Vaccines in Primary Immunodeficiency

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Children's National

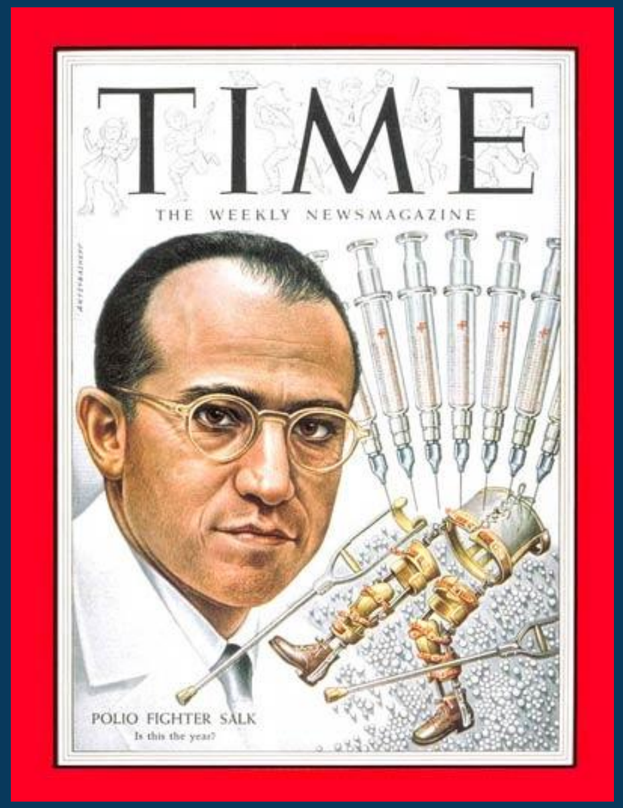
Speaker Disclosures

- MDK:
  - Consultant:CSL Behring, M3 Global Research, Guidepoint Global Research
  - Author, Uptodate (Wolter-Kluwer)
  - DSMB: Ensoma

- KW:
  - Sponsored Research: Cogent Biosciences, GSK, Regeneron Pharmaceuticals, DBV Technologies, Pharming Healthcare
  - Consultant/Advisory Boards: Amgen, Pharming Healthcare, ADMA Biologics

Background

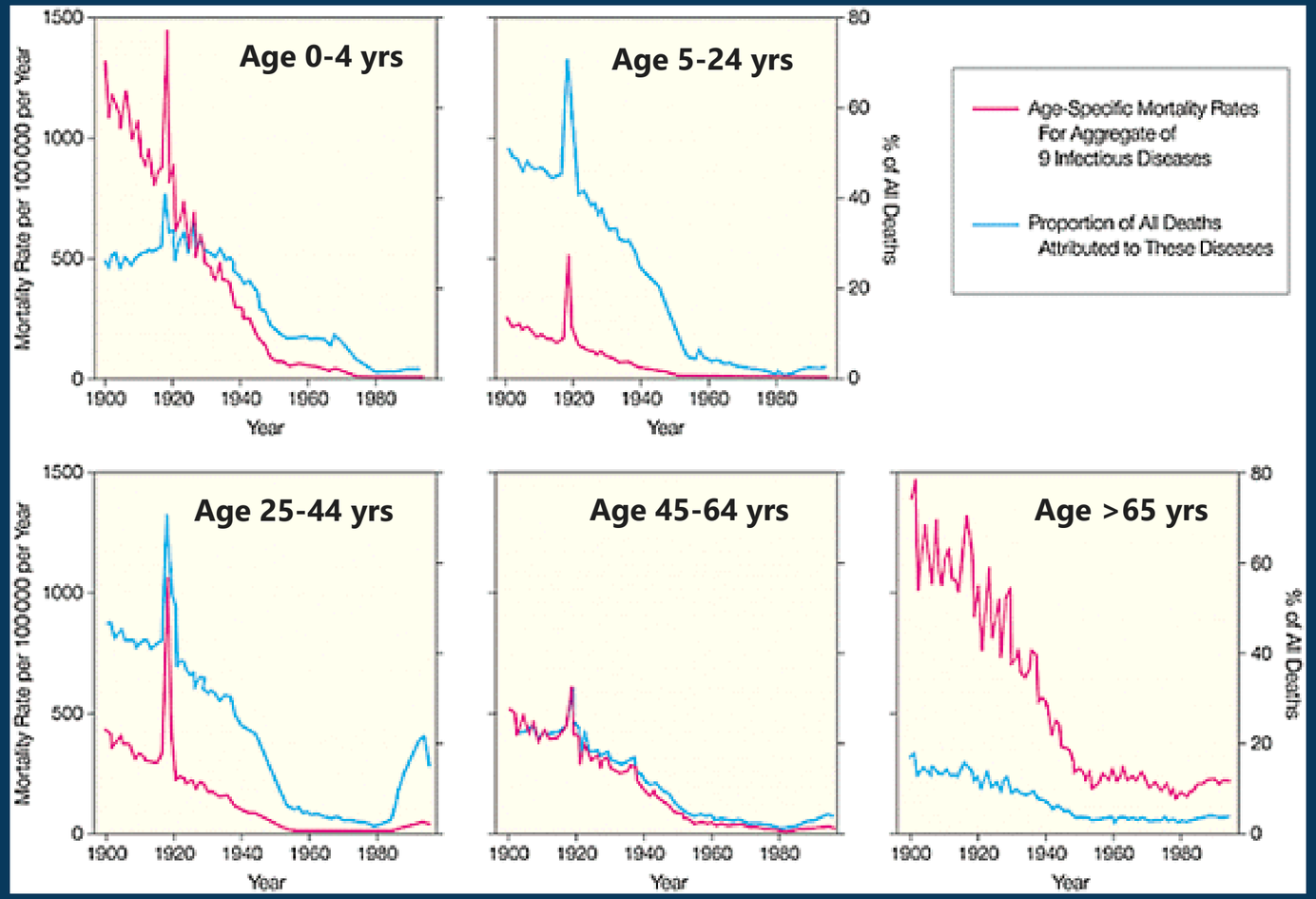
- Vaccination remains one of the most life-saving public health measures in history.





