Measles – Historical Perspective on Disease Impact and Vaccine Development

Robert L. Atmar, M.D.

Baylor College of Medicine

Disclosures

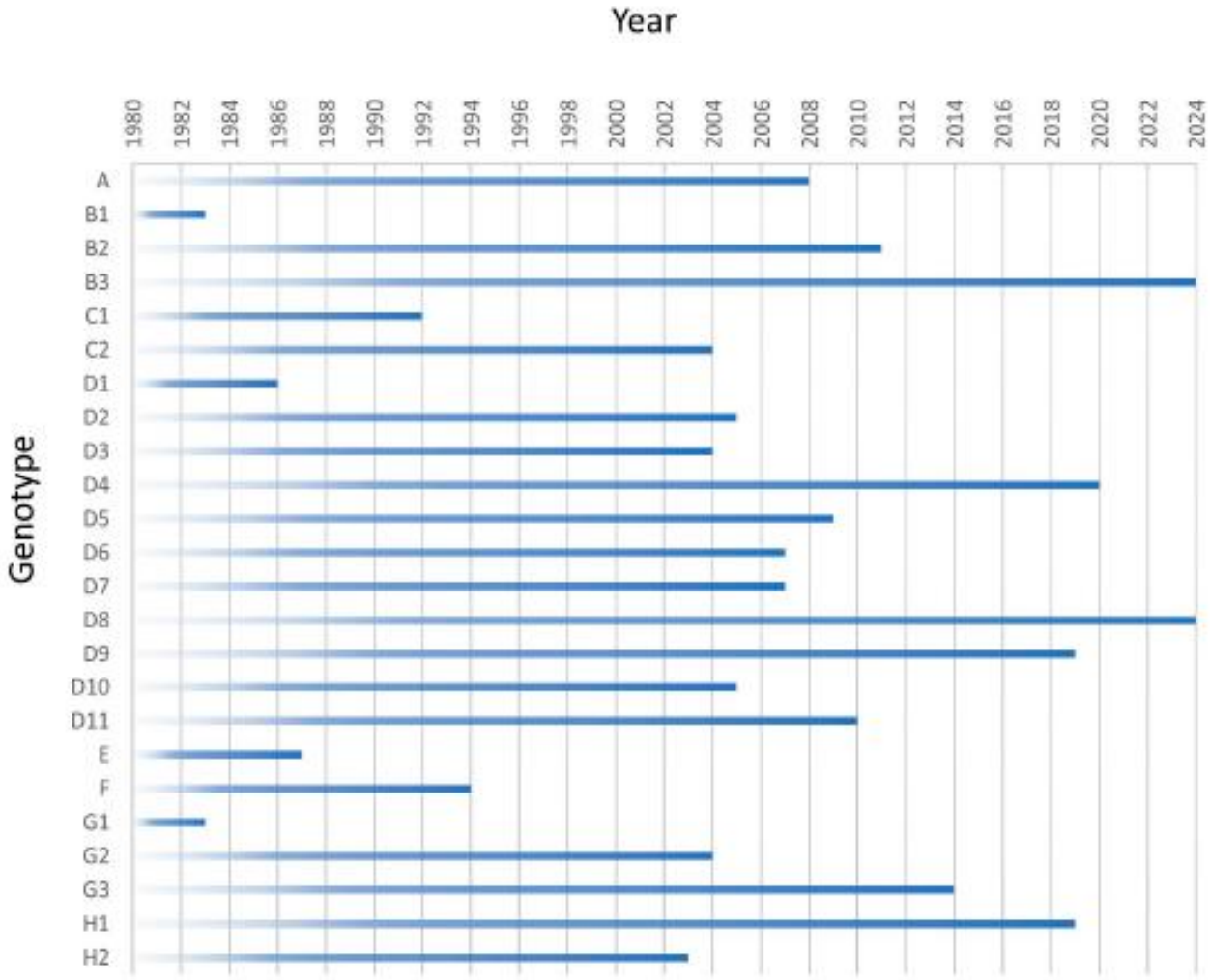
- **Nothing to disclose**

Measles - History

- Recognized as early as 7th century by Al Yehudi
- Rhazes described as distinct from smallpox in 10th century
- 1846 Faroe Island outbreak – characteristics described by Danish physician Peter Panum
- 1911 – Goldberger and Anderson recognized as virus (filterable agent)
- 1954 – Enders and Peebles grew the virus in human and monkey kidney cell lines

