Immunization Program 101

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VERMONT
DEPARTMENT OF HEALTH

Agenda

- Vermont's Immunization Program
  - Universal Purchase
  - Funding
- Vaccine Approval Process
- Vaccine Safety
- Why Do Some Vaccines Work Better Than Others?
- Upcoming Vaccines and Advances

Vermont’s Immunization Program Structure

The Basics

- Vermont is a universal vaccine state, providing vaccines to enrolled providers at no cost for use with all patients, regardless of insurance status.
  - Made possible by the Vermont Vaccine Purchasing Program (VVPP)
- Insurer funding is combined with federal funding to support the purchase of vaccines from the CDC federal contract at the lowest price.
- People (under 65 years old) without health insurance may receive vaccines at no cost through the Health Department Local Offices.
- The program cannot currently provide vaccines for those 65 years and older because insurers (i.e., Medicare) do not pay into this program for the people they cover.
- Many providers and pharmacies have vaccines available for those 65 and older.

Immunization Program Oversight

The program has the responsibility to abide by the following:

- ❑ CDC Cooperative Agreement
  - → Immunization Program Operations Manual
- ❑ CDC Supplemental Funding
  - → COVID-19 funding (rescinded March 24, 2025)
  - → Small-scale and large-scale response funding
- ❑ Vermont Vaccine Purchasing Program (VVPP)
  - → VVPP Plan of Operations
- ❑ Vermont Laws – Statutory Requirements
  - → Title 18, Chapter 21

Immunization Program funding comes from multiple sources

Operational Program Funding (including staff)

- Federal: CDC 70%
- State: Medicaid, General Funds 5%
- Health insurers - VVPP 25%

Vaccine Funding

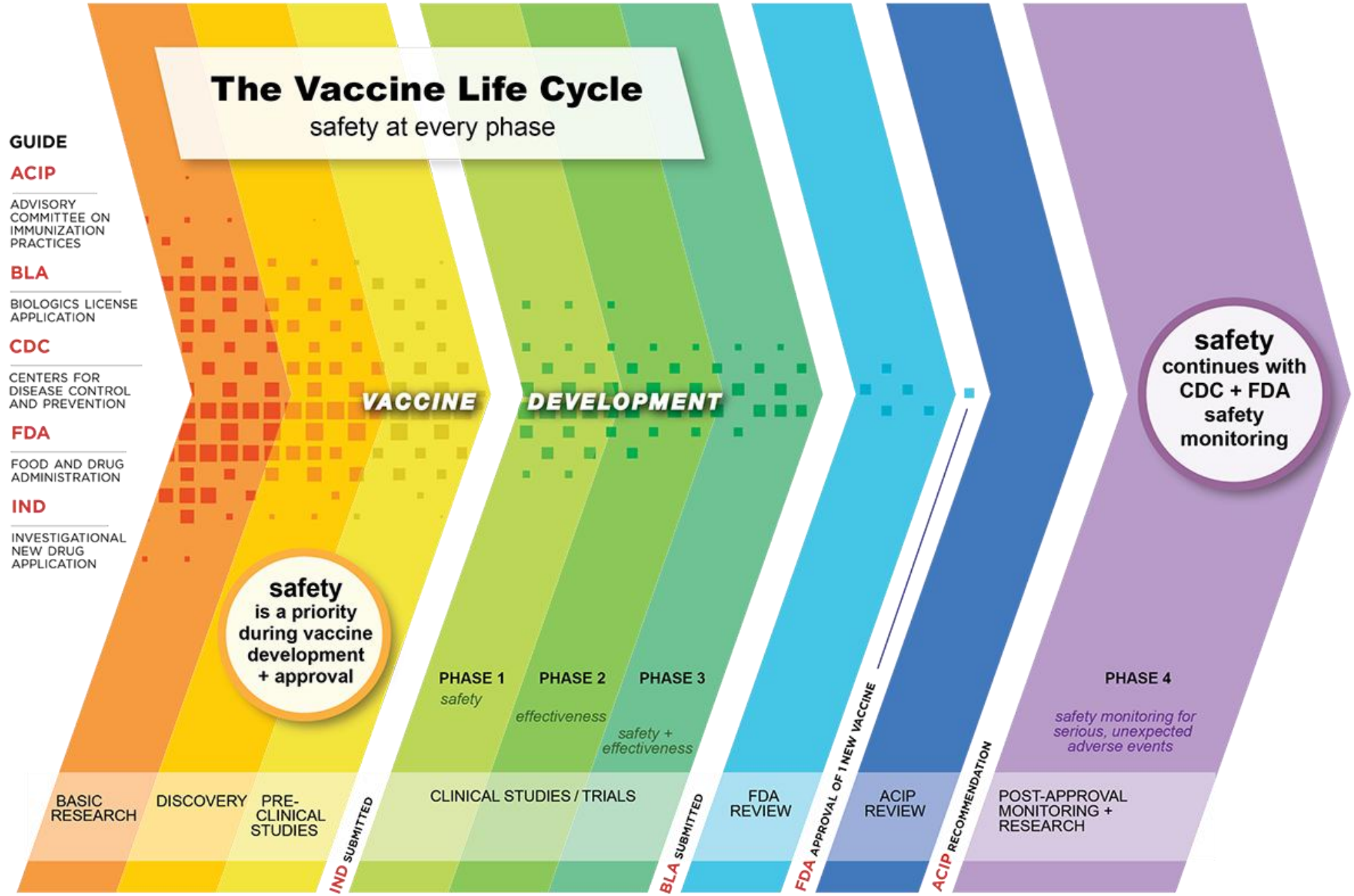
- Vaccine for Children – Federal Funds – 54% of all pediatric vaccine costs
- 317 – Federal Funds –uninsured adults
- VVPP – Insurers - 46% of pediatric and 90% of adult (19-64) vaccine costs

CDC Funding Requirements

Programmatic Strategies (2025)

- Strengthen Program Infrastructure and Management
- Increase Vaccine Access
- Improve Vaccination Equity
- Promote Vaccine Confidence and Demand
- Enhance Data and Evaluation
- Strengthen Program Support for Partners
- Enhance Vaccination Response Readiness

How Vaccines are Approved


The Vaccine Life Cycle
safety at every phase
GUIDE
ACIP
ADVISORY COMMITTEE ON IMMUNIZATION PRACTICES
BLA
BIOLOGICS LICENSE APPLICATION
CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION
FDA
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VACCINE DEVELOPMENT
safety is a priority during vaccine development + approval
PHASE 1
safety
PHASE 2
effectiveness
PHASE 3
safety + effectiveness
PHASE 4
safety monitoring for serious, unexpected adverse events
safety continues with CDC + FDA safety monitoring
BASIC RESEARCH
DISCOVERY
PRE-CLINICAL STUDIES
IND SUBMITTED
CLINICAL STUDIES / TRIALS
BLA SUBMITTED
FDA REVIEW
FDA APPROVAL OF 1 NEW VACCINE
ACIP REVIEW
ACIP RECOMMENDATION
POST-APPROVAL MONITORING + RESEARCH

How are New Vaccines Developed and Tested?