Winning the fight against infectious diseases in the 20th century

Mortality rate/100,000 annually



Armstrong GL *et al* *JAMA* 1999

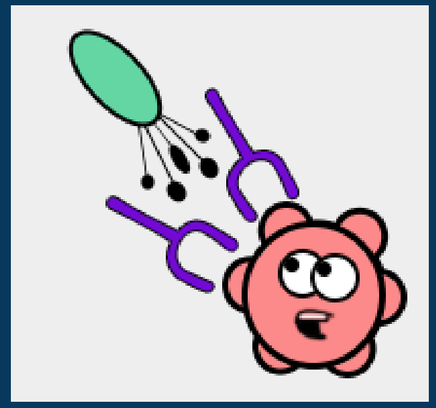
How vaccines work

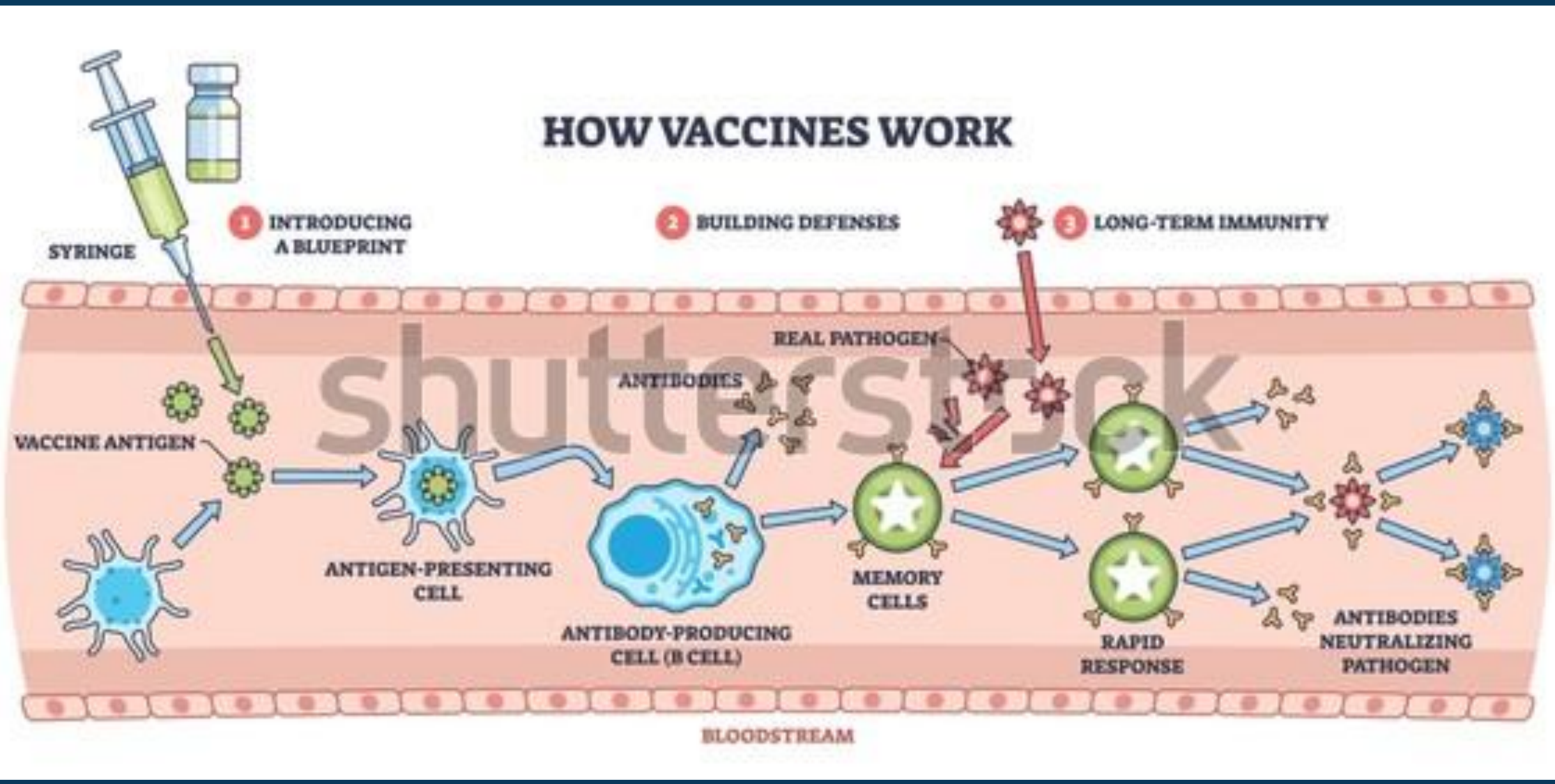
- By presenting bacterial/viral particles to the immune system, immune memory develops

Adaptive Immune cells (T-cells, B-cells) recognize the foreign particles



The immune system produces immune proteins (antibodies) and Killer T-cells to clear infectious particles




HOW VACCINES WORK
SYRINGE
1 INTRODUCING A BLUEPRINT
2 BUILDING DEFENSES
3 LONG-TERM IMMUNITY
REAL PATHOGEN
ANTIBODIES
VACCINE ANTIGEN
ANTIGEN-PRESENTING CELL
ANTIBODY-PRODUCING CELL (B CELL)
MEMORY CELLS
RAPID RESPONSE
ANTIBODIES NEUTRALIZING PATHOGEN
BLOODSTREAM
shutterstock

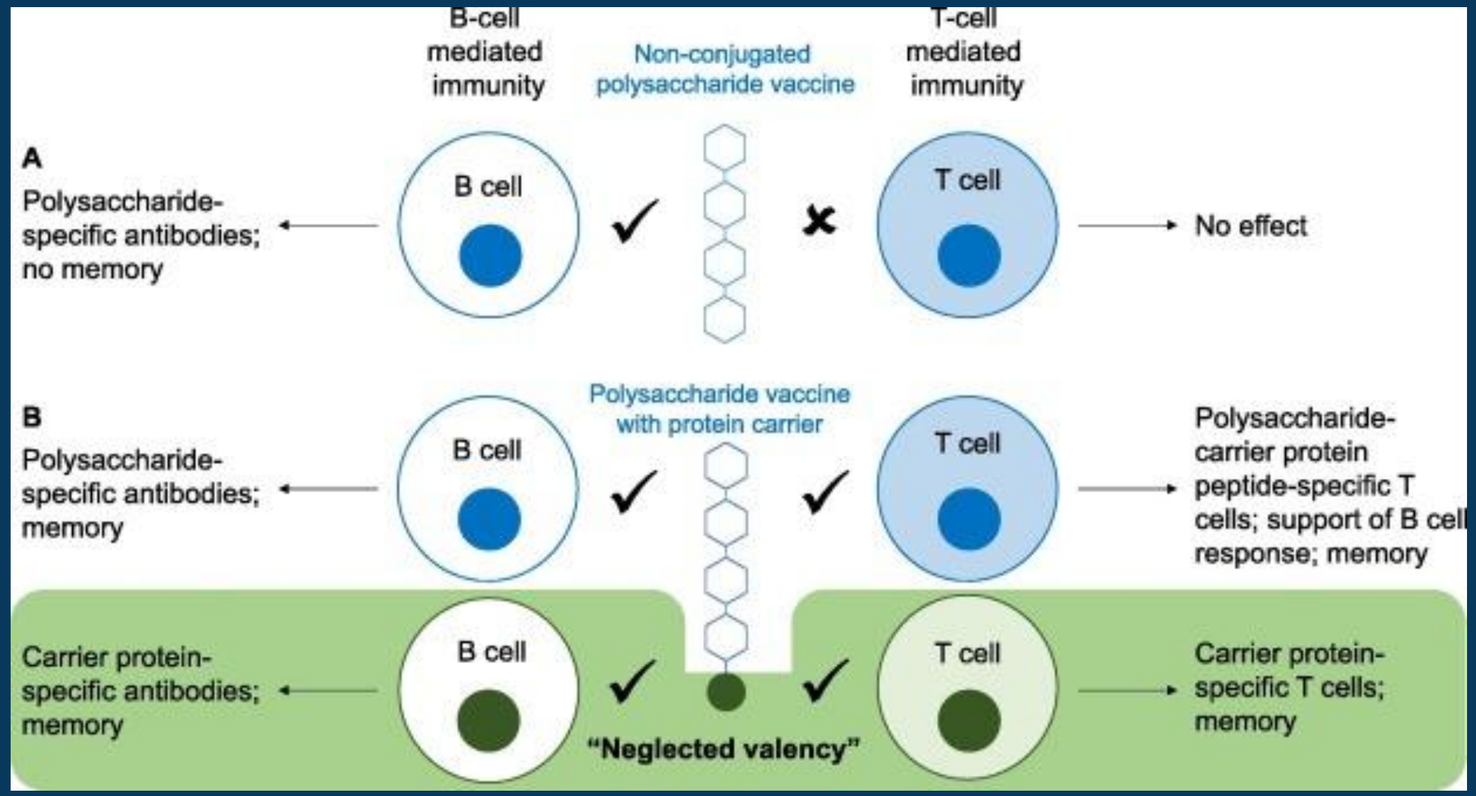
Vaccination in special populations

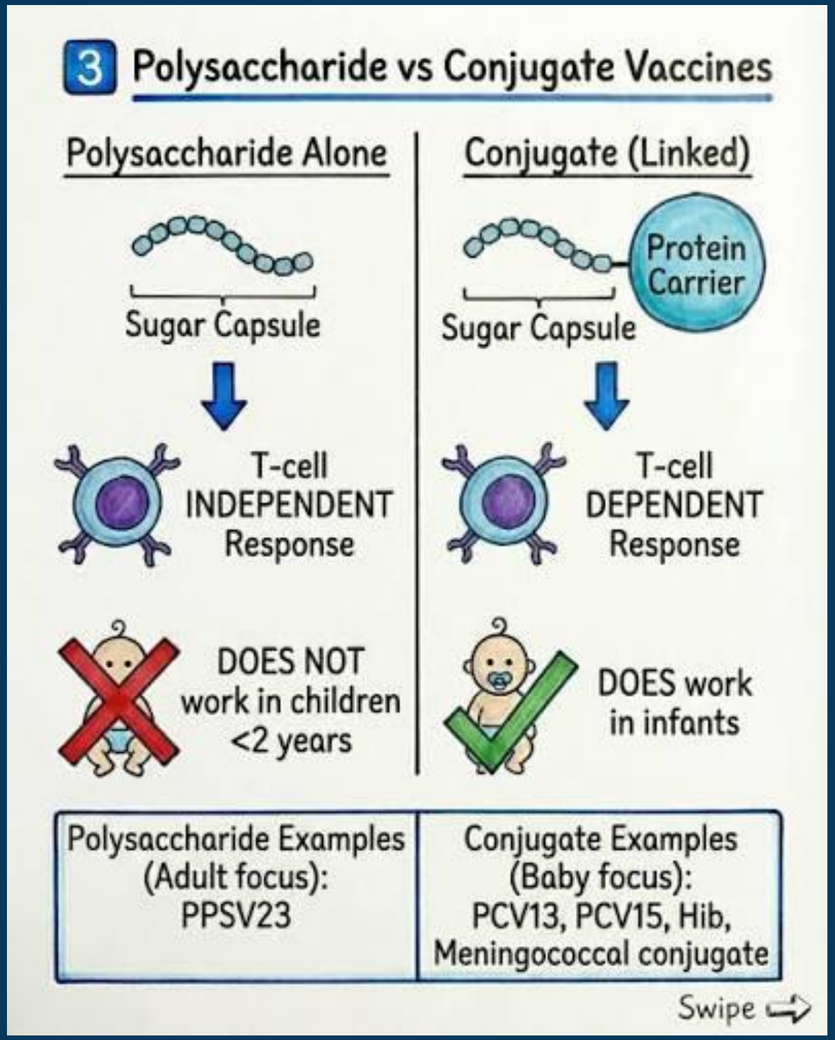
- **Vaccines may be less effective or sometimes harmful in immunocompromised patients**
  - Primary Immunodeficiency
  - Bone marrow / cord blood transplant recipients
  - Solid organ transplant recipients
  - Uncontrolled HIV patients
  - Patients on immunosuppressive medications

