

# ***Dynamics of RotaShield Uptake in the US Infant Population, a Vaccine that was Withdrawn After 9 Months of Use***

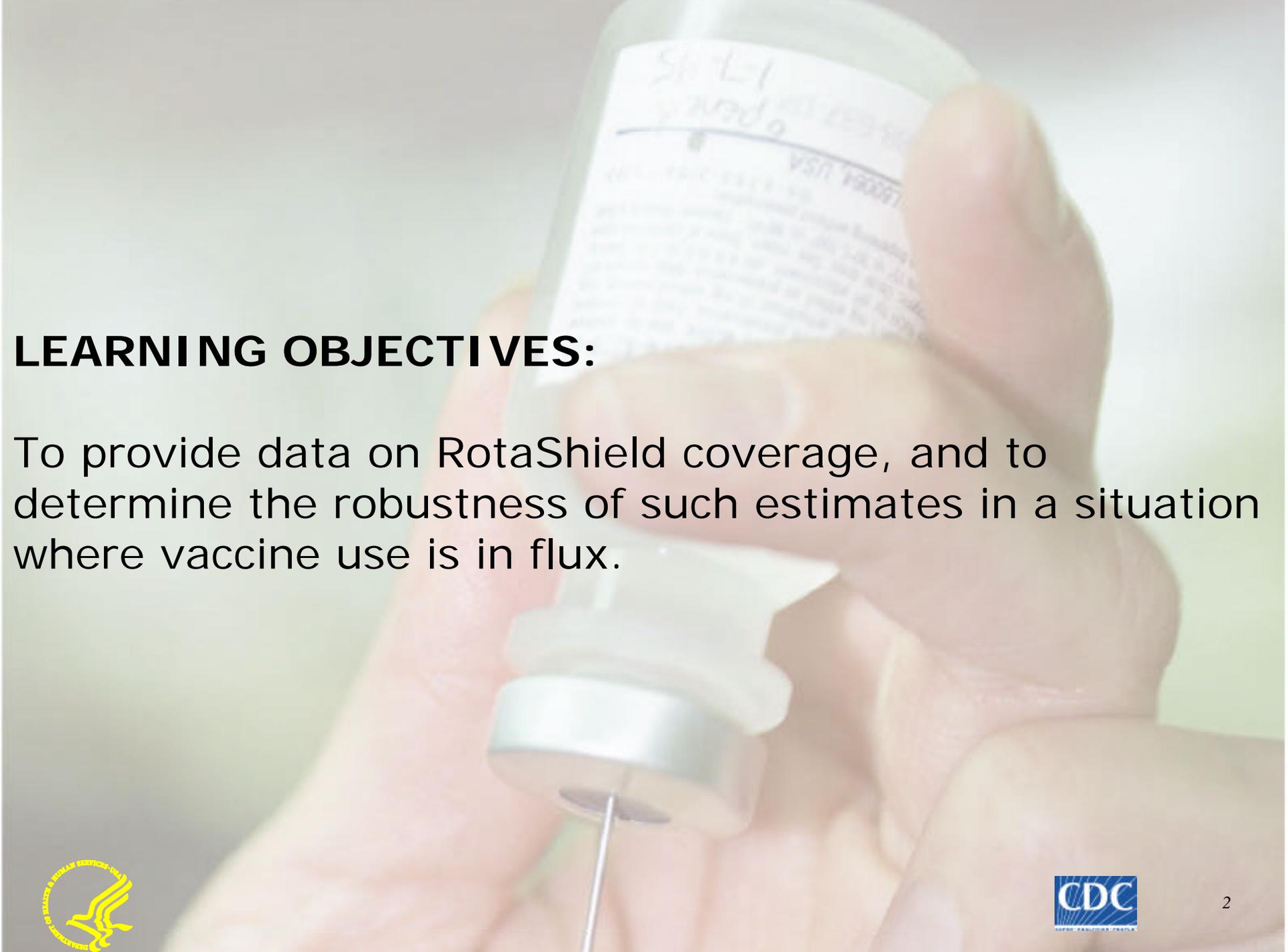
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## LEARNING OBJECTIVES:

To provide data on RotaShield coverage, and to determine the robustness of such estimates in a situation where vaccine use is in flux.



## **BACKGROUND:**

The National Immunization Survey (NIS) measures vaccination coverage for the childhood vaccines in the U.S. RotaShield, a vaccine against Rotavirus diarrhea, was used during October 1998–July 1999 and withdrawn after 9 months due to adverse events (intussusception) (1-3).

## **OBJECTIVE:**

Quantifying RotaShield coverage presents a unique challenge to NIS data interpretation because the short usage period produced a complex pattern of uptake. We addressed the effect on coverage rates of assumptions regarding population-at-risk for RotaShield immunization.

