2020. https://www.cdc.gov/vaccines/imzmanagers/coverage/adultvaxview/pubs-resources/vaccination-coverage-adults-2019-2020.html; 2. CDC. Vaccination Coverage among Adults in the United States, National Health Interview Survey, 2021. https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/vaccination-coverageadults-2021.html.

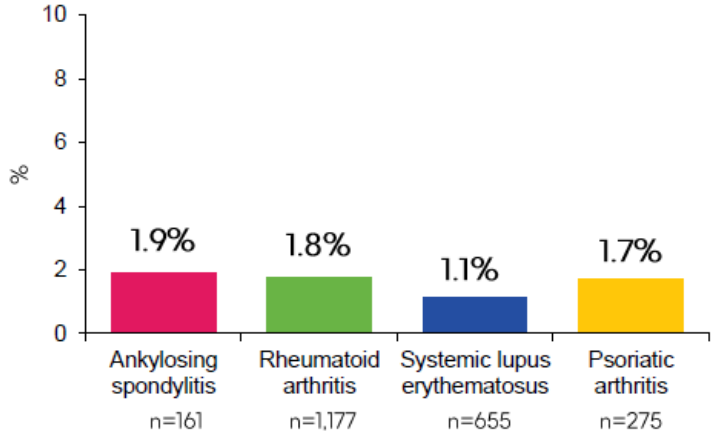
Vaccination Rates

RESULTS: RZV uptake

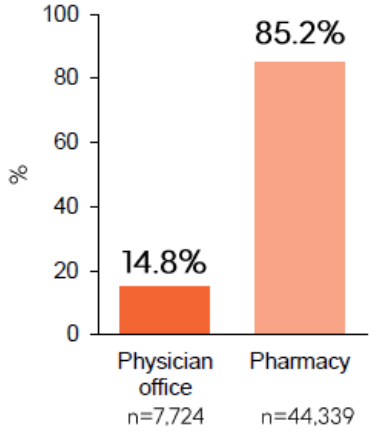
Cumulative RZV uptake was 9.5% and ranged from 7.0% to 10.4% by condition through June 2023



Cumulative RZV uptake among adults 19-49 years of age ranged from **1.1% to 1.8%** by condition



Majority of patients received their **1st RZV dose at a pharmacy**



A majority (67.9%) of in-clinic RZV vaccinations were given by family or internal medicine physicians

Gatwood J, et al. Recombinant Zoster Vaccine Uptake in US Adult with Rheumatic Disease: A Mixed Methods Analysis. ACR 2024.