Types of Vaccines

	Viral	Bacterial
Inactivated (killed)	Inactivated influenza Poliovirus (Salk) Rabies vaccine COVID-19	DTAP/TDAP Prevnar/Pneumovax Haemophilus (Hib) Menactra / Menveo
Live-attenuated (weakened)	Rotavirus (Rotateq) MMR Varicella (Varivax) Yellow fever Oral Poliovirus *(not in US/Canada)*	BCG (outside US) Oral typhoid vaccine
Recombinant	SARS-Cov-2 mRNA vaccine Influenza mRNA vaccine Shingrix (VZV) RSV vaccines	

Different vaccines cause a different response





Understanding a Vaccine Challenge

	Protein	Conjugated Polysaccharide	Unconjugated Polysaccharide
Immunizations	Diphtheria Tetanus	*Haemophiuls influenzae* Prevnar	***Salmonella Typhi*** Pneumovax
T-lymphocyte help?	Yes	Yes	No
Age	All ages	All ages	Only >2 years of age can induce response

Understanding a Vaccine Challenge

Vaccine	Allowed Age (years)	T cell independent or dependent	Time frame to reach peak antibody levels	Protective level (⁺µg/mL or *IU/mL)
H. influenzae type b conjugate	Any	Dependent	3-4 weeks after third dose	1.0⁺
Tetanus	Any	Dependent	2-3 weeks after initial series	0.15*
Meningococcal conjugate	Any	Dependent	2-4 weeks	2+
Prevnar15	Any	Dependent	4 weeks	0.35⁺
Prevnar20	Any	Dependent	4 weeks	0.35⁺
Prevnar21	Any	Dependent	4 weeks	0.35⁺
Pneumovax23	>2	Independent	4 weeks	1.3⁺
S. typhi	>2	Independent	4 weeks	1.0+
Rabies virus	Any	Dependent	3 weeks after third dose	0.5*

Understanding a Vaccine Challenge

- Typically providers try to measure pre- and post-vaccine antibody levels to look for immune response
- It is best to use the same lab for pre- and post-comparison
- If a patient is on Ig replacement, common vaccine antibody levels aren't usually checked
  - Exception: *S. typhi*, which is not substantially in Ig products

Practical Pneumococcal Vaccine Specific Considerations

- It is helpful to know which Prevnar vaccine was given and when before interpreting post-PPSV23 response
  - It is helpful for patients to have their vaccination records or sign medical release to obtain them
  - Pneumovax is NOT the same as Prevnar
  - Each Prevnar is a little different in its protection
- Pneumovax challenge has limited value in countries where pneumococcal disease is endemic



Vaccination is a Choice

- It is important for patients and families to discuss all vaccinations with their doctors as each may have risks and benefits
  - Live attenuated vaccines are safe for many but not all patients with PI
  - Live attenuated vaccines can cause infection in some patients with low or poor functioning T cells
  - Some PI may warrant more frequent vaccinations to add protection

Risk of Live Vaccines in PI

BCG vaccination in patients with severe combined immunodeficiency: Complications, risks, and vaccination policies

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Persistent systemic rotavirus vaccine infection in a child with X-linked severe combined immunodeficiency

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Clinical and Experimental Immunology ORIGINAL ARTICLE doi:10.1111/cei.12421

Vaccine-associated varicella and rubella infections in severe combined immunodeficiency with isolated CD_4 lymphocytopenia and mutations in *IL7R* detected by tandem whole exome sequencing and chromosomal microarray

D. K. Bayer,* C. A. Martinez,†

Summary

Vaccines in Patients with PI

In Severe T-cell defects:

SCID, Complete Digeorge syndrome, NEMO,

MHC II deficiency, related disorders

Live vaccines strictly contraindicated

(Rotateq, MMR, Varicella, BCG, Oral polio, Oral typhoid)

Inactivated vaccines likely safe but also likely ineffective.

Vaccines in Patients with PI

In mild to moderate T-cell defects:

DiGeorge Syndrome without Athymia

Ataxia Telangiectasia

Cartilage Hair Hypoplasia

Other select forms of combined immunodeficiency

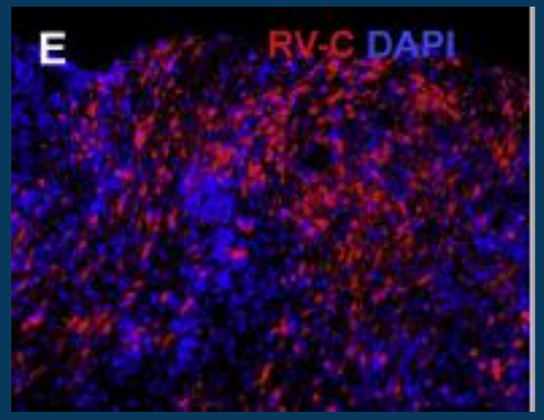
Selected live vaccines may be safe, but evaluation is required first.

Inactivated vaccines safe and may be beneficial.

Complications from MMR Vaccine in CID

- Granulomatous disease described in rare patients with T-cell deficiency disorders
  - Vaccine strain Rubella isolated from lesions
  - Disorders:
    - Ataxia Telangiectasia
    - Nijmegen Breakage Syndrome
    - RAG1/2 deficiency
    - Ligase 4 deficiency
    - WHIM syndrome
    - MHC II deficiency





Perelycina L *et al.,*
J All Clin Immunol 2016

Buchbinder D *et al,*
J Clin Immunol 2019

Vaccines in Patients with PI

<u>In severe B-cell deficiencies</u>:

X-linked agammaglobulinemia

Common variable immunodeficiency

Inactivated vaccines safe but may not be beneficial.

- **Recommended: Inactivated influenza, RSV, COVID-19**

Live vaccines generally avoided (especially when on Ig replacement)

Vaccines in Patients with PI

In mild to moderate B-cell deficiencies:

Selective IgA deficiency

IgG subclass deficiencies

Inactivated vaccines safe and likely beneficial.

Routine live vaccines may be given and are recommended.

Vaccines in Patients with PI

<u>In Phagocyte deficiencies</u>:

Chronic granulomatous disease

Leukocyte adhesion deficiency,

Live bacterial vaccines contraindicated

Oral polio, Oral typhoid, BCG (outside US)

Inactivated vaccines and live viral vaccines safe and recommended.

Vaccines & Immunoglobulin Replacement

- **Immunoglobulin provides protection against many vaccine-preventable illnesses**
  - **Exceptions:**
    - **Annual influenza strains**
      - Annual inactivated Influenza vaccine recommended for patients and caregivers.
    - **HPV:** inactivated vaccines recommended
    - **COVID-19** vaccines recommended
- **Live virus vaccinations are contraindicated when on Immunoglobulin replacement**

Vaccination For Close Contacts

- Generally speaking, doctors recommend close contacts (e.g. family, caregivers, household members) to those with PI are fully vaccinated to reduce exposure to illness
- Some live attenuated vaccines can lead to exposure to the virus in body fluids and stool for a few weeks, so patients may need to limit contact with recently vaccinated individuals
  - MMR, Varivax: transmission very unlikely
    - If local rash occurs after varivax: cover it with a dressing and call your immunologist.
  - **EXCEPTIONS**:
    - Avoid oral poliovirus (not used in US)
    - Avoid oral typhoid vaccine (Inactivated available).

Vaccines For Close Contacts

Recommendations for live viral and bacterial vaccines in immunodeficient patients and their close contacts

Medical Advisory Committee of the Immune Deficiency Foundation

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Houston and Shenandoah, Tex, Bethesda, Columbia, and Baltimore, Md, Durham, NC, Iowa City, Iowa, Buffalo and New York, NY, Boston, Mass, Memphis, Tenn, Cincinnati, Ohio, Denver, Colo, Miami, Fla, Shelburne, Vt, Seattle, Wash, San Francisco and Los Angeles, Calif, Milwaukee, Wis, and Philadelphia, Pa

Vaccines are

safe and effective

at preventing
serious diseases.