## **METHOD:**

Using NIS interview data from January 2000-March 2002, we studied three birth cohorts with infants born during 1) March 1998-May 1999, 2) September 1998-March 1999, and 3) December 1998-April 1999. The first cohort represents all infants who were ever 1-7 months of age during the RotaShield use period and thus targeted for a 1st dose - but with very different person-time at-risk. The second and third birth cohorts are subsets focused on infants at-risk for a 1st RotaShield dose over several months. Each subset was re-weighted to represent all U.S. infants in each age cohort.



## RESULT:

We identified 27,693, 13,031, and 9,082 children with provider-reported data in three age cohorts, respectively. In the first cohort, we estimated that 1.1 million RotaShield doses were administered to 569,000 infants. The cohort-specific RotaShield coverage rates ( $\geq 1$  doses) were 11.4%, 17.4% and 20.0%, respectively. We observed substantial variation in state level coverage ranging from 1%-23% in the first to 1%-32% in the second, and 1%-41% in the third cohort. Uptake of 1st Rotashield dose increased from low levels in October-November 1998, and reached stable levels by January 1999.



# *National Immunization Survey (NIS)*

- ❖ *Large ongoing RDD survey, conducted by CDC since 1994 (1)*
- ❖ *Measures vaccination coverage among children aged 19-35 months at National, State, and urban area levels*
  - ◆ *78 Immunization Action Plan (IAP) areas: 50 States, District of Columbia, and 27 large urban areas*
- ❖ *Monitors Healthy People 2000 and 2010 goals of immunization coverage*
  - ❖ *≥90% Coverage: 4DTP, 3Polio, 1MMR, 3HepB, 3Hib, and 4:3:1:3 series*
- ❖ *Monitors introduction of new vaccines (e.g., Varicella, Rotavirus, and Pneumococcal)*
- ❖ *'Earliest warning system' for changes in immunization coverage*
- ❖ *Evaluate administration of age-appropriate immunizations*



# *NIS Data Collection*

## ❖ *Household Screener and Interview (by telephone)*

- ◆ **Parent/Guardian** (*most knowledgeable person*)
- ◆ **Socio-demographic information:** *mother and child*
- ◆ **Vaccination History from**
  - *Shot card or memory recall*
- ◆ **Vaccination dates** (shot card only)
- ◆ **Provider's contact information with consent**

## ❖ *Provider Record Check Study (by mail)*

- ◆ **Provider's office** (e.g., staff, nurse, manager)
- ◆ **Mail, Fax, Telephone**
- ◆ **Vaccination history from**
  - *Completed IHQ or copy of medical records*
- ◆ **Matched on DOB, Gender, Name**
- ◆ **Provider's information** (e.g., facility type, participation in immunization registry and VFC)



# *RotaShield Vaccine*

**Developed at NIH  
Al Kapikian *et al.***

**Manufactured by  
Wyeth Laboratories Inc.**

**Licensed by FDA  
August 1998**

▪ ***Used during Oct'98 – July'99***

~ **600,000 infants vaccinated with**

~ **1.1 million RotaShield doses**

▪ **VAERS: 15 intussusception cases reported to CDC**

▪ ***RotaShield discontinued on July 16, 1999***

**20 years**

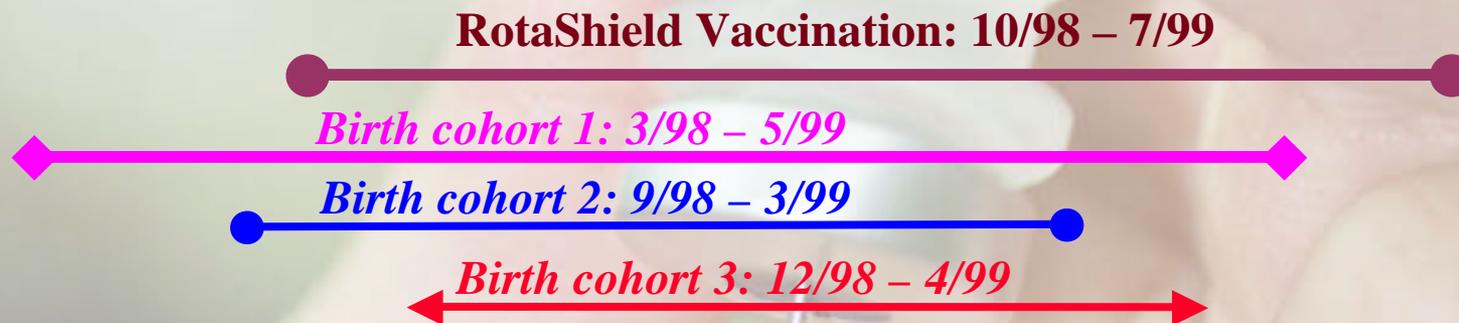
**Vaccine  
80-100%  
effective**

**9 months**



# *RotaShield Vaccination (Oct'98- July'99)*

- ❖ *Recommended age: 2, 4, and 6 months*
- ❖ *NIS Data collection for rotavirus vaccination started in 1999*
- ❖ *Source of Data: NIS Q1/2000 – Q1/2002*
- ❖ *Selected three arbitrary birth cohorts to evaluate variation in coverage estimates:*
  - ◆ *Cohort 1: children born in March 1998 – May 1999*
  - ◆ *Cohort 2: children born in September 1998 – March 1999*
  - ◆ *Cohort 3: children born in December 1998 – April 1999*