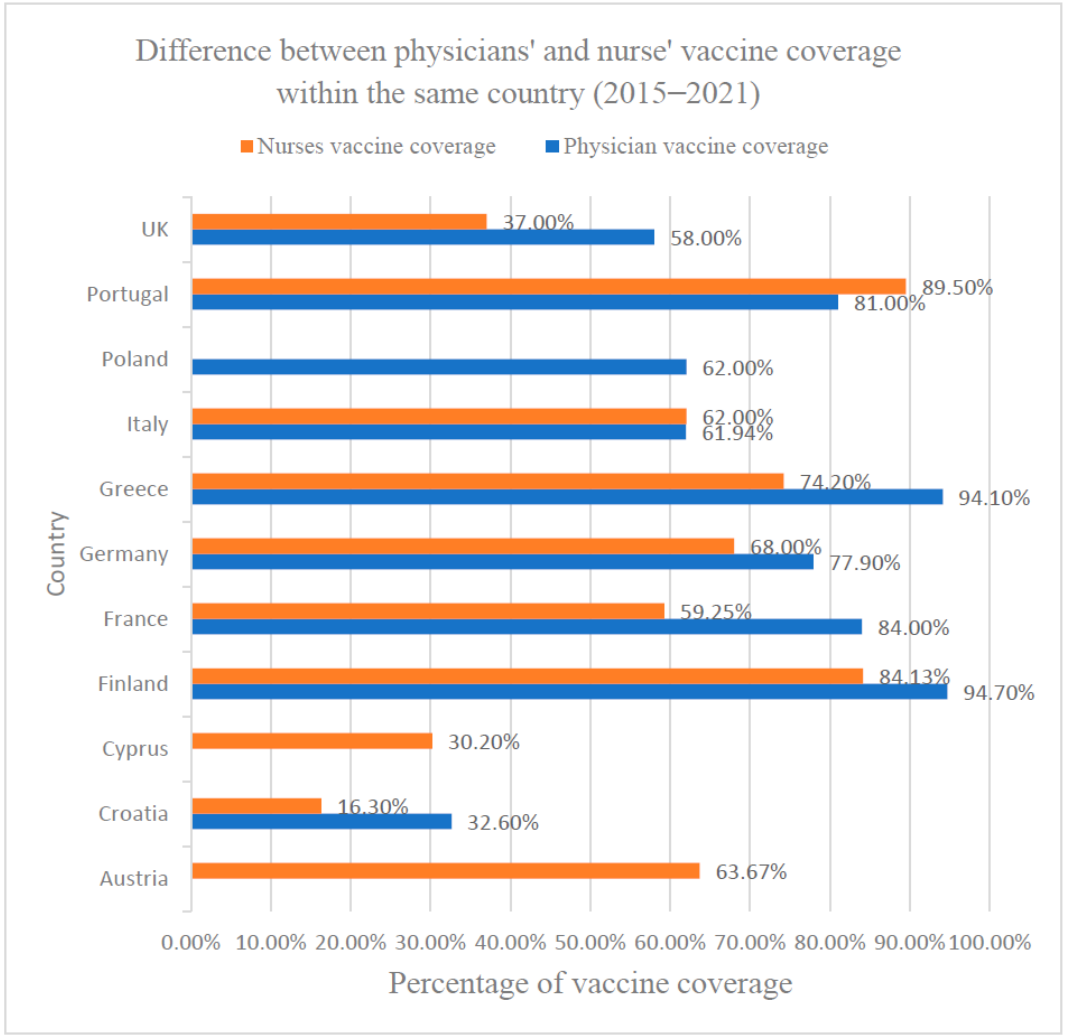
Vaccine Hesitancy- It is also HCW

In our 2015 paper, we looked at Vaccinations in Autoimmune Disease patients

- ***Only 20%*** *of patients were receiving both influenza and pneumococcal vaccines in Rheumatology practices*
- ***Safety concerns*** that have been raised beyond viral or pathogen-associated disease include Guillain-Barre syndrome (GBS) and other autoimmune disorders, autism, thimerosal-associated toxicity, and other neurologic complications.
- ***AD specific concerns*** included development of disease flares, new AD processes, autoantibodies emergence,
- ***Presence of adjuvants***
  - Alleged associations between squalene and Gulf War syndrome, and aluminum and macrophagic myofasciitis
- ***Lack of knowledge of when to dose vaccines***
- ***Safety concerns*** – no increase in viral diseases, or autoimmune disease severity or illness found in large trials
  - No increase in GBS
  - No increase in complications
- ***AD specific concerns***
  - No increase in disease flares in large trials
  - Autoantibodies were seen as only transient in clinical trials, no clinical effect
- ***Adjuvants***
  - All vaccines containing adjuvants are tested before licensing and have been used since 1940s
  - Adjuvanted vaccines do increase reaction at the injection site (better immune response)
  - Only one observational study suggested possible association between aluminum and eventual development of asthma
  - No clinical trial has demonstrated an association between adjuvanted vaccines and development of AD

McKinnon JE, et al, 2015; CDC.gov; Tavares Da Silva F, 2015

Vaccine Hesitancy- It is also **HCW**



This includes several vaccines like Influenza, Covid-19 and others.

Positive Factors	Total Studies (n)	Country
Protection of Others	15	Cyprus, Czech Republic, France, Greece, US, Egypt, Tunisia, Singapore, Lebanon, Palestine, UAE
Control Pandemic/Disease	11	Cyprus, China, Czech Republic, Egypt, France, Greece, Lebanon, Switzerland, Turkey, UAE
Protect Themselves	11	Cyprus, Greece, Switzerland, Egypt, Tunisia, China, Singapore, Lebanon
Knowledge of COVID-19 and the Vaccine	11	Albania, Cyprus, Greece, Kosovo, Spain, US, China, Azerbaijan, Lebanon
Increased Perception of Risk	11	France, China, Singapore, Saudi Arabia, UAE
Trust in Government and Health Authorities	10	Albania, Cyprus, Greece, Kosovo, Spain, Tunisia, China, Lebanon
Increased Fear of COVID-19	9	Albania, Cyprus, Czech Republic, France, Greece, Kosovo, Spain, Lebanon, Palestine
Vaccine Safety	9	China, Greece, India, Azerbaijan, Saudi Arabia, Turkey
Increased Susceptibility to Disease	6	Switzerland, Egypt, China, Iraq, Lebanon, Palestine, Turkey
Negative Factors		
Vaccine Safety/Side Effects	32	Albania, Cyprus, Czech Republic, France, Germany, Greece, Italy, Kosovo, Slovakia, Spain, Switzerland, UK, US, Tunisia, Lebanon, China, Palestine, Turkey, UAE
Effectiveness and Efficacy	18	Albania, Cyprus, Czech Republic, Greece, Italy, Kosovo, Slovakia, Spain, UK, US, Tunisia, China, Lebanon, Palestine, Turkey
Previous COVID-19 Infection	16	Albania, Cyprus, Czech Republic, France, Greece, Italy, Kosovo, Slovakia, Spain, UK, US, Egypt, Azerbaijan, Lebanon, Turkey
Quick Vaccine Development	11	Cyprus, France, Greece, Italy, UK, India, Lebanon
Lack of Trust	11	Cyprus, Czech Republic, Greece, Italy, UK, Turkey
Lack of Information/Knowledge	10	Cyprus, Germany, Greece, India, Palestine
Misinformation	7	Switzerland, Egypt, Palestine
Infection not Severe/Harmful to Self	6	Cyprus, Switzerland, Egypt, UAE
Vaccine Content	4	France, Italy, Lebanon, Turkey
Vaccine Novelty	4	US
Wanting Others to take it First	4	US
Insufficient Time	3	Egypt, China
Vaccine Approval Process	2	Cyprus

Kaur M, et al, 2023; Ghare F, et al, 2023

Vaccine Safety

- **Vaccine adjuvants and safety**
  - Aluminum and monophosphoryl lipid A. Aluminum, in the form of alum, has been used for nearly 90 years in vaccines
  - New adjuvants are also being used successfully including MF59, AS03 (influenza vaccines)
- **Vaccines DO NOT CAUSE autism**
  - No links in larger studies (Hviid et al., 2003; Madsen et al., 2002; Schechter and Grether, 2008; Taylor et al., 2014).
  - Institute of Medicine, CDC did not find associations
- **Thimerosal and Preservatives**
  - Thimerosal was reduced/eliminated from childhood vaccines due to theoretical concerns
  - There are several other preservatives used today to prevent contaminations of the vaccines

Fields Virology, 2023; Goodman & Gilmans, 2023.

