

# **Assessing Rotavirus Vaccine Effectiveness in Connecticut Using the State Immunization Registry**

**Alice Guh, MD, MPH**

**Connecticut State Department of Public Health**

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# Rotavirus in the Pre-vaccine Era

- **Leading cause of severe acute gastroenteritis (GE) in young children**
  - **>55,000 hospitalizations**
  - **>200,000 emergency department (ED) visits**
- **Most severe cases among 6–24 months age group**
- **>95% infected by age 5**

# Rotavirus Vaccine

<b>Vaccine Characteristics</b>	<b>RotaTeq®</b>	<b>Rotarix®</b>
<b>Licensure</b>	<b>February 2006</b>	<b>April 2008</b>
<b>Type</b>	<b>Live, Pentavalent, Human-bovine</b>	<b>Live, monovalent, Human-attenuated</b>
<b>Oral dosing</b>	<b>3-dose: 2, 4, 6 mos</b>	<b>2-dose: 2, 4 mos</b>
<b>Efficacy against any GE severity*</b>	<b>74% (95%CI: 67, 80)</b>	<b>87% (95% CI: 80, 92)</b>
<b>Efficacy in reducing hospitalizations*</b>	<b>96% (95%CI: 91, 98)</b>	<b>100% (95%CI: 82, 100)</b>

\*Through one rotavirus season

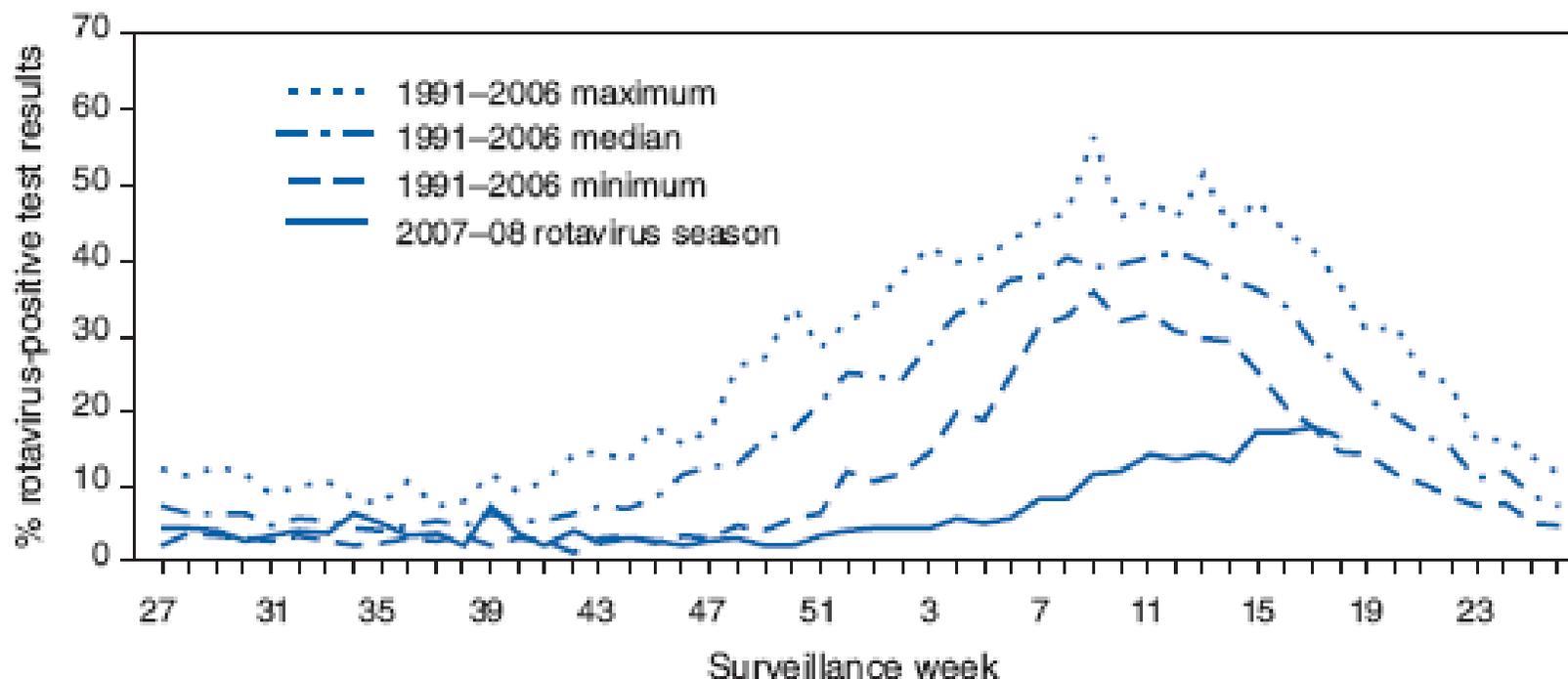
# Vaccine Uptake

- **Lacking nationally representative data**
- **U.S. sentinel sites with population-based immunization systems**
  - Children aged 13 months
  - 3-dose coverage was 33.7% in March 2008
- **Connecticut Immunization Registry and Tracking System**
  - Children aged 1 year
  - 3-dose coverage was 50% in June 2008