# *Sample Size and RotaShield Coverage by Birth Cohorts, Q1/2000- Q1/2002 NIS*

<b>Birth Cohort</b>	<b>Sample size (n)</b>	<b>U.S. Population (N)</b>	<b>Infants with 1+ doses of RotaShield (N)</b>	<b>Rotavirus Vaccine Coverage (%)</b>
<b>Cohort 1*</b>	<b>27,693</b>	<b>5,006,744</b>	<b>568,938</b>	<b>11.4</b>
<b>Cohort 2</b>	<b>13,031</b>	<b>2,313,909</b>	<b>402,575</b>	<b>17.4</b>
<b>Cohort 3</b>	<b>9,082</b>	<b>1,629,355</b>	<b>325,943</b>	<b>20.0</b>

**\* 1.1 million RotaShield doses administered in cohort 1**

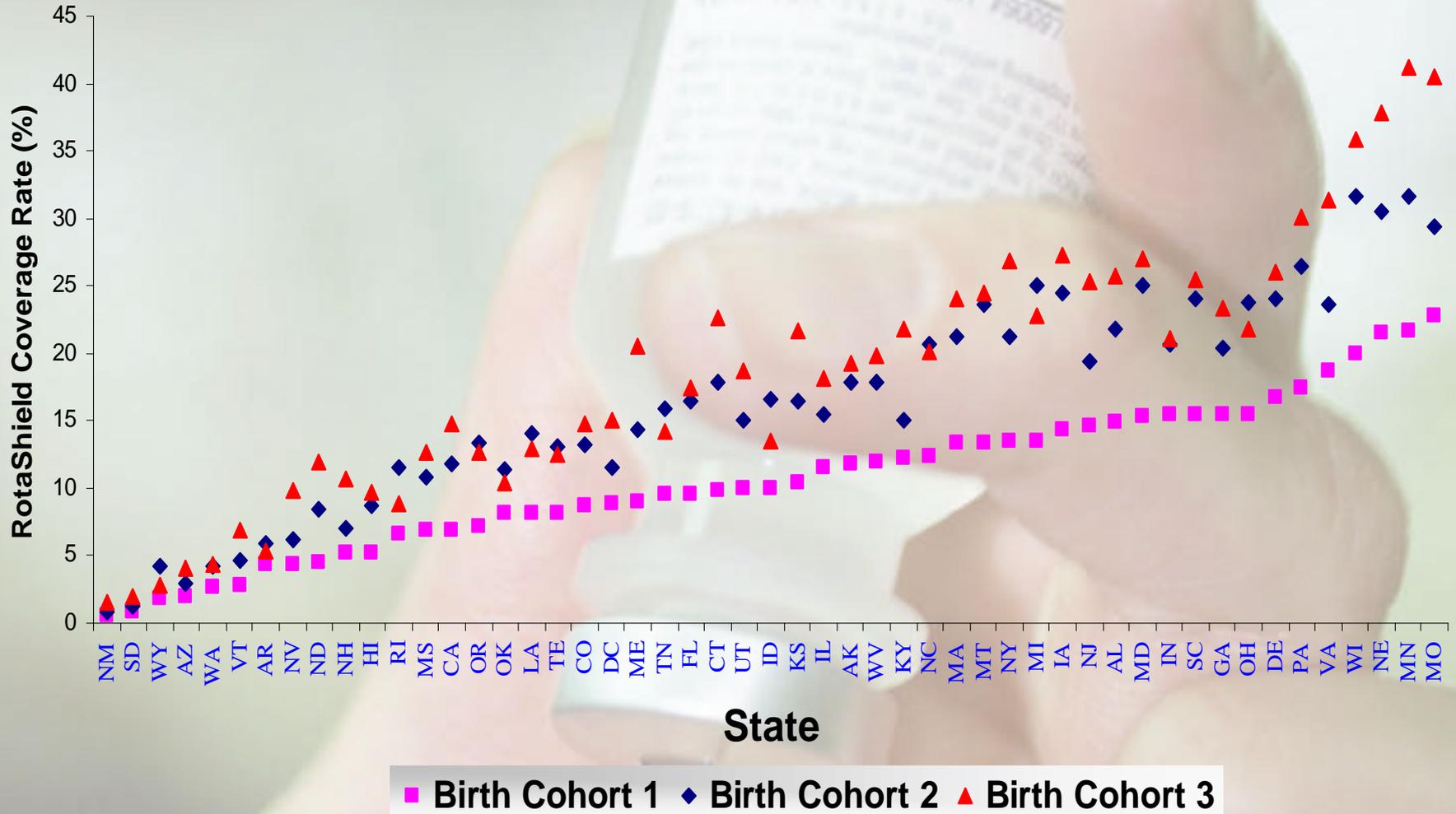


# *Demographic Characteristics of Infants Who Received At Least One Dose of RotaShield by Birth Cohorts*

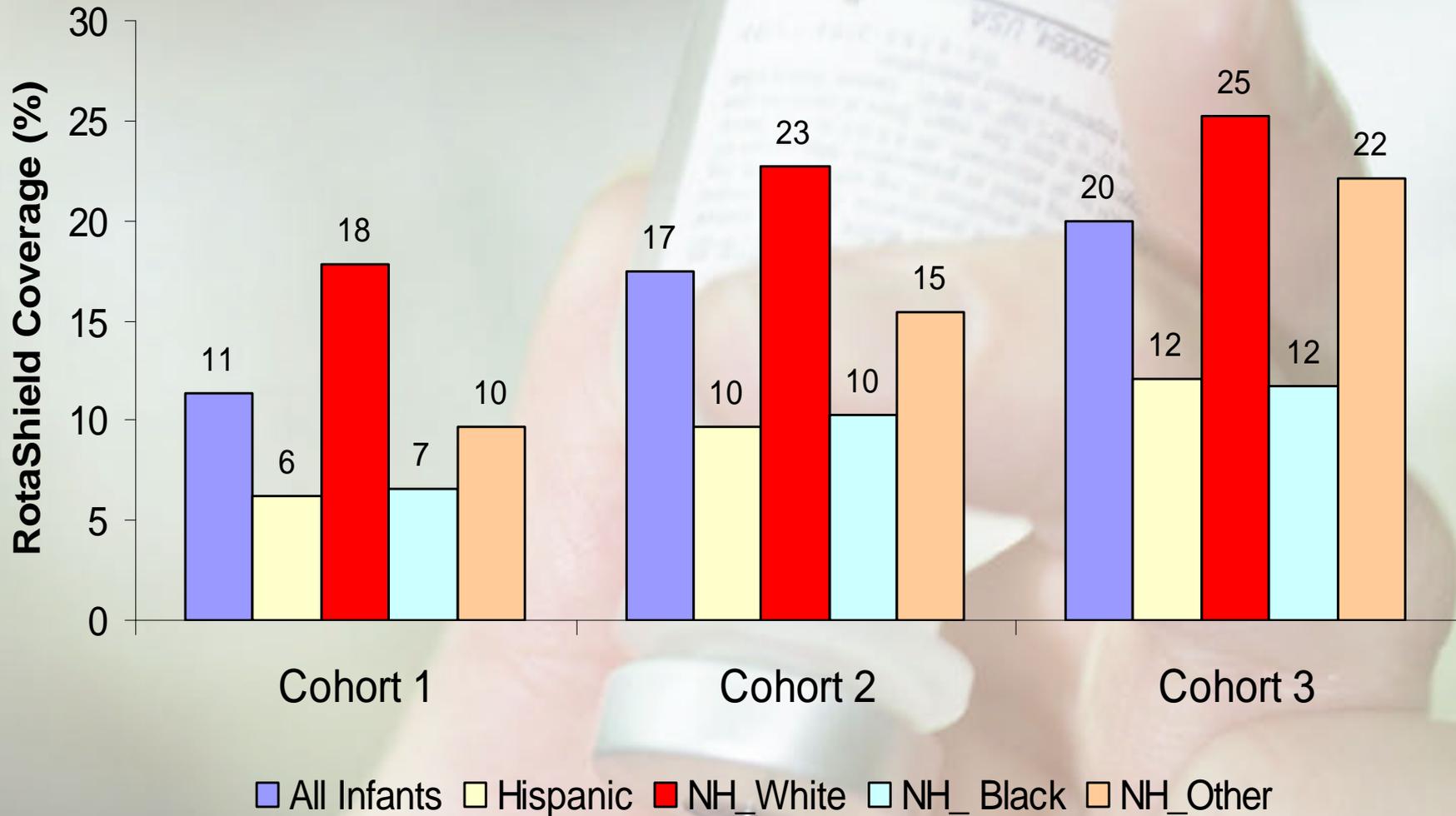
	<b>Cohort 1 n=2968</b>	<b>Cohort 2 n=2105</b>	<b>Cohort 3 n=1674</b>
<b>Age at 1<sup>st</sup> dose in days</b>			
Min	23	23	23
Mean	96	91	79
Median	69	68	64
Max	744	744	587
<b>Race/Ethnicity (%)</b>			
Hispanic	11.7	12.2	13.2
NH White	74.7	73.2	71.9
NH Black	9.3	9.7	9.5
NH Other	4.4	4.9	5.4



