National Center for Immunization & Respiratory Diseases
Division of Viral Diseases

25 Years of Varicella Vaccination Program in the United States: Health and Economic Impact during 1995–2019

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Varicella: from rite of passage to vaccine-preventable disease.

- **Historically, varicella was considered disease of little consequence, too mild to warrant prevention**
- **Mid-1950s: first reported fatal varicella cases in children treated with newly introduced immunosuppressive therapy unmasked the lethal potential of the varicella-zoster virus (VZV)[1]**

Child with leukemia who died of varicella, ~1970 (courtesy of Dr. Anne Gershon)

[1]Cheatham et al. Am J Pathol 1956; 32:1015-35.

Varicella: from rite of passage to vaccine-preventable disease.

1960s/70s

Iatrogenic immunosuppression: systemic steroid therapy, organ transplant, childhood cancer

- Leukemia cured in 80% of children but many died of varicella before immune reconstitution

1974

Varicella vaccine (Japan), VZV attenuated, healthy children and adults and children with leukemia in remission[1]

- Initial controversy in the U.S.: risk for latency and persistence of immunity

1980s

US trials in children with leukemia demonstrated vaccine efficacy and safety[2]

- Subsequent studies showed safety and efficacy in healthy children and adults

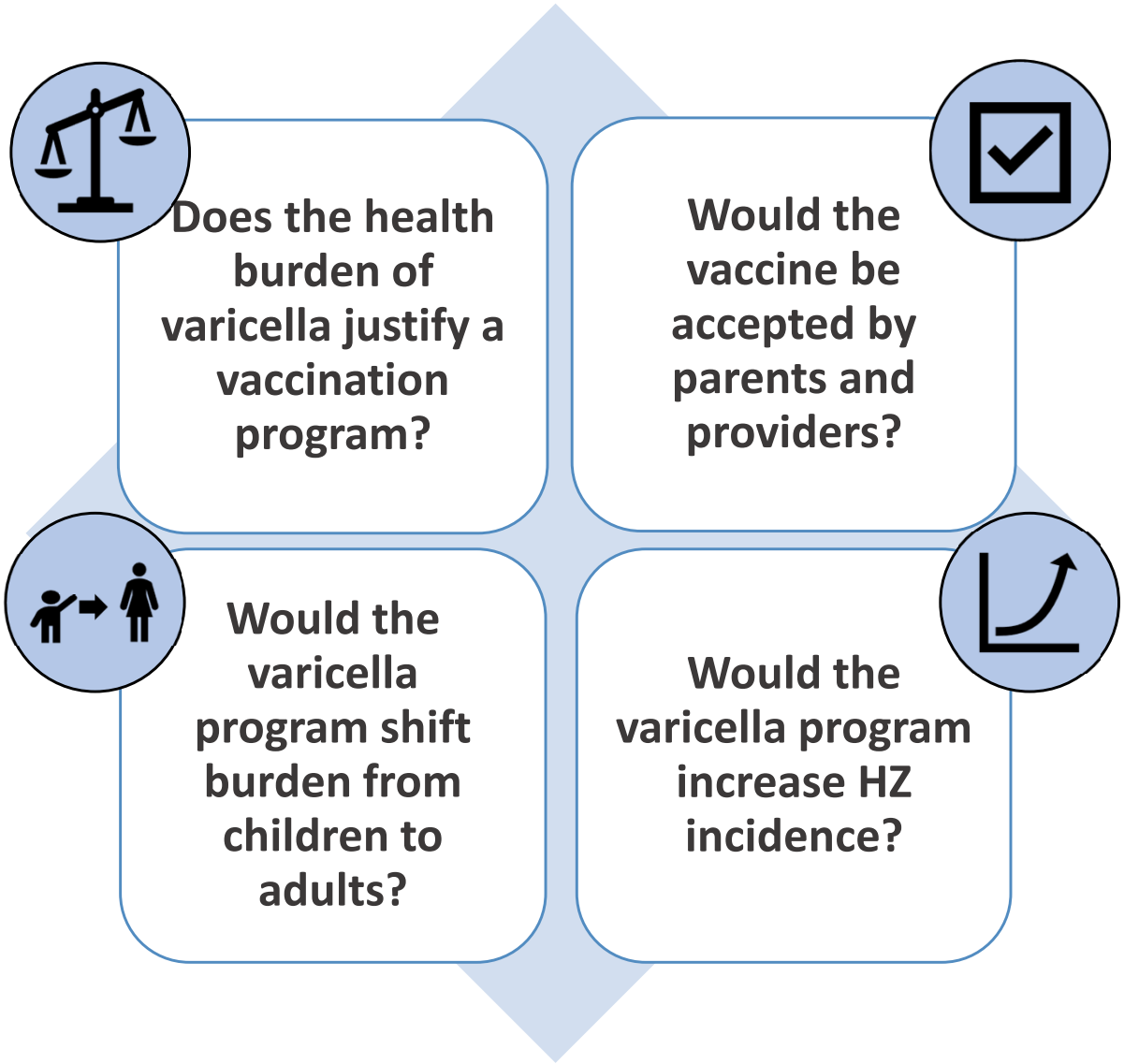
1995

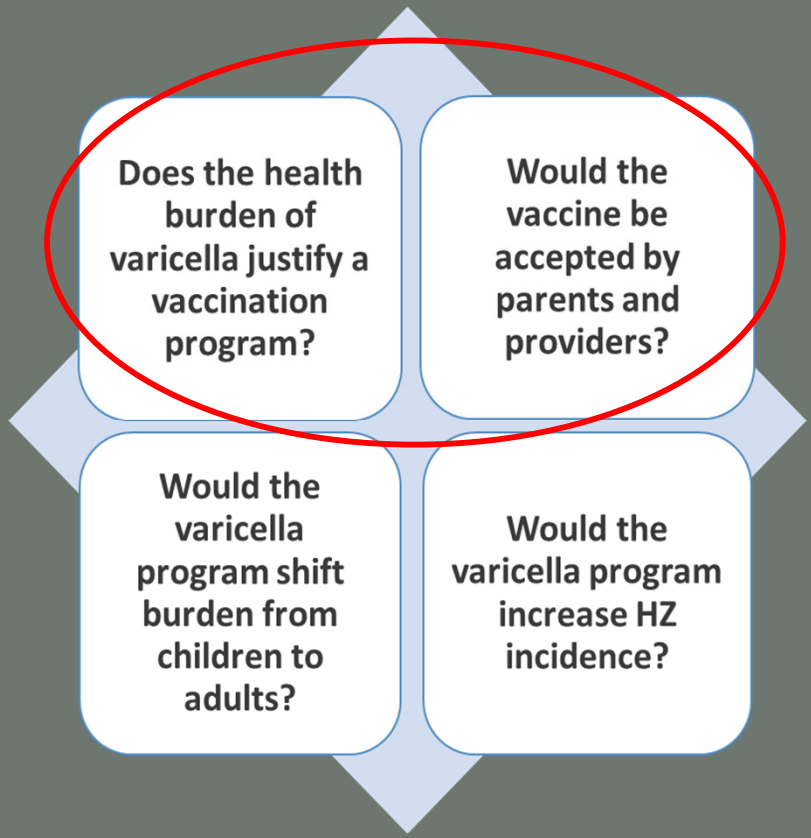
Varicella vaccine licensed in the U.S.