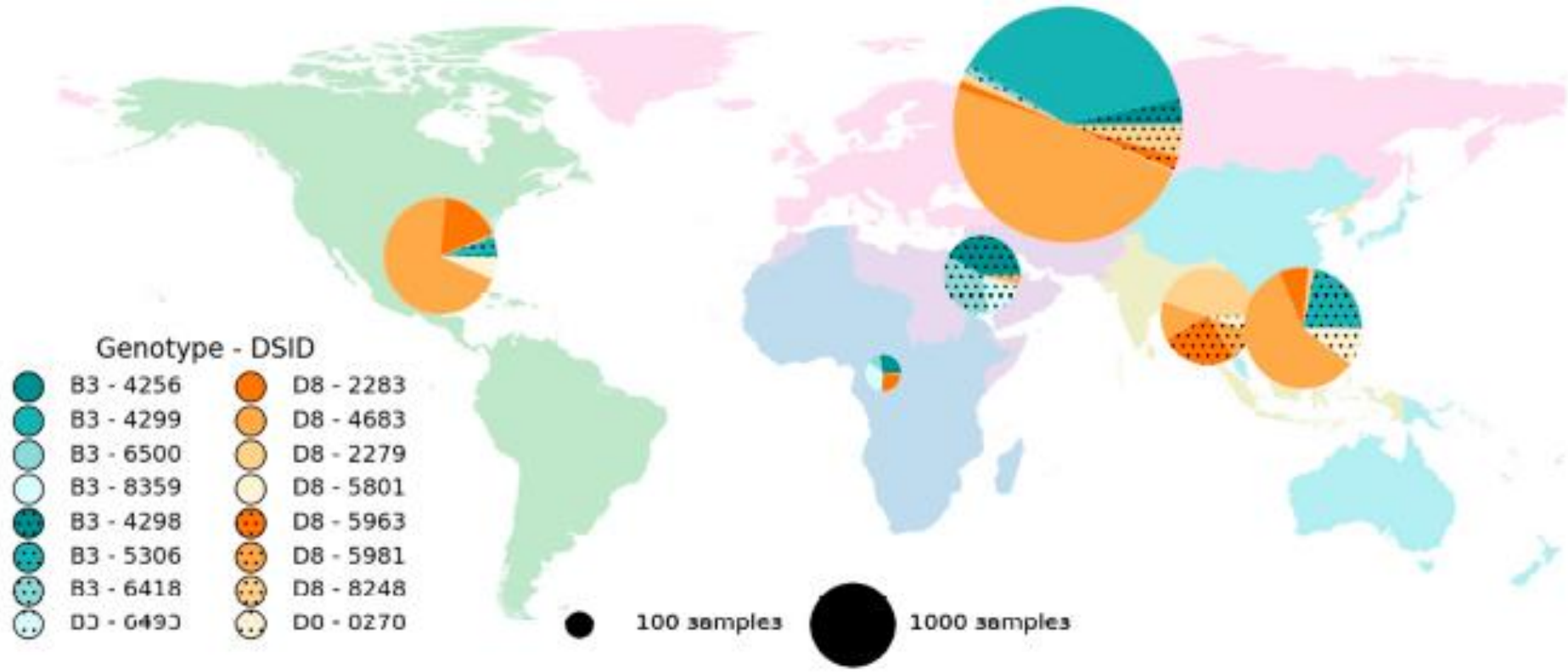
Rubeola – the Virus

- **Single-stranded RNA virus in the *Paramyxoviridae* family, genus *Morbillivirus***
- **Eight viral proteins**
- **24 genotypes (A, B1-B3, C1-C2, D1-D11, E, F, G1-G3, H1-H2), but only a few commonly circulating globally**
- **One serotype**



Bankamp et al. *Vaccines* 2024;12:810

Global Distribution of Measles Virus Genotypes by WHO Region: 2019-2023



NOTE: D8 – 9171 (Ontario lineage) not common

Bankamp et al. *Vaccines* 2024;12:810

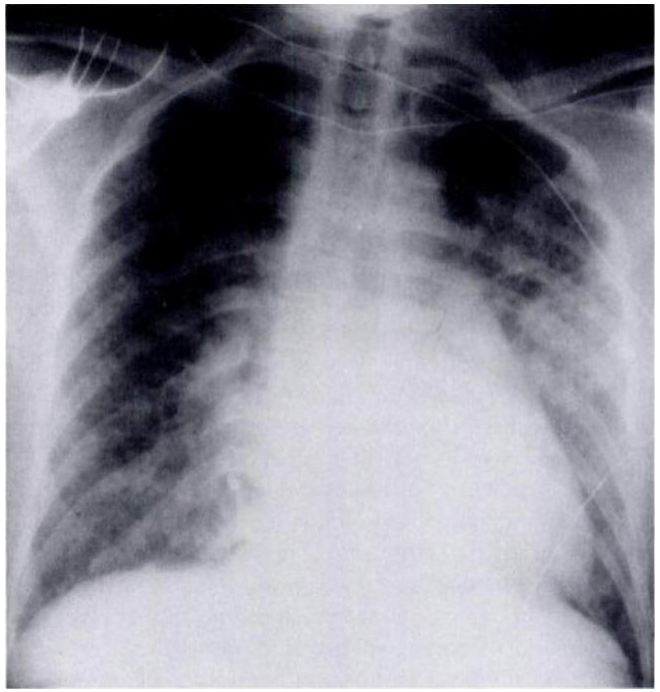
Measles - Disease

- Incubation period – 10-14 days (range 7-21 days)
- Prodrome – fever, malaise, cough, coryza, conjunctivitis (3 C's)
- Rash
  - Enanthem – Koplik's spots 2 days before skin rash and 1-2 days after
  - Exanthem – maculopapular; head → trunk → extremities; onset 2-4 days after prodrome onset and can last 4-8 days
- Transmissibility – greatest in 4 days before and after rash onset

https://www.cdc.gov/measles/signs-symptoms/photos.html

Measles - Complications

- Respiratory – viral or *bacterial*
  - Pneumonia (most common cause of death globally)
  - Otitis media – in ~10% of children
- Diarrhea (2nd most common cause of death globally)
- Blindness (due to corneal scarring in areas with vitamin A deficiency)
- CNS
  - Post-infectious encephalitis (1 per 1000-2000 cases)
  - SSPE – 1 per 10K-100K cases (years later)
- Death – CFR 3-6% in some countries (1-3/1000 in US)