Phase	Typical Size	Focus
1	20–100 people	Gathering research on safety in humans, side effects, immune response, dose/response relationship.
2	Hundreds of people	Participants with characteristics of intended recipients; ideally includes people of diverse backgrounds. Gathering additional safety information (side effects and risks) and effectiveness.
3	Thousands of people	Confirming effectiveness, monitoring common and less common side effects. Studies include a control group to help define benefits for those who got the vaccine compared to people who did not.
4 (Post licensure)	Thousands of people	FDA may require post-licensure studies to evaluate vaccine safety and effectiveness over a longer period of time.

Vaccine Development – 101 | FDA

Role of the FDA

FDA's Center for Biologics Evaluation and Research (CBER) is responsible for regulating vaccines in the US

Vaccines and Related Biological Products Advisory Committee (VRBPAC)

- Reviews preliminary data to determine if clinical trials are appropriate
- Reviews the manufacturer's Biological License Application (BLA), including
  - Pre-clinical and clinical data
  - Details about manufacturing process
  - Information and inspection results about manufacturing facility
  - Manufacturer's proposed prescribing information

- Monitoring and oversight continues after vaccine licensure

Role of the ACIP

As new vaccines near/attain licensure, **CDC staff work closely with the Advisory Committee on Immunization Practices (ACIP) to conduct reviews** on impending vaccines as a foundation for vaccine recommendations/policy, with a focus on:

- Public Health Importance
- Benefits (Vaccine Efficacy)
- Harms (Vaccine Safety)
- Values
- Acceptability
- Resource use
- Equity
- Feasibility

How are Vaccines Added to the VFC Program?

ACIP determines which vaccines will be added to the VFC program

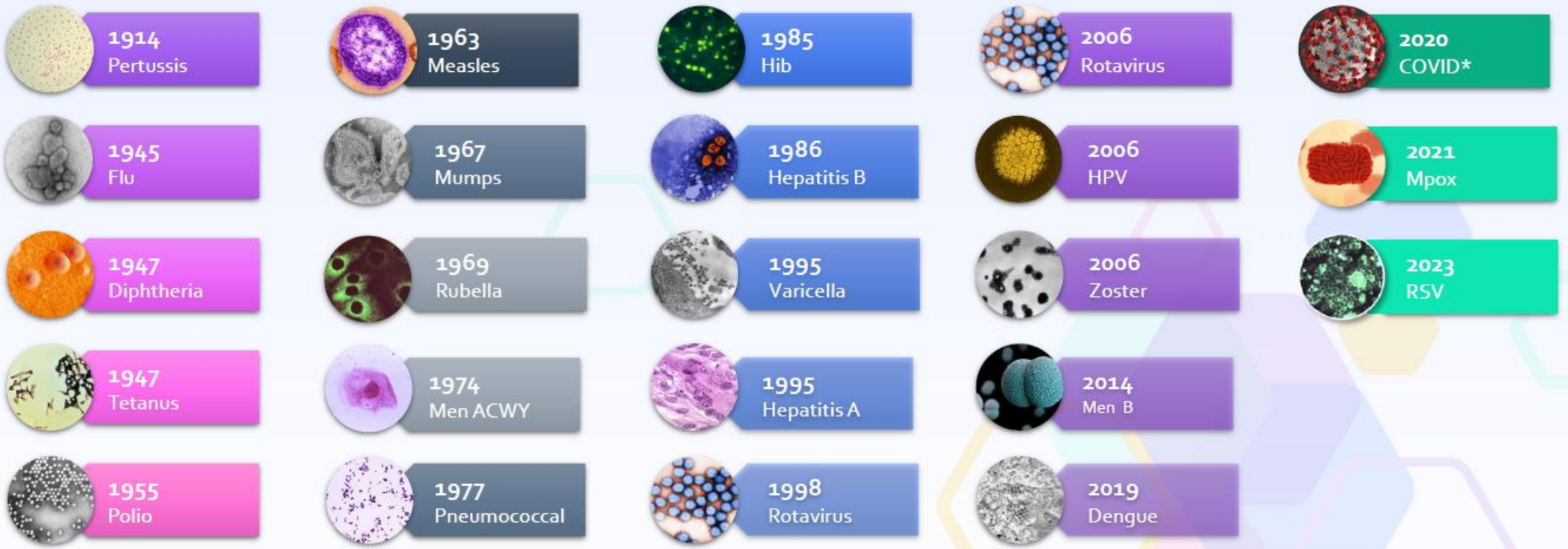
- ACIP's determination is documented in VFC resolutions, which require a separate ACIP vote
- Vaccines become available for use in the VFC program once they have been added to CDC's vaccine contracts and purchased by CDC

VFC resolutions are posted on CDC's website at: ACIP Resolutions for Vaccines for Children (VFC) Program

Following ACIP recommendations and resolutions (for VFC), steps are taken to add new vaccines to CDC's contracts

- Timeline to update contract is ~2–4 months post ACIP, often longer for new contracts
- Depends on timing of recommendation/resolution, product availability, alternative products

When were vaccines against VPDs that we prevent today through routine immunization first licensed?



*Authorized for Emergency Use by the US FDA.

VRBPAC and ACIP Members

VRBPAC

- Generally, meets six times per year
- 15 core members
  - Serve terms for up to four years
  - Additional temporary members (up to 10) can be appointed if needed
- Subcommittees can be formed

ACIP

- Generally, meets 3 times per year
- Up to 19 voting members
  - Independent medical and public health experts who do not work for CDC
  - Voting members have four-year terms
- Six ex officio members who represent other federal agencies related to immunizations
- 30 representatives of liaison organizations that have immunization expertise

Vaccine Safety

Defining Terms

Safety

Vaccine effectiveness (VE)

