



# Background on Measles, Mumps, Rubella, and Varicella (MMRV) Vaccine

Arjun Srinivasan, MD, MS, MBA

Acting Chief Medical Officer

National Center for Immunization and Respiratory Diseases

ACIP Meeting

September 18, 2025

# Measles, mumps, rubella, and varicella caused significant disease burden pre-vaccine in the United States

- During the last major **rubella** epidemic in the U.S. (1964-1965), in 1 year:
  - **11,000** pregnant women lost their babies
  - **2,100** newborns died
  - **20,000** born with congenital rubella syndrome, causing deafness, heart defects and developmental delay



- Before the introduction of **measles** vaccine (1963), each year an estimated:
  - **48,000** hospitalizations
  - **400-500** deaths



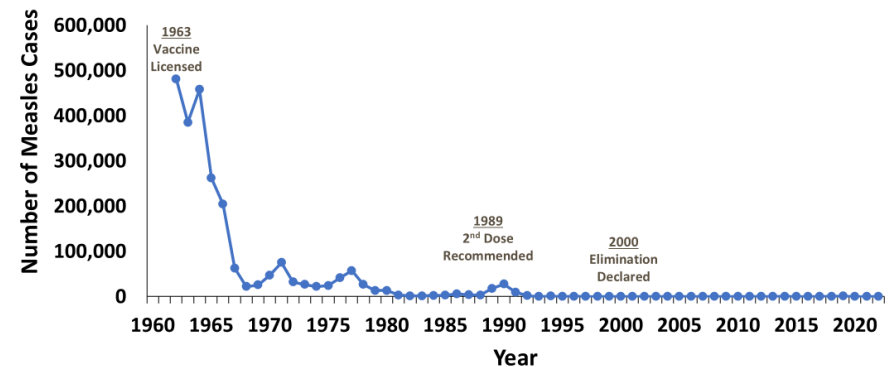
- **Mumps** was the leading cause of viral encephalitis and sudden onset deafness
- Each year in the early 1990s (before **varicella** vaccine):
  - **10,500-13,500** hospitalizations
  - **100-150** deaths



# Dramatic reductions in measles, mumps, rubella, and varicella in the United States after introduction of vaccines

- The introduction of monovalent measles, mumps, rubella vaccines (1963-1969), followed by trivalent MMR (1971), then monovalent varicella (1995) and the quadrivalent MMRV (2005) vaccines, coupled with attaining and maintaining high coverage rates (>90%) in the United States (U.S.) led to:
  - **Elimination** of endemic measles in 2000
  - **Elimination** of endemic rubella in 2004
  - **99% decline** in mumps cases by early 2000
  - **97% decline** in varicella incidence by 2019

Measles Cases in the U.S., 1963-2023



## MMRV vaccine in the United States

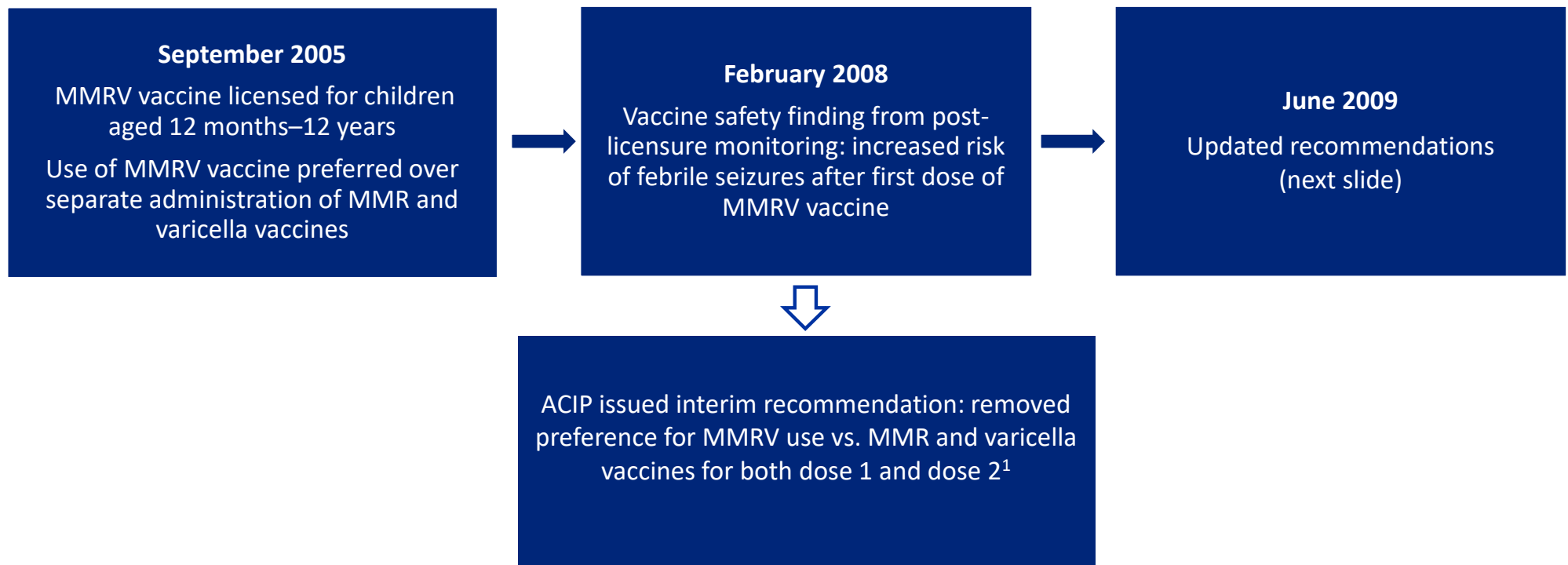
- Two options for measles, mumps, rubella, and varicella vaccination: MMRV vaccine or MMR vaccine + varicella vaccine
  - Recommended as two doses: routine ages - 1<sup>st</sup> dose: 12-15 months; 2<sup>nd</sup> dose: 4-6 years
- The MMRV vaccine available in the U.S. (ProQuad, Merck & Co, Inc) was **licensed by FDA** in September 2005 based on **noninferior immunogenicity** of the antigenic components compared with simultaneous administration of MMR vaccine and varicella vaccine
  - **Efficacy** of the measles, mumps, rubella, and varicella components of MMRV vaccine was **previously established** in clinical studies with the monovalent vaccines
  - Burden of disease for these diseases **too low** to perform efficacy clinical trials in the U.S.