Vaccine Side Effects- Myocarditis

- Studies have shown that the prognosis for myocarditis post vaccination is favorable, particularly in young patients.
  - In the study by Semenzato L and colleagues, they proceeded to further evaluate the complications post myocarditis due to COVID-19 infections, vaccination and other causes
  - Using the French National Health Data System- all 4635 patients hospitalized in France with myocarditis from December 2020 to June 2022 were evaluated

Table 3. Associations Between Clinical Outcomes and Myocarditis Groups Over 18 Months

Outcome	Postvaccine myocarditis (n = 558)		Post–COVID-19 myocarditis (n = 298)		Conventional myocarditis (n = 3779)	
	No. of events (%)	Weighted hazard ratio[a]	No. of events (%)	Weighted hazard ratio[a]	No. of events (%)	Weighted hazard ratio[a]
Rehospitalization for myopericarditis	18 (3.2)	0.75 (0.40-1.42)	12 (4.0)	1.07 (0.53-2.13)	220 (5.8)	1
Cardiovascular event (excluding myopericarditis)	15 (2.7)	0.54 (0.27-1.05)	22 (7.4)	1.01 (0.62-1.64)	277 (7.3)	1
Heart failure, heart rhythm and conduction disorders, cardiomyopathy[b]	6 (1.1)	0.53 (0.07-4.28)	11 (3.7)	1.23 (0.58-2.63)	132 (3.5)	1
Hospitalization for any cause	68 (12.2)	0.69 (0.50-0.94)	63 (21.1)	1.04 (0.73-1.48)	739 (19.6)	1
Death from any cause	1 (0.2)		4 (1.3)		49 (1.3)	1
Composite outcome 1[c]	32 (5.7)	0.55 (0.36-0.86)	36 (12.1)	1.04 (0.70-1.52)	497 (13.2)	1
Composite outcome 2[c]	75 (13.4)	0.64 (0.48-0.85)	76 (25.5)	1.03 (0.75-1.40)	874 (23.1)	1

[a] Weighted Cox regression model was used to standardize comparisons according to sociodemographic characteristics and comorbidities of conventional myocarditis described in Table 2. Associations could not be estimated when the number of events was rare (<5).

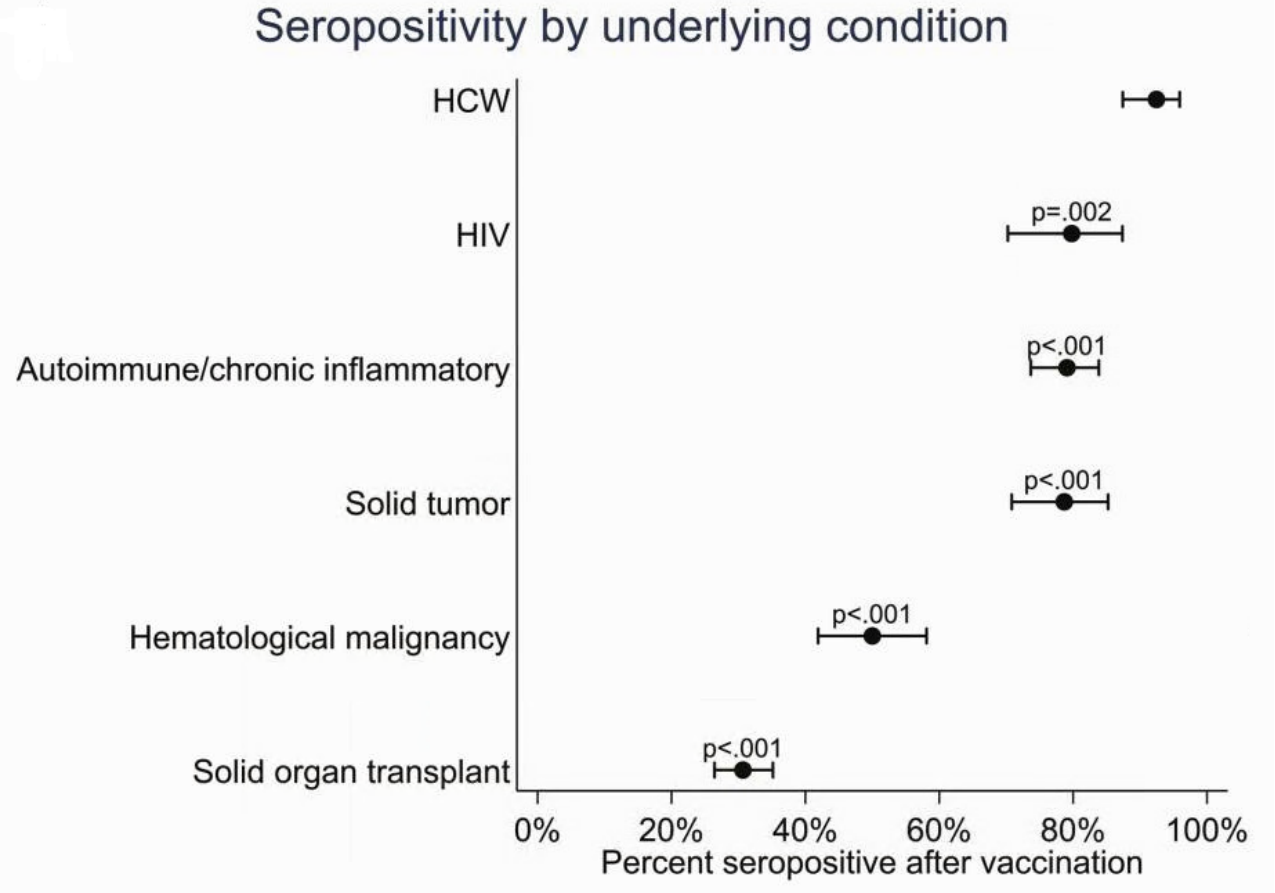
[b] During the follow-up, infarction occurred in 3/558 patients (0.5%) with postvaccine myocarditis, 4/298 (1.3%) with post-COVID-19 myocarditis, and 56/3779 (1.5%) with conventional myocarditis; cardiac rhythm disorders occurred in 3/558 (0.5%), 5/298 (1.7%), and 52/3779 (1.4%) patients, respectively; and heart failure occurred in 3/558 (0.5%), 7/298 (2.3%), and 45/3779 (1.2%) patients, respectively.

[c] Composite outcome 1: rehospitalization for myopericarditis, cardiovascular event, or death from any cause. Composite outcome 2: rehospitalization for myopericarditis, cardiovascular event, hospitalization for any cause (>1 night stay), or death from any cause.

"Patients with post–COVID-19 mRNA vaccination myocarditis, contrary to those with post–COVID-19 myocarditis, show a ***lower frequency of cardiovascular complications*** *than those with conventional myocarditis at 18 months. However, affected patients, mainly healthy young men, may require medical management* up to several months after hospital discharge."