Immunogenicity

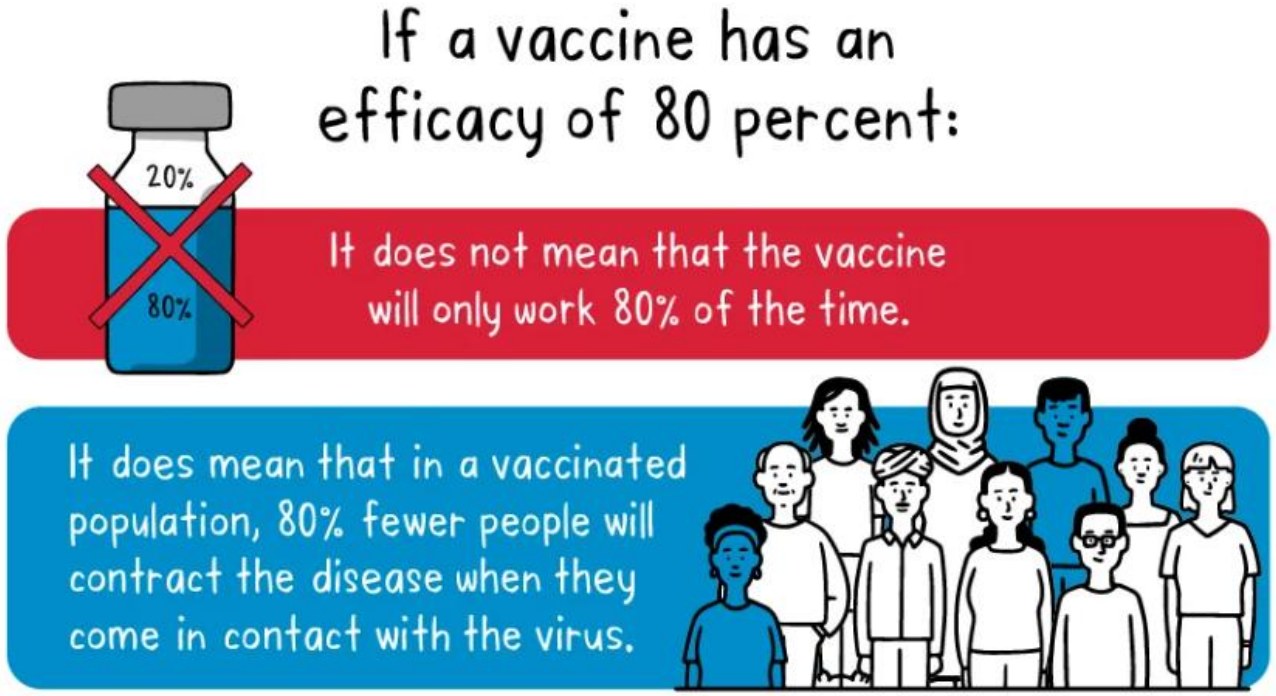


Image from: World Health Organization: Vaccine efficacy, effectiveness and protection

No Vaccine is 100% Safe

“Vaccines are neither completely safe nor always effective at disease prevention, leading some people to misunderstand the relative benefit and risk of vaccination.”

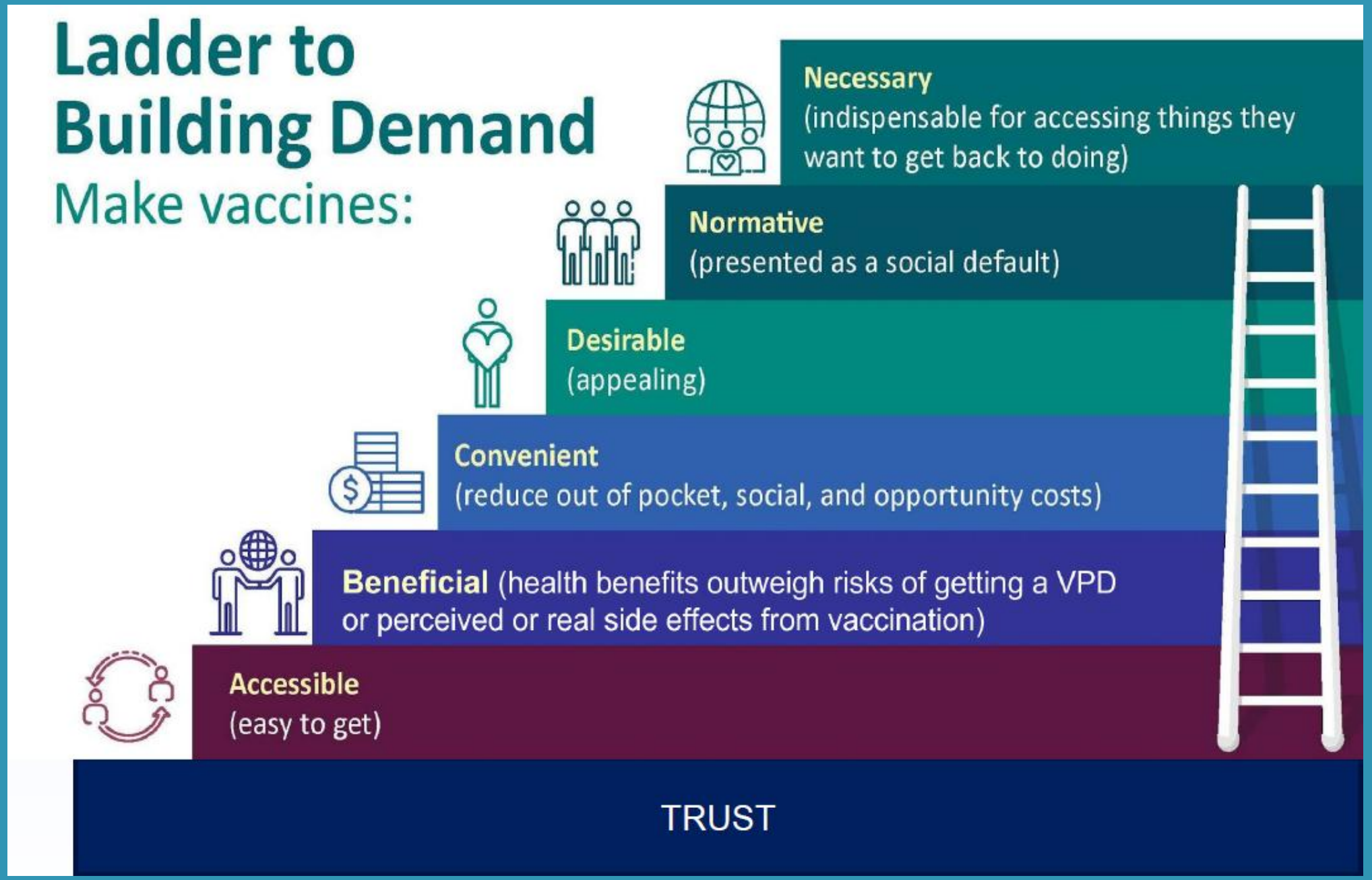
Understanding Vaccine Safety and the Roles of the FDA and the CDC | New England Journal of Medicine

The first definition of the word safe is "harmless." This definition would imply that any negative consequence of a vaccine would make the vaccine unsafe. Using this definition, no vaccine is 100 percent safe. Almost all vaccines can cause pain, redness or tenderness at the site of injection. And some vaccines cause more severe side effects. A vaccine's benefits must clearly and definitively outweigh its risks.

Vaccine Safety: Are Vaccines Safe? | Children's Hospital of Philadelphia

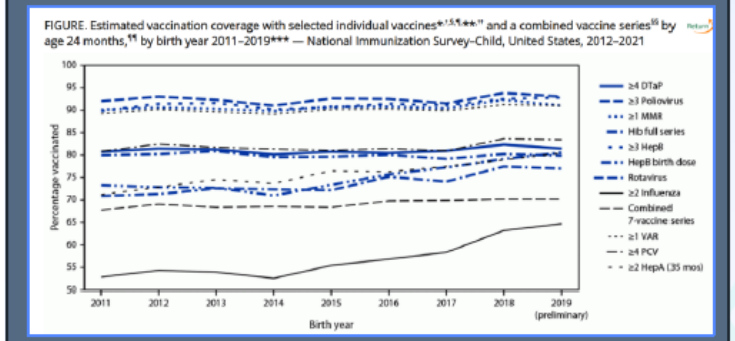
Ladder to Building Demand

Make vaccines:



Monitoring and Evaluation Following Licensure

Ongoing monitoring and evaluation activities focus on vaccine coverage, effectiveness, safety, and impact on the epidemiology of the disease(s) being prevented.

