Varicella Vaccination Program in the United States

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August 13, 2014

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Varicella disease

- Highly contagious, itchy vesicular rash (250-500 lesions)
  - Generally mild in childhood but severe cases occur
  - Complications include virally and bacterially mediated (e.g., skin and soft tissue infection, sepsis, pneumonia, neurologic, hemorrhagic)
- At increased risk of complications
  - Adults
  - Immunocompromised persons
  - Pregnant women
  - Newborns

Varicella public health burden

- Direct medical costs
  - Physician visits, hospitalizations, deaths
- Outbreak related costs
  - Schools, other closed settings especially involving adults (hospitals, ships, prisons etc.)
- Healthcare associated costs
  - Exposures and illness in healthcare settings
- Societal costs
  - Days of school and/or work missed for case and caretaker
  - Medications, other

Varicella disease epidemiology in the US – Pre-vaccine era

- **Annual Burden**
  - ~ 4 million cases (approximate to birth cohort)
  - ~ 11,000-13,500 hospitalizations (~ 4.0-6.0/100,000 population per year)
  - ~ 100-150 deaths (~ 0.4-0.6 /million population per year)
  - Congenital varicella syndrome ~ 44
    - Risk = 1-2% for pregnancies affected 0-20 weeks
- **Greatest disease burden in children**
  - > 90% of cases
  - 70% hospitalizations
  - 50% deaths

The US varicella vaccination program – Recommendations

- 1995: 1st country to introduce varicella vaccine as part of routine childhood immunization program
  - 1-dose policy for children 12 – 18 months
  - 2-dose vaccination of susceptibles $\geq$13 years (4 – 8 weeks apart)
- 2006: Routine 2- dose vaccination of children
  - 1st dose: 12 – 15 months
  - 2nd dose: 4 – 6 years
  - Catch-up vaccination (2nd dose if previously received 1 dose) and vaccination of all eligible persons without evidence of immunity

Cost effectiveness

- **Analyses of 1-dose and 2-dose programs versus no vaccination suggested***
  - **I-dose program cost beneficial or breaks even from medical perspective**
    - **$4.40 saved for every $1 spent**
  - **2 dose program is cost beneficial from societal perspective**
    - **Societal $2.70**

*Not included: Varicella outbreak costs, herpes zoster – in vaccinees (expected decline) or in those with history of varicella (modeled increase)

US EXPERIENCE WITH ONE DOSE VARICELLA VACCINE

Varicella effectiveness and safety

- 1-dose vaccine effectiveness:
  - 85% varicella of any severity
  - >95% severe disease
- Vaccine safety*:
  - Excellent safety profile with >55 million vaccine doses distributed
  - Vaccine Adverse Event Reporting System – national passive system to report adverse events
    - Rate of severe adverse events**: 2.6/100,000 doses distributed
  - Rash, fever, and injection-site reactions accounted for 2/3 of all reports