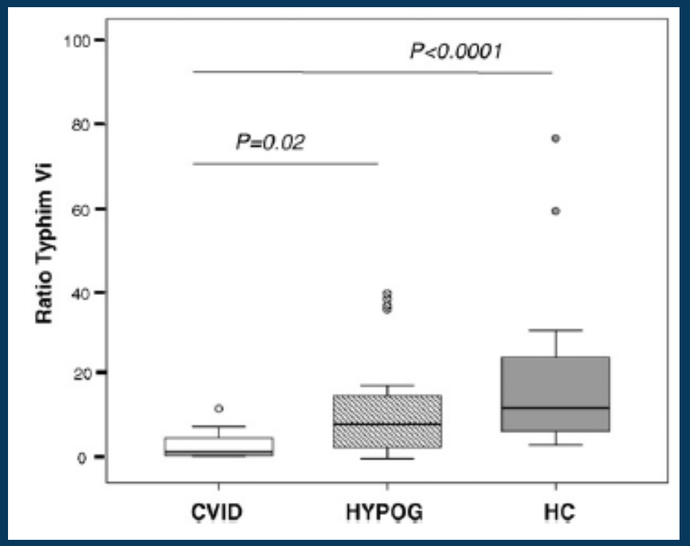


National Immunization
Awareness Month

Vaccine Responses with Antibody Deficiency

- EMPATHY study (2016)
  - 41% of patients with CVID responded to inactivated Typhoid vaccine

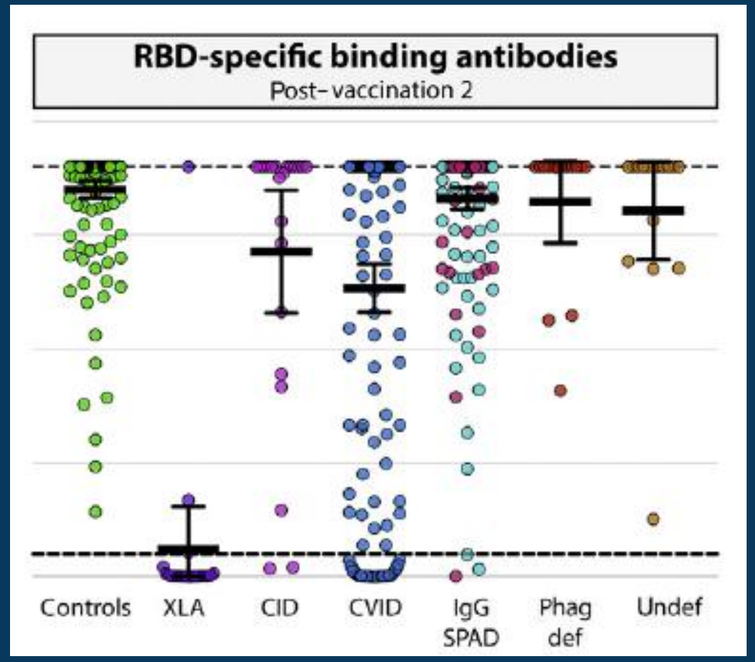
- Influenza vaccine studies
  - In 3 studies, 20-30% of antibody deficiency patients had detectable responses to inactivated influenza vaccine

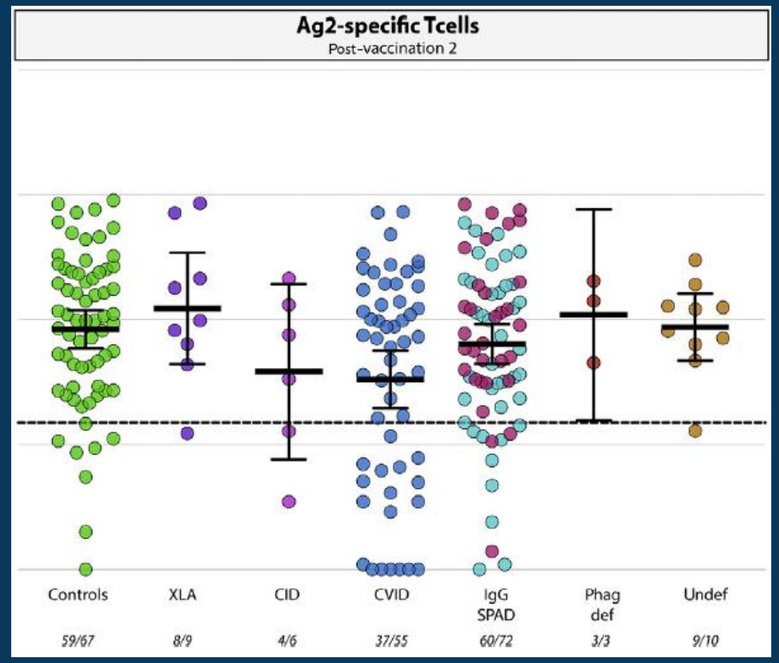


Sanchez-Ramon S *et al., Clin Immunol* 2016

COVID-19 Vaccines in PI

- Many patients with PID have some responses to COVID-19 vaccines and boosters
- T cell responses are identified in many patients with PI





Dalm *et al J Allergy Clin Immunol*. 2022

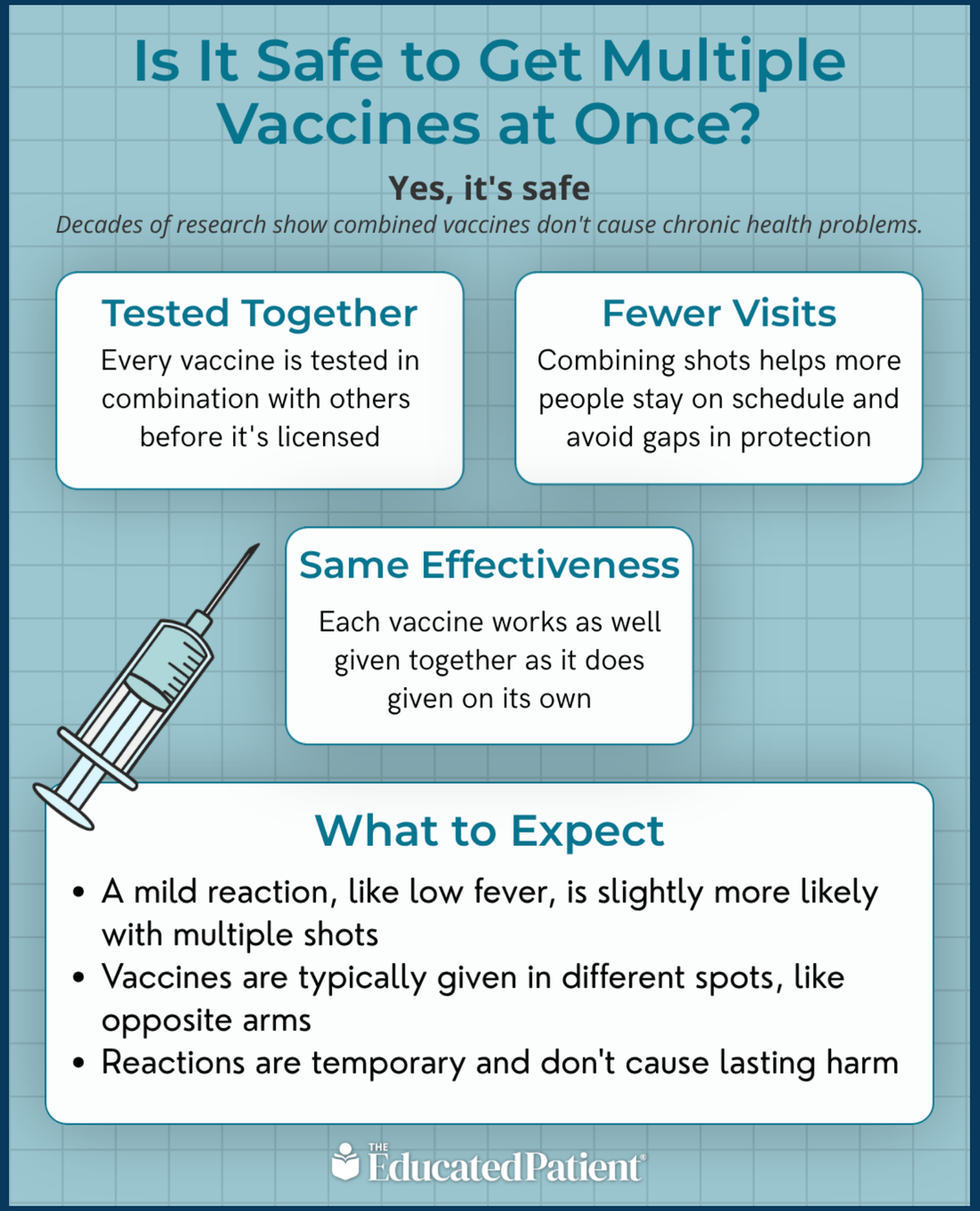
RSV Vaccines and Monoclonal Antibodies

- New vaccines reduce severe RSV by up to 80%

Vaccine product	Doses / intervals	Age approvals
Abryso	1 dose	60 years and in pregnant women (32-36 weeks gestation)
Arexvy	1 dose	60 years
mRESVIA	1 dose	60 years