- First country with a routine varicella vaccination program

Gershon at al. JID 2021. Marin et al. JID 2022. In press. [1]Takahashi et al. Lancet 1974 [2]Gershon et al. JAMA 1984.

Debate around the time of varicella vaccine recommendations





U.S. Varicella Vaccination Program

Before vaccine, varicella represented a significant health burden (medical and societal) in the United States.

Annual average, pre-vaccine

- **Cases ~4 million**
- **Hospitalizations ~10,500–13,500**
- **Deaths ~100–150**
- **Congenital varicella syndrome ~44**
- **Greatest disease burden in children**
  - >90% cases, 70% hospitalizations, 50% deaths

Wharton et al. 1996, Galil et al. 2001, Davis et al. 2004, Meyer et al. 2000, Nguyen et al. 2005, Enders and Miller. 2000

Varicella vaccine policy in the United States

- **1995: Routine one-dose**
  - One dose routinely at age 12–18 months with catch-up vaccination of older children
  - Two doses for susceptible persons aged ≥13 years
- **2007: Policy changed to routine 2-dose**
  - 1st dose at age 12–15 months
  - 2nd dose at age 4–6 years
  - Catch-up vaccination of persons who had received one dose
  - Vaccination of all eligible persons without evidence of immunity

Rationale for policy change

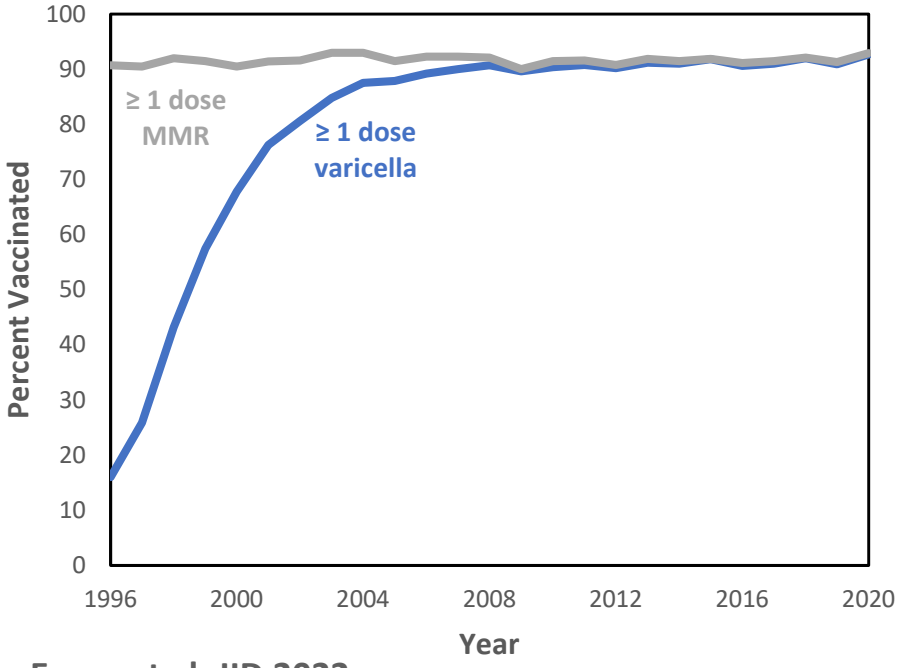
- Low-level community transmission continued
- Outbreaks in highly 1-dose vaccinated school populations (smaller, less frequent)

MMWR 2007;56(RR-4):1–39. Available at www.cdc.gov

Program implementation was highly successful.