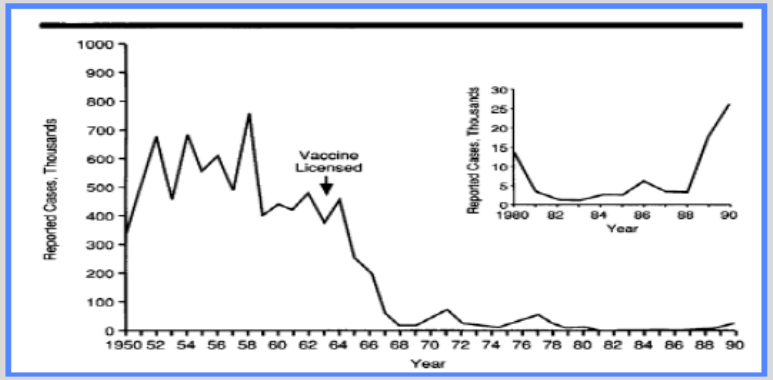


Combined vaccine series coverage results from NIS, 2011-2019 (*MMWR Morb Mortal Wkly Rep* 2023;72(2):33–38)

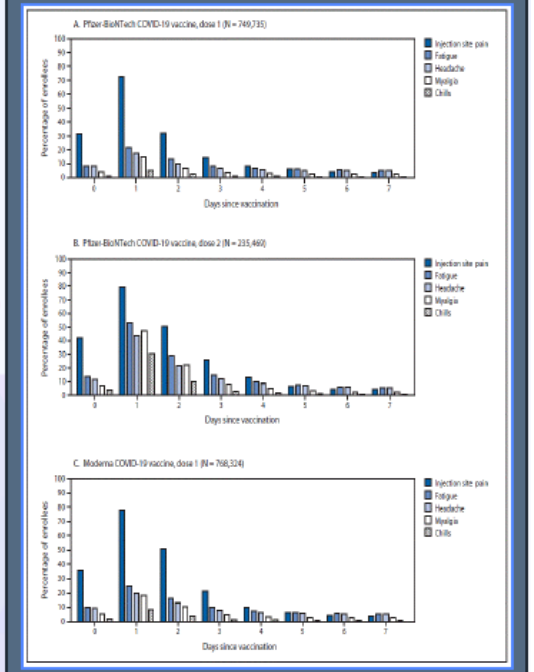
Table 3. Incremental Vaccine Effectiveness of MMR3 versus MMR2.*

Days after Vaccination with MMR3	Mumps Cases		Effectiveness of MMR3 vs. MMR2	P Value
	2 Vaccine Doses	3 Vaccine Doses		
	no.		*% (95% CI)*	
7 Days	230	23	60.0 (38.4–74.0)	<0.001
14 Days	232	21	63.2 (42.3–76.5)	<0.001
21 Days	235	18	68.3 (48.6–80.4)	<0.001
28 Days	241	12	78.1 (60.9–87.8)	<0.001

Effectiveness of a third dose of MMR vaccine for mumps outbreak control (*N Engl J Med* 2017; 377(10):947-956)



Incidence of measles in the pre- and post-vaccine time periods (*JAMA* 1991;266 (11):1547-1552)



First month of COVID-19 vaccine safety monitoring (*MMWR Morb Mortal Wkly Rep* 2021;70(8):283–288)

National Vaccine Safety Monitoring in the US

Vaccine Adverse Event Reporting System (VAERS)

- National, early warning, passive surveillance system co-managed by CDC and FDA
- Anyone can report
- Not designed to determine if an adverse event (AE) was caused by the vaccine

Vaccine Safety Data Link (VSD)

- Involves network of integrated healthcare organizations and networks across the US
- Uses electronic health data to monitor and assess the safety of vaccines
- Evaluates vaccine safety concerns from literature and reports to VAERS, other vaccine safety systems.

Clinical Immunization Safety Assessment (CISA)

- National collaborating network that includes medical research centers
- Clinical consultation-based
- Designed to help understanding of AE at the individual patient level

Emergency Preparedness /Vaccine Safety

- Utilizes v-safe, a vaccine safety monitoring system that sends confidential check-ins to vaccine recipients via text; launched as part of CDC's National COVID-19 Vaccination program
- VAERS, VSD, and CISA are also used

VAERS

- Passive surveillance – relies on individuals and healthcare providers to submit reports of adverse health events after vaccination
- Followed up with additional research on reports of adverse events that are unexpected events or appear more often than expected

Strengths

- Casts a wide net (anyone can submit)
- Early warning/hypothesis-generating system

Limitations

- Passive surveillance – doesn't capture all adverse events
- No control group to compare rates
- Reports can lack details or have errors

Clinical Immunization Safety Assessment (CISA)

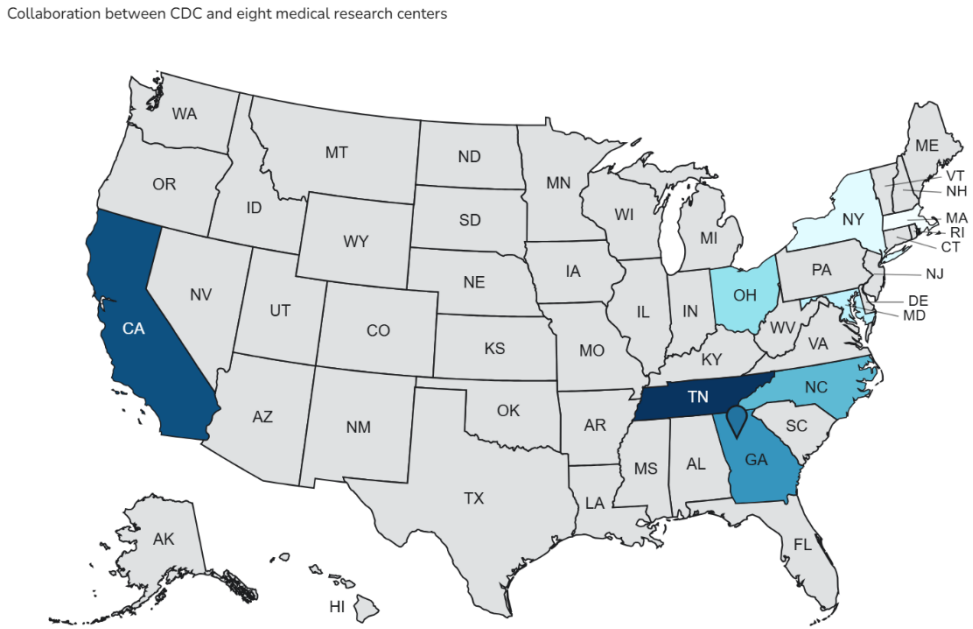
The Clinical Immunization Safety Assessment (CISA) Project is a network of vaccine safety experts from CDC, research centers and other partners.