Semenzato L, et al. JAMA, 2024

Prospective Evaluation of Coronavirus Disease 2019 (COVID-19) Vaccine Responses Across a Broad Spectrum of Immunocompromising Conditions: the COVID-19 Vaccination in the Immunocompromised Study (COVICS).



Haidar G, Agha M et al. *Clin Infect Dis*. 2022 Aug 24;75(1):e630-e644. PMID: 35179197

Covid Vaccine Myths according to AARP

- The vaccines were developed too quickly
- The vaccines will alter your DNA
- If you had COVID-19, you don't need to get vaccinated
- The vaccines cause variants
- The vaccines use a live version of the coronavirus
- The vaccines contain microchips or can cause you to be magnetic
- The vaccines can cause fertility problems
- You shouldn't get the vaccine if you ever had an allergic reaction
- COVID doesn't affect kids as much, so they don't need the vaccine
- If the vaccines worked, we wouldn't need to update them

www.aarp.org. Publish May 17th, 2023

Vaccine Successes!

Primary Goals of Vaccination

- ***Prevention or modification of infectious diseases***
  - *Most viral vaccines are aimed to prevent or modify the disease **without** necessarily prevention infection*
  - *Vaccines can prevent diseases like post exposure disease for rabies, rubella virus, hepatitis B virus and others*

- ***Control of epidemic infection within populations (HERD Immunity)***
  - *Vaccines can provide community immunity with **oral live poliovirus vaccines** leading to reduction in poliomyelitis,*

- **Vaccines as cancer prevention**
  - *HBV prevents liver cancer and HPV vaccines prevent cervical and other cancers related to HPV*

Fields Virology, 2023; Rodrigues CM, Plotkin SA, 2020

Primary Goals of Vaccination

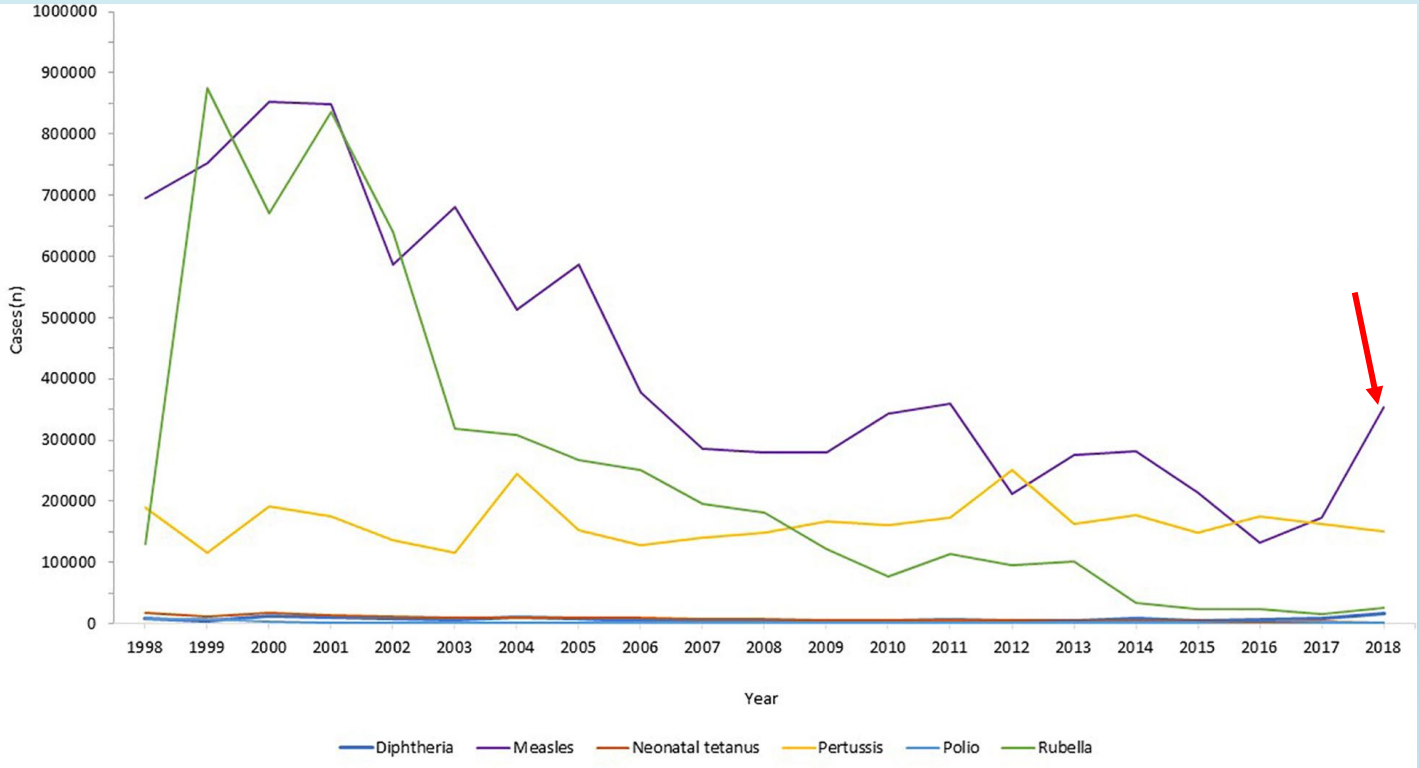
- **Vaccination as immunotherapy**
  - *This is seen in VZV vaccination where the use of live vaccine reduces the incidence of Herpes Zoster and postherpetic neuralgia*
  - ***Similar strategies are used for HPV, and evaluated for HIV and HBV***

- **Vaccination for eradication or elimination of a disease,**
  - This is possible for diseases where humans are the only host and natural reservoir. This was achieved with Smallpox vaccination with vaccinia virus vaccine.
  - Semi-eradication has been achieved with vaccines against polio, measles, mumps, rubella, rabies and VZV, yellow fever and Japanese encephalitis

Fields Virology, 2023; Rodrigues CM, Plotkin SA, 2020

TABLE 1 | Vaccine impact in United States comparing the incidence of diseases prior to the implementation of vaccine (Roush and Murphy, 2007), described as the pre-vaccine era and the vaccine coverage (Hill et al., 2017) and disease incidence (Centers for Disease Control and Prevention, 2017) in 2017, as reported by the Centers for Disease Control and Prevention.