# Post-Vaccine Era

- **National network of U.S. laboratories**
  - 2007–2008 vs previous 15 seasons
  - Rotavirus delayed in onset by 2–4 months, diminished in magnitude by >50%

**FIGURE 1. Percentage of rotavirus tests with positive results from participating laboratories, by week of year — National Respiratory and Enteric Virus Surveillance System, United States, 1991–2006 rotavirus seasons and 2007–08 rotavirus season\***

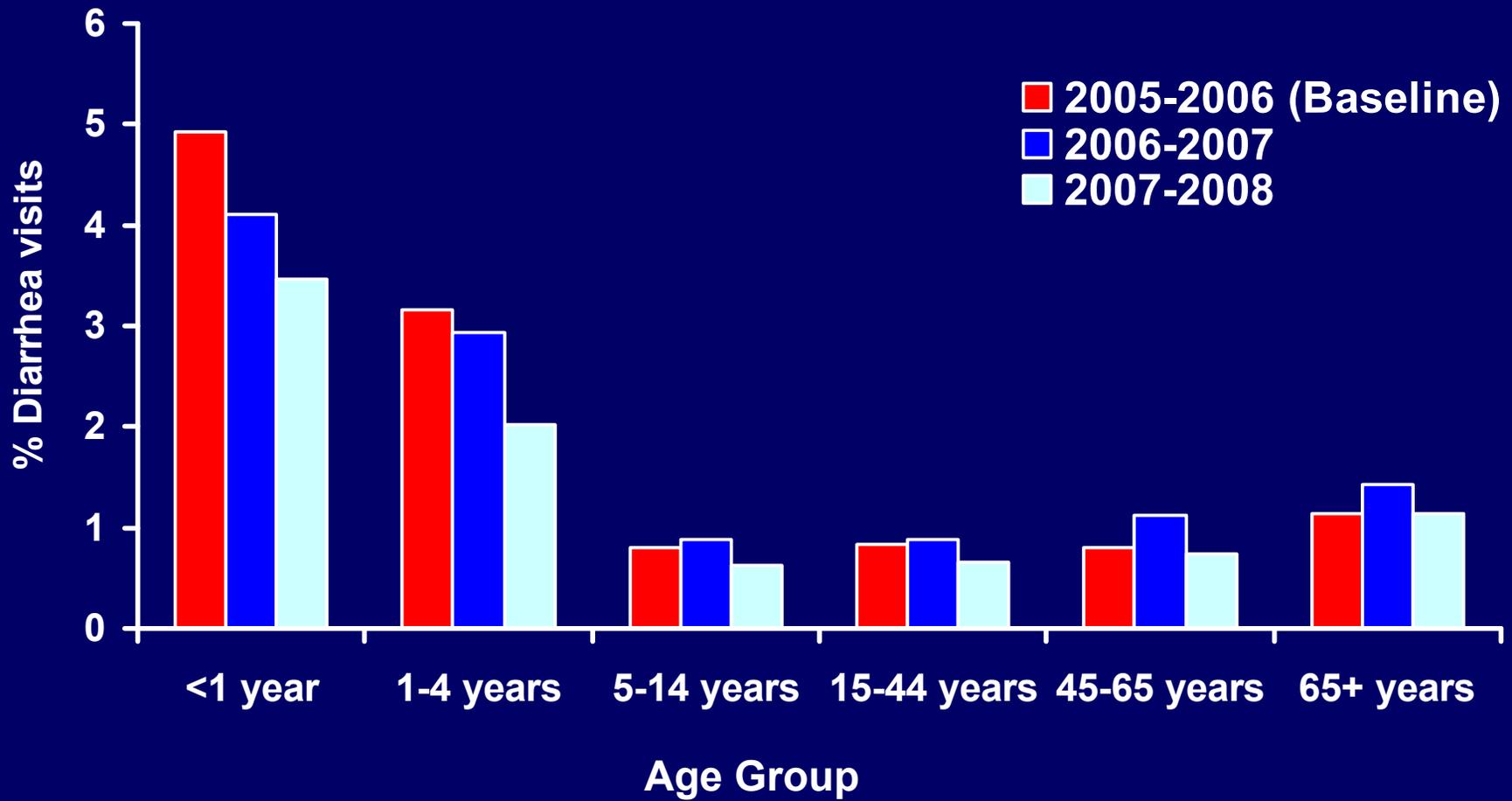


\* 2008 data current through week ending 3 May 2008. Data from July 2006–June 2007 were excluded from the (1991–2006) prevaccine baseline data because some persons tested likely received vaccine during that period.