Chest 1993;103:1625

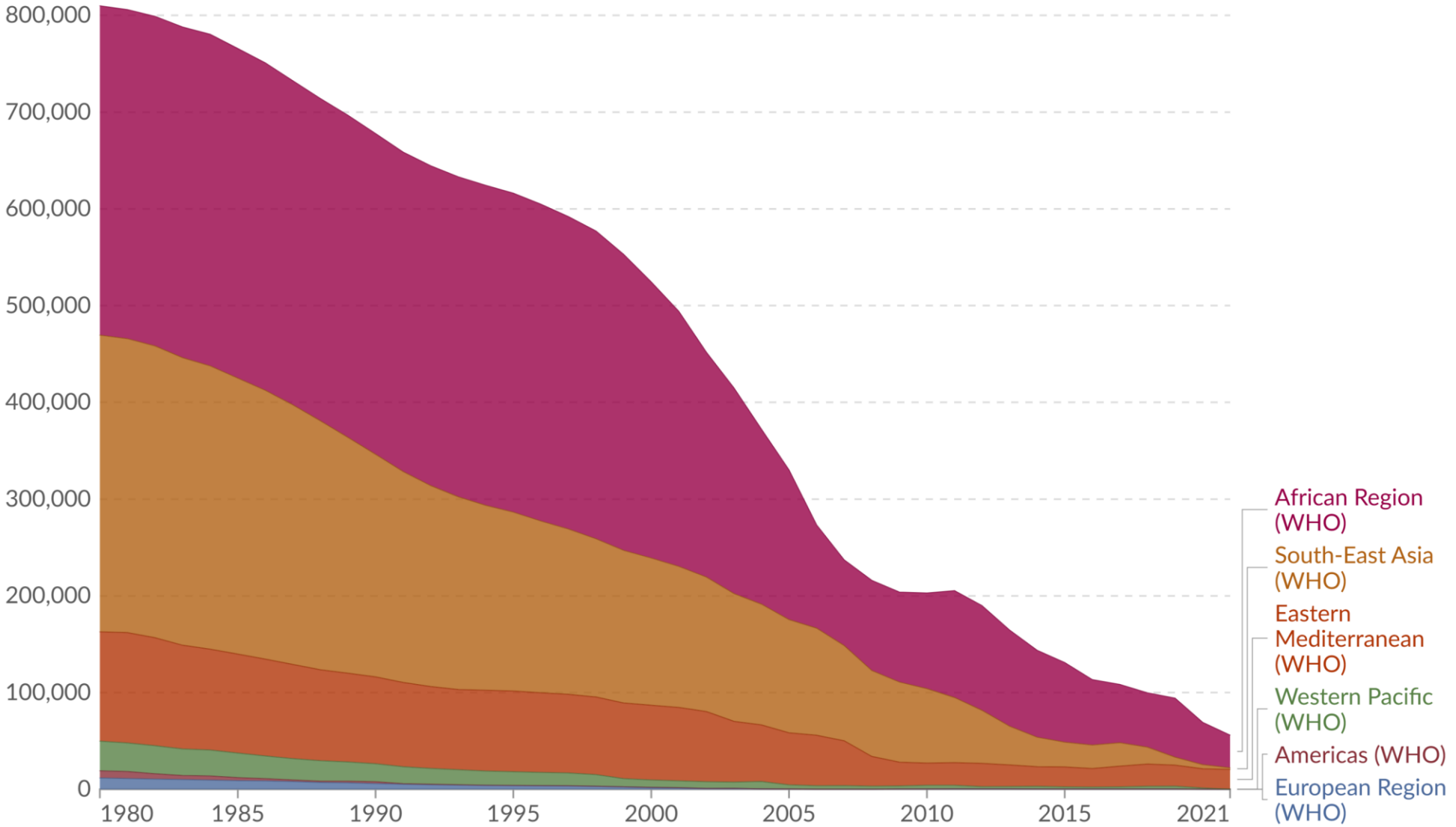
Measles – Other Clinical

- Pregnant women
  - Prematurity, spontaneous abortion (not congenital abnormalities)
  - ? Increased pneumonia
- Immunocompromised
  - May have pneumonia without rash
  - Increased complications (pneumonia, hospitalizations, encephalitis)
  - Increased mortality
- Hepatitis and sinusitis in adults as additional complications

Deaths due to measles by region, 1980 to 2021

Our World in Data

Estimated annual number of deaths due to measles[1].

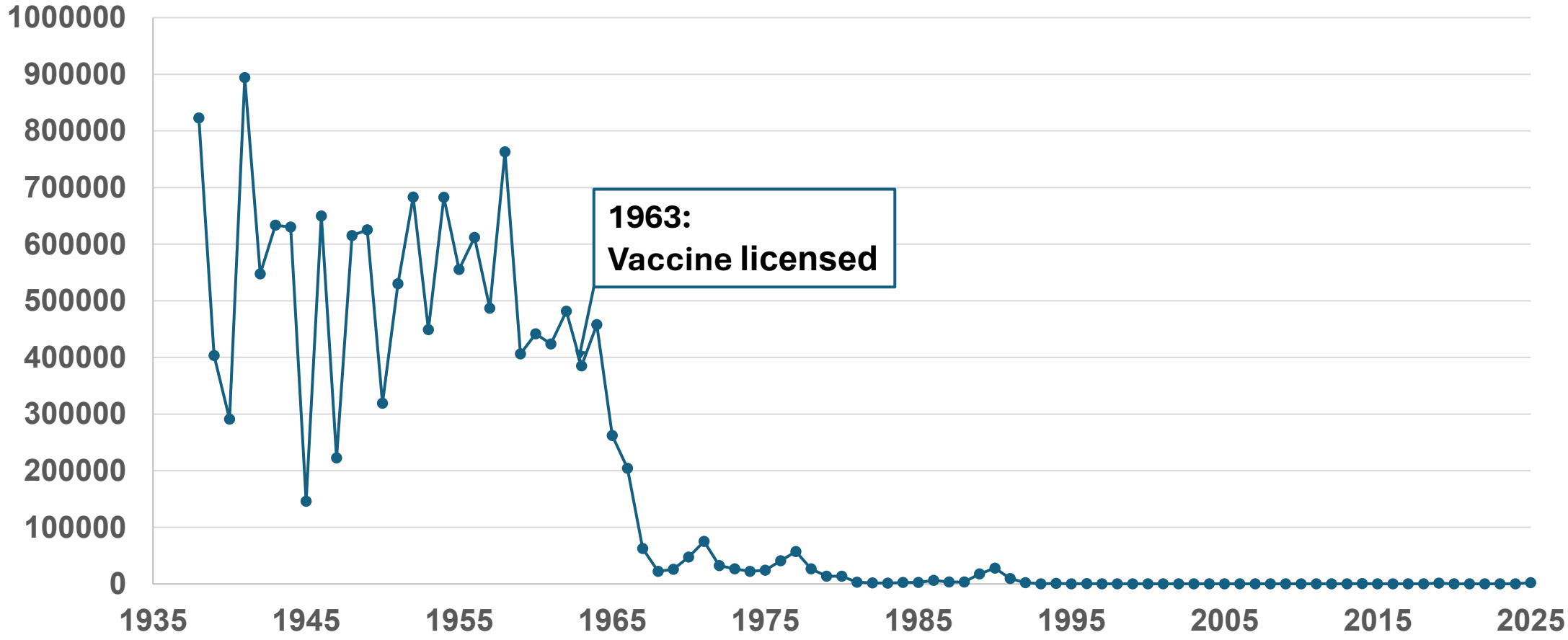


Data source: IHME, Global Burden of Disease (2024)

OurWorldinData.org/vaccination | CC BY

https://ourworldindata.org/grapher/deaths-due-to-measles-gbd

Reported Cases of Measles in US 1938-2025



https://ourworldindata.org/grapher/number-of-measles-cases

Measles Vaccines

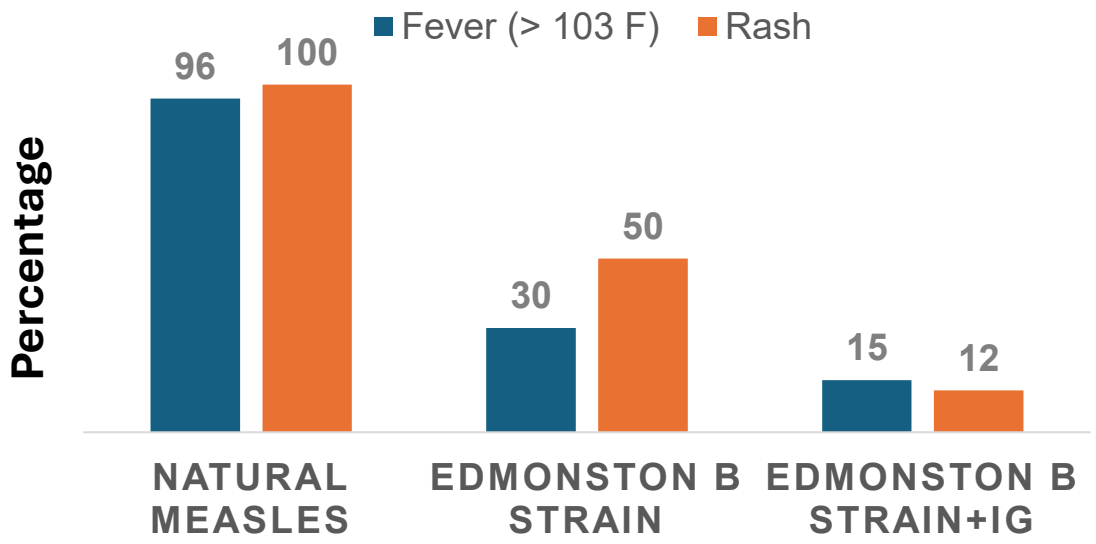
- **Inactivated (formalin-inactivated, alum-precipitated)**
  - **1963-1967**
  - **Short term immunity**
  - **Atypical measles syndrome – rash palms/soles spreads centripetally; erythematous → maculopapular → vesicular, petechial or purpuric; lung involvement common; altered immune response and immune complex formation**