Vaccine	Peak cases in prevaccine era (year)	Vaccine coverage in children 19–35 months old (% [95% CI])	Cases in 2017 (*n*)	Disease reduction (%)
Smallpox	110, 672 (1920)	–	0	100
Diphtheria	30, 508 (1936)	94.0 (93.3 – 94.7)	0	100
Measles (non-imported)	763, 094 (1958)	91.5 (90.6 – 92.3)	99	99.99
Mumps	212, 932 (1964)	91.5 (90.6 – 92.3)	6,109	97.13
Rubella	488, 796 (1964)	91.5 (90.6 – 92.3)	7	100.00
Congenital rubella syndrome	20, 000 (1964 – 65)	–	5	99.98
Pertussis	265, 269 (1934)	94.0 (93.3 – 94.7)	18,975	92.85
Polio (paralytic)	21, 269 (1952)	92.7 (91.9 – 93.5)	0	100
Tetanus	601 (1948)	94.0 (93.3 – 94.7)	33	94.51



Rodrigues CM, Plotkin SA, 2020. WHO

Other Benefits

- **Reduction** in secondary infections that complicate vaccine-preventable diseases
- Vaccines are highly beneficial on a population level and **cost-effective** in comparison to other public health interventions.
- Productivity gains
  - Economic growth
  - Healthy children have improved learning
- Minimizing the impact of diseases on families
- Cost-Effective preparedness for Outbreaks
- Impact on life expectancy and opportunity

Vaccine Successes

- **Smallpox became the first human infectious disease to be eradicated by vaccination**
- **HBV vaccine was the first vaccine to regarded as an anticancer vaccine**
- ***HPV is the second anticancer vaccine***
- **Polio vaccination has nearly eradicated polio and almost eliminated polio induced paralysis**
- **Herd immunity- protect those that cannot be vaccinated**
  - *Think protection of newborns, pregnant women, immunosuppressed patients*

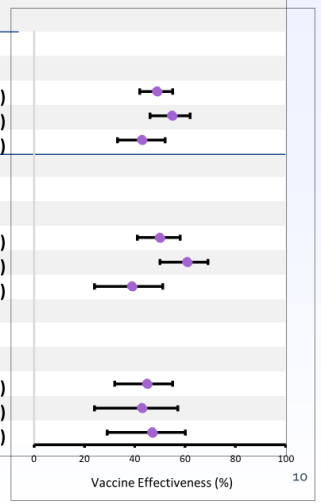
Rodrigues CMC, Plotkin SA, 2020; Fields Virology, 2023.

Primary Aims of COVID-19 Vaccines
- Prevent symptomatic infection
- Prevent hospitalizations

ICATT: VE of *2023-2024 COVID-19 vaccine* against *symptomatic infection* among adults aged ≥18 years, by age group and time since dose

September 2023 – February 2024

COVID-19 dosage pattern/age group	Total tests	SARS-CoV-2-test-positive, N (%)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No updated (2023-2024) monovalent dose (ref)	10,829	4,080 (38)	676 (427 to 859)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	1,537	408 (27)	61 (33 to 86)	**49 (42 – 55)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	735	170 (23)	32 (20 to 46)	**55 (46 – 62)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	720	214 (30)	82 (71 to 95)	**43 (33 – 52)**
18-49 years				
No updated (2023-2024) monovalent dose (ref)	8,676	3,152 (36)	691 (439 to 877)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	943	229 (24)	61 (34 to 85)	**50 (41 – 58)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	452	87 (19)	32 (19 to 46)	**61 (50 – 69)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	445	130 (29)	81 (70 to 94)	**39 (24 – 51)**
≥50 years				
No updated (2023-2024) monovalent dose (ref)	2,153	928 (43)	593 (400 to 800)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	594	179 (30)	62 (32 to 89)	**45 (32 – 55)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	283	83 (29)	32 (21 to 44)	**43 (24 – 57)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	275	84 (31)	84 (72 to 98)	**47 (29 – 60)**



Link-Gelles, et al. MMWR 2024: http://dx.doi.org/10.15585/mmwr.mm7304a2 (Results updated with additional month of data since publication.)

10

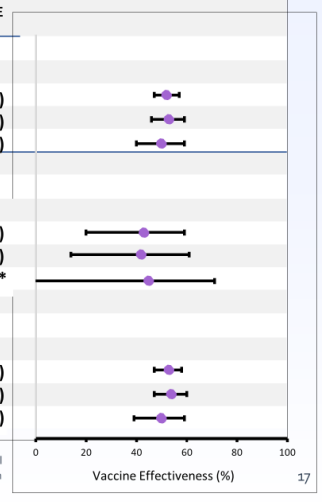
VISION: VE of *2023-2024 vaccine* against *hospitalization* among immuno*competent* adults aged ≥18 years, by age group