# Rotavirus in Connecticut

- **Not a reportable disease**
- **Not part of state universal vaccine distribution**
- **State population-level effect of vaccine is unknown**
- **CT ED Syndromic Surveillance System**
  - 2007–2008 vs 2005-2006 data
  - Diarrhea visits among children aged <1–4 years decreased by 32%

# Annual Percent of ED Visits by Age Group and Season — 2005–2008



# Objectives

- **Using the Connecticut Immunization Registry and Tracking System (CIRTS):**  
**Determine post-licensure rotavirus vaccine effectiveness (VE) in preventing hospitalizations of Connecticut infants for rotavirus GE**

# CIRTS

- **1998 — statewide**
- **Approximately 92% newborns enrolled yearly**
- **Computerized entries of individual vaccination data for children aged <5 years**
- **Obtain data from providers at ages 7- and 19-months**
- **Contains birthdate and address**

# CIRTS — Alternative VE Study Method

<b>Study Method Characteristics</b>	<b>Alternative*</b>	<b>Traditional</b>
<b>Vaccination history of cases and controls</b>	<b>CIRTS</b>	<b>Provider records, patient interviews</b>
<b>Selection of control subjects</b>	<b>CIRTS</b>	<b>Medical charts, patient interviews</b>
<b>Labor-intensive</b>	<b>No</b>	<b>Yes</b>
<b>Time-consuming</b>	<b>No</b>	<b>Yes</b>

**\*Demonstrated to be acceptable and accurate method by Muhammad et. al in pneumococcal conjugate VE study (2008)** 11

# Methods

- **Case-control study**
- **Existing patient data\***
  - **CIRTS**
  - **Two main pediatric hospitals in Connecticut**
    - **Connecticut Children Medical Center (CCMC)**
    - **Yale New Haven Hospital (YNHH)**

\*Approved by IRB / HIC of CT DPH, CCMC, and YNHH

# Case Selection

- **Case definition**
  - Positive stool test for rotavirus antigen
  - Child aged  $\geq 2$  months but  $< 3$  years
  - Hospitalized at CCMC / YNHH with rotavirus GE during July 2006–December 2008
- **Case identification**
  - Retrospective review of hospital laboratory data
  - Standardized medical chart abstraction
  - CIRTS access for rotavirus vaccination status