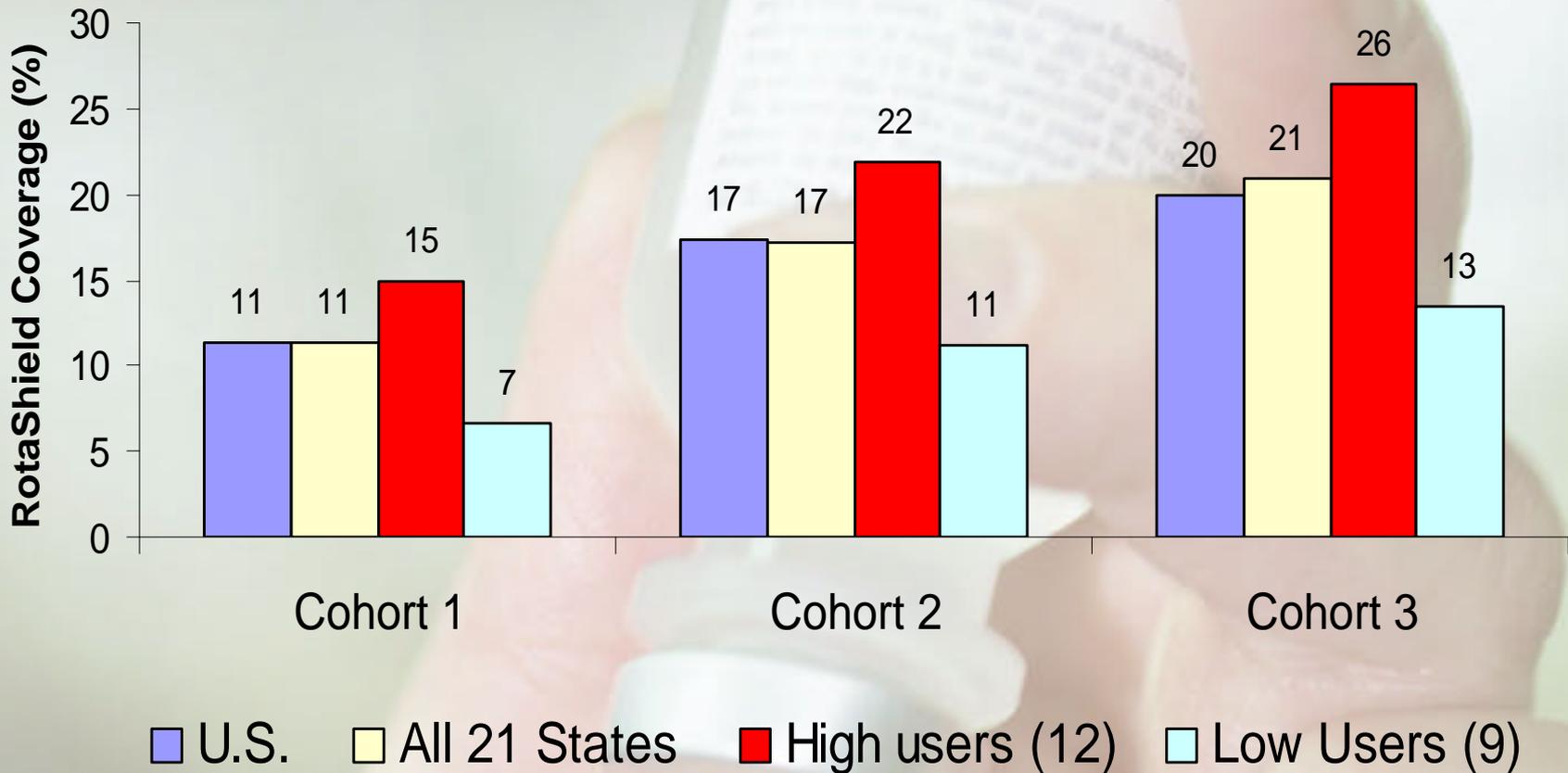
# Comparison of State-Specific RotaShield Coverage by Three Birth Cohorts, Q1/2000-Q1/2002 NIS