September 2023 – January 2024

COVID-19 dosage pattern/age group	COVID-19 case-patients N (Col %)	COVID-19 control-patients N (Col %)	Median interval since last dose among vaccinated among those vaccinated, days (IQR)	Adjusted VE (95% CI)
≥18 years				
No updated (2023-2024) monovalent dose (ref)	4,194 (91)	28,715 (87)	627 (383-765)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	395 (9)	4,199 (13)	42 (24-62)	**52 (47-57)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	270 (6)	3,056 (9)	32 (19-45)	**53 (46-59)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	125 (3)	1,143 (3)	73 (66-81)	**50 (40-59)**
18-64 years				
No updated (2023-2024) monovalent dose (ref)	938 (96)	11,342 (95)	685 (447-829)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	38 (4)	657 (5)	38 (22-58)	**43 (20-59)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	28 (3)	503 (4)	30 (19-44)	**42 (14-61)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	10 (1)	154 (1)	74 (67-81)	**45 (-6-71)***
≥65 years				
No updated (2023-2024) monovalent dose (ref)	3,256 (90)	17,373 (83)	549 (370-745)	**Ref**
Updated (2023-2024) monovalent dose, ≥7 days	357 (10)	3,542 (17)	43 (25-62)	**53 (47-58)**
Updated (2023-2024) monovalent dose, 7-59 days earlier	242 (7)	2,553 (12)	32 (19-46)	**54 (47-60)**
Updated (2023-2024) monovalent dose, 60-119 days earlier	115 (3)	989 (5)	73 (66-81)	**50 (39-59)**

VE estimates adjusted for age, sex, race and ethnicity, geographic region, and calendar time. MMWR to be published February 29, 2024

*Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation.



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Link-Gelles, et al. MMWR 2024: http://dx.doi.org/10.15585/mmwr.mm7304a2 (Results updated with additional month of data since publication.)

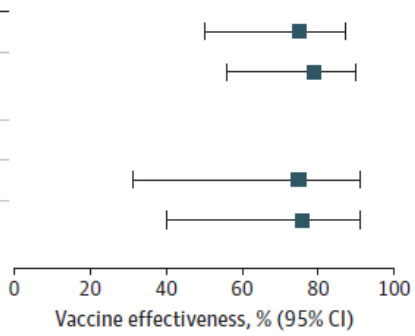
RSV Vaccine Effective Against Hospitalization

- Prelicensure trials were not able to evaluate efficacy against RSV-associated hospitalization
- Included recombinant RSVPreF3 adjuvanted (Arexvy, GlaxoSmithKline) and Recombinant RSVPreF (Abrysvo, Pfizer, Inc.)
- Case-control trial of adults ≥60yo
  - Hospitalized with acute respiratory illness
  - 24 hospitals, 19 states
  - 10/1/2023 to 3/31/2024
  - 2978 adults included

- Key Results
  - VE against RSV-associated hospitalization was 75% (95% CI-50%-87%)

Figure. Vaccine Effectiveness Against Respiratory Syncytial Virus (RSV)–Associated Hospitalization Among Adults 60 Years and Older

Group	Vaccinated RSV case patients, No./total No. (%)	Vaccinated control patients, No./total No. (%)	Days since RSV vaccination, median (IQR)	Vaccine effectiveness, % (95% CI)
Adults aged ≥60 y, unweighted[a]	9/367 (2.5)	256/2611 (9.8)	84 (54-125)	75 (50-87)
Adults aged ≥60 y, inverse probability of vaccination weighting[b]	9/367 (2.5)	256/2611 (9.8)	84 (54-125)	79 (56-90)
Age group, y, unweighted[a]				
60-74	4/214 (1.9)	118/1542 (7.7)	88 (57-128)	75 (31-91)
≥75	5/153 (3.3)	138/1069 (12.9)	81 (50-123)	76 (40-91)



Surie D, et al, JAMA, 2024

Current Adult Vaccinations

Recommended Adult Immunization Schedule
for ages 19 years or older

UNITED STATES
2025

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, egg-based)	IIV3	Multiple
	aIIV3	Fluad
	HD–IIV3	Fluzone High–Dose
Influenza vaccine (inactivated, cell–culture)	ccIIV3	Flucelvax
Influenza vaccine (recombinant)	RIV3	Flublok
Influenza vaccine (live, attenuated)	LAIV3	FluMist
Measles, mumps, and rubella vaccine	MMR	M–M–R II, Priorix
Meningococcal serogroups A, C, W, Y vaccine	MenACWY–CRM	Menveo
	MenACWY–TT	MenQuadfi
Meningococcal serogroup B vaccine	MenB–4C	Bexsero
	MenB–FHbp	Trumenba
Meningococcal serogroup A, B, C, W, Y vaccine	MenACWY–TT/ MenB–FHbp	Penbraya
Mpox vaccine	Mpox	Jynneos
Pneumococcal conjugate vaccine	PCV15	Vaxneuvance
	PCV20	Prevnar 20
	PCV21	Capvaxive
Pneumococcal polysaccharide vaccine	PPSV23	Pneumovax 23
Poliovirus vaccine (inactivated)	IPV	Ipol
Respiratory syncytial virus vaccine	RSV	Abrysvo, Arexvy, mResvia
Tetanus and diphtheria vaccine	Td	Tenivac
Tetanus, diphtheria, and acellular pertussis vaccine	Tdap	Adacel, Boostrix
Varicella vaccine	VAR	Varivax
Zoster vaccine, recombinant	RZV	Shingrix

Vaccine	19–26 years	27–49 years	50–64 years	≥65 years
COVID–19	1 or more doses of 2024–2025 vaccine (See Notes)			2 or more doses of 2024-2025 vaccine (See Notes)
Influenza inactivated (IIV3, ccIIV3) **Influenza recombinant** (RIV3)	1 dose annually			1 dose annually (HD–IIV3, RIV3, or aIIV3 preferred)
Influenza inactivated (aIIV3; HD–IIV3) **Influenza recombinant** (RIV3)	Solid organ transplant (See Notes)			
Influenza live, attenuated (LAIV3)	1 dose annually			
Respiratory syncytial virus (RSV)	Seasonal administration during pregnancy (See Notes)		60 through 74 years (See Notes)	≥75 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 health care 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, PCV21, 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	2 doses			
Inactivated poliovirus (IPV)	Complete 3-dose series if incompletely vaccinated. Self–report of previous doses acceptable (See Notes)			

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

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

Recommended vaccination based on shared clinical decision–making

No Guidance/ Not Applicable

https://www.cdc.gov/vaccines/hcp/imz-schedules/downloads/adult/adult-combined-schedule.pdf