*Chaves et al. JID 2008

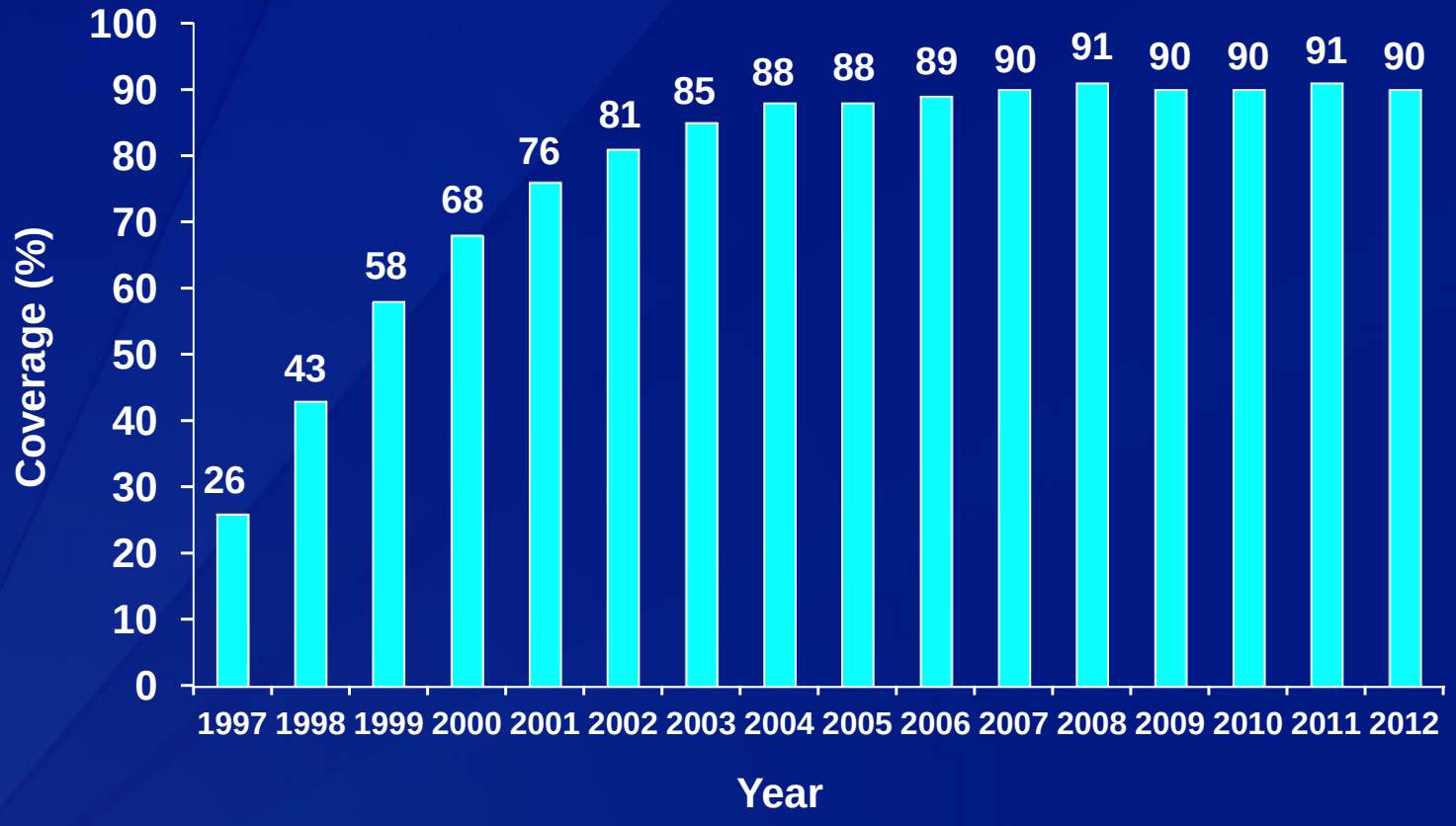
** Rash, hepatitis, pneumonia, herpes zoster, meningitis, encephalitis; 2 vaccine strain VZV deaths, one immunocompromised and one with significant medical history suggestive of immunocompromise

Varicella: clinical features in vaccinated persons ("breakthrough varicella")

- ~15-20% of 1-dose vaccinated persons develop breakthrough varicella if exposed to VZV
- Varicella in vaccinated persons usually milder (fewer lesions and shorter duration of rash) than varicella in unvaccinated persons
- 25-30% breakthrough cases not mild and have clinical features more similar to unvaccinated cases
- 1-dose vaccinees with <50 lesions 1/3 as contagious as unvaccinated persons
- Vaccinees with ≥50 lesions as contagious as unvaccinated persons

MMWR 2007 Varicella Recommendations, Arvin 1996, Seward JAMA 2004, Chaves JID 2008