Strengths

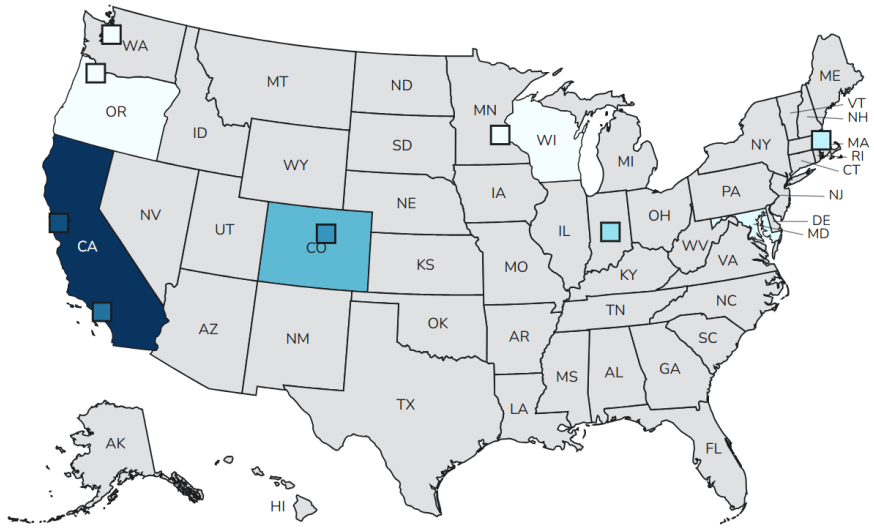
- Conducts prospective, multi-site clinical studies with hundreds of subjects and ability to recruit controls
- Assesses vaccine safety in sub-populations
- Detailed clinical data on patients and ability to collect biological samples from patients

Limitations:

- Limited ability to study rare adverse events due to small sample sizes
- Clinical trials can be labor/resource intensive
- Can be challenging to recruit and retain subjects



Vaccine Safety Datalink (VSD)



- Established in 1990
- Conducts population-based monitoring and conducts studies on adverse effects following immunization.
- Uses electronic health record data from member sites to assess vaccine safety and detect adverse events in near-real time.

Benefits:

- Timely vaccine safety studies
- Use of a control group

Limitations:

- May not have enough patients for detecting extremely rare adverse events
- May not capture vaccine administration data outside of health system
- Cannot determine if an association between an adverse event and vaccination is causal

[About the Vaccine Safety Datalink (VSD) | Vaccine Safety Systems | CDC]

V-safe

V-safe originally launched in December 2020 to monitor the safety of COVID-19 vaccines and later expanded to include mpox and RSV vaccines.

- Voluntary CDC smart phone-based monitoring program for vaccine safety in the US

Strengths

- Anyone can enroll
- Quickly validates safety data from clinical trials or identify potential safety issues
- Regular reminders to complete a survey help capture more safety data
- CDC can follow-up with participants and submit VAERS reports, as needed

Limitations

- May not properly represent the post-vaccination experiences of the entire population

FDA monitoring and surveillance systems

MedWatch

- Used for products like nirsevimab (when administered alone)

Post-licensure Rapid Immunization Safety Monitoring System (PRISM)

- Largest vaccine safety surveillance system in U.S. using database of health insurance claims
- *Strengths*: Linked to some immunization and birth registries; access to denominator data for vaccine exposure
- *Limitations*: lag in time for accessing data; Medicare population not well represented; may not be representative of those without insurance

The Biologics Effectiveness and Safety (BEST) Initiative

- Active surveillance system with large-claims data, EHR data and linked claims-EHR data
- *Strengths:* near real-time analysis; use of a control group; ability to assess safety of vaccine in sub-populations
- *Limitations:* May not be representative of those without insurance coverage; cannot determine if an association between adverse event and vaccination is causal

Examples of Assessing Safety Signals

	Concern	How was it detected?	Follow up assessment	Ass'n? / Action?
1996	Vaccine-associated paralytic polio (VAPP) & OPV	VAERS	VSD; Data from other countries & PAHO; NIS; IOM review	YES / YES Transition from oral polio vaccine to inactivated polio vaccine in U.S.
2008-2011	DVT from HPV vaccination	VAERS & VSD	VSD, Denmark, Sweden, Canada: Cohort studies	NO / NO No change to vaccination schedules
2021	Johnson & Johnson COVID-19 vaccine & VITT (rare form of blood clot)	VAERS & data from Europe	Additional data out of Europe; CISA; VSD; VA Data	YES / YES Vaccine use limited and FDA eventually rescinded EUA.
2021	mRNA COVID-19 vaccines & myo/pericarditis	Data from Israel	VAERS; V-safe; CISA; VSD; Military Health System & PCORnet data; DoD; Data from other countries	NO / Partial No change to vaccination schedules. HOWEVER, an optional 8-week interval between 1st & 2nd dose was added to recommendations.

Slide from Carson, Paul. April 4, 2024. *Vaccines Under the Microscope: How Can We Know They Are Safe?* (Plenary presentation). Massachusetts Adult Immunization Conference, Boston, MA. Vaccines-Under-the-Microscope.pdf

Examples of Assessing Safety Signals

	Concern	How was it detected?	Follow up assessment	Ass'n? / Action?
2001	Use of thimerosal in vaccines & autism	NONE (Public Concern)	VAERS; VSD; CISA; IOM; Data from other countries	NO / YES Data doesn't support association. HOWEVER, thimerosal removed from childhood vaccines in U.S.
2012	HPV vaccine & primary ovarian insufficiency (POI)	NONE (Public Concern)	VAERS; CISA; VSD; Data from other countries; WHO	NO / NO Data doesn't support association between HPV vaccination & POI.
2023	Pfizer's bivalent COVID-19 vaccine & stroke in 65+ yoa	VSD	VAERS; CMS & VA data; BEST; Data from other countries	NO / NO Data doesn't support association between Pfizer's COVID-19 vaccination and stroke in 65+ yoa.
2022-23	Aluminum in vaccines & asthma	NONE (Public Concern)	VSD; Data from other countries	MAYBE / YES Majority of data doesn't support association, however this will continue to be studied.