Atypical measles rash
A: m-p and purpuric rash
B: purpuric rash of palm

***BMJ Case Rep* 2015; bcr2015211054**

Measles Vaccines

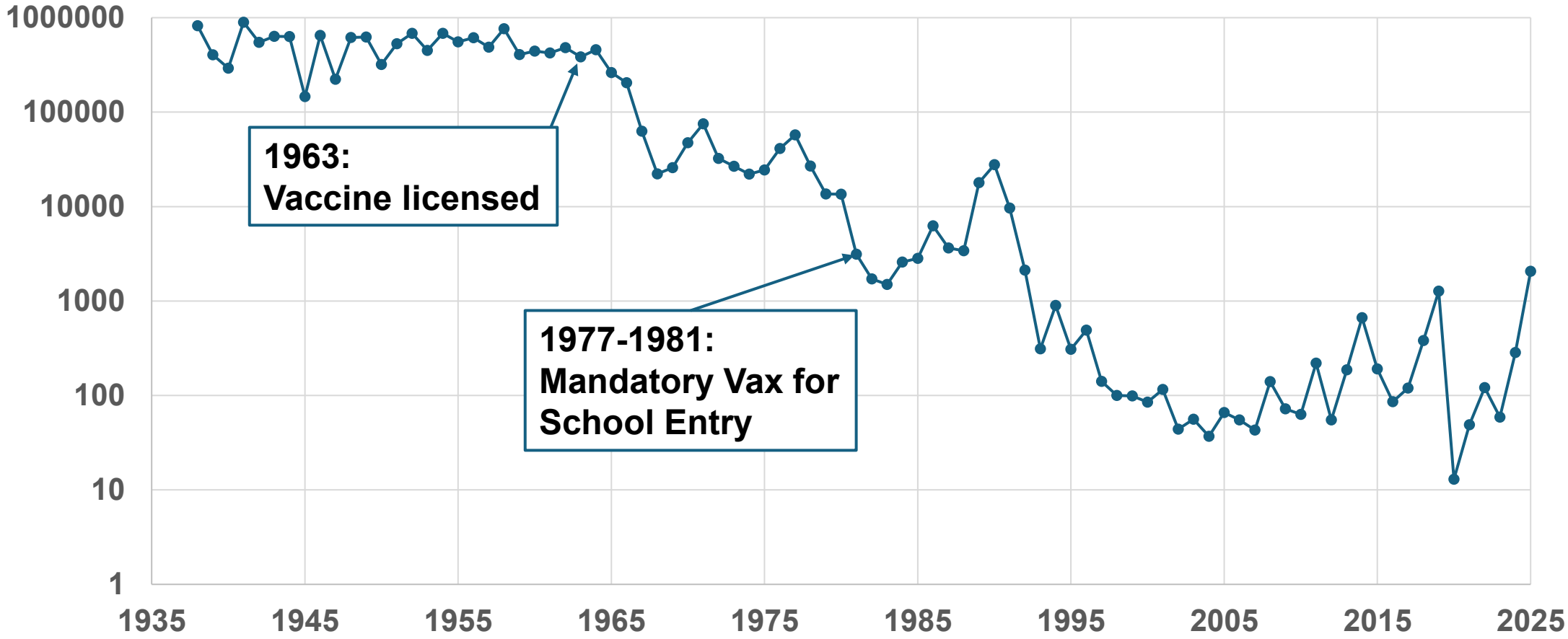
- **Live-attenuated (Edmonston B) – Genotype A**
  - **1967-1975**
  - **Fever, rash common**
  - **Administered with Ig → modified measles syndrome; some signs can be absent**



Measles Vaccines

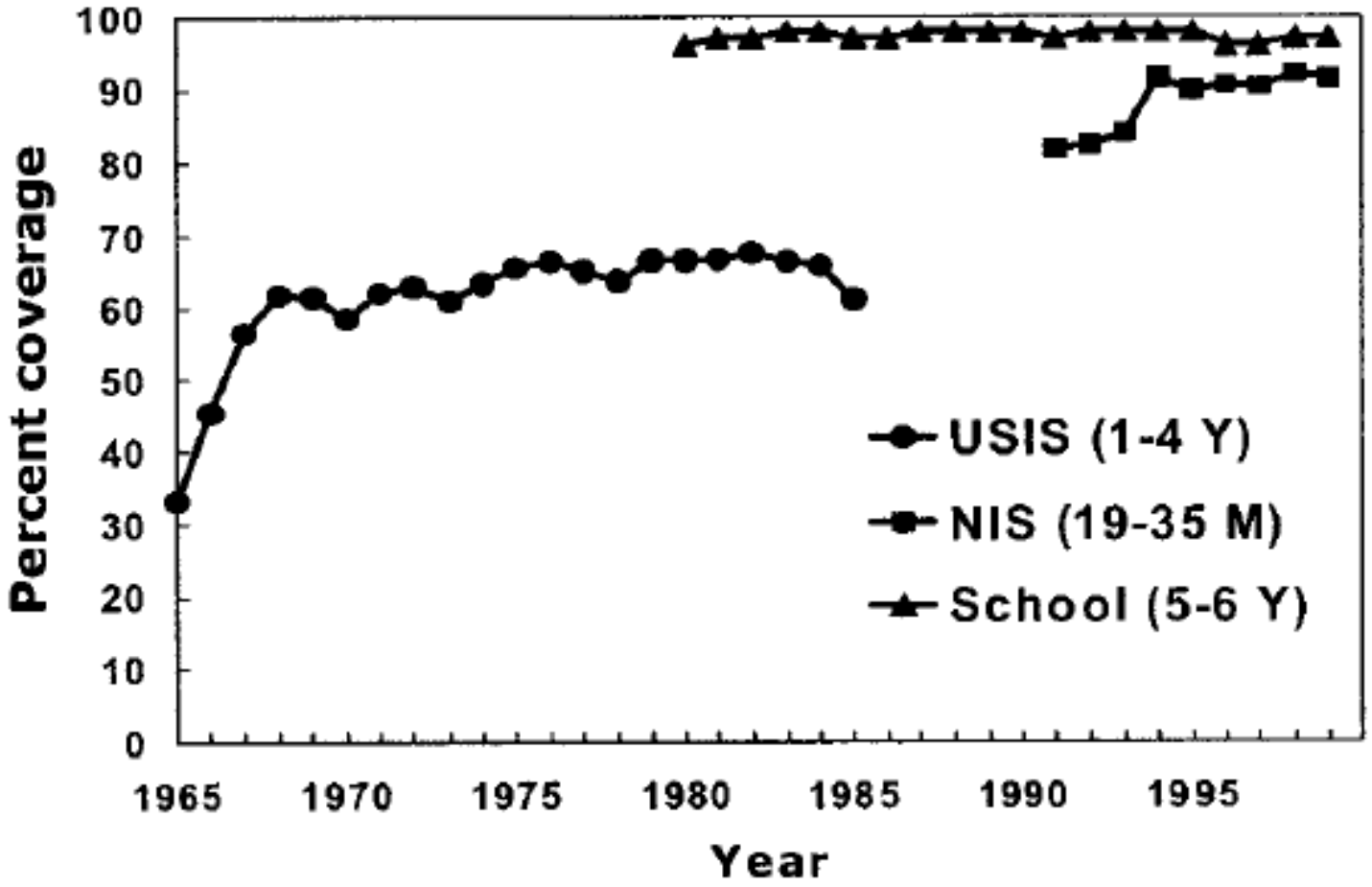
- **Live-attenuated – further attenuated through serial passage; fever (≥ 103 F in 5-15%)**
  - **Moraten (Merck): 1968 – present**
  - **Schwarz (GSK): 2022 – present**
- **Part of MMR: 1971 – present**
- **Part of MMRV: 2005 – present**