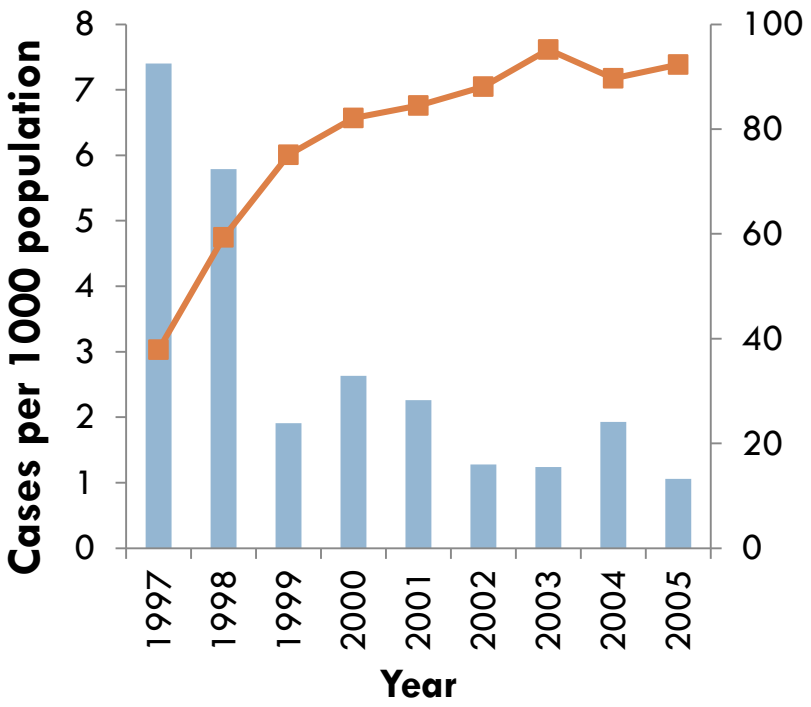
One-dose varicella vaccination coverage, children 19-35 months National Immunization Survey, 1997-2012



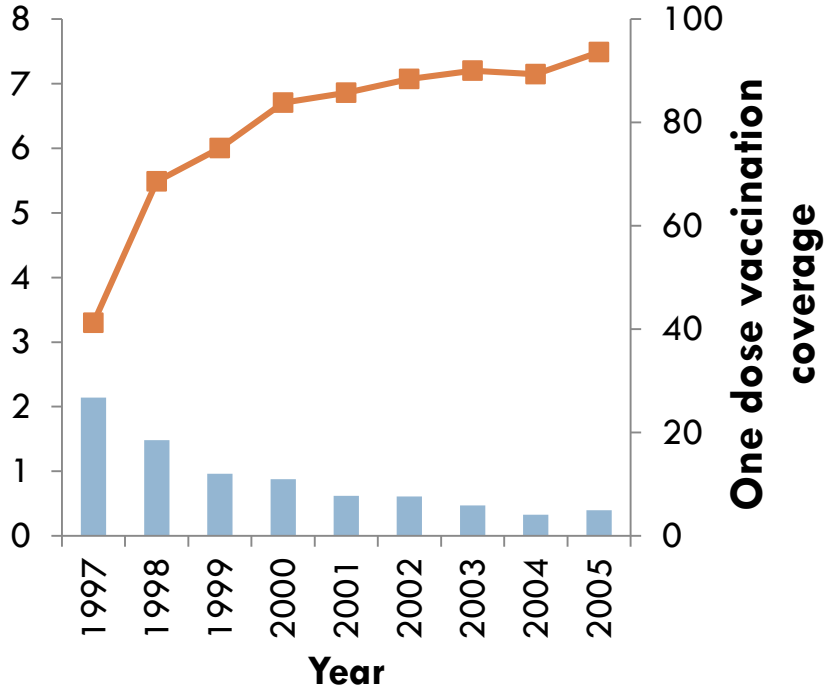
*National Immunization Survey (NIS), coverage available at www.cdc.gov/vaccines/stats-surv/default.htm#nis

One-dose varicella vaccination program impact – Varicella Active Surveillance Project (VASP) sites, 1995-2005