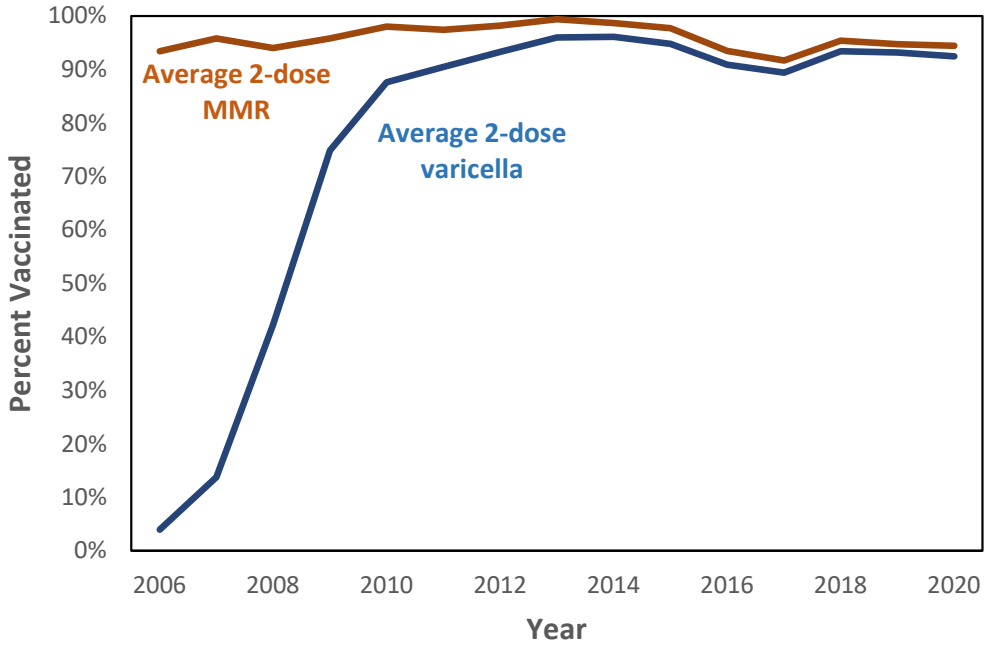
Vaccination coverage for ≥1 dose varicella and ≥1 dose MMR, children age 19–35 months, US 1996–2020

Data Source: National Immunization Survev



Vaccination coverage for ≥2 doses varicella and ≥2 doses MMR, children by age 7 years — 6 US states, 2006–2020

Data Source: Immunization Information System



Elam-Evans et al. JID 2022.

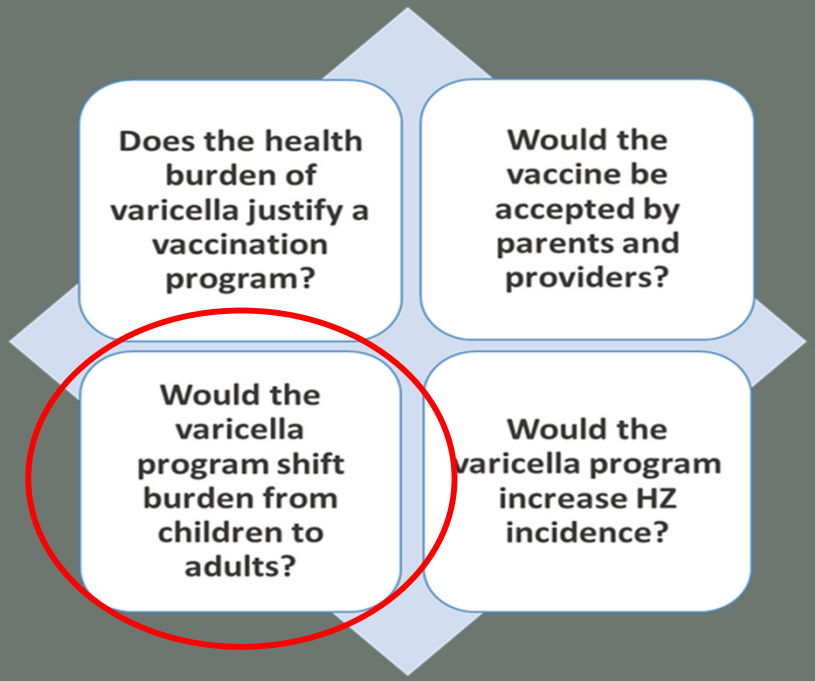
Post-licensure vaccine effectiveness among children

Varicella Endpoint	1 dose VE	2 dose VE
Varicella of any severity	**82%** (Meta-analysis)	**92%** (Meta-analysis)
Moderate and Severe disease	**97%** (Median)	
Severe* disease	**100%** (range= 97-100)	

HIV+ children (2 doses, 1 study)- **82**% (95% CI 24%–100%)[1]

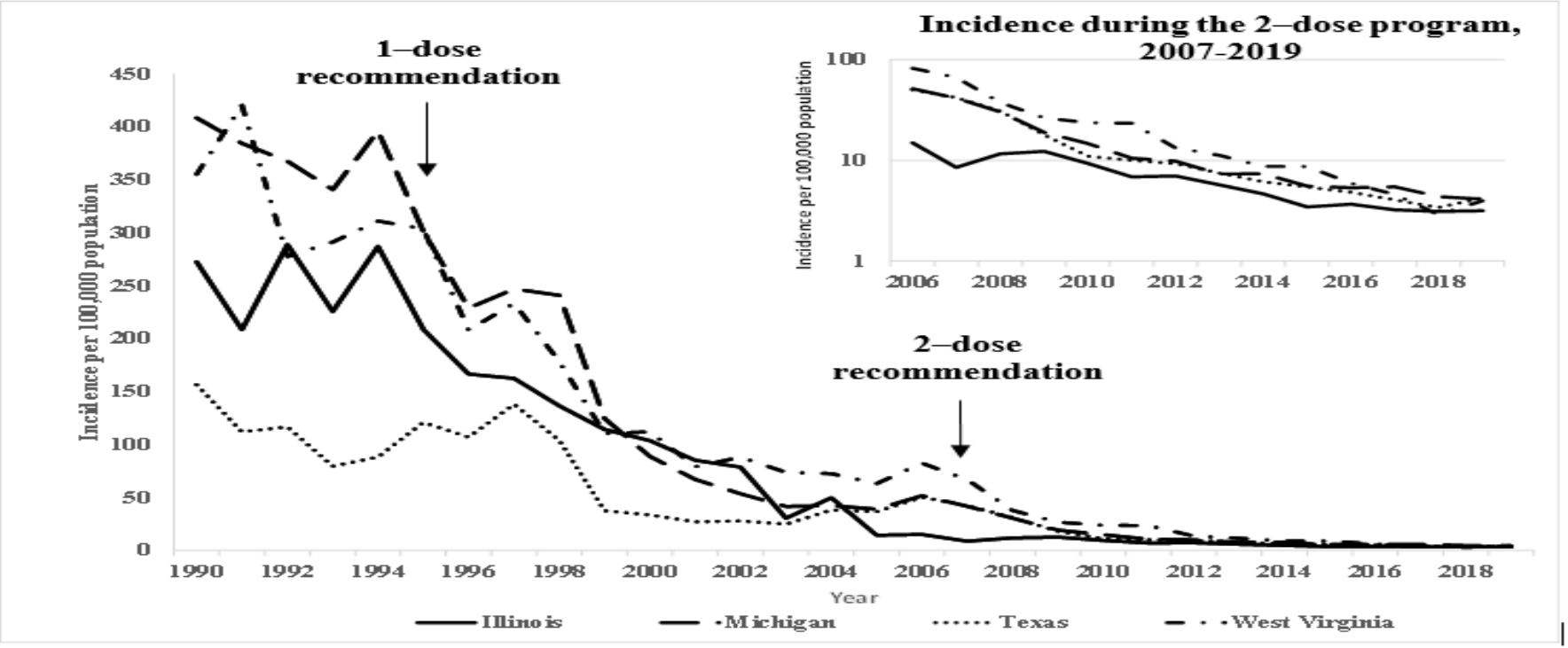
*Definitions: 1) Varicella with >500 lesions or a complication requiring physician visit; 2) disease severity scale used in clinical trials: # lesions, fever, systemic signs and subjective assessment of illness