# Comparison of RotaShield Coverage by Race/Ethnicity of Infants and Three Birth Cohorts, Q1/2000-Q1/2002 NIS



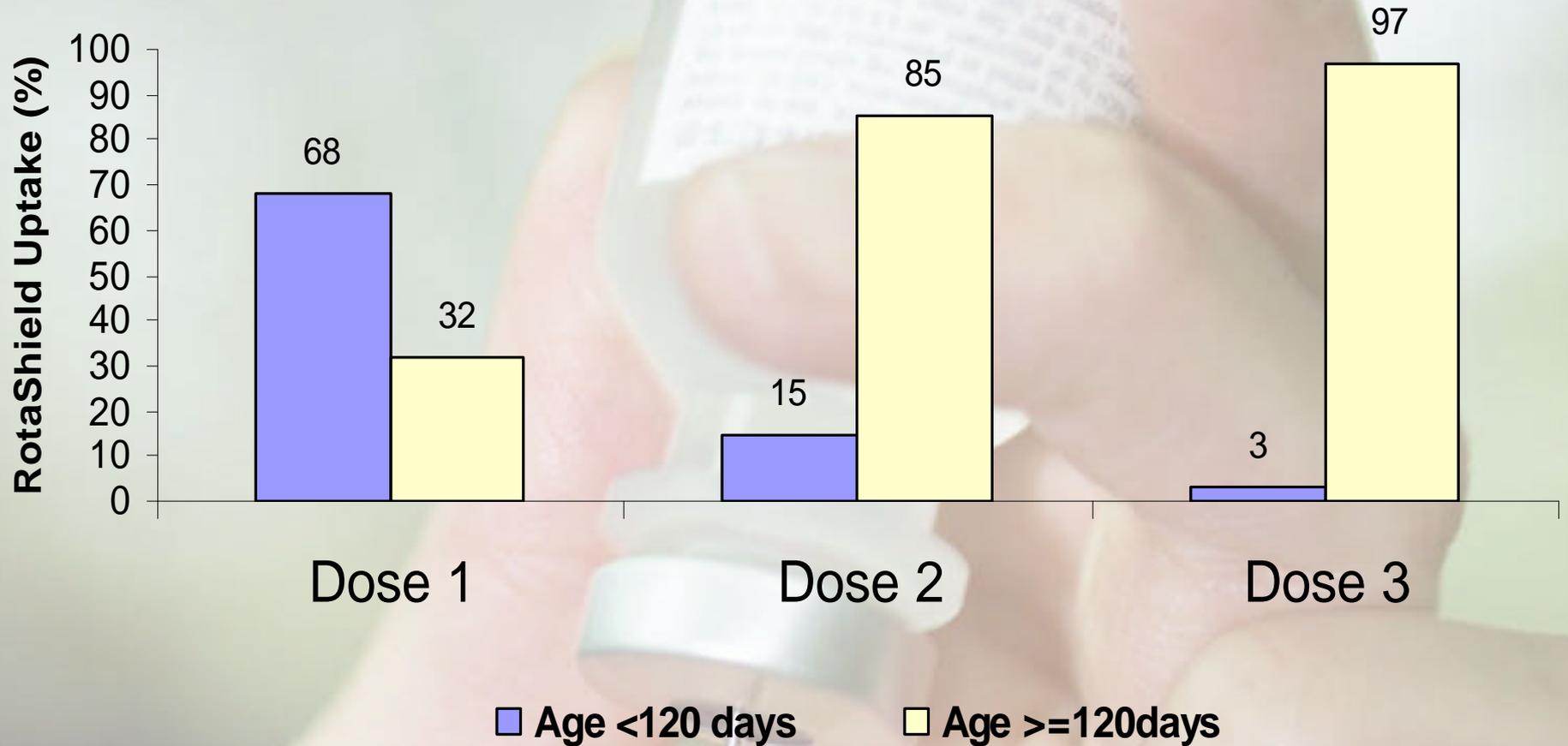
# RotaShield Coverage by High or Low User States\* and Three Birth Cohorts, Q1/2000-Q1/2002 NIS