## Clinical trials for MMRV vaccine

- Immunogenicity after the **first dose** of MMRV vaccine vs. MMR + varicella vaccines in children aged 12 to 23 months was assessed in **4 randomized clinical trials**
  - 5446 received MMRV, 2038 received MMR + varicella vaccines at separate injection sites
  - End points assessed (seroconversion rates and geometric mean titers) were similar and met the pre-established criteria for noninferiority<sup>1</sup>
- Immunogenicity after the **second dose** of MMRV vaccine vs. MMR vaccine (+/- varicella vaccine) in children aged 4-6 years was assessed in **1 randomized clinical trial**
  - 399 received MMRV, 205 received MMR + placebo, 195 received MMR + varicella vaccine; also met pre-established criteria for noninferiority
- 2008-2009 ACIP Work Group assessment: given the noninferior immunogenicity, **effectiveness** was assumed to be **equal**

<sup>1</sup>Lower bound of the 95% CI for the difference in measles, mumps, and rubella seroconversion rates >-5.0%, lower bound of the 95% CI for the difference in varicella seroprotection rates was either >-15% [one study] or >-10.0% [three studies]

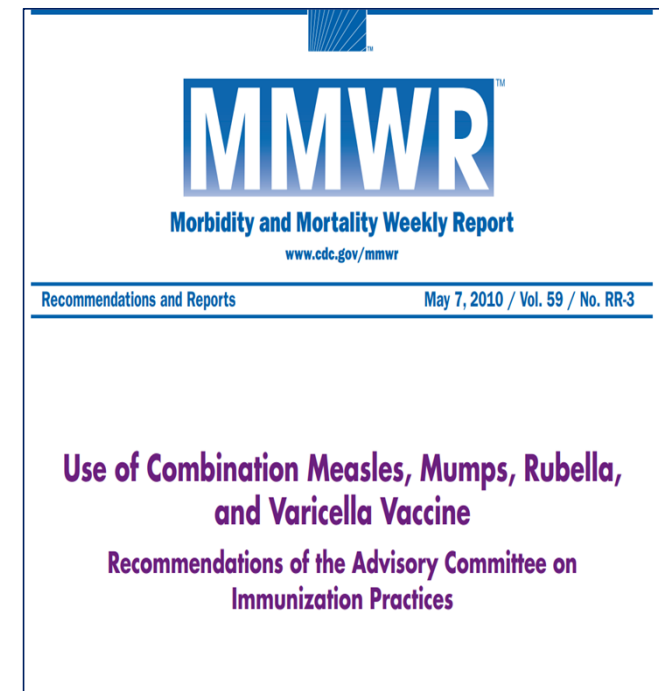
# Timeline of recommendations for MMRV vaccine use in the United States



<sup>1</sup>At the time, MMRV vaccine had not been distributed in the U.S. since July 2007 because of manufacturing constraints unrelated to safety or efficacy: [Notice to Readers: Update on Supply of Vaccines Containing Varicella-Zoster Virus](#). MMRV vaccine became available again in the U.S. in 2012.