Marin et al. Pediatrics 2016. [1]Son et al. JID 2010.



Impact of 25 Years of the U.S. Varicella Vaccination Program on Varicella

Varicella incidence* declined >97%, 1990–2019.

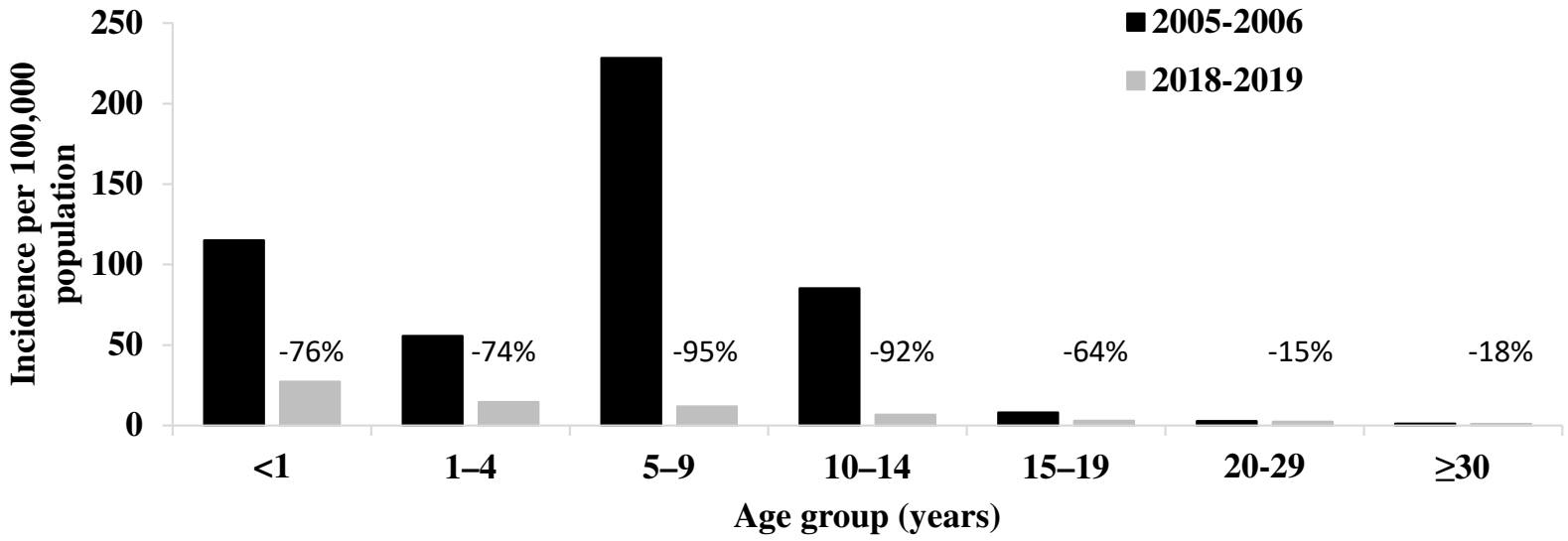


*4 states with consistent reporting of cases to the National Notifiable Diseases Surveillance System.

Marin et al. JID, 2022.

Varicella incidence declined in all age groups during the 2-dose program*.