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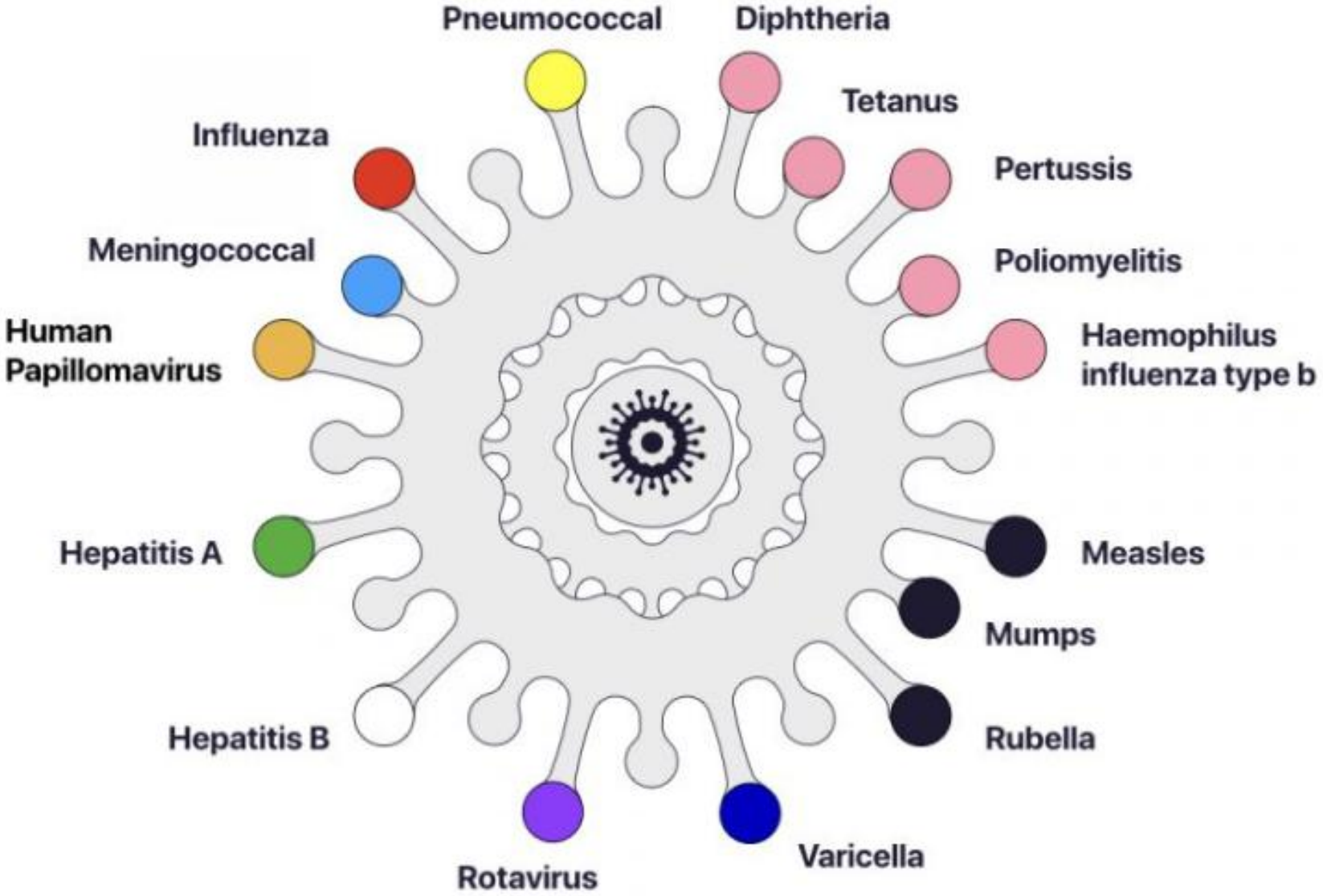
Why do Some Vaccines Work Better Than Others?

Vaccine-Preventable Diseases



What Does it Mean for a Vaccine to be Effective?

It depends on the virus.

And how much it's spreading.

And the type of vaccine.

And the immune response stimulated by the vaccine.

In short, it’s complicated.

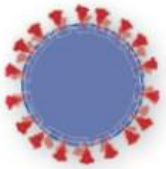
Why Do Some Vaccines Work Better Than Others?

Viral Spread

How much a virus is spreading impacts how well the vaccine works

The prevalence of the virus changes over time

Some viruses mutate and develop variants

	WHOLE-PATHOGEN VACCINES		VIRAL VECTORS		SUBUNIT VACCINES				NUCLEIC ACIDS	
										
	ATTENUATED	INACTIVATED	REPLICATING	NON-REPLICATING	PROTEIN SUBUNIT	POLYSACCHARIDE/ CONJUGATE	TOXOID	VIRUS-LIKE PARTICLES	RNA	DNA
DESCRIPTION	Living pathogen that has been weakened (but not killed) in the laboratory	Whole pathogen killed by heat, chemicals or radiation	A carrier virus that is able to infect human cells (such as an adenovirus) is introduced carrying genetic material that codes for the specific viral antigen in order to elicit the immune response.	A carrier virus (such as an adenovirus) that is able to infect human cells ***but cannot replicate*** is introduced carrying genetic material that codes for the specific viral antigen in order to elicit the immune response.	Purified viral antigens	Surface polysaccharide antigens, primarily from bacterial pathogens	Chemically inactivated toxins from pathogen	Particles that contain virus surface proteins that can elicit an immune response, but lack viral genetic material (so cannot replicate)	mRNA injected directly into muscle tissue and translated into specific pathogen protein antigens by host cellular machinery.	Plasmid containing pathogen DNA that encodes for specific antigens, injected directly into cellular tissue.
EXAMPLES	MMR vaccine	Polio vaccine, Rabies vaccine, Typhoid vaccine	Animal vaccines such as for Rift Valley fever virus, avian influenza	Animal vaccines such as for Rift Valley fever virus, avian influenza	Candidate Zika vaccine	Candidate vaccines for SARS, Bird flu (H5N1, H1N1), Zika	Diphtheria vaccine, Tetanus vaccine	Human papillomavirus vaccine	Candidate Zika vaccine	Candidate vaccines for SARS, Bird flu (H5N1, H1N1), Zika
PROS	Elicits strong immune response	Contains actual pathogen so will direct proper immune response	Efficient delivery of genetic material into host cells and tissues	Efficient delivery of genetic material into host cells and tissues	No chance of infection by pathogen	No chance of infection by pathogen	Raise direct immune response to pathogenic component	Easy access into cells	Directs the expression of viral antigens without threat of viral infection or need for integration into host DNA	Directs the expression of viral antigens without threat of viral infection
CONS	Slight potential for microbe reactivation	May require an adjuvant to stimulate complete immune response	May be suppressed by existing host immune response	May be suppressed by existing host immune response	Requires efficient delivery mechanism that protects against degradation	May require an adjuvant to stimulate complete immune response	May require an adjuvant to stimulate complete immune response	May be suppressed by existing host immune response	Difficult delivery into cells	Difficult delivery into cells

[Vaccine Comparison - American Society for Microbiology]