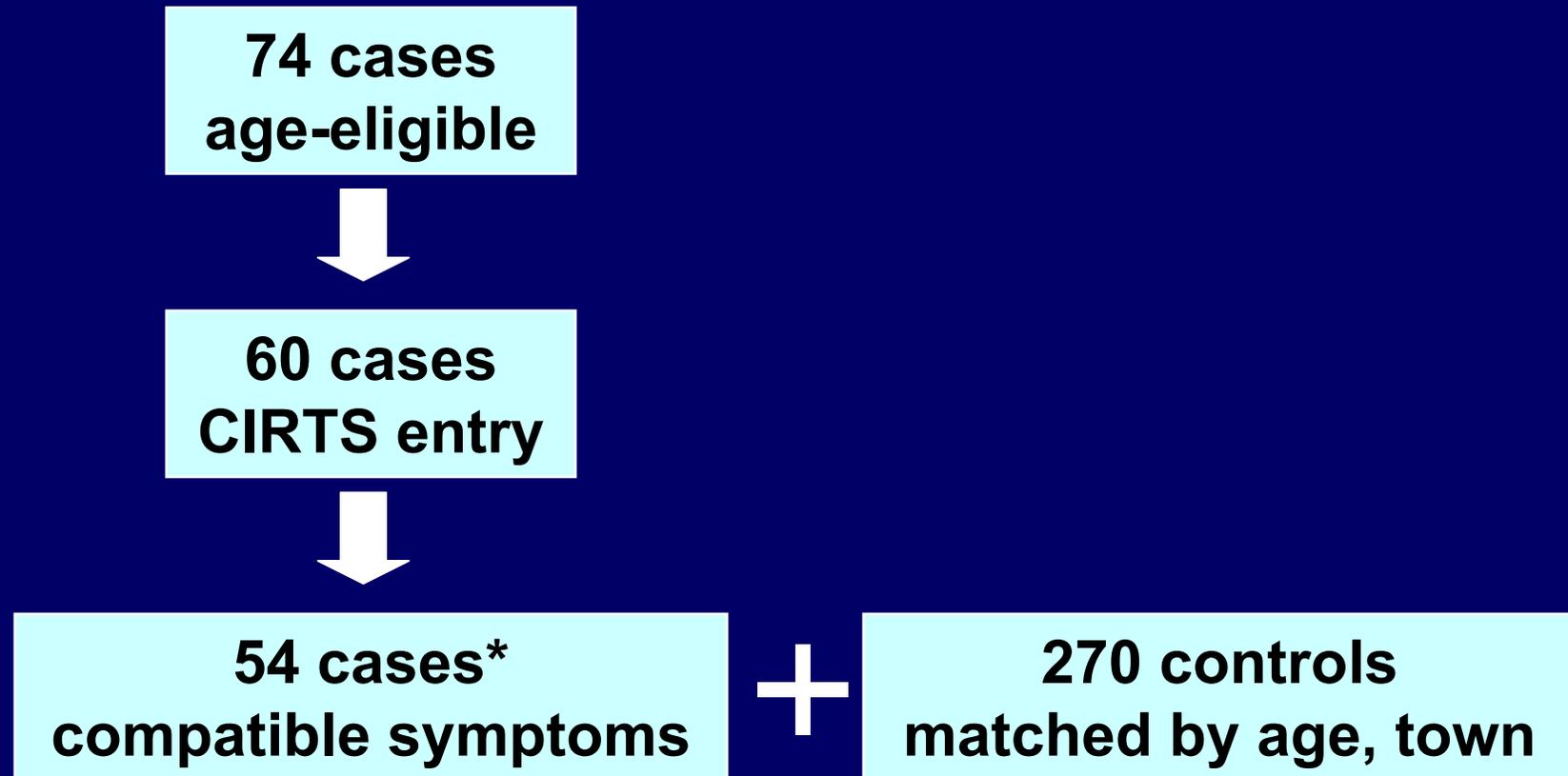
# Control Selection

- **Control definition**
  - Child not hospitalized at CCMC / YNHH for rotavirus GE (no positive stool test) during July 2006–December 2008
  - Match case-patient: within 14 days of birthdate, town of residence
- **Control identification**
  - CIRTS access for selection by birthdate, town
  - CIRTS access for rotavirus vaccination status

# Case-control Study Design

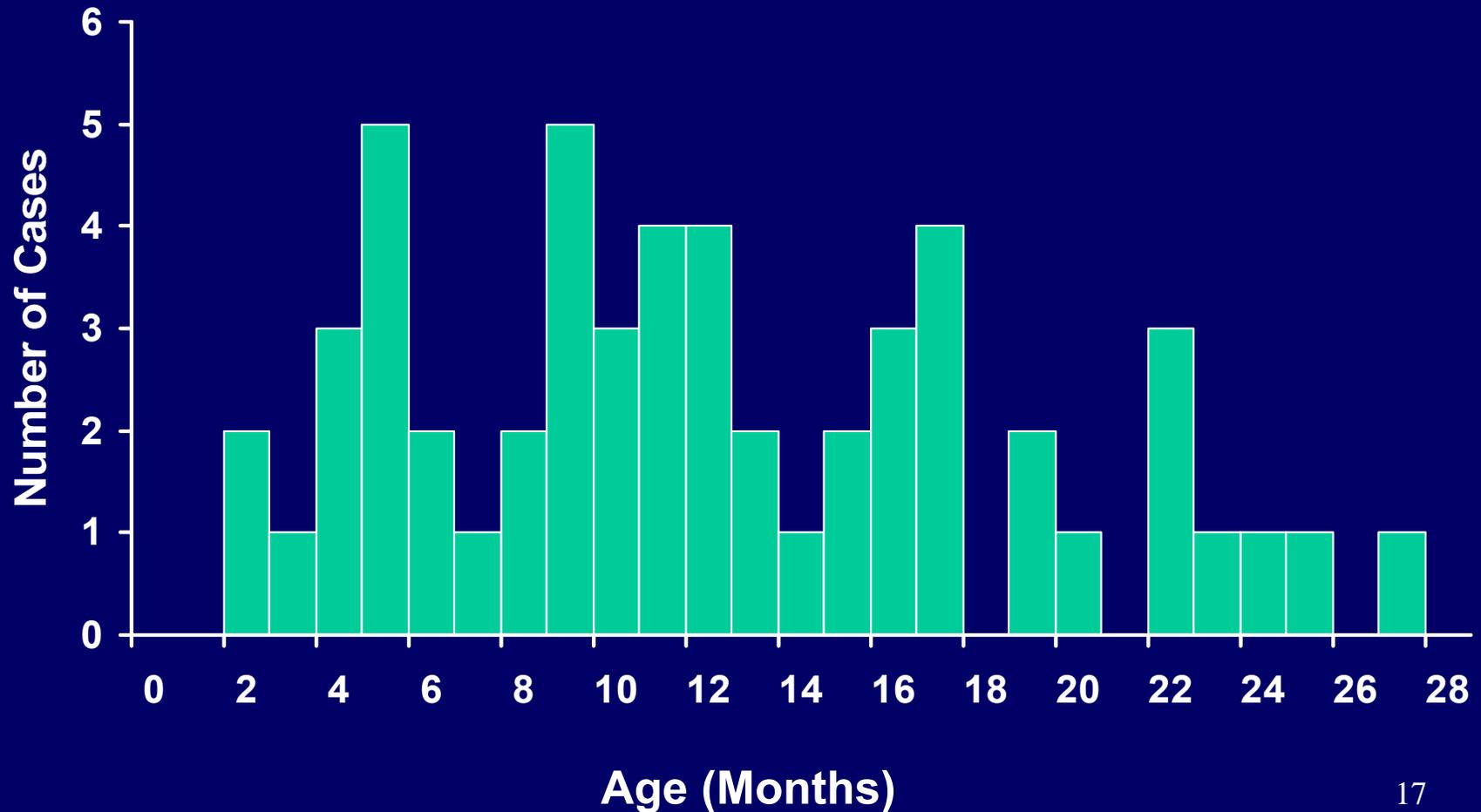
- Matched analysis
- 1 case : 5 controls
- Receipt of 1 valid dose of rotavirus vaccine
  - At age 6–12 weeks
  - $\geq 7$  days prior to illness onset of case-patients
- Odds ratio (OR), 95% confidence intervals
- $VE = (1 - \text{matched OR}) \times 100\%$