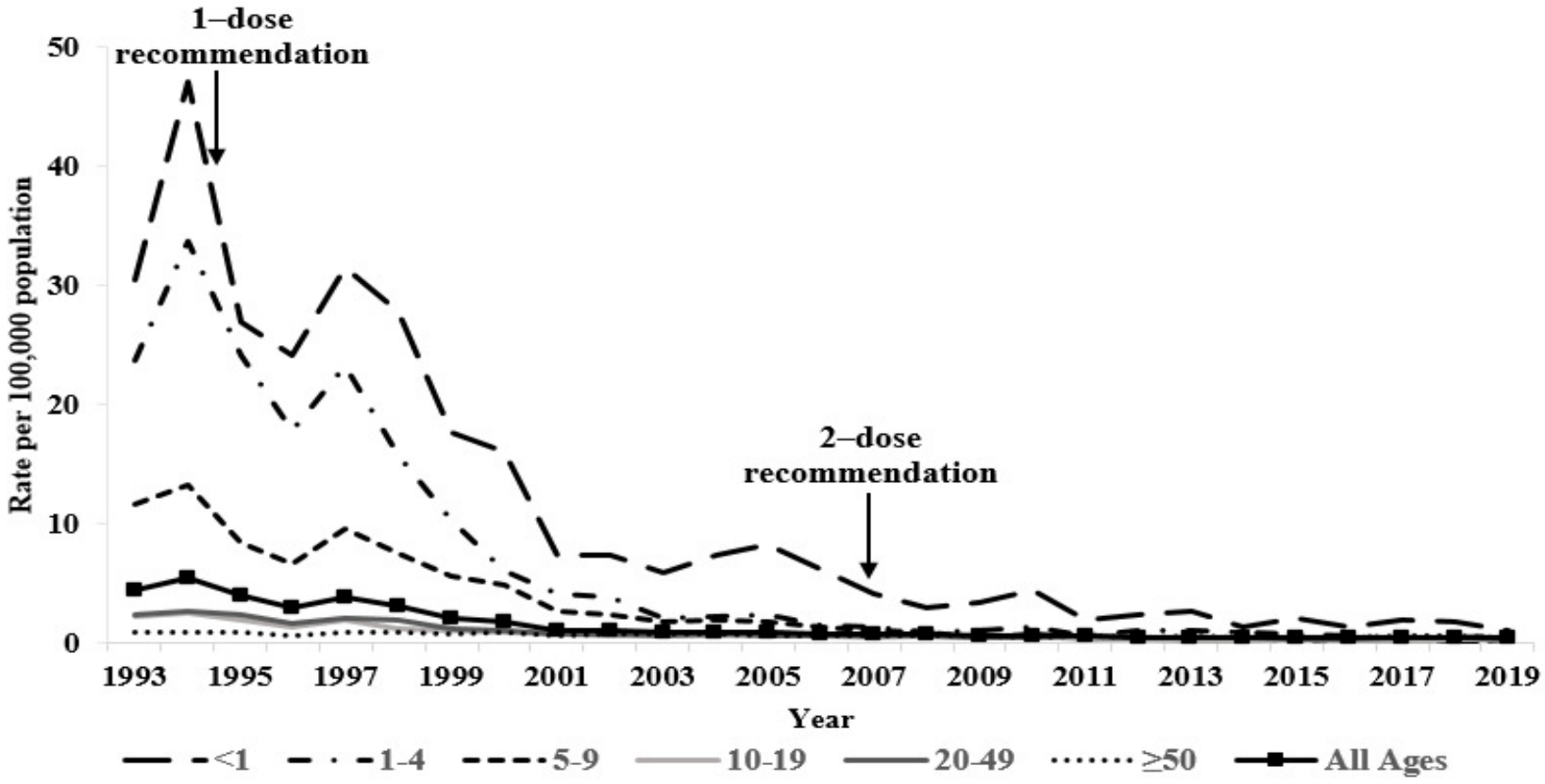
In 7 states with consistent reporting, the number of outbreaks declined 82%§



*29 states and the District of Columbia reported age data during 2005–2006 (end of 1-dose program) and 38 during 2018–2019 (mature 2-dose program); National Notifiable Diseases Surveillance System data; **Marin et al. JID 2022.**

§Outbreak: ≥5 varicella cases; **Leung et al. JID 2022.**

Varicella hospitalizations declined 90% during 1993–2019.



Marin et al. JID 2022. Data: HCUP National Inpatient Sample (NIS).

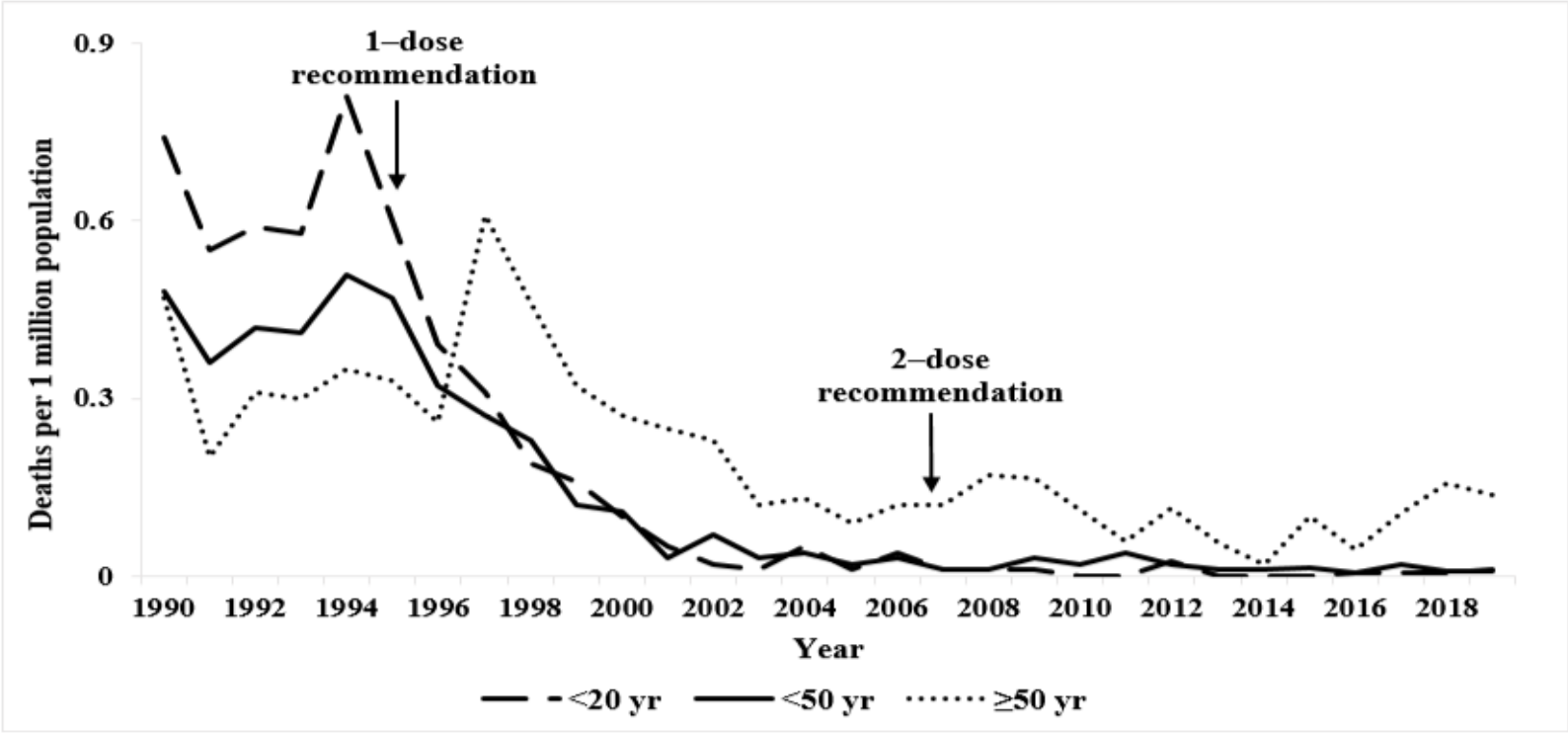
>10,500 hospitalizations are prevented now annually, including >1,250 among infants.