Antelope Valley, CA



West Philadelphia, PA



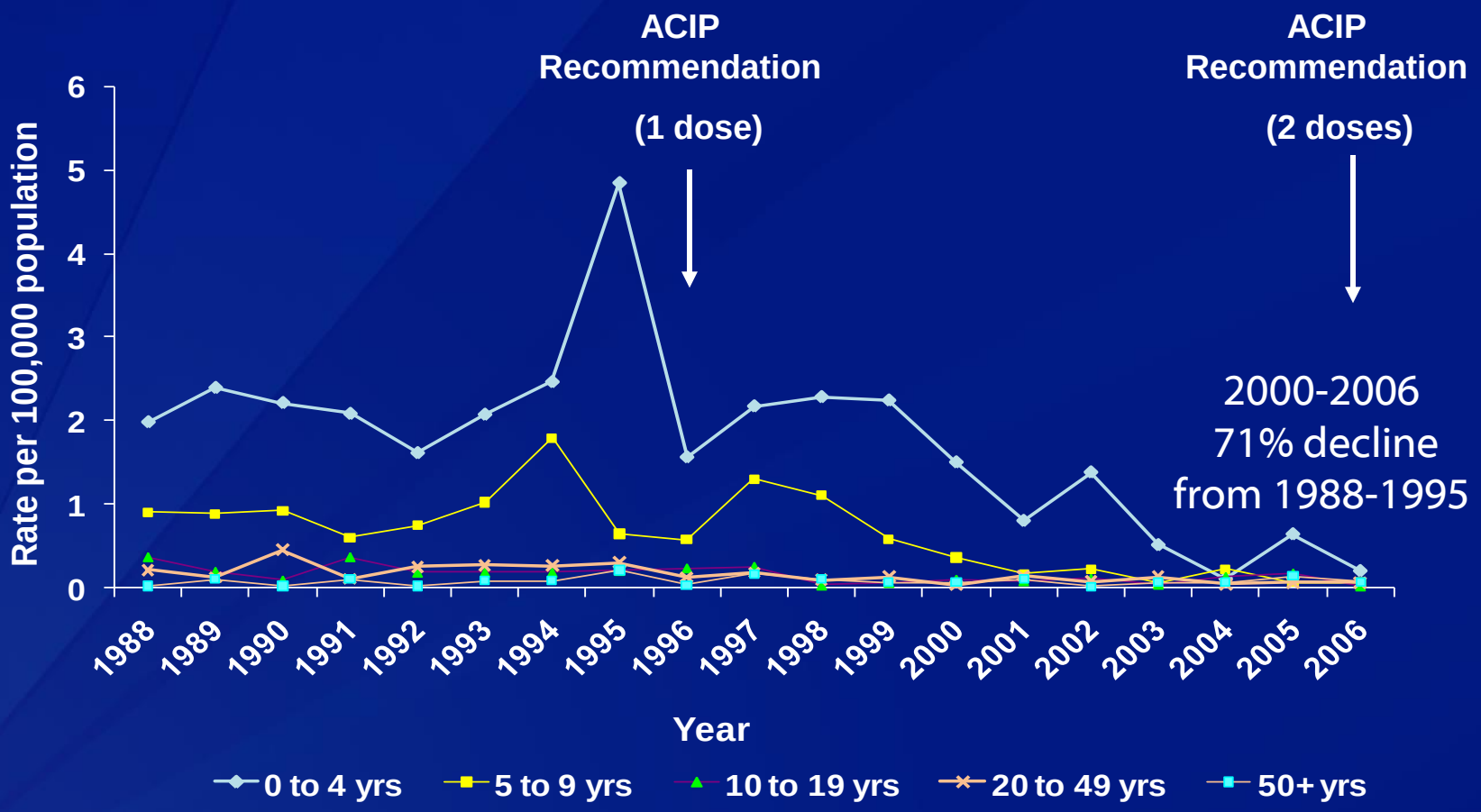
Overall incidence

One dose vaccination coverage

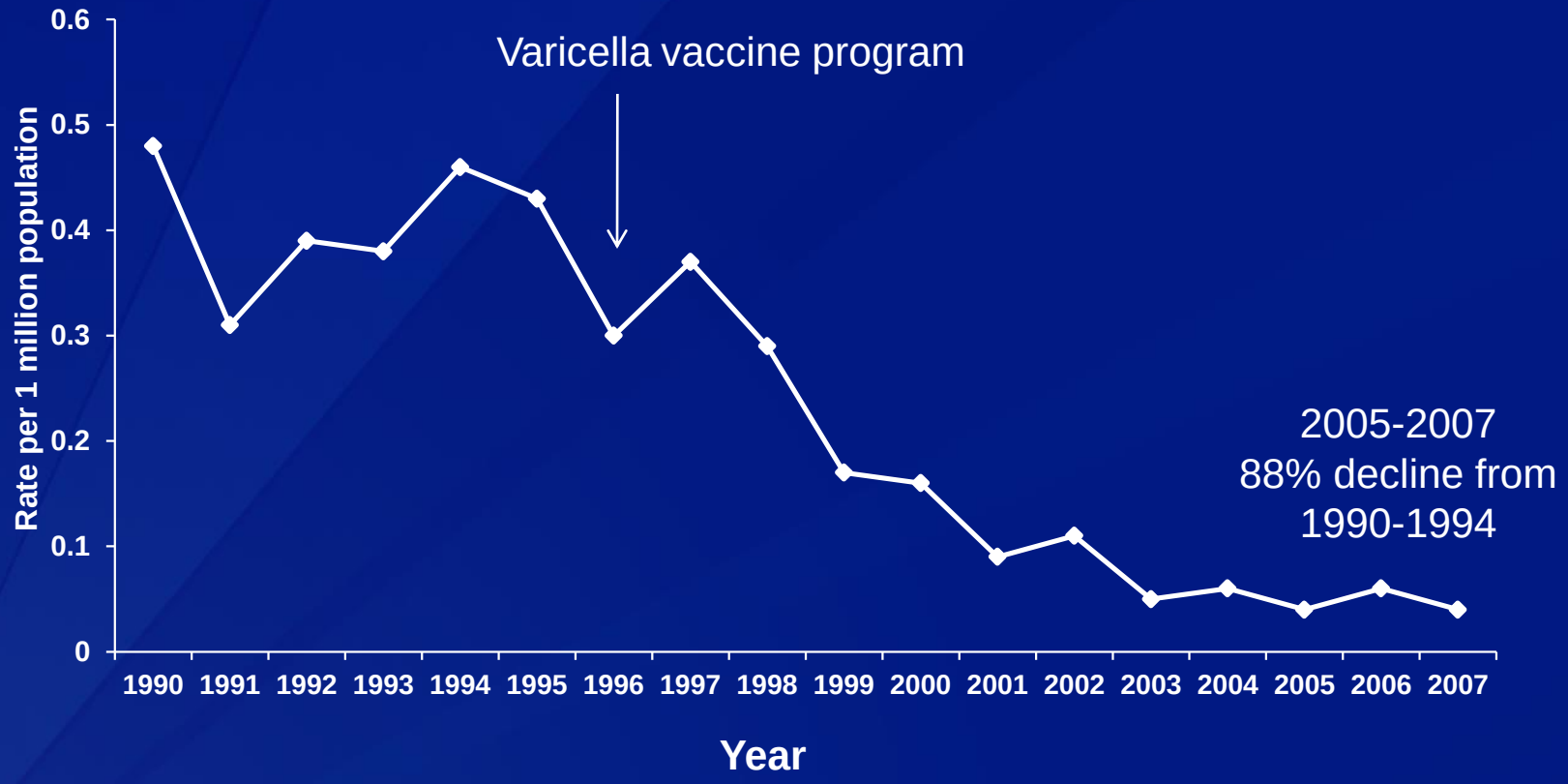
Reduction in age-specific incidence rates – VASP sites, 1995-2005

Age (years)	Antelope Valley, CA (%)	West Philadelphia, PA (%)
<1	84	77
1-4	95	89
5-9	92	95
10-14	64	98
15-19	86	78
20+	82	67
Total	**90**	**93**