# Study Sample



\*Remaining 6 (10%) of 60: 2 without GE, 4 missing charts

# Age of Case-Patients by Symptom Onset (n=54)

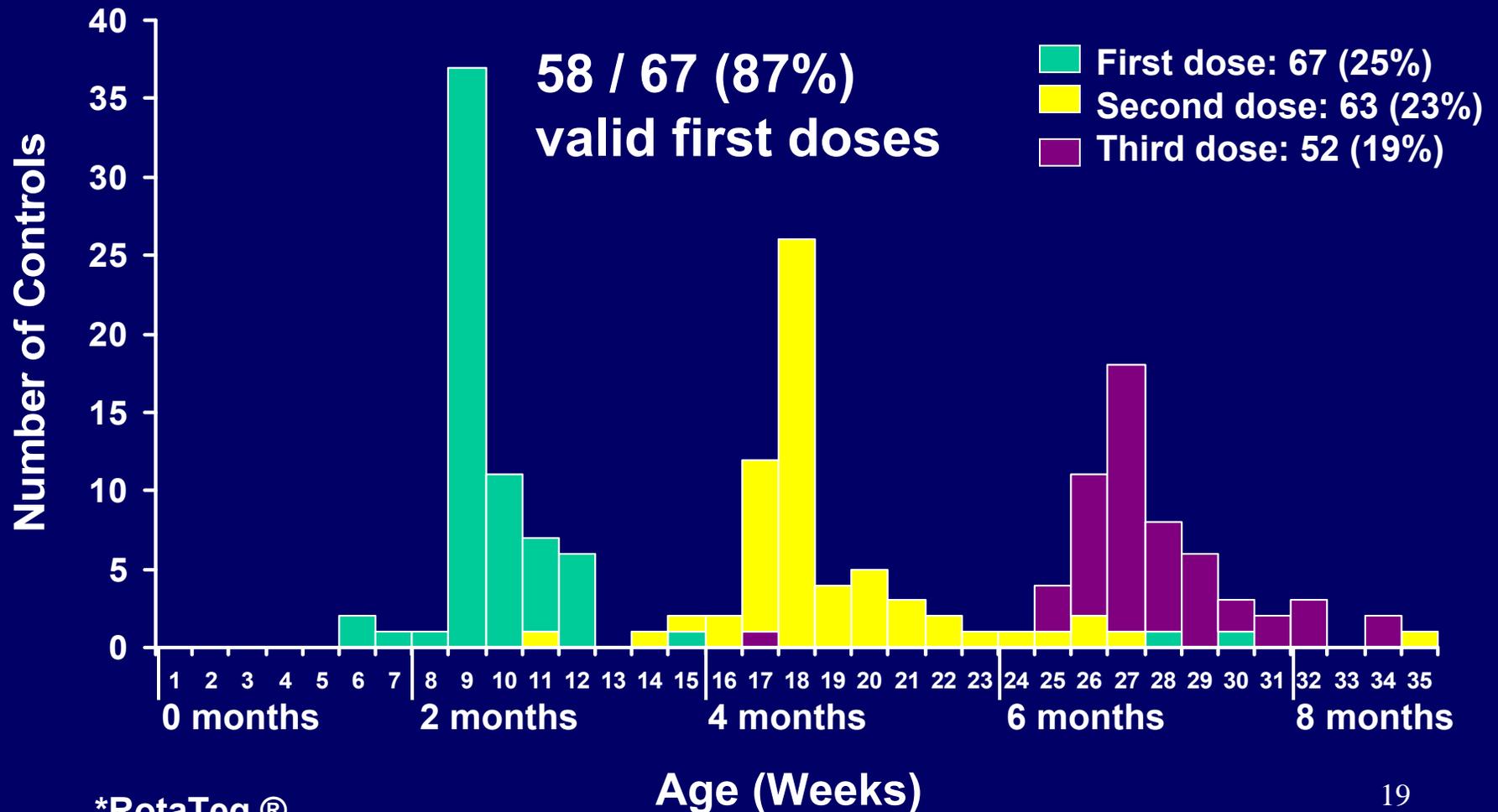


# Case-patient Characteristics (n=54)

Characteristics	No.	(%)
Median age in months (range)	11 (2–27)	
Male	31	(57)
<b>Symptoms</b>		
Diarrhea ( $\geq 2$ episodes / day)	53	(98)
Vomiting ( $\geq 1$ episode / day)	50	(94)
