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

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Atlanta, GA
February 23, 2023
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)](image)

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

Iatrogenic immunosuppression: systemic steroid therapy, organ transplant, childhood cancer
- Leukemia cured in 80% of children but many died of varicella before immune reconstitution

US trials in children with leukemia demonstrated vaccine efficacy and safety
- Subsequent studies showed safety and efficacy in healthy children and adults

1960s/70s
- Varicella vaccine (Japan), VZV attenuated, healthy children and adults and children with leukemia in remission
  - Initial controversy in the U.S.: risk for latency and persistence of immunity

1974
- 1980s
- Varicella vaccine licensed in the U.S.
  - First country with a routine varicella vaccination program

1995

Debate around the time of varicella vaccine recommendations

- Does the health burden of varicella justify a vaccination program?
- Would the vaccine be accepted by parents and providers?
- Would the varicella program shift burden from children to adults?
- Would the varicella program increase HZ incidence?
U.S. Varicella Vaccination Program

- Does the health burden of varicella justify a vaccination program?
- Would the vaccine be accepted by parents and providers?
- Would the varicella program shift burden from children to adults?
- Would the varicella program increase HZ incidence?
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

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**
  - 1<sup>st</sup> dose at age 12–15 months
  - 2<sup>nd</sup> 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)

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 Survey

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

<table>
<thead>
<tr>
<th>Varicella Endpoint</th>
<th>1 dose VE</th>
<th>2 dose VE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varicella of any severity</td>
<td>82%</td>
<td>92%</td>
</tr>
<tr>
<td></td>
<td>(Meta-analysis)</td>
<td>(Meta-analysis)</td>
</tr>
<tr>
<td>Moderate and Severe disease</td>
<td>97%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Median)</td>
<td></td>
</tr>
<tr>
<td>Severe* disease</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(range= 97-100)</td>
<td></td>
</tr>
</tbody>
</table>

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

*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

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

Does the health burden of varicella justify a vaccination program?

Would the vaccine be accepted by parents and providers?

Would the varicella program shift burden from children to adults?

Would the varicella program increase HZ incidence?

*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.

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

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Average annual no. hospitalizations 1993-95</th>
<th>Average annual no. hospitalizations 2018-19</th>
<th>Decline in hospitalization rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1</td>
<td>1,338</td>
<td>55</td>
<td>-96%</td>
</tr>
<tr>
<td>1-4</td>
<td>4,309</td>
<td>80</td>
<td>-98%</td>
</tr>
<tr>
<td>&lt;20</td>
<td>8,574</td>
<td>285</td>
<td>-97%</td>
</tr>
<tr>
<td>&lt;50</td>
<td>11,573</td>
<td>783</td>
<td>-94%</td>
</tr>
<tr>
<td>All ages</td>
<td>12,189</td>
<td>1,390</td>
<td>-90%</td>
</tr>
</tbody>
</table>


Most of the decline occurred during the 1-dose program.
Deaths practically eliminated among <20-year-olds.

Deaths with varicella as the underlying cause, persons aged <50 years-old, 1990-2019


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

- Effective, safe, and accepted vaccine
- 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

High vaccine coverage reached

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
Acknowledgements

Co-authors
- Jessica Leung
- Kathleen Dooling
- Tara Anderson
- Adriana Lopez
- Michael Melgar
- Aaron Curns
- Fangjun Zhou

Nurses, physicians, pharmacists
State and local health department staff
Varicella active surveillance project staff
CDC Division of Viral Diseases past/present staff

JID supplement contributors
- Jane Seward
- Anne Gershon
- Laurie D. Elam-Evans
- Eugene Shapiro
- Sheila Dollard
- Ann Arvin
- Marci Drees
- Ismael Ortega-Sanchez
- Rafael Harpaz
- Alexandra Hess
- Lauren Pearson
- Olga Munteanu
- Janine Cory
- Nina Masters
Thank You

For more information, contact CDC
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