Varicella hospitalization rates from NHDS, by year and age group – US, 1988–2006

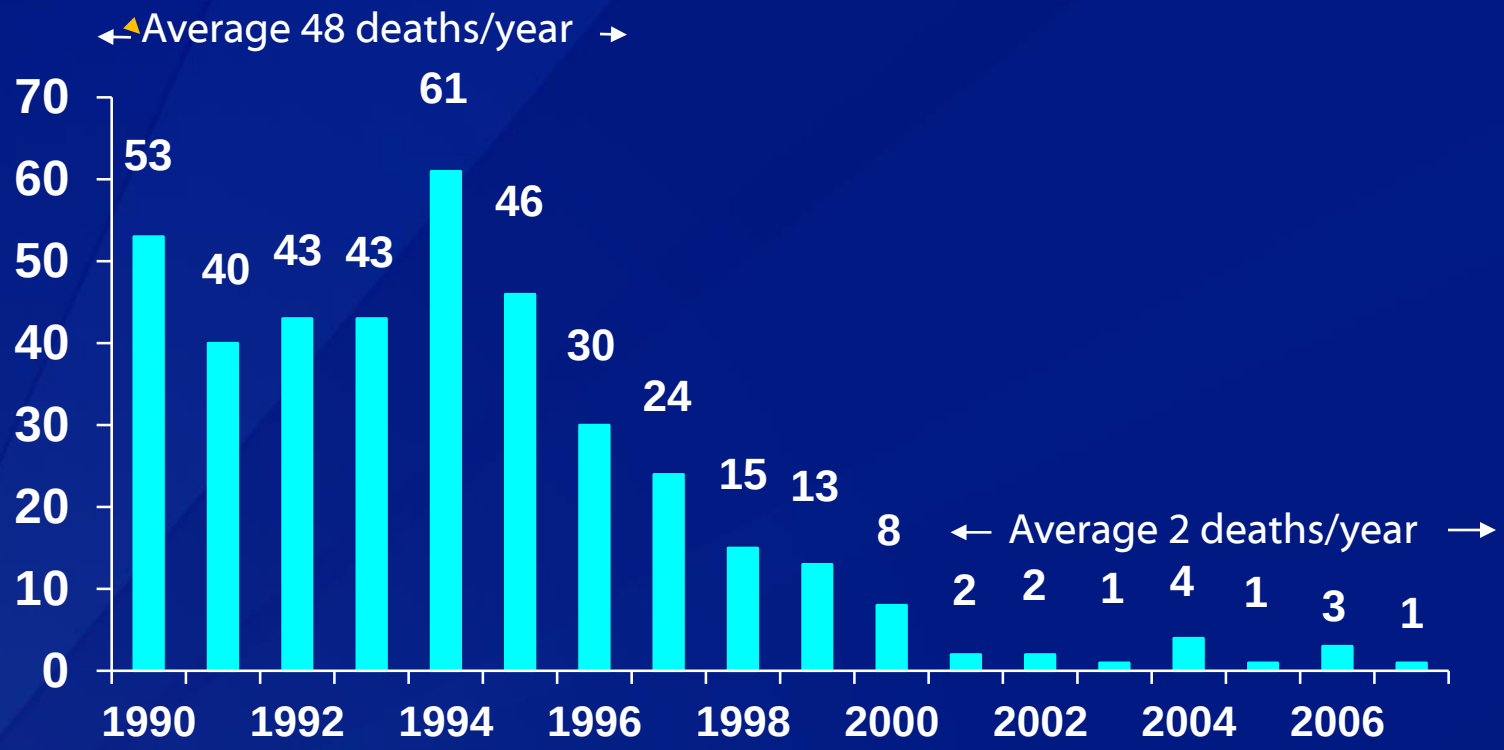


Varicella-related* mortality rates, by year, US, 1990–2007



Nguyen HQ, Jumaan AO, Seward JF.. N Engl J Med 2005;352:450–8 & Marin CDC unpublished data
*Varicella as the underlying cause of death

Varicella deaths* among children and adolescents < 20 years, US, 1990-2007



* NCHS, varicella as underlying cause of death

Reduction in varicella health care costs

- Total estimated direct medical expenditures for varicella hospitalizations and ambulatory visits
  - 1994-1995 $85 million
  - 2002 $22 million
  - 74% decline