Age Group	Average annual no. hospitalizations 1993-95	Average annual no. hospitalizations 2018-19	Decline in hospitalization rate
<1	1,338	55	-96%
1-4	4,309	80	-98%
<20	8,574	285	-97%
<50	11,573	783	-94%
All ages	**12,189**	**1,390**	**-90%**

Marin et al. JID 2022. Data: HCUP National Inpatient Sample (NIS).

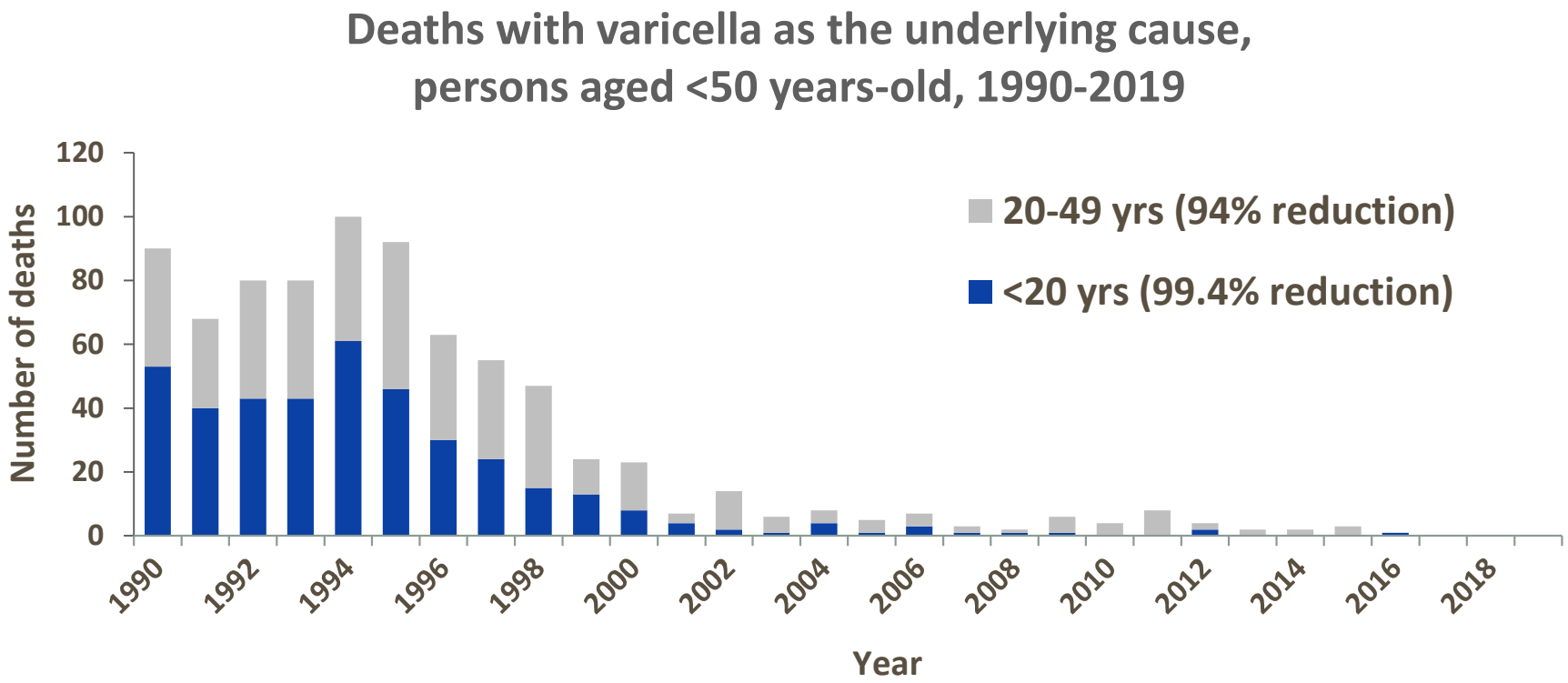
Varicella mortality declined 89% during 1990–2019.

Most of the decline occurred during the 1-dose program.