Examples

Covid-19 Vaccines

Prevent severe disease

Prevent hospitalization and death

Most effective in the first 6 months post vaccination

Flu Vaccines

Make disease milder

Less effective at preventing disease

Seasonal administration – formulation changes year to year

Human Papillomavirus Vaccines

Protect against 90% of cancers caused by HPV

Minimize infection

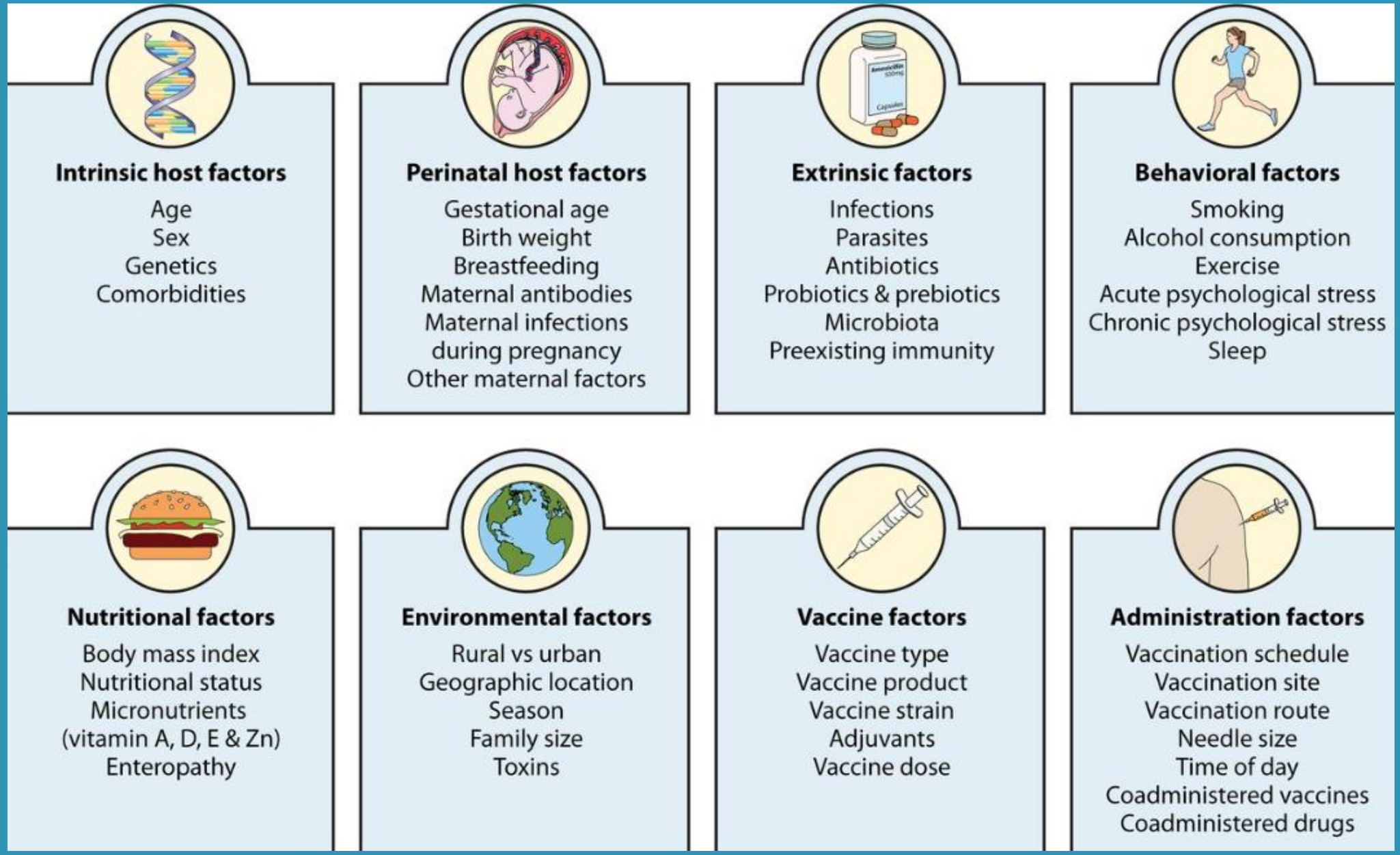
Most effective if given before exposure

Measles (MMR) Vaccine

Nearly 100% effective at preventing disease

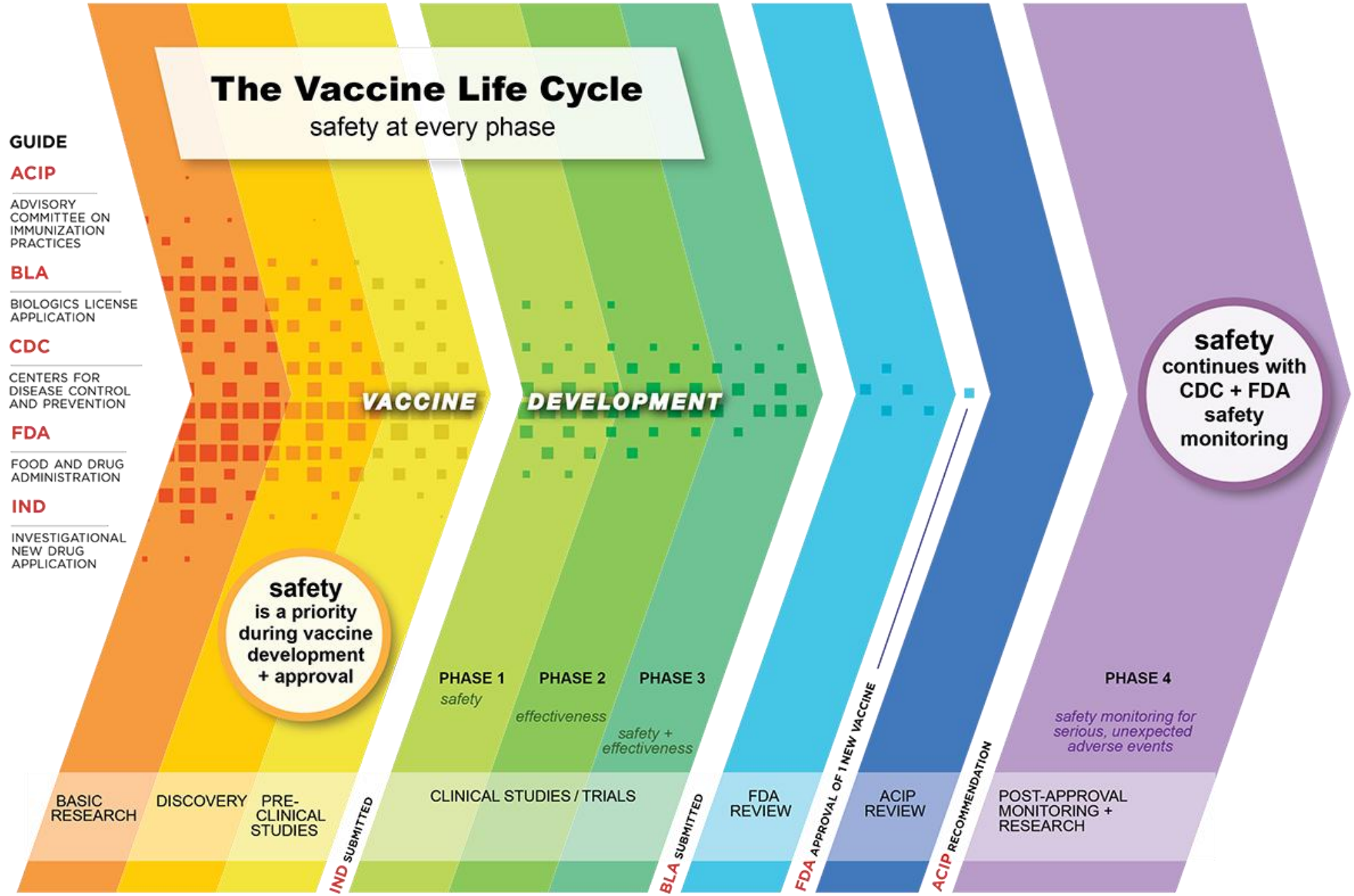
Lifetime protection

The Host Matters



Factors That Influence the Immune Response to Vaccination | Clinical Microbiology Reviews

Upcoming Vaccines and Advances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Pipeline Overview

	Pre-Clinical Studies	Phase I	Phase II	Phase III	BLA	Total
Vaccines	223	83	64	23	3	396
Antibodies	85	28	28	22	1	164

Vaccines in Phase II Development

- Chickenpox and Shingles (2)
- Chikungunya Virus (1)
- Clostridium difficile (1)
- Covid-19 (8)
- Cytomegalovirus Infection (1)
- Dengue Fever (1)
- Hantavirus (1)
- HIV Prevention (1)
- HPV Treatment (1)
- Influenza (4)
- Malaria (5)
- Mpox (1)
- Norovirus (3)
- Plague (1)
- Pneumococcal Vaccines (4)
- RSV (2)

Vaccines in Phase III Development

- Clostridium difficile (1)
- Covid-19 (7)
- Dengue Fever (1)
- Ebola (1)
- Escherichia coli (1)
  - Discontinued due to low efficacy
- HIV prevention
  - Discontinued due to low efficacy
- Lyme Disease (1)
- Pandemic Influenza (1)
- Pneumococcal (1)
- Rabies (2)
- RSV Prevention (1)
  - Intranasal vaccine designed specifically for toddlers
- Seasonal Influenza (2)

mAbs in Development

Phase II