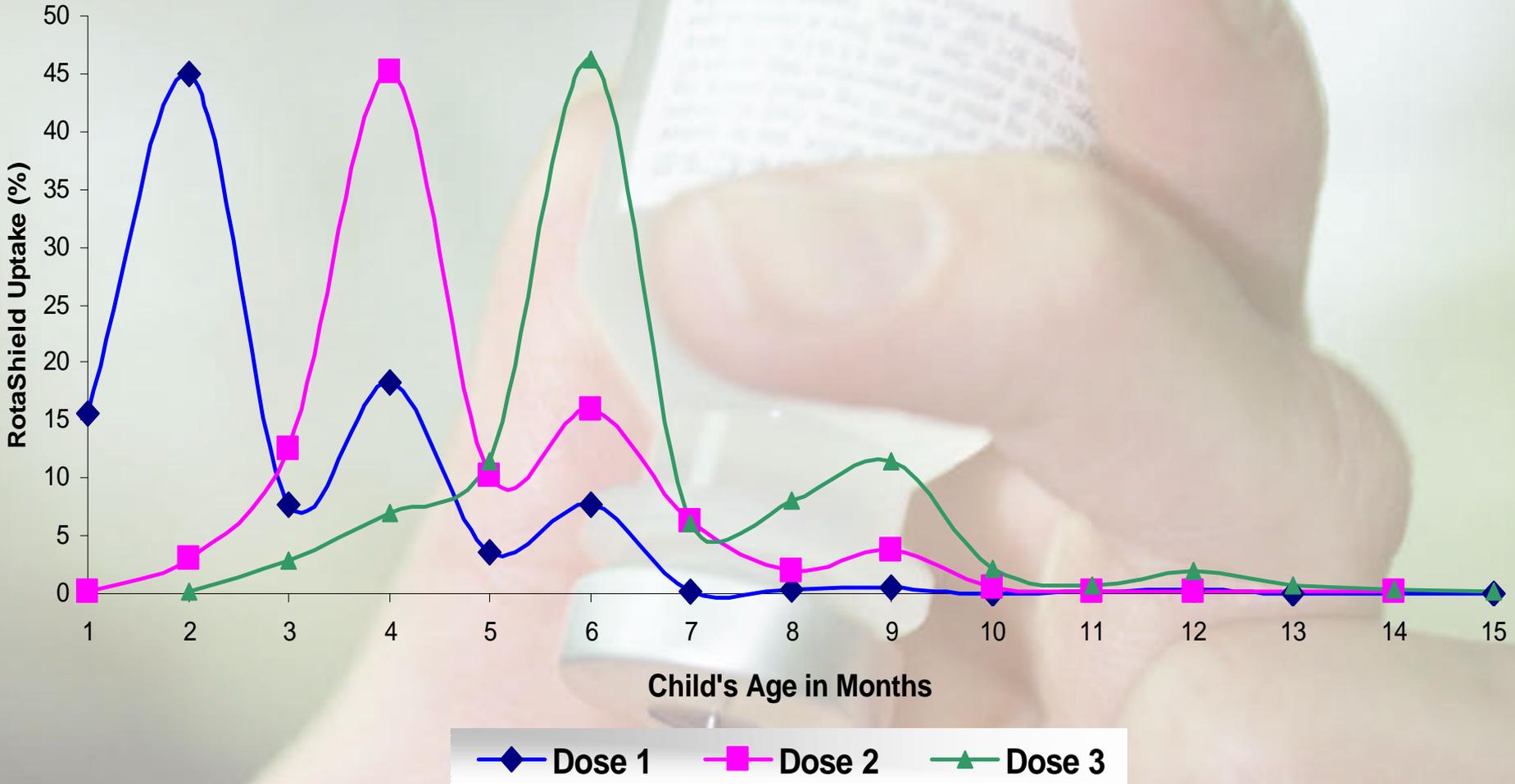
\*21 high and low user states were selected based on availability of hospitalization data from the AHRQ and NIS coverage ( $\geq 10\%$ ,  $< 10\%$ ) for the 1<sup>st</sup> rotavirus dose among children born in Cohort 1



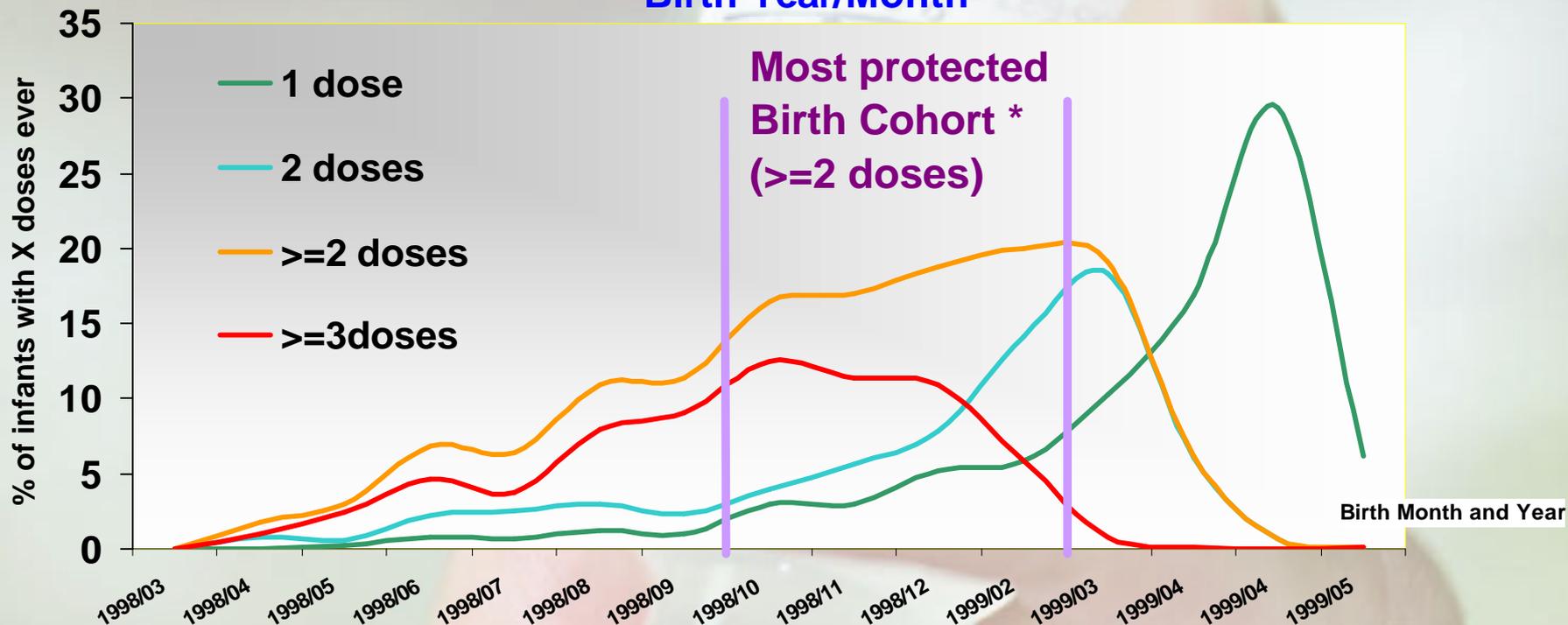
# RotaShield Uptake by Dose and Age at Vaccination among Infants Born in Cohort 1 (3/98-5/99)