Reported Cases of Measles in US 1938-2025



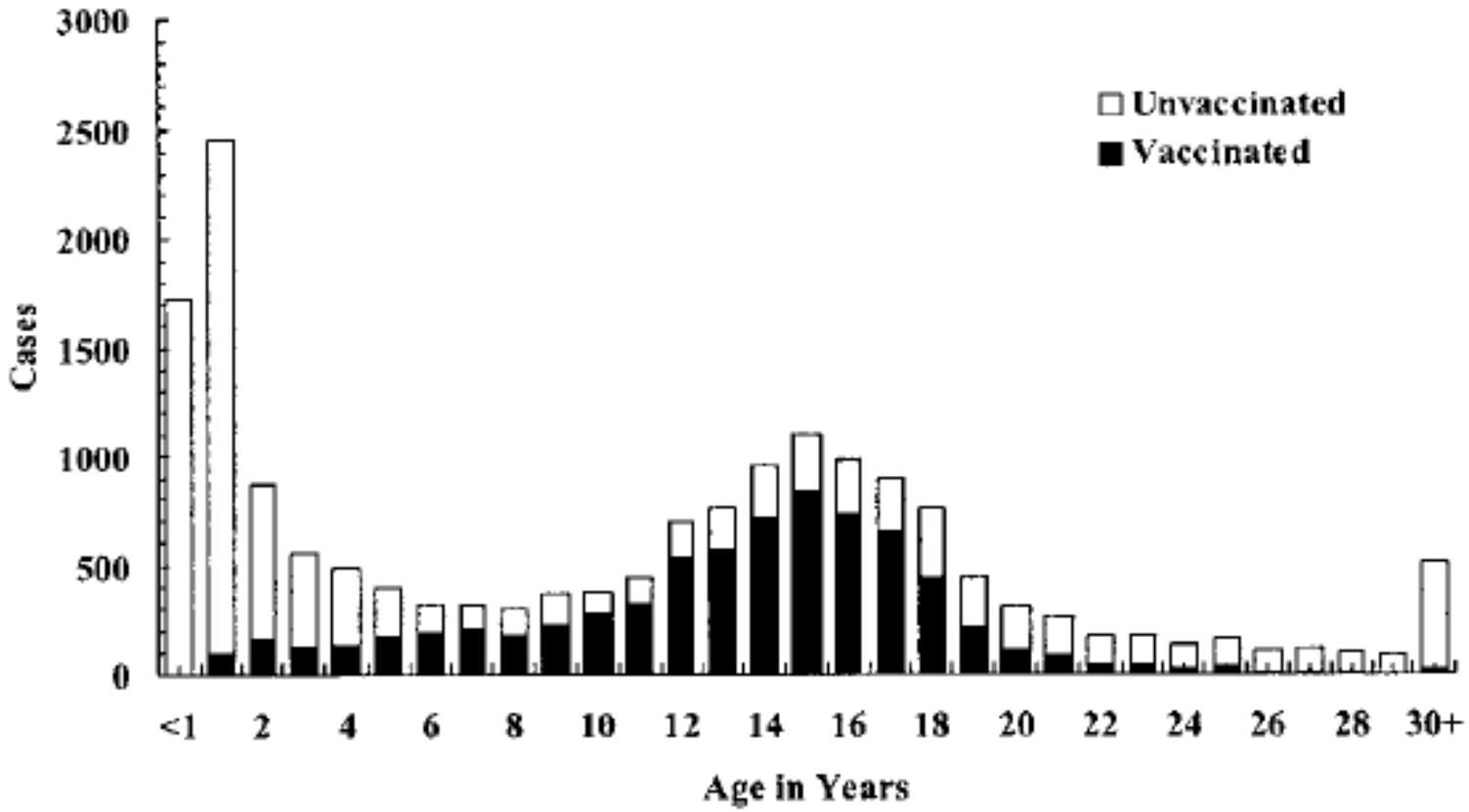
https://ourworldindata.org/grapher/number-of-measles-cases