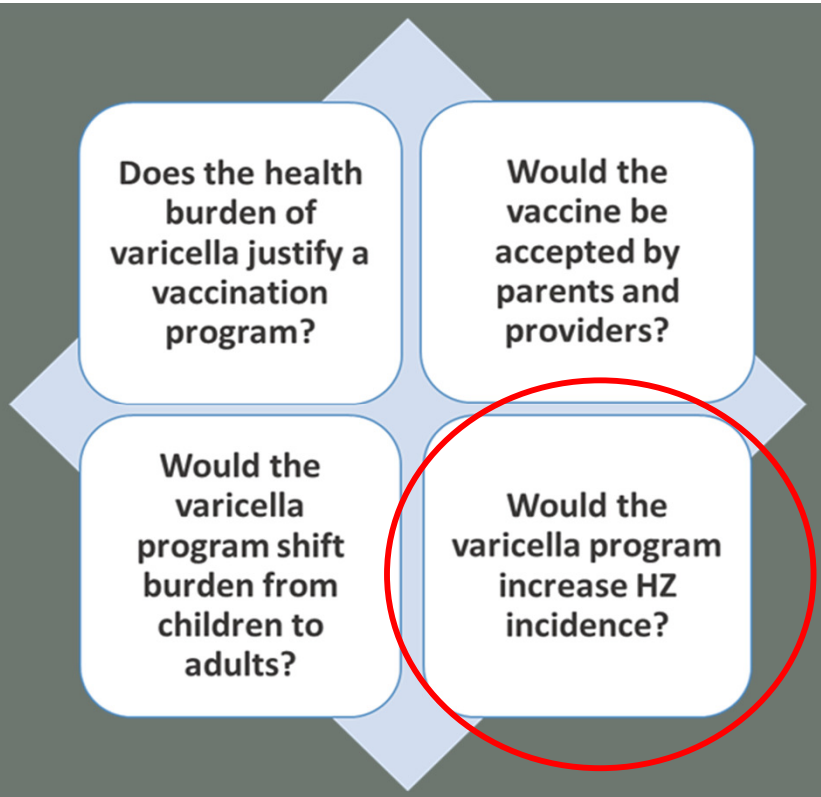
Varicella as the underlying cause of death. National Center for Health Statistics data.
Marin et al. JID 2022.

Deaths practically eliminated among <20-year-olds.



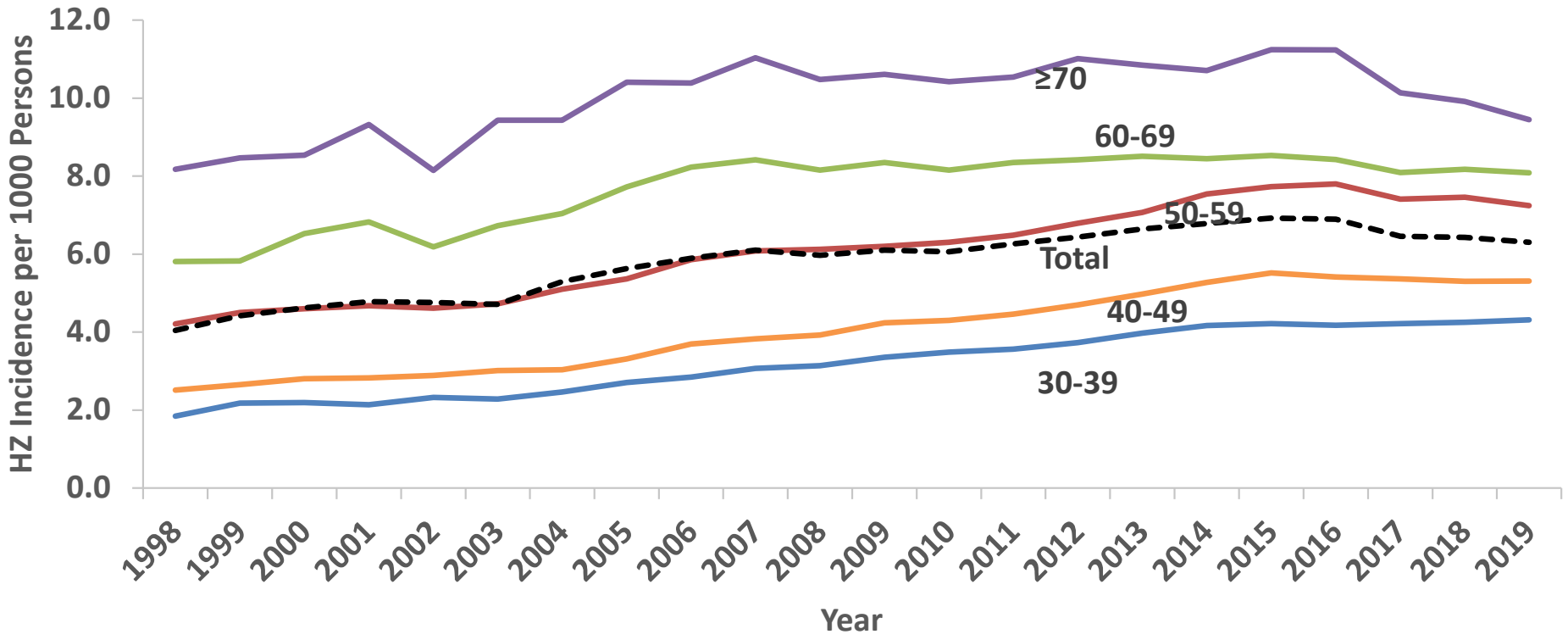
No varicella deaths (underlying or contributing) reported in the <20 years age group in 2011, 2013, 2014, 2017, 2018. Data: National Center for Health Statistics

Marin et al. JID 2022.