RSV Vaccines in PI

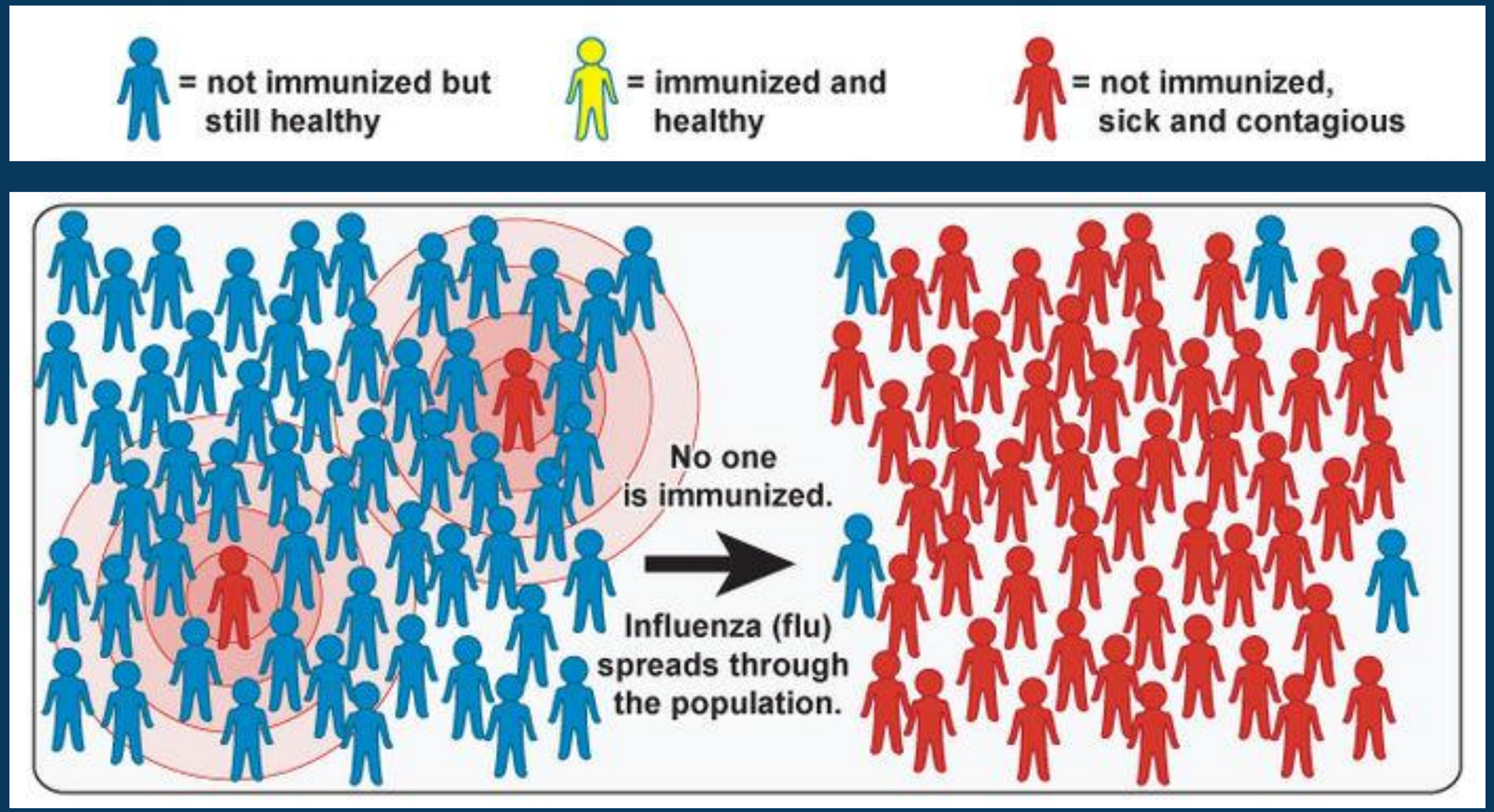
- RSV efficacy was evaluated in immunocompromised population
  - Decreased antibody response
  - In first season, RSV vaccines are effective at reducing hospitalization 65-75%
  - In second season, immunity wanes



- Is it ok to get a vaccine if/when you are sick?
  - In most cases YES if you are recovering from illness
  - We do not typically recommend vaccination if you actively have a fever

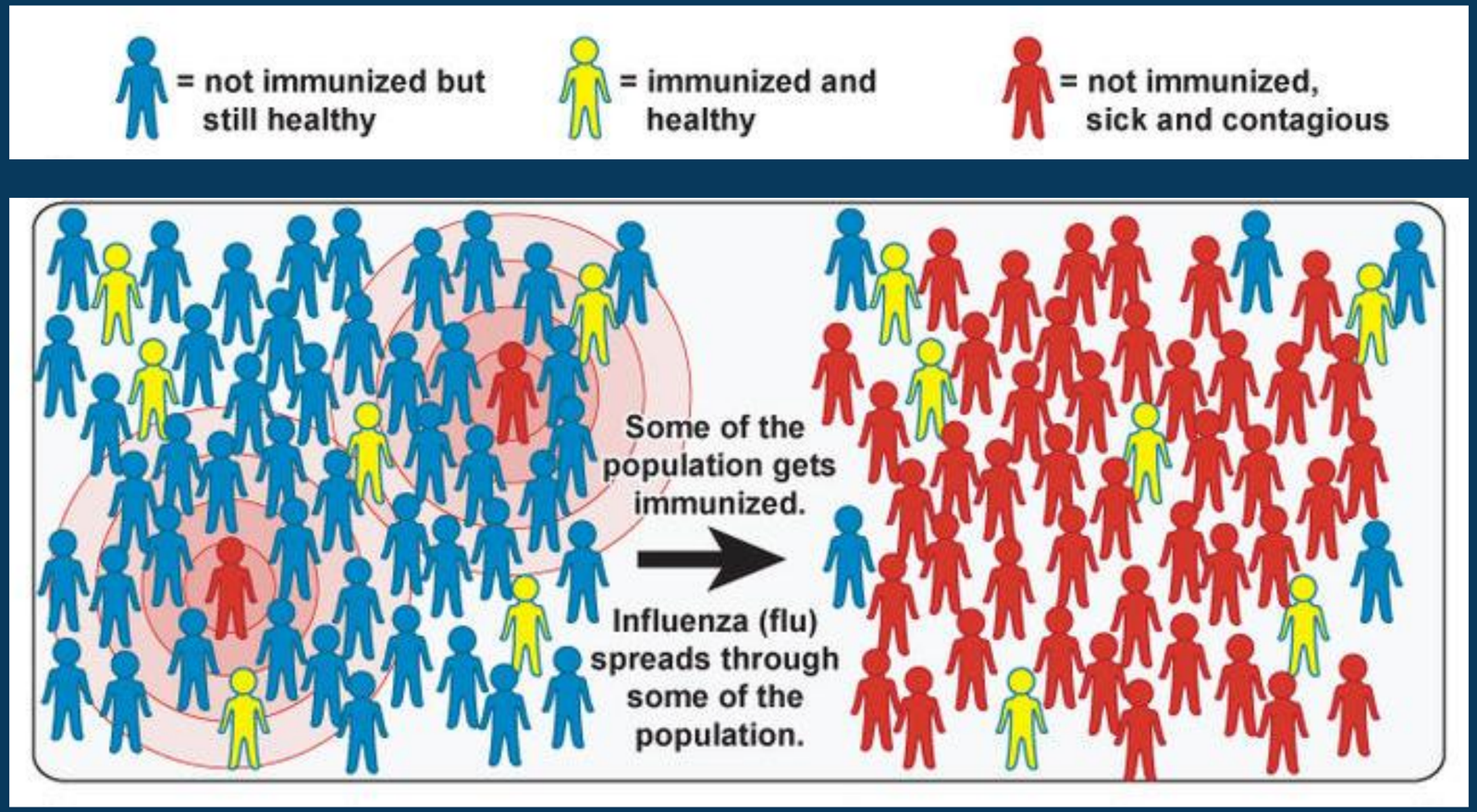
Vaccines and Public Health

- Vaccination prevent disease spread through “herd immunity”