Measles Vaccine First Dose Coverage by Age Group – US, 1964-1999



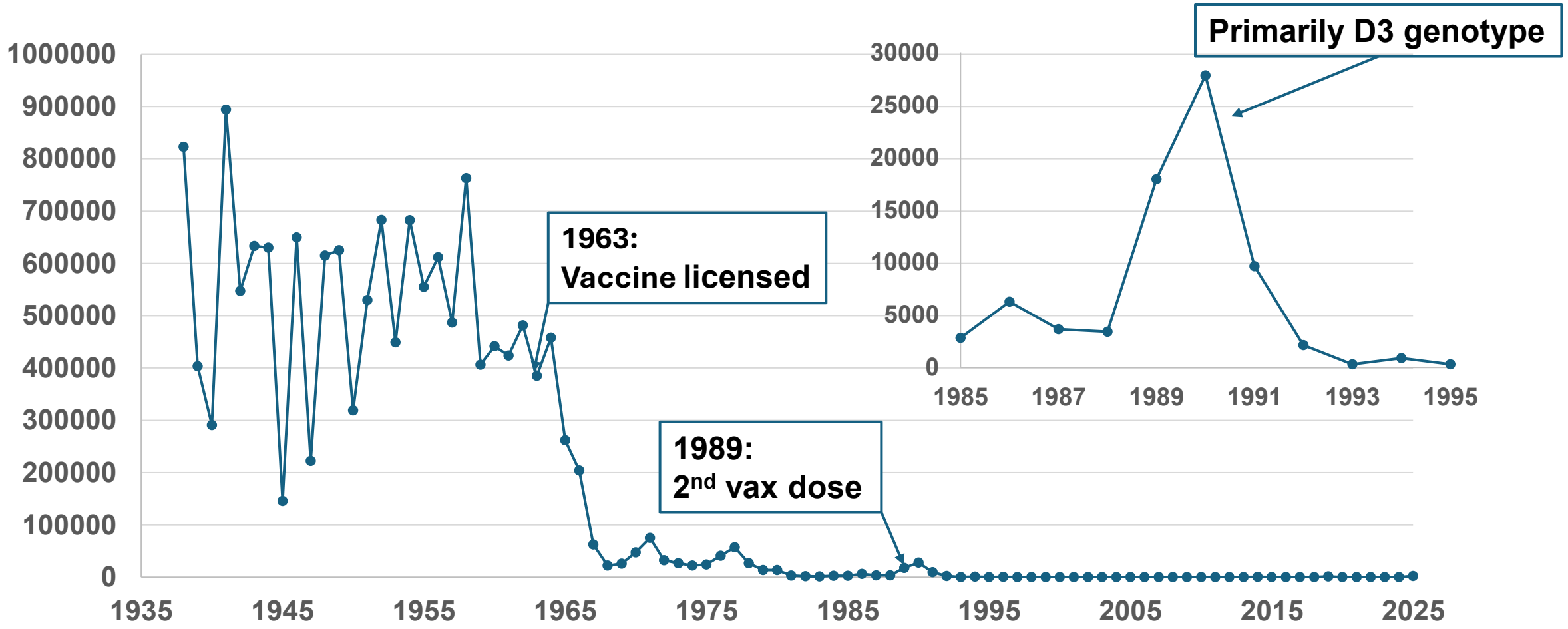
Hinman et al. *J Infect Dis* 2004;189(suppl 1): S17

Reported Measles Cases in US by Age and Vaccination Status – 1985-1988



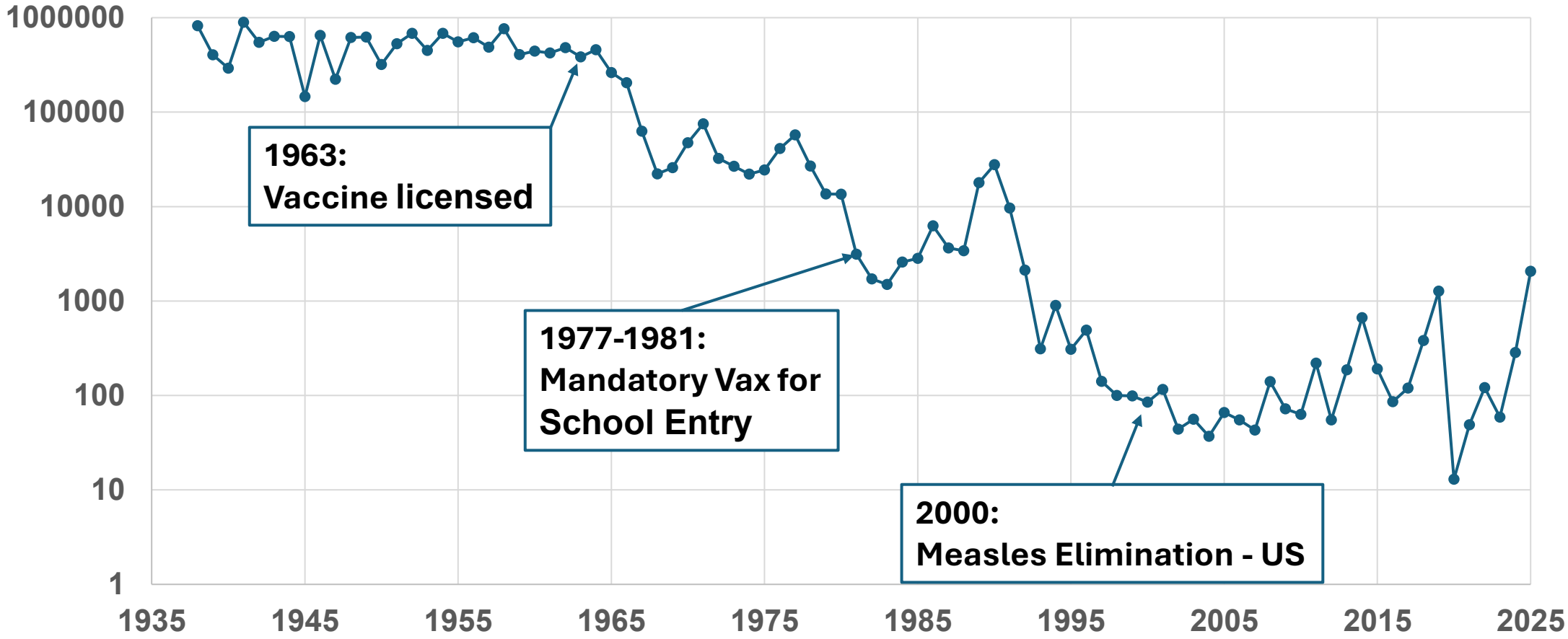
Hinman et al. *J Infect Dis* 2004;189(suppl 1): S17