Zhou et al, JAMA, 2005

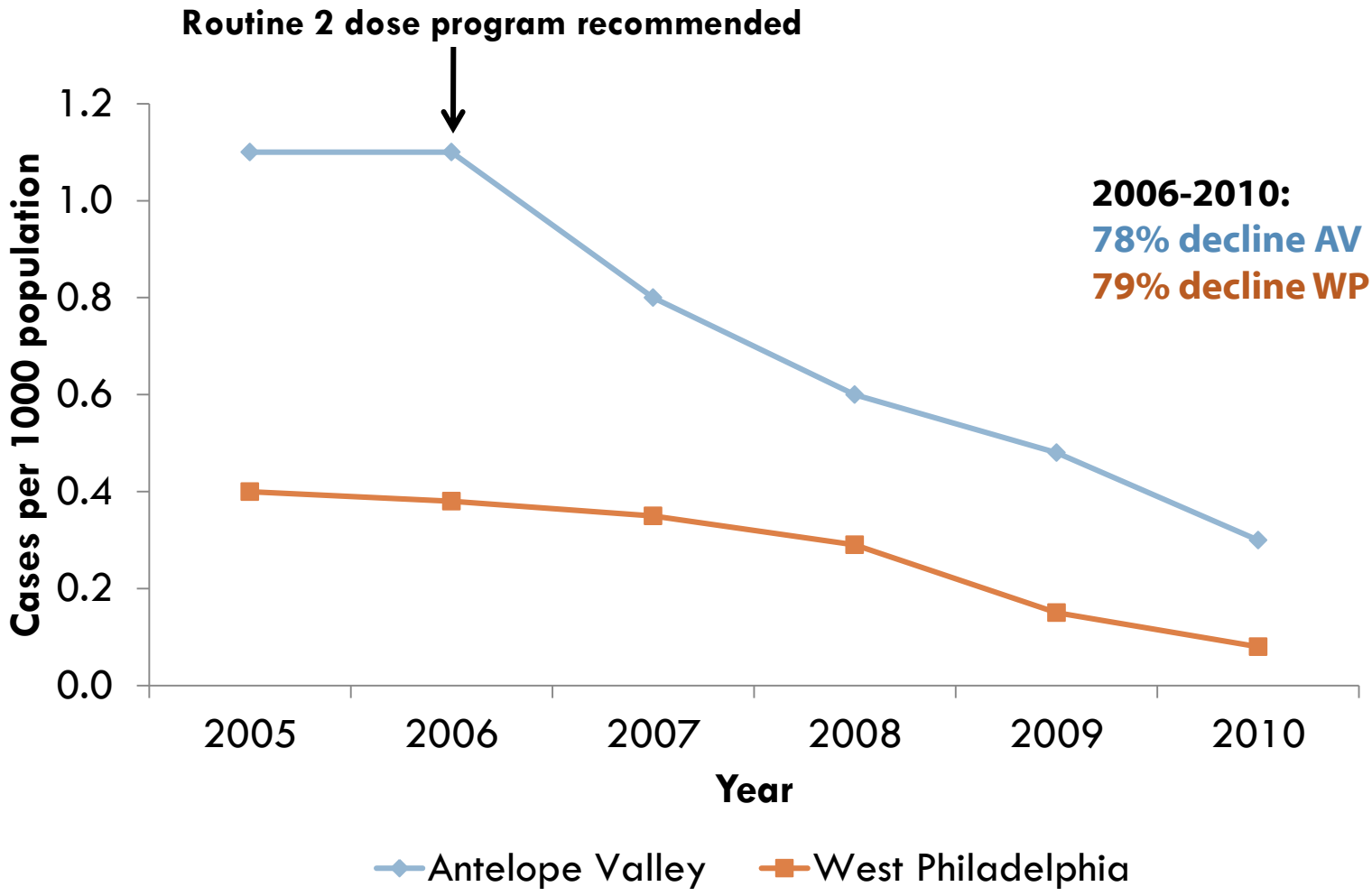
Change to a 2-dose vaccine policy - Rationale -

- **Varicella epidemiology**
  - **Ongoing endemic transmission with outbreaks in highly vaccinated school populations (coverage >96%)**
- **Breakthrough cases are contagious**
- **Vaccine effectiveness one dose ~80-85%**
  - **Incomplete protection after 1st dose**
- **Improved vaccine efficacy* with 2 doses**
  - **98%** **varicella of any severity**
  - **100%** **severe disease**

* Improved efficacy confirmed by field experiences which found a median of 95% 2-dose varicella vaccine effectiveness against varicella of any severity.