Abdominal pain	4	(8)
Fever ( $\geq 100.4^\circ$ F)	42	(78)
Dehydration	48	(89)
Receipt of $\geq 1$ vaccine dose*	3	(6)
Valid dose	2	(4)

\*RotaTeq ®

# Age of Control Subjects by Rotavirus Vaccination\* (n=270)



\*RotaTeq®

# Matched Analysis

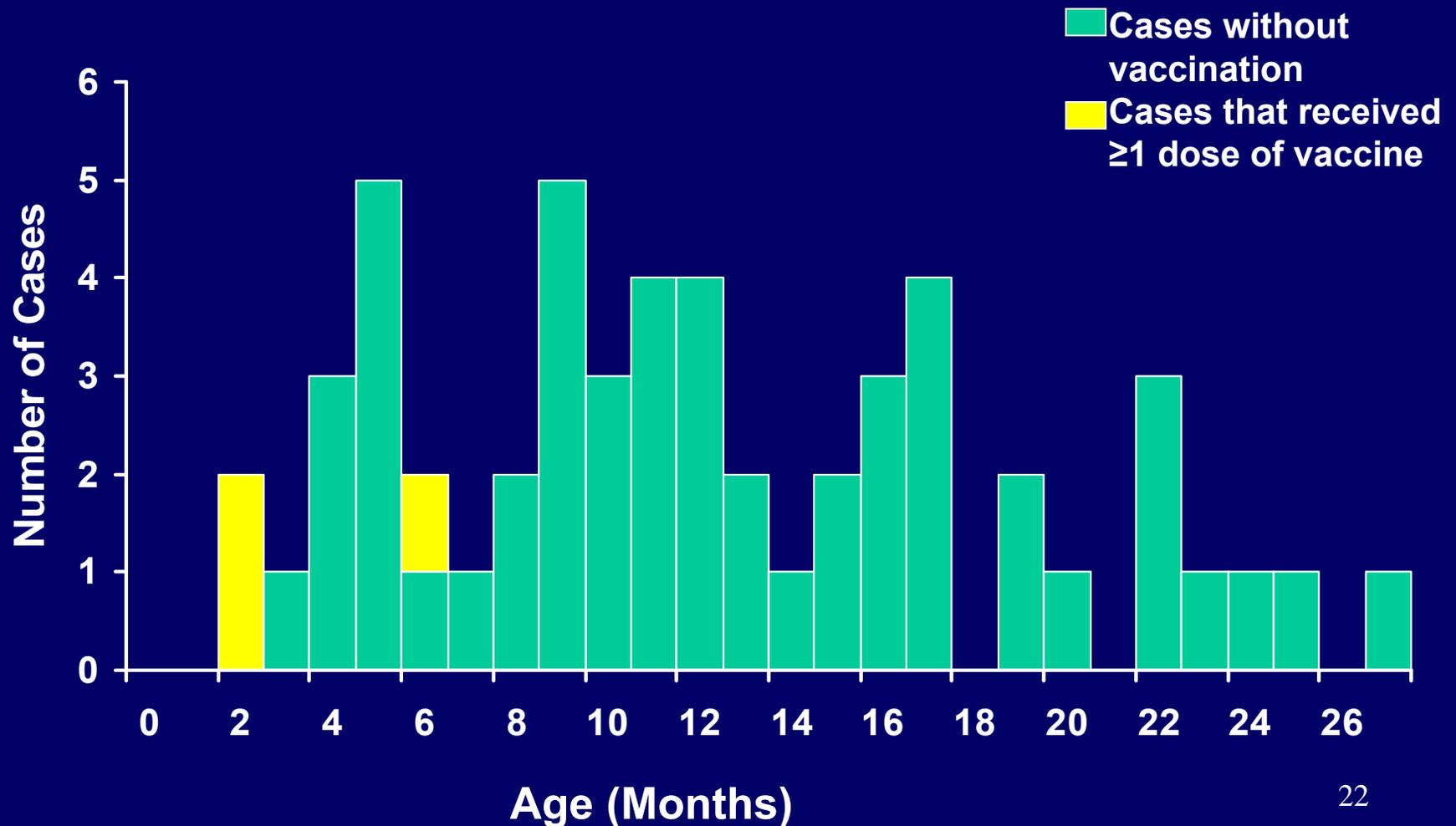
		Controls		
		1 dose	No dose	
Cases	1 dose	4	6	10
	No dose	54	206	260