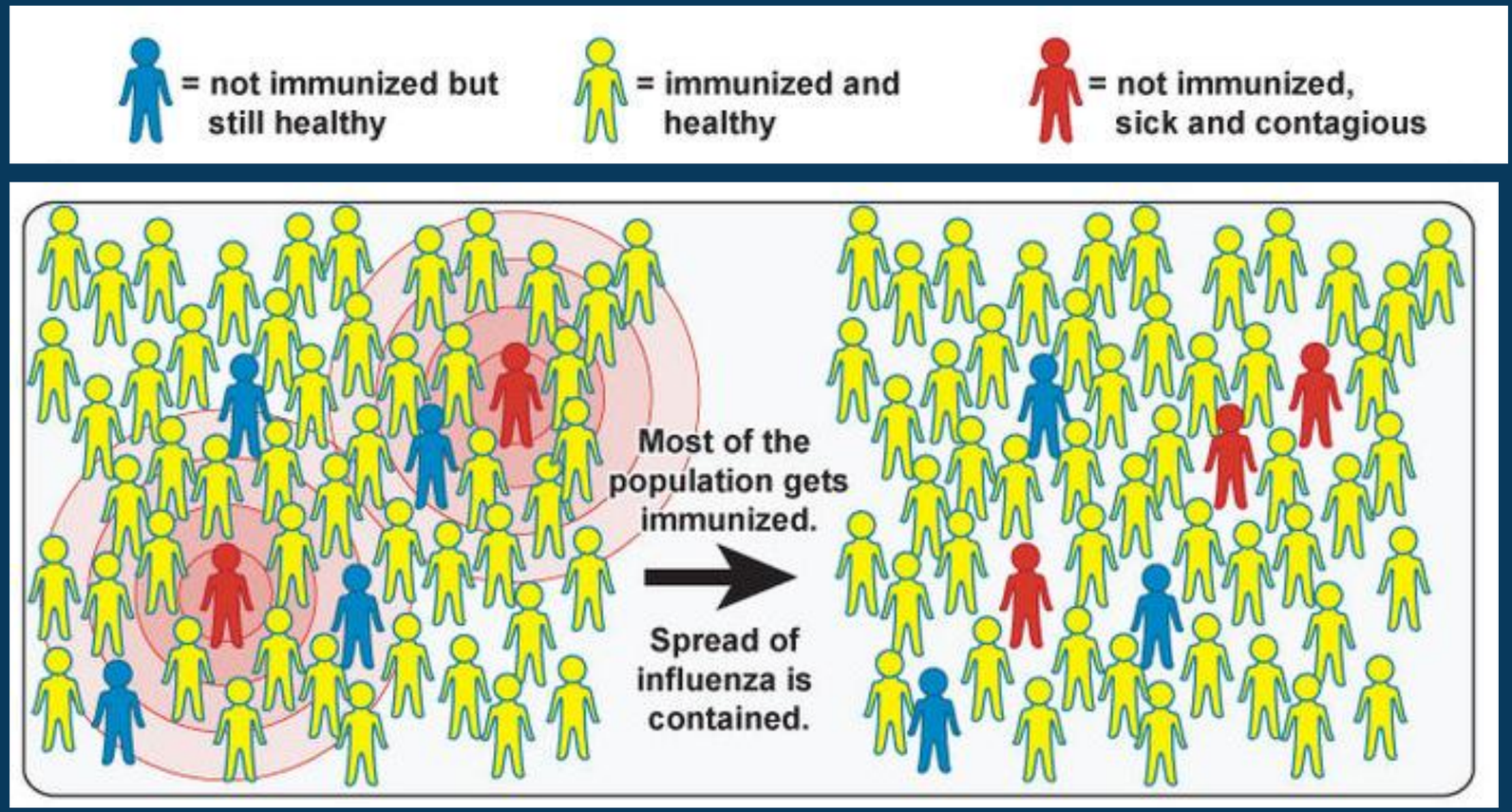
Vaccines and Public Health

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Vaccines and Public Health

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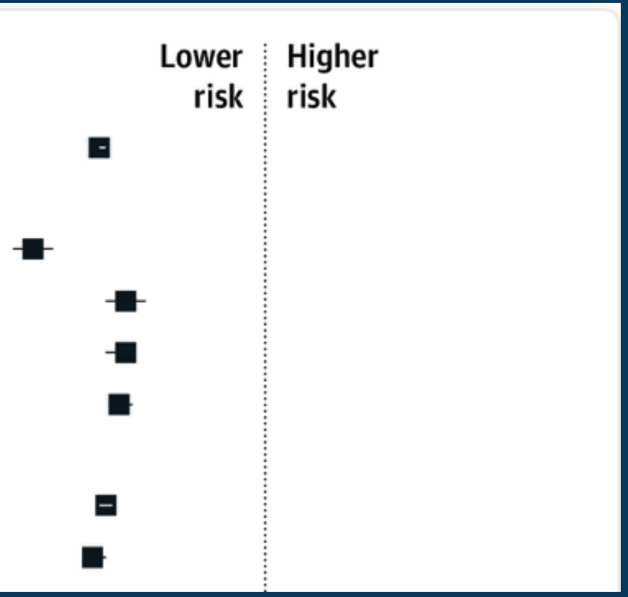
Herd immunity is critical for protecting the young and immunocompromised

- In the US:
  - 3 million infants under 1 year old
  - ~18 million individuals with cancer
  - ~500,000 individuals with primary immunodeficiency
  - 400,000 solid organ transplant recipients
  - 20,000 bone marrow transplants (annually)

COVID-19 vaccines and mortality

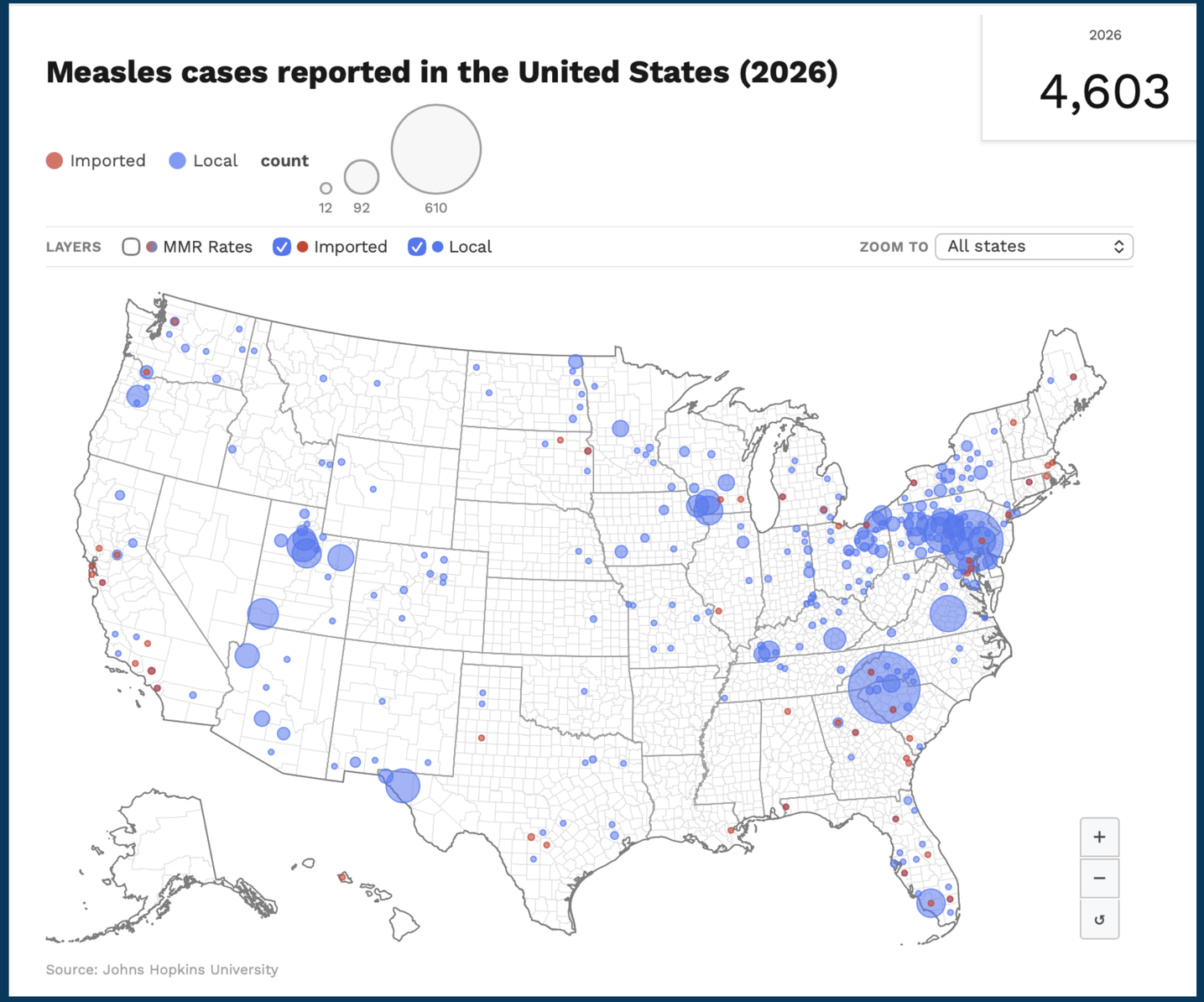
- Vaccines reduced risk of COVID-19 death by 74% in large multi-year French study
  - No increase in secondary co-morbidities