Reported Cases of Measles in US 1938-2025



https://ourworldindata.org/grapher/number-of-measles-cases

Reported Cases of Measles in US 1938-2025



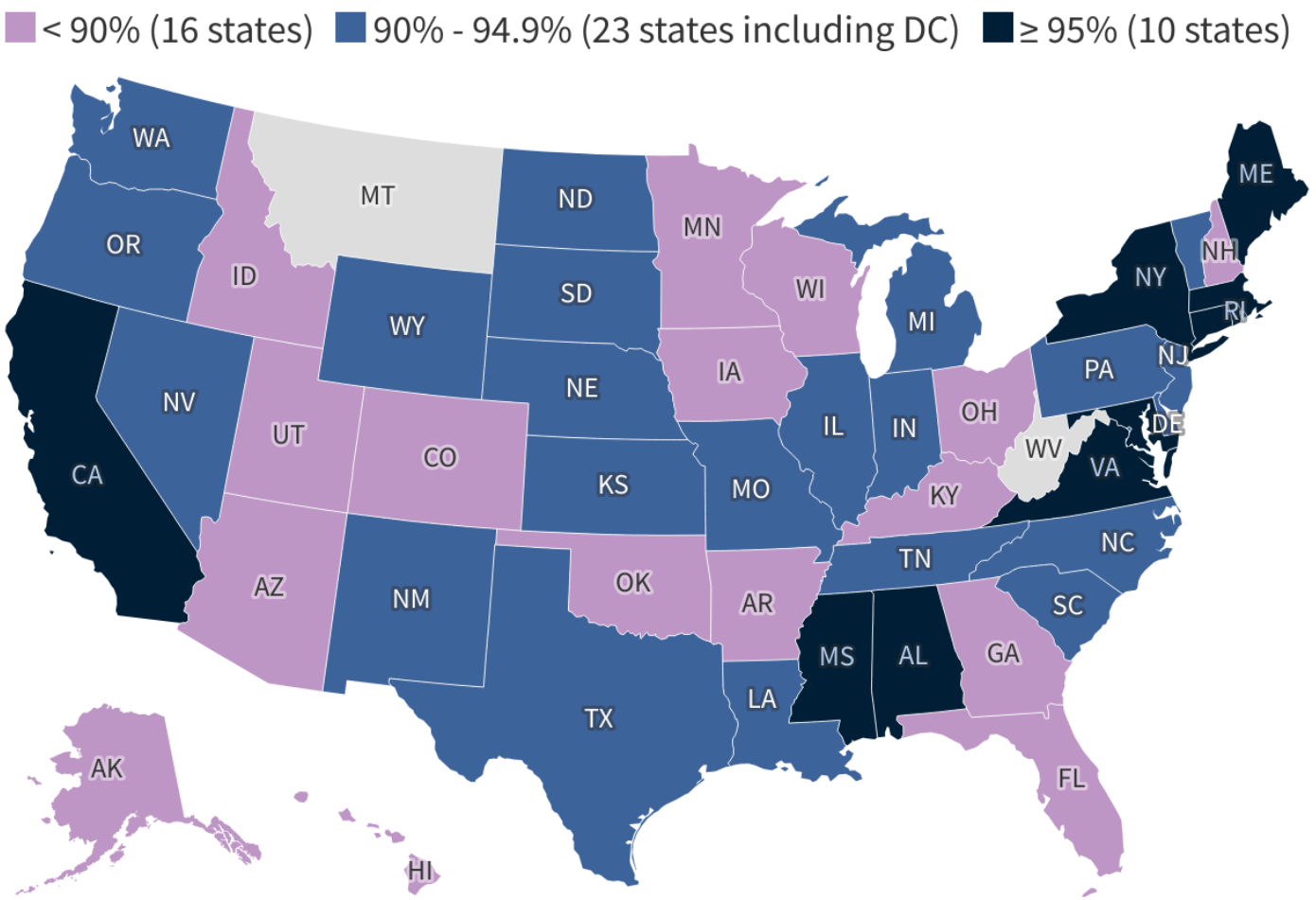
https://ourworldindata.org/grapher/number-of-measles-cases

10 Lessons Learned in Measles Prevention/Elimination

- Requires high vax rates by age 2 years
- School immunization requirements ensure high rates
- A 2nd vax dose improves population immunity
- School immunization requirements can ensure 2nd dose administered
- Coverage assessment crucial
- Measles surveillance critical
- Lab back-up needed to confirm diagnosis
- Tracking genotypes critical for tracking circulation (endemicity?)
- International introduction will continue after elimination
- Collaboration with other countries needed to reduce introduction

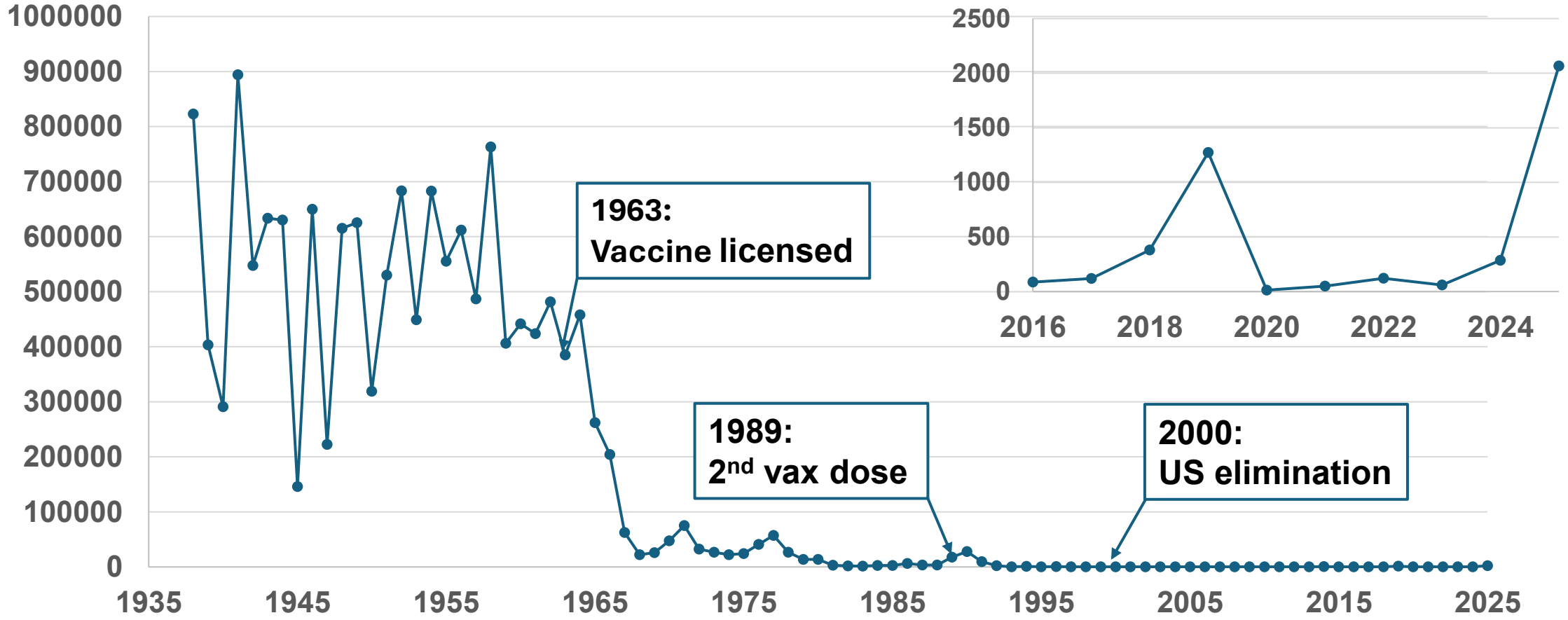
Hinman et al. *J Infect Dis* 2004;189(suppl 1): S17