**Matched OR = 0.11 (95% CI: 0.04, 0.26)**

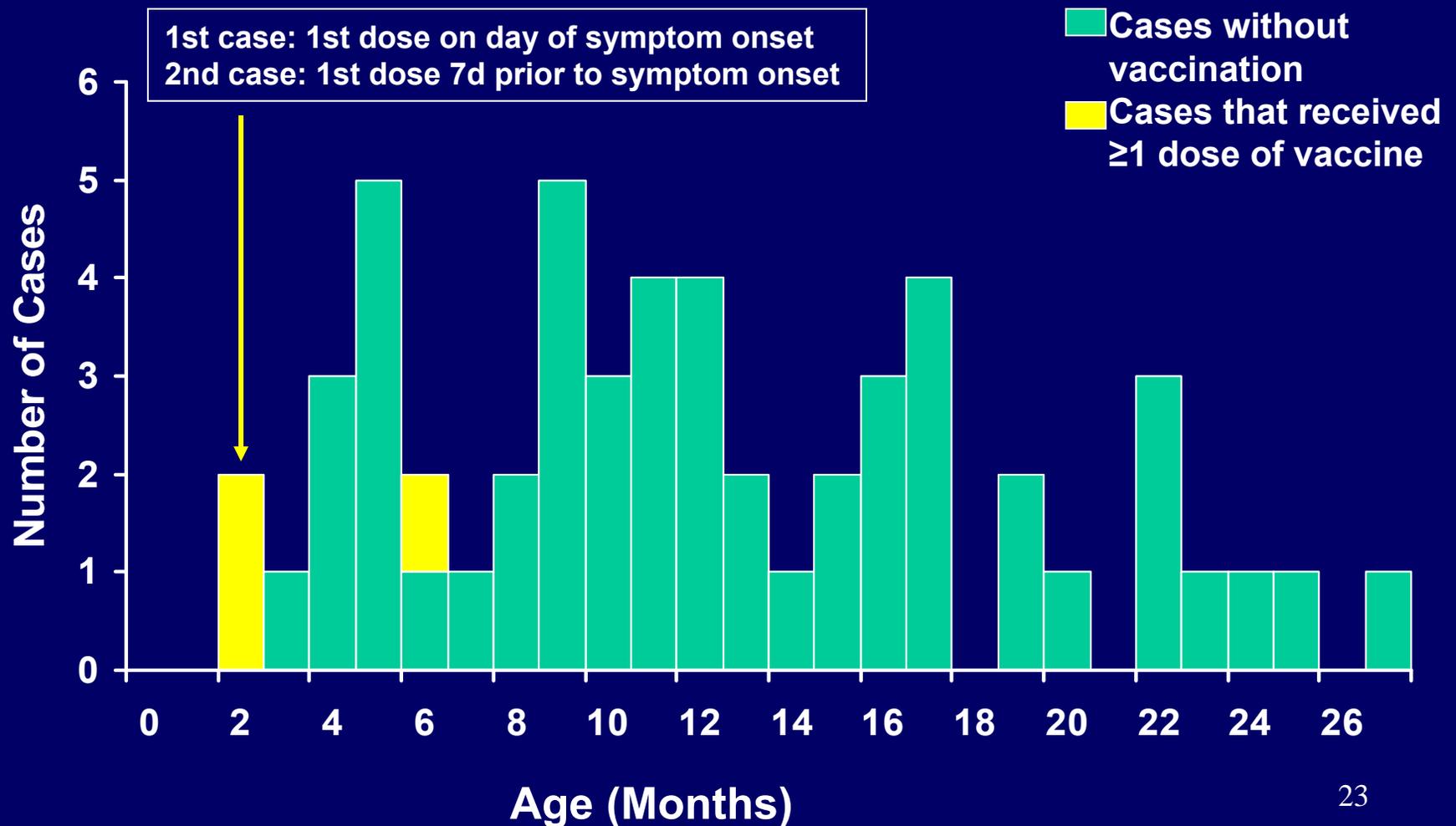
# VE in Preventing Hospitalizations

- **Current study VE — 1 dose**  
**89% (95% CI: 74, 96)**
- **Pre-licensure RotaTeq® VE — 3 doses**  
**96% (95%CI: 91, 98)**