Table 2 Recommended Adult Immunization Schedule by Medical Condition or Other Indication, United States, 2025

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 medical conditions or 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	Health care Personnel[b]
			<15% or <200mm³	≥15% and ≥200mm³							
COVID–19		See Notes									
Influenza Inactivated Influenza recombinant		Solid organ transplant (See Notes)	1 dose annually								
LAIV3					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			Liver disease (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
IPV		Complete 3-dose series if incompletely vaccinated. Self–report of previous doses acceptable (See Notes)									

- Recommended for all adults who lack documentation of vaccination, **OR** lack evidence of immunity
- Not recommended for all adults, but recommended for some adults based on either age **OR** increased risk for or severe outcomes from disease
- Recommended vaccination 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

Recent Vaccine News! October 23-24, 2024

Pneumococcal Vaccines

- ACIP recommends a pneumococcal conjugate vaccine (PCV) for all PCV-naïve adults aged ≥50 years
- ACIP recommends **PCV21** as an option for adults aged ≥19 years who currently have a recommendation to receive a dose of PCV.

COVID-19 Vaccines

In addition to previously recommended 2024-2025 vaccination:

- ACIP recommends **a second dose*** of 2024-2025 COVID-19 for adults ages 65 years and older
- ACIP recommends **a second dose**** of 2024-2025 COVID-19 vaccine for people ages 6 months-64 years who are moderately or severely immunocompromised
- ACIP recommends **additional doses (i.e., 3 or more doses)** of 2024-2025 COVID-19 vaccine for people ages 6 months and older who are moderately or severely immunocompromised under ***shared clinical decision making***

Meningococcal Vaccines

- ACIP recommends MenB-4C (Bexsero®) be administered as a 2-dose series at 0 and 6 months when given to healthy adolescents and young adults aged 16–23 years based on shared clinical decision-making for the prevention of serogroup B meningococcal disease
- ACIP recommends MenB-4C (Bexsero®) be administered as a 3-dose series at 0, 1–2, and 6 months when given to persons aged ≥10 years at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to N. meningitidis isolates; and persons at increased risk during an outbreak)

ACIP Recommendations | ACIP | CDC

Recent Vaccine News!

RSV Vaccines – Adults

- ACIP recommends adults 75 years of age and older receive a single dose of RSV vaccine.
- ACIP recommends adults 60–74 years of age and older who are at increased risk of severe RSV disease receive a single dose of RSV vaccine.

Influenza Vaccines

- ACIP reaffirms the recommendation for routine annual influenza vaccination of all persons aged ≥6 months who do not have contraindications.
- ACIP recommends high-dose inactivated (HD-IIV3) and adjuvanted inactivated (aIIV3) influenza vaccines as acceptable options for influenza vaccination of solid organ transplant recipients aged 18 through 64 years who are on immunosuppressive medication regimens, without a preference over other age-appropriate IIV3s or RIV3.

Recent Vaccine News!

Chikungunya Vaccine

Recommendations for use of chikungunya vaccine among travelers:

ACIP recommends chikungunya vaccine for persons aged ≥18 years **traveling to a country or territory** where there is a chikungunya outbreak

In addition, chikungunya vaccine may be considered for the following persons traveling to a country or territory without an outbreak but with evidence of chikungunya virus transmission among humans within the last 5 years

- Persons aged **>65 years**, particularly those with underlying medical conditions, who are likely to have at least moderate exposure* to mosquitoes, OR
- Persons staying for a cumulative period of **6 months** or more

*Moderate exposure could include travelers who might have at least 2 weeks (cumulative) of exposure to mosquitoes in indoor or outdoor settings.

ACIP recommends chikungunya vaccine for **laboratory workers** with potential for exposure to chikungunya virus

Recent Vaccine News!

Mpox Vaccines

ACIP recommends vaccination with **the 2-dose JYNNEOS** vaccine series for persons aged 18 years and older at risk for mpox. Dose 2 administered 28 days after dose 1

Persons at risk:

- Gay, bisexual, and other men who have sex with men, transgender or nonbinary people who in the past 6 months have had one of the following:
  - A new diagnosis of ≥1 STD, ≥1 sex partner
  - Sex at a commercial sex venue
  - Sex in association with a large public event in a geographic area where mpox transmission is occurring
- Sexual partners of persons with the risks described in above
- Persons who anticipate experiencing any of the above

CDC.gov

Future Vaccines

- **In ClinicalTrials.gov, there are 825 studies starting or actively recruiting for vaccine studies**

- There are **300 trials** in phase II and III currently registered and/or enrolling

- **Funding**
  - NIH- 107
  - Industry- 331
  - By other federal agencies- 36
  - Others- 605

Examples of Trials in Clinicaltrials.gov

- Active Health Education to Increase **HPV** Vaccine Coverage in Youth: A Stepped-wedge, Cluster, and Randomized Trial
- Therapeutic Vaccine Based on aDC1 **Dendritic Cells** for the Control of Viremia After ATI in **HIV** Infected Individuals
- Safety and Immunogenicity of SARS-CoV-2 Protein Subunit Recombinant Vaccine in Healthy Children
- Understanding Poor Vaccine Responses to Hepatitis B Vaccination
- **Intradermal** Influenza Vaccination
- Tumor Vaccines for Solid Tumors
- Vaccine Hesitancy in Black/African Americans With Rheumatic Diseases

Clinicaltrials.gov.

Over 310 mRNA vaccines and treatments are currently in development

Table 1. Ongoing Clinical Trials With mRNA Vaccines (Excluding COVID-19 Vaccines).