US EXPERIENCE WITH TWO DOSE VARICELLA VACCINE

Two-dose varicella vaccination program impact – VASP sites, 2005-2010



Reduction in age-specific incidence rates – VASP sites, 2006-2010

Age (years)	Antelope Valley, CA (%)	West Philadelphia, PA (%)
<1	81.5	6.1
1-4	55.9	72.7
5-9	88.3	92.9
10-14	78.5	95.7
15-19	36.1	43.8
20+	55.6	58.6
Total	77.5	78.7

Varicella outbreak characteristics VASP - Antelope Valley, CA,1995-2010

Characteristic	1995-1998	1999-2001	2002-2005	2006-2007	2008-2010
Number of outbreaks	236	42	46	19	4
Median cases (range)	15 (5-124)	11.5 (5-56)	9 (5-45)	9 (5-17)	8 (5-10)
% of outbreaks with 10 or more cases	72%	55%	41%	37%	25%
Duration outbreak	45 (7-198)	39 (1-149)	30 (3-90)	29 (4-61)	43 (5-52)
Age case patients, median (range)	6 (0-59)	6 (0-40)	9 (0-49)	9 (0-19)	13 (6-41)
Percent cases vaccinated	2%	21%	49%	70%	68%

Source: CDC and Varicella active surveillance project. 2006-2007 and 2008-2010 unpublished data, please do not distribute.

Severe varicella disease in the 2-dose era

- Varicella-related hospitalizations in active surveillance sites during 2006–2010 declined >40% compared with 2002–2005 and >85% compared with 1995–1998
- Analysis of national varicella hospitalization data in progress
- Updated mortality analysis (unpublished data)
  - No varicella deaths were reported among persons <20 years in 2010-2011 versus an annual average of 2 deaths in the 1-dose era and 48 deaths during the pre-vaccine era

Varicella vaccine and herpes zoster (HZ)

- Effect in community will depend on effect in vaccinated and unvaccinated cohorts
- In vaccinated healthy and immunocompromised children
  - Varicella vaccine also prevents herpes zoster
    - VE 68% - 100%
  - Declines in HZ incidence in vaccinated cohorts described US, Canada
- In persons with history of varicella
  - Models predicted increases based on assumptions about role of and duration of external boosting from exposure to children with varicella
  - Real world data?

Is risk for HZ increasing in the US?

Yes, but …..

No evidence that this increase is related to the varicella vaccination program

- **Increased risk predates program**
- **Increased risk in countries without varicella vaccination program**
- **Increase seen in unvaccinated cohorts across all ages**
- **An increase in some unrecognized risk factor for HZ is responsible?**

Conclusions: impact of varicella vaccination program in US

- ~20 years of experience with routine use of varicella vaccine in the US
- Varicella vaccine
  - Good safety profile with rare confirmed serious adverse events, most commonly in immunocompromised children
  - Markedly decreases the risk and severity of varicella and, over the short term, herpes zoster in vaccinated children
  - One dose is ~ 85% effective in preventing all varicella and ~ 100% effective in preventing severe varicella and 68-100% effective in preventing HZ; higher 2-dose effectiveness against all varicella
- Vaccine impact documented
  - Declines in varicella incidence, hospitalizations and mortality to very low levels
  - Herd immunity effect, no increase in incidence or severe outcomes in adults
  - Increases in herpes zoster cannot be attributed to varicella vaccination programs

THANK YOU

For more information please contact Centers for Disease Control and Prevention

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