# RotaShield Uptake by Dose and Age of Infants Born in Cohort 1 (3/98-5/99)



# Exposure to RotaShield Vaccine Among Infants Born in Cohort 1 (1998-99) from 12 "High User" States by Birth Year/Month



\* These data define the birth cohort born during Oct98-March99 as most likely to have had benefits of the aborted Rotashield vaccination program in terms of a reduction in Rotavirus-related diarrhea hospitalizations during the winter 2000 Rotavirus season. Assuming  $\geq 2$  doses protect 100%, the expected reduction in rotavirus diarrhea in this "protected" cohort is 15-20% in "high user" States.

# Conclusion

- ❖ *Our estimate of 1.1 million RotaShield doses ever used agreed with Wyeth-Lederle net sales (~1.2 million doses) and also with an estimate provided by Smith et al. (2).*
- ❖ *Estimates of RotaShield coverage depended profoundly on the arbitrary choice of birth cohorts at-risk for RotaShield. Narrowing the birth cohort for infants who were at the recommended age (2-6 months old) for beginning their RotaShield schedule increased the estimates of National coverage from 11% to 20%.*
- ❖ *Earlier studies had not taken this factor into consideration when they reported RotaShield coverage estimates of 11% (2)*
- ❖ *Substantial variation was observed in RotaShield coverage by state (e.g., 1% - 23% in cohort 1) and cohort*

*❖ Contrary to earlier findings, we expect a measurable decline in national rates of intussusceptions during the RotaShield use period when compared to surrounding years (4).*

*❖ This finding strengthens the observation of no increase in intussusceptions during RotaShield use period was unexpected (see 3-5 and Simonsen et al., NIC 2003 poster #63)*

*❖ Among 12 States with high RotaShield coverage, the expected decrease in intussusception hospitalizations could be as high as 27%;*

*❖ Assuming children with 2+ doses of RotaShield would be 100% protected against rotavirus diarrhea, we would expect 15-20% reduction in rotavirus diarrhea in this \*protected" cohort in "high user" States.*

# References

- 1) Smith PJ, Battaglia MP, Huggins VJ, Hoaglin DC, Roden A-S, Khare M, Ezzati-Rice TM, and Wright RA. Overview of the Sampling design and statistical methods used in the National Immunization Survey. *American Journal of Preventive Medicine*, 2001, 20:4 (Supplement 1): pp 17-24
- 2) Smith PJ, Schwartz B, Mokdad A, Block AB, McCuauy M, and Murphy TV. The first oral rotavirus vaccine 1998-1999: Estimates of coverage from the National Immunization Survey. In press.
- 3) CDC. Intussusception among recipients of rotavirus vaccine – United States, 1998-1999. *MMWR* July 16, 1999/ 48(27), pp 577-581
- 4) Murphy TV, Gargiullo PM, Massoudi MS, et al. *The New England Journal of Medicine*, February 22, 2001, 344, pp564-572
- 5) Simonsen L, Morsens DM, Elixhauser M, Gerber M, Van Raden M, and Blachwelder WC. Effect of rotavirus vaccination programme on trends in admission of infants to hospital for intussusception. *Lancet*, October 13, 2001, 358, pp 1224-1229