Vaccine	Formulation Type/Route of Administration	Indication	Clinical Trial Number	Phase	Sponsor	Status
eOD-GT8 60mer mRNA	Nanoparticle/Intraperitoneal	HIV	NCT05414786	1	International AIDS Vaccine Initiative	Recruiting
Core-g28v2 60mer mRNA vaccine and eOD-GT8 60mer mRNA vaccine	Nanoparticle/Intramuscular injection	HIV	NCT05001373	1	International AIDS Vaccine Initiative	Recruiting
BG505 MD39.3 mRNA, BG505 MD39.3 gp151 mRNA, and BG505 MD39.3 gp151 CD4KO mRNA	NA/Intramuscular injection	HIV	NCT05217641	1	National Institute of Allergy and Infectious Diseases (NIAID)	Recruiting
mRNA-1345	Lipid nanoparticle/Intramuscular injection	Respiratory Syncytial Virus (RSV)	NCT05127434	2/3	Moderna	Recruiting
		RSV	NCT04528719	1	Moderna	Recruiting
mRNA-1345 and mRNA-1273.214	Lipid nanoparticle/Intramuscular injection	RSV	NCT05330975	3	Moderna	Recruiting
Influenza vaccines (mRNA-1020, mRNA-1030, and mRNA-1010)	Lipid nanoparticle/Intramuscular injection	Influenza (A and B strains)	NCT05333289	1/2	Moderna	Recruiting
		Influenza (A and B strains)	NCT05375838	1/2	Moderna	Recruiting
mRNA-1010	Lipid nanoparticle/Intramuscular injection	Seasonal influenza	NCT04956575	1/2	Moderna	Recruiting
		Seasonal influenza	NCT05415462	3	Moderna	Recruiting
Influenza vaccines {monovalent influenza modRNA vaccine (mIRV), bivalent influenza modRNA vaccine (bIRV AB, bIRV AA, and bIRV BB) quadrivalent influenza modRNA vaccine (qIRV)}	NA/Intramuscular injection	Influenza	NCT05052697	1/2	Pfizer	Recruiting
Seasonal quadrivalent influenza mRNA vaccine CVSQIV	NA/Intramuscular injection	Influenza	NCT05252338	1	CureVac AG	Recruiting
Self-amplifying ribonucleic acid (saRNA) vaccines (PF-07852352, PF-07836391, PF-07836394, PF-07836395, PF-07836396, and PF-07867246)	NA/Intramuscular injection	Influenza	NCT05227001	1	Pfizer	Recruiting
mRNA NA vaccine	NA/Intramuscular injection	Influenza	NCT05426174	1	Sanofi Pasteur	Recruiting
			NCT05085366	3	Moderna	Recruiting
mRNA-1647	NA/Intramuscular injection	Cytomegalovirus infection	NCT04232280	2	Moderna	Recruiting
			NCT05105048	1	Moderna	Recruiting
mRNA -1215	Lipid nanoparticle/Intramuscular injection	Nipah virus	NCT05398796	1	National Institute of Allergy and Infectious Diseases (NIAID)	Recruiting
W_ova1 vaccine	Liposome/Intravenous injection	Ovarian cancer	NCT04163094	1	University Medical Center Groningen	Active, not recruiting
National Cancer Institute (NCI)-4650	Lipid nanoparticle/Intramuscular injection	Cancer (Melanoma, Colon, Gastrointestinal, Genitourinary, and Hepatocellular)	NCT03480152	1/2	National Cancer Institute (NCI)	Terminated
BNT113	Liposome/Intradermal vaccine	Carcinoma, Squamous Cell, Head and Neck Neoplasm, Cervical Neoplasm, Penile Neoplasms Malignant	NCT03418480	1/2	University of Southampton	Recruiting
	Liposome/Intradermal vaccine	Unresectable Head and Neck Squamous Cell Carcinoma Metastatic Head and Neck Cancer Recurrent Head and Neck Cancer Melanoma Stage III Melanoma Stage IV Unresectable Melanoma	NCT04534205	2	BioNTech SE	Recruiting
BNT111	NA/Intravenous infusion		NCT04526899	2	BioNTech SE	Recruiting
Individualized Cancer RNA Immunotherapy (IVAC®) vaccines: IVAC_W_bre1_uID and IVAC_W_bre1_uID/IVAC_M_uID	NA/Intravenous injection	Triple Negative Breast Cancer (TNBC)	NCT02316457	1	BioNTech SE	Active, not recruiting
RNA tumor vaccine	NA/Intramuscular injection	Solid tumor	NCT05202561	1	First Affiliated Hospital Bengbu Medical College	Recruiting

Gote V, et al. 2023; Kutikuppala LVS, et al, 2024.

“I always get sick when I get the vaccines”

“Why are they forcing me to get this vaccine”

“Will this vaccine affect me having children”

“I don’t want you to do any Tuskegee experiment on me”

“Are you trying to kill me”

“I don’t trust the government or pharmaceuticals”

“I already got 2 shots, how many more do you want me to do”

“Why get vaccinated, I still got the infection”

My approach

- **Be patient**, ask again but don't put too much pressure
- Acknowledge that the government mislead with vaccines benefits, patients know!
- Give **realistic expectations** for the vaccines- Prevent severe disease, Prevent hospitalizations
- Be prepared for the patient to be antagonistic, educate and give risks/benefits
- Ask if people had the vaccine or the disease in their family or friends
  - Most folks, if they see Shingles, will agree to get the shingles shot even if it hurts!
- Remember there is no such thing as **settled science!** New side effects can emerge (myocarditis)
- If the patient agrees to just one vaccine, that is **ONE MORE** than before!
- **Build trust**, don't sell hype or politics or be judgmental!

Last words:

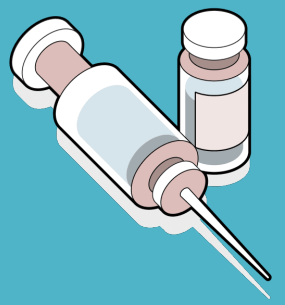
A New Study Appears to Stunningly Contradict Newton and Einstein's Theory of Gravity

Goo esidents
star

Breakdown of the Newton–Einstein Standard Gravity at Low Acceleration in Internal Dynamics of Wide Binary Stars
Kyu-Hyun Chae

Published 2023 July 24

Remember that science doesn’t settle! Be inquisitive!



Science is always evolving!

Thank you