Characteristic	Unvaccinated, No. of events/total No.	Vaccinated, No. of events/total No.	wHR (95% CI)
Overall	32 662/5 932 443	98 429/22 767 546	0.75 (0.75-0.76)
Age, y			
18-29	2 769/1 777 782	6 604/6 553 907	0.65 (0.62-0.68)
30-39	4 488/1 737 069	11 254/5 535 008	0.79 (0.76-0.82)
40-49	8 333/1 322 270	27 771/5 889 066	0.79 (0.76-0.80)
50-59	17 080/1 095 322	52 800/4 789 565	0.78 (0.77-0.80)
Sex			
Male	22 062/3 056 404	64 946/11 078 943	0.76 (0.75-0.77)
Female	10 600/2 876 039	33 483/11 688 603	0.74 (0.73-0.76)

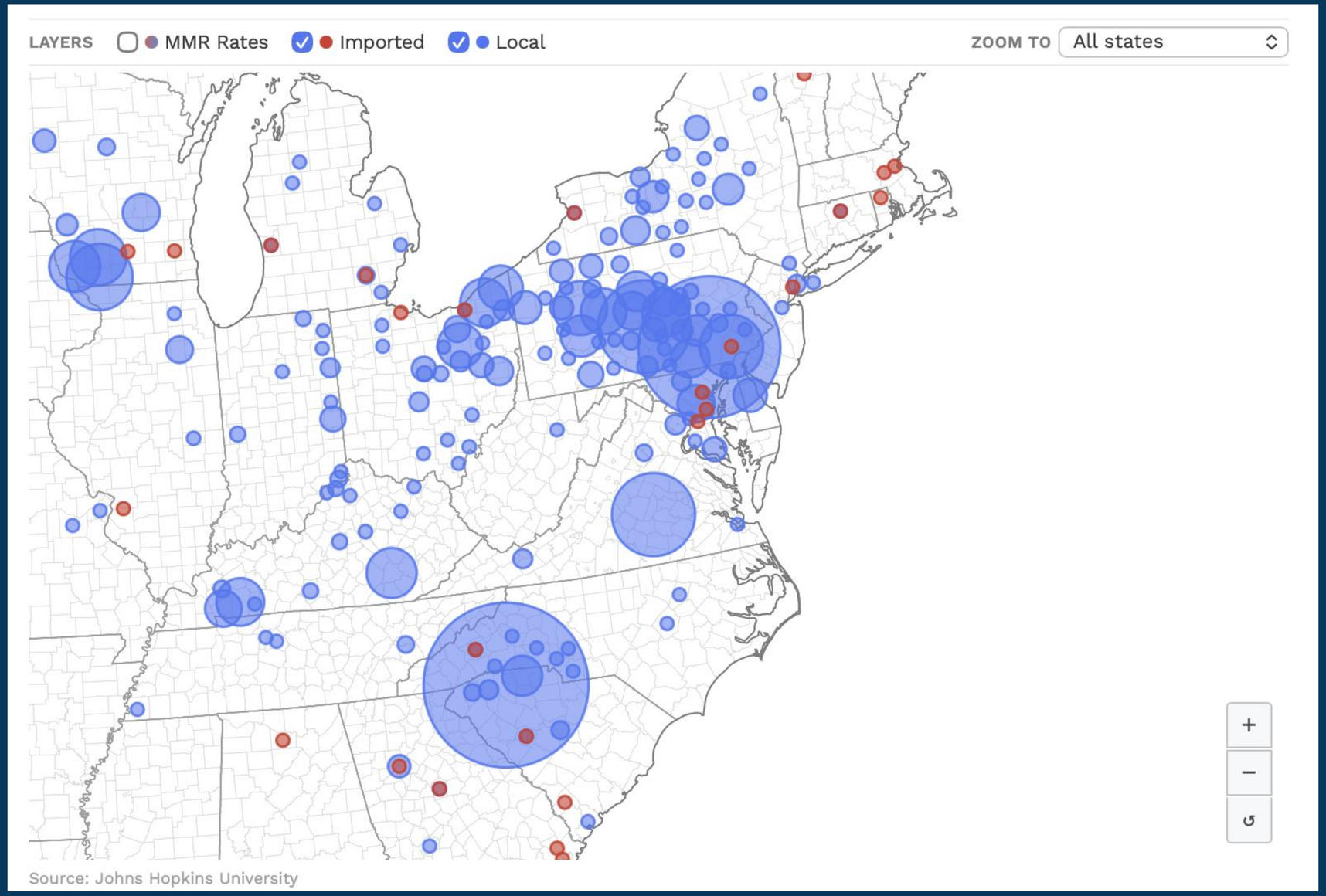


Semenzato L *et al JAMA Network Open*, 2025

2026 US Measles Outbreak



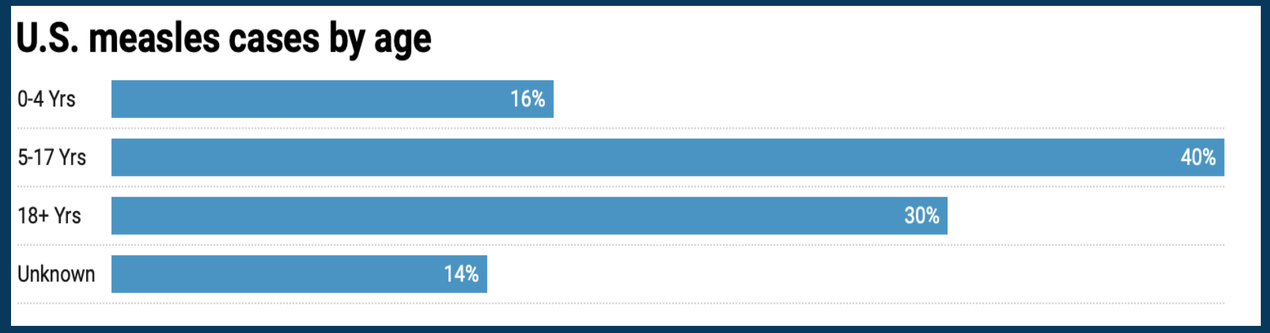