MMR Vaccine Coverage For Kindergarteners Has Decreased



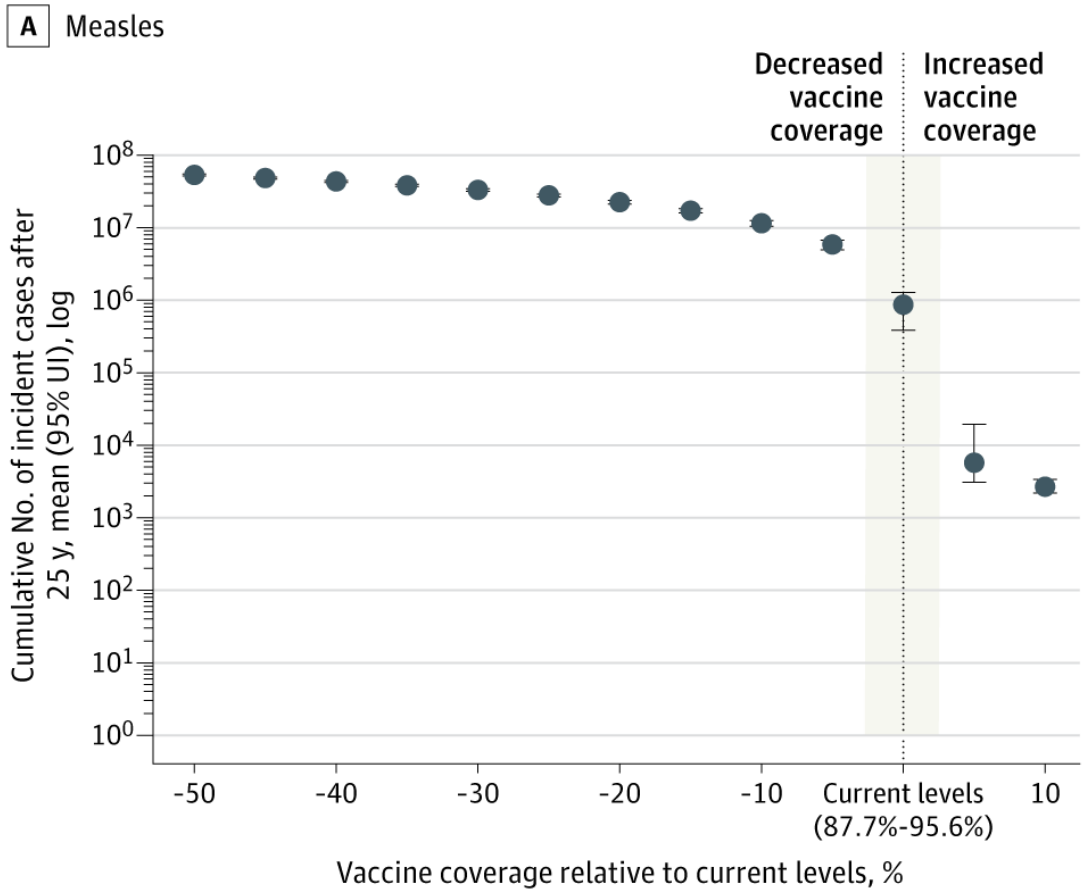
https://www.kff.org/medicaid/kindergarten-routine-vaccination-rates-continue-to-decline/

Reported Cases of Measles in US 1938-2025



https://ourworldindata.org/grapher/number-of-measles-cases

Modeling of Measles Re-Emergence at Current Vaccination Rates in US



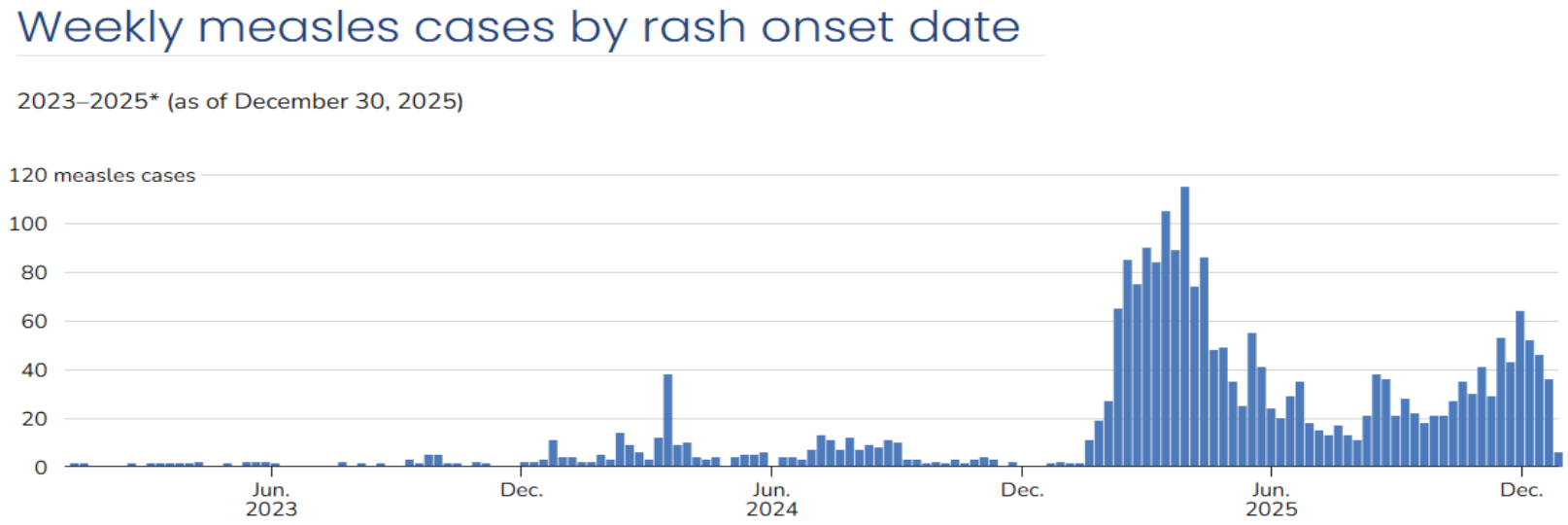
25-year period – current vax rates

- **851,300 cases**
- **170,200 hospitalizations**
- **2550 deaths**
- **851 with post-neurological sequelae**

Kiang et al. *JAMA* 2025;333:2176

Loss of Elimination Status in US May Be Imminent

- **Sustained circulation of D8 (mostly DSID 9171) virus in US since January 20, 2025 (beginning of West Texas outbreak) – last TX case 7/1/25, 762 total linked to outbreak**
- **Cases in New Mexico (100 cases from 2/14/25-8/14/25) epidemiologically linked to W Texas**
- **Outbreak in Arizona (205 cases Aug to present)/Utah (156 cases total) continues; DSID 9171, but also found in Mexico and Canada (in Mennonite communities)**
- **Outbreak in South Carolina continues (176 cases in outbreak from Sep to present)**



https://www.cdc.gov/measles/data-research/index.html#cdc_data_surveillance_section_10-measles-cases-in-2025

Summary

- Measles is a vaccine-preventable illness that can cause severe disease and mortality
- Measles vaccination eliminated endemic transmission in the US in 2000, although repeated introduction from international locations continued to occur
- Decreased vaccine uptake has allowed reintroduction of measles and large outbreaks in unvaccinated groups; further decreases in coverage will lead to more cases and greater impact on the population