- BK Virus (2)
- Covid-19 Treatment (13)
- Hepatitis B Treatment (1)
- HIV / AIDS Treatment (8)
- Pseudomonas Specific Agents (1)
- Seasonal Influenza (1)
- Sepsis and Septic Shock (1)
- Staphylococcal Vaccines (1)
- Hepatitis D (1)
- Clostridium difficile (1)

Phase III

- Covid-19 (4)
- Hepatitis D (2)
- Respiratory Tract Infections (1)
  - Excluding Pneumonia

Submitted to FDA for BLA

- RSV Prevention (1)

Messenger RNA Vaccines

Before the pandemic mRNA vaccines were already developed

With fast development and production times, mRNA vaccines are ideal for protection against new infectious diseases and variants of existing ones

mRNA vaccines in development now (not a complete list):

- Avian Bird Flu
- All Coronaviruses
- C. difficile
- CMV
- EBV
- Genital Herpes (HSV-2)
- Hepatitis C
- HIV
- Influenza
- Leptospirosis
- Lyme Disease
- Malaria
- Norovirus
- Tuberculosis
- Therapeutics
- Varicella

Vaccines to Treat Cancer

Preventative cancer vaccines- reduce your risk of cancer by protecting against certain viral infections that can cause the disease.

We already have two, Hepatitis B and HPV

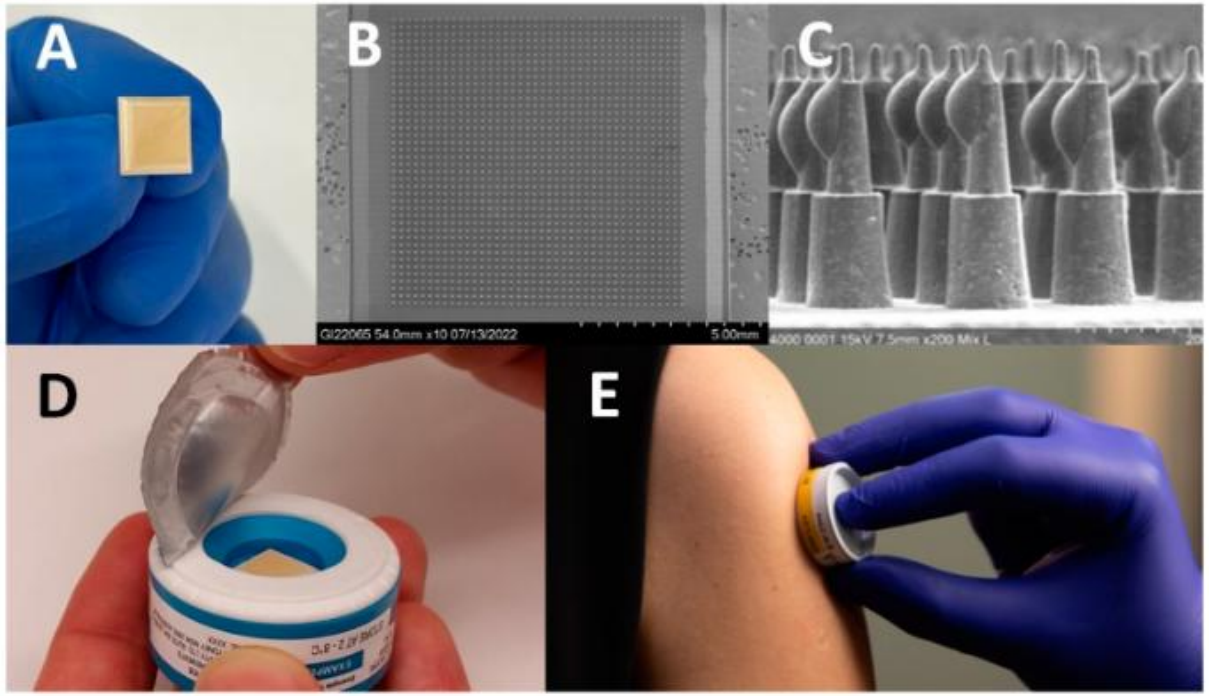
- Unleash immune cells to attack cancer while sparing healthy cells
- Be combined with other cancer therapies
- Trigger a long-lasting immune response that can potentially prevent cancers from spreading or returning

Therapeutic cancer vaccines train the body to protect itself against its own damaged or abnormal cells — including cancer cells.

- Stop a tumor from growing or spreading
- Destroy cancer cells still in the body after treatments
- Keep cancer from coming back

New Vaccine Advances

Microarray patches



Self Administered Flu Vaccine