# Updated ACIP recommendations for MMRV vaccine use in the United States (current recommendations)

- **For the first dose** of measles, mumps, rubella, and varicella vaccination **at age 12–47 months, either MMR vaccine and varicella vaccine or MMRV vaccine may be used.** Providers who are considering administering the MMRV vaccine should discuss the benefits and risks of both vaccination options with the parents or caregivers.
  - CDC provided implementation guidance: unless the parent or caregiver expresses a preference for the MMRV vaccine, CDC recommends that MMR vaccine and varicella vaccine be administered for the first dose in this age group.
- **For the first dose at age  $\geq 48$  months and for the second dose at any age (15 months–12 years), MMRV is generally preferred** over separate injections of MMR vaccine and varicella vaccine



## Post-licensure effectiveness

- No post-licensure vaccine effectiveness estimates are available for the MMRV vaccine used in the U.S.
  - With measles and rubella being eliminated in the U.S., mumps and varicella at very low levels, there were **not enough cases of disease or outbreaks** in children to assess vaccine effectiveness in the U.S.
  - **Those vaccinated with MMRV or MMR and varicella vaccines continue to have very low rates of disease for measles, mumps, rubella, and varicella in the U.S.**
  - There have been **no reports** to CDC indicating concern for lower MMRV vaccine effectiveness compared to use of the separate component vaccines, consistent with the immunogenicity results seen in the clinical trials



## MMRV vaccine utilization

- MMRV vaccine accounts for **15%** of **first dose**<sup>1</sup> measles, mumps, rubella, and varicella vaccination among children aged 19-35 months and **75%** of **second dose**<sup>2</sup> vaccination among children aged 4-6 years
  - First dose range by state: 5.1%-31.8%
  - Second dose range by jurisdiction: 46%-96%

<sup>1</sup>Data from National Immunization Survey-Child, 2023

<sup>2</sup>Data from 39 jurisdictions' Immunization Information Systems (IIS), children age 4-6 years by Dec 31, 2024 who received an MMR-containing vaccine

## Summary

- **MMRV vaccine** is **one of the two options** for vaccination of U.S. children for protection against measles, mumps, rubella, and varicella
- The two vaccination options (MMRV vaccine or separate injections of MMR vaccine and varicella vaccine) are considered **equivalent** in terms of protection against disease
- Due to the current recommendations, most MMRV vaccine use in the U.S. is among children age 4–6 years (for the second dose of MMR and varicella vaccination)
- Vaccination for measles, mumps, rubella, and varicella has led to at least **97% reduction** in all four diseases compared with the pre-vaccine era

For more information, contact CDC 1-800-CDC-INFO (232-4636) TTY: 1-888-232-6348  
[www.cdc.gov](http://www.cdc.gov)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

# References: Pre-vaccine burden of measles, mumps, rubella, and varicella

- Bloch AB, Orenstein WA, Stetler HC, et al. Pediatrics 1985;76:524-32. [Health impact of measles vaccination in the United States](#)
- CDC. MMWR 2005;54:279–82. [Elimination of rubella and congenital rubella syndrome—United States, 1969–2004](#)
- Marin, et al., JID, 2022, [Monitoring Varicella Vaccine Impact on Varicella Incidence in the United States: Surveillance Challenges and Changing Epidemiology, 1995–2019](#)
- Marin, et al., JID, 2022, [Decline in Severe Varicella Disease During the United States Varicella Vaccination Program: Hospitalizations and Deaths, 1990–2019](#)
- National Communicable Disease Center. [Rubella surveillance](#). Bethesda, MD: US Department of Health, Education, and Welfare; 1969.
- Shapiro, et al., JID, 2022, [The Effectiveness of Varicella Vaccine: 25 Years of Postlicensure Experience in the United States](#)
- Witte JJ, Karchmer AW. Public Health Rep, 1968 Feb;83(2):5-100. [Surveillance of mumps in the United States as background for use of vaccine](#)

# References: Current/recent epidemiology for measles, mumps, rubella, and varicella

- **Measles:** Measles Cases and Outbreaks: CDC Website: <https://www.cdc.gov/measles/data-research/index.html>
- **Mumps:** Tappe J, et al. Vaccine 2024;42(25): [Characteristics of reported mumps cases in the United States: 2018-2023.](#)
- **Rubella:** Rubella in the United States: <https://www.cdc.gov/rubella/vaccine-impact/index.html>
- **Varicella:** [Shapiro E and Marin M. The effectiveness of varicella vaccine: 25 years of post-licensure experience in the United States. \*The Journal of Infectious Diseases\* 2022; 226 \(4\): S425–S430; Marin M, Leung J, Anderson TC, Lopez A. Monitoring Varicella Vaccine Impact on Varicella Incidence in the United States: Surveillance Challenges and Changing Epidemiology, 1995–2019. \*The Journal of Infectious Diseases\* 2022; 226 \(4\): S392–399.](#)