2026 US Measles Outbreak

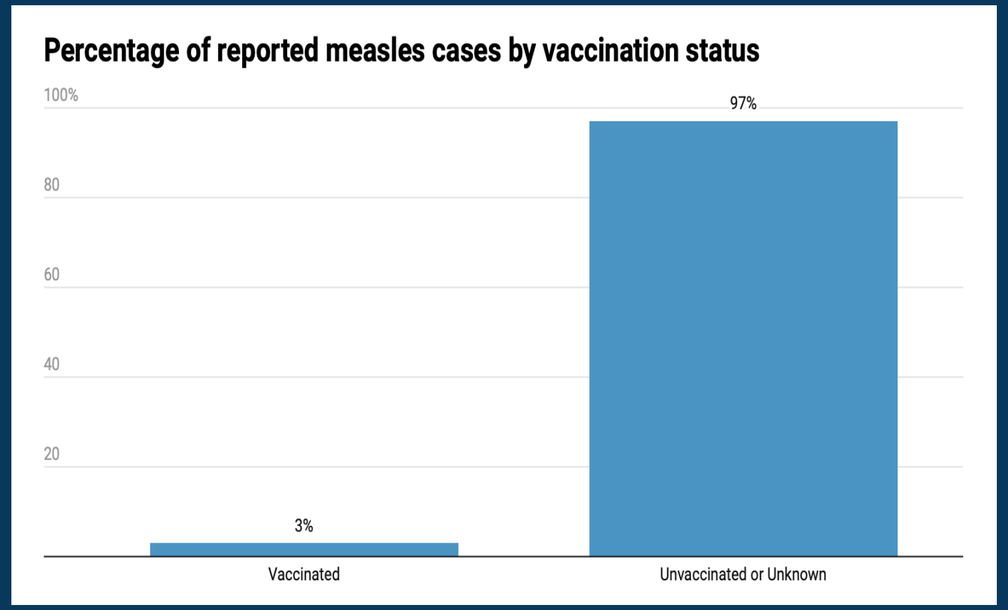


2026 US Measles Outbreak

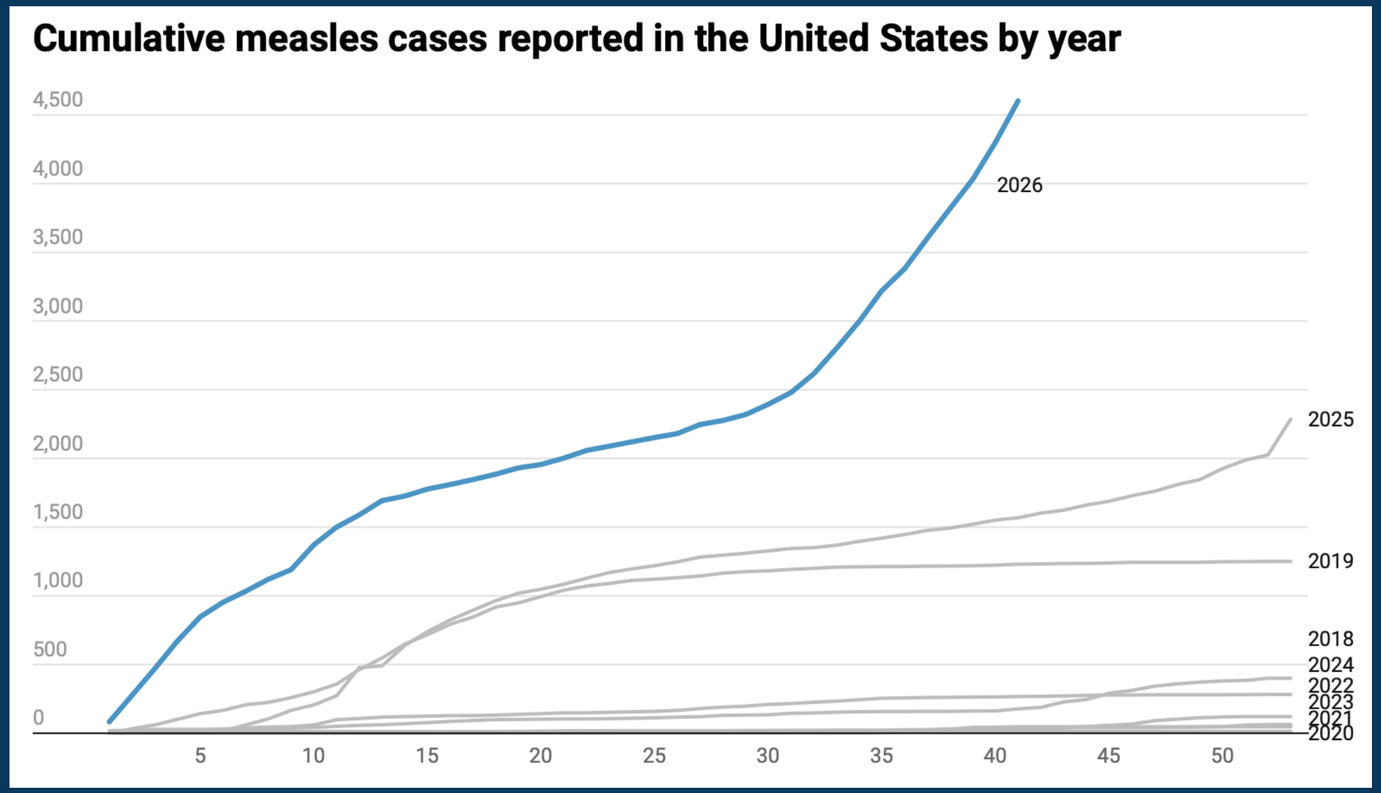
Statistics for 2026 Measles outbreak:

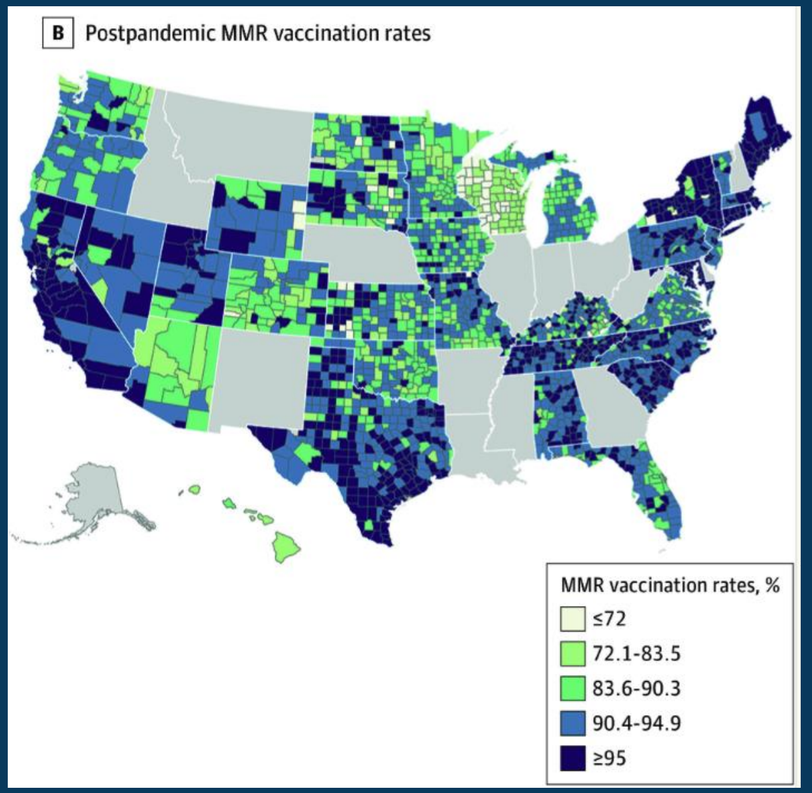
- 10% hospitalization rate
- 6 probable measles deaths*





2026 US Measles Outbreak

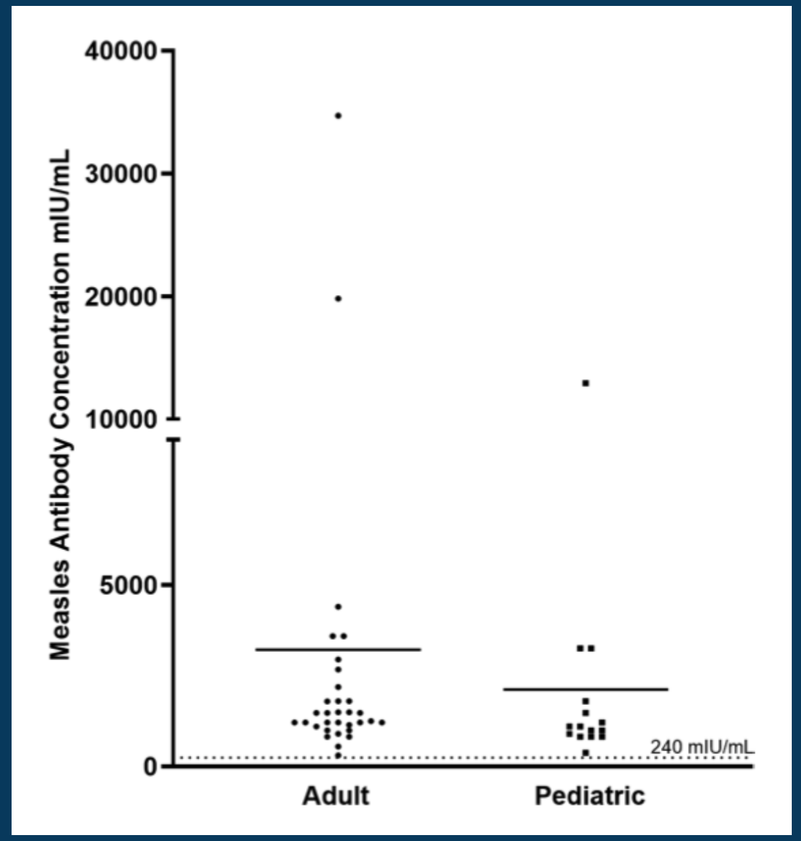




Response to Measles outbreak

- Healthy relatives: vaccinate
- PI patients:
  - Ig products are protective

- Advocate
- Vote



Rajendram V *et al Plos One* 2025



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Acknowledgements





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