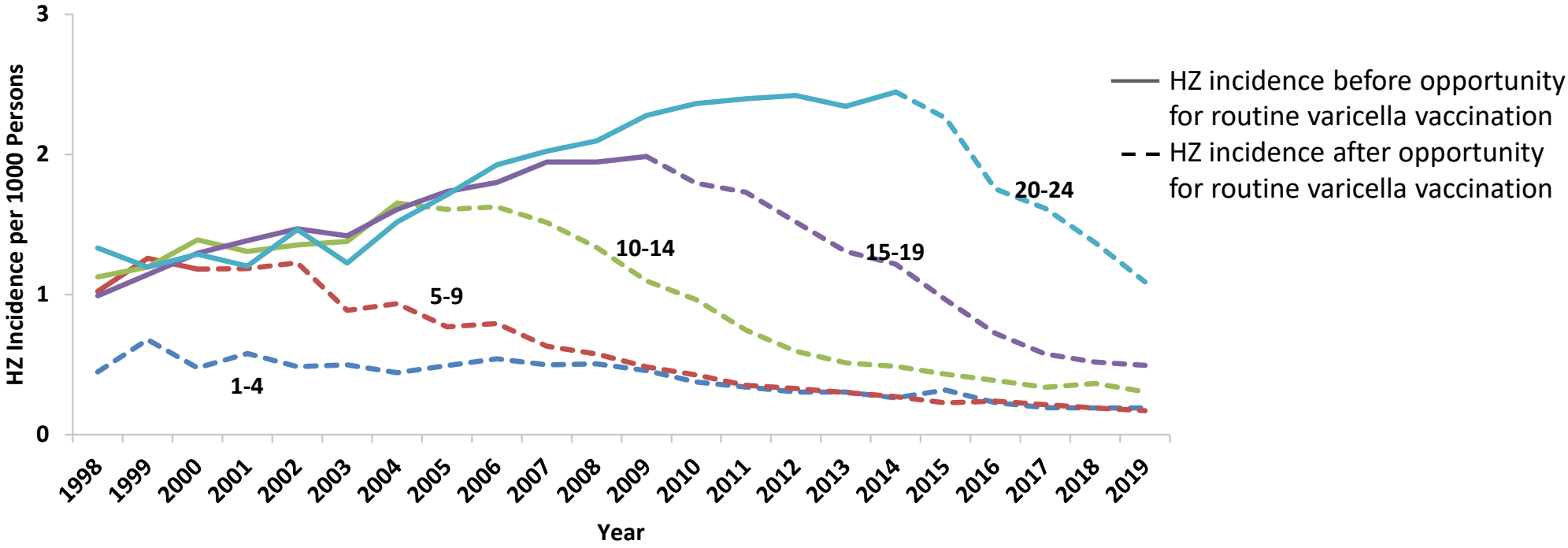
Herpes Zoster Trends During the U.S. Varicella Vaccination Program

In persons aged ≥30 years, HZ incidence increased during the earlier study years, with decelerations in later years.



Leung et al. JID 2022. MarketScan 1998–2019.

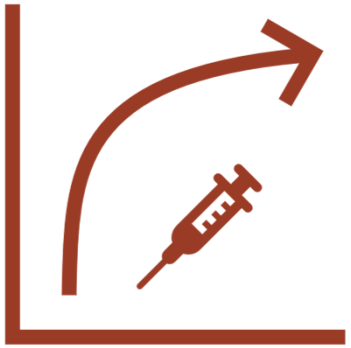
In children and young adults, HZ incidence declined in a step-wise pattern once each age group was comprised by persons born during the varicella vaccination program.



Leung et al. JID 2022. MarketScan 1998–2019.

US varicella vaccination resulted in substantial disease prevention and societal savings over 25 years of program implementation.

Effective, safe, and accepted vaccine



High vaccine coverage reached

Prevented morbidity & mortality

91 million cases

238,000 hospitalizations

1,933-2,446 deaths

Highly cost saving

$23.4 billion

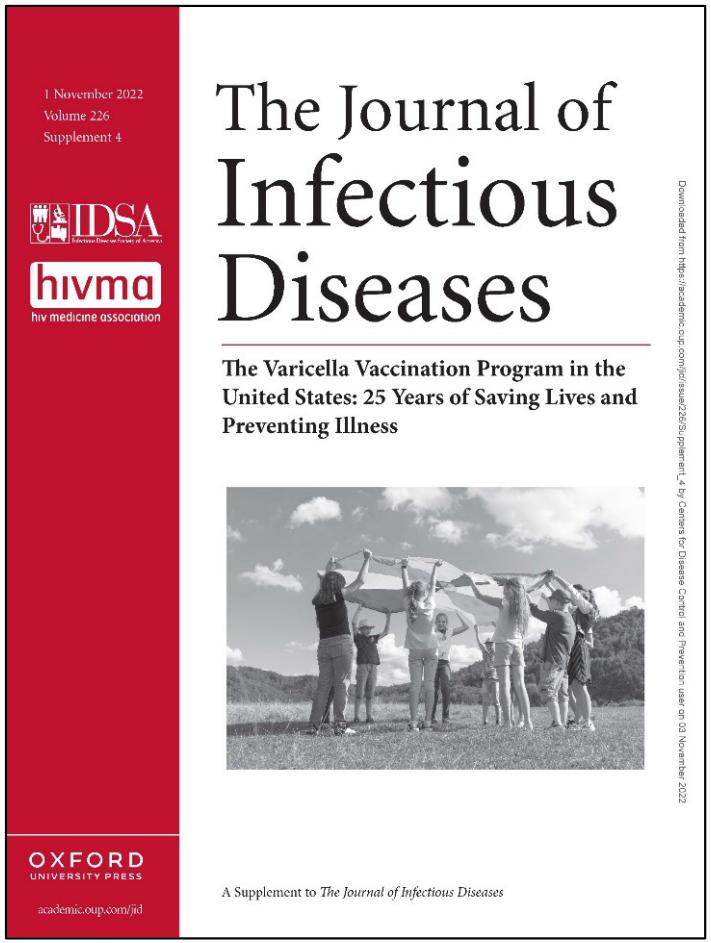
in net societal savings

No increase in HZ due to varicella program

Reduced HZ incidence in children/adolescents

The varicella vaccination program in the US: 25 years of saving lives and preventing illness

The Journal of Infectious Diseases **supplement**
November 1st, 2022



https://academic.oup.com/jid/issue/226/Supplement_4

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Thank You

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