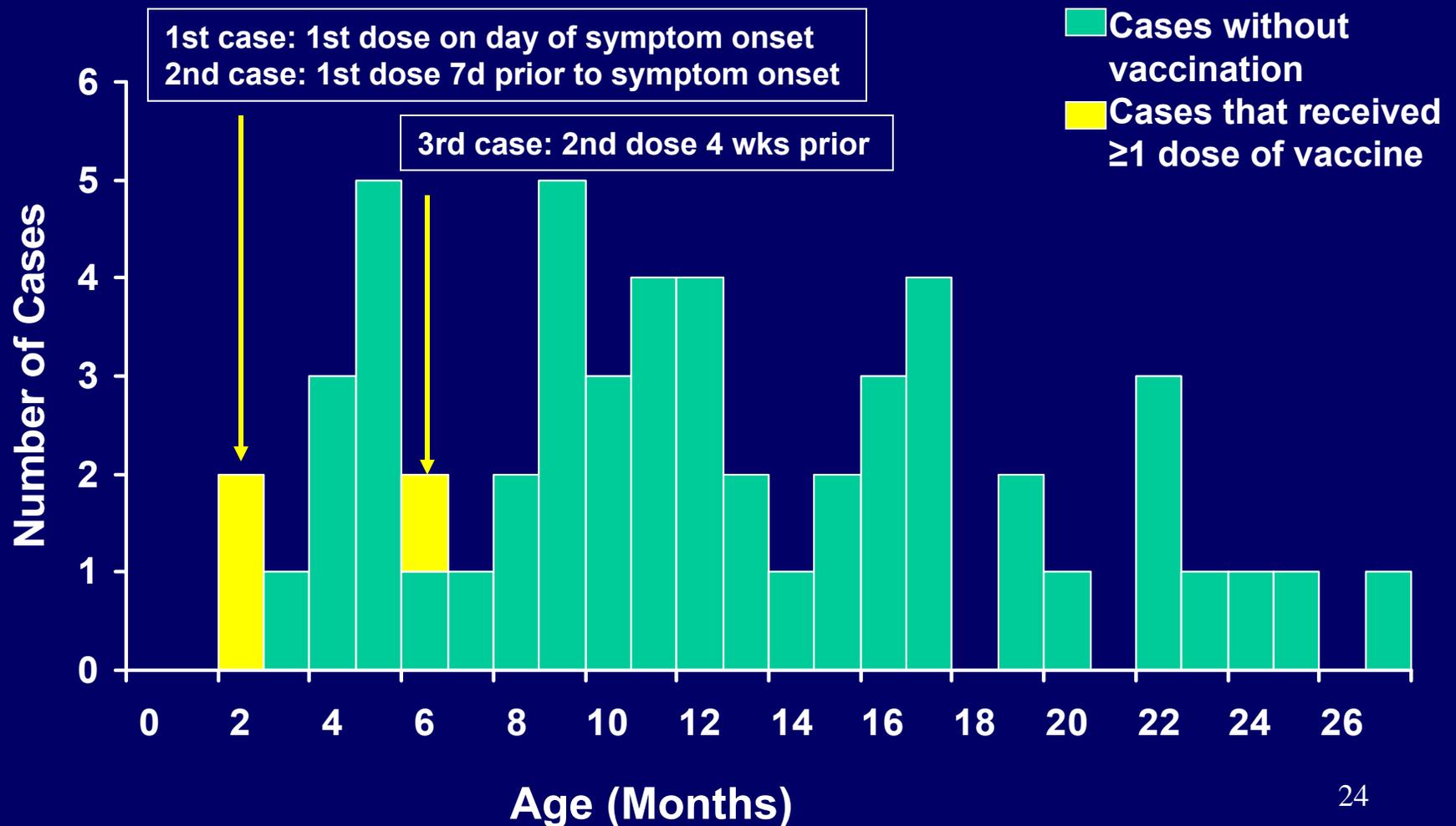
# Age of Case-Patients by Symptom Onset (n=54)



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# Age of Case-Patients by Symptom Onset (n=54)



# Limitations

- **Lacked power to assess VE of 2- or 3-doses**
- **Might not be representative of whole state**
- **Possible difference in vaccine opportunities**
- **CIRTS entry might not be complete**
- **Potential misclassification of controls**

# Conclusions

- **High VE in post-licensure era in preventing hospitalization of Connecticut children for rotavirus GE**
- **Possible vaccine failure with <3 doses**
- **Comparable to pre-licensure VE**
- **CIRTS has proven to be a useful VE study method**

# Recommendations

- **Provide rotavirus vaccine at no cost to providers to enhance statewide immunization efforts**
- **Validate the use of CIRTIS by comparing with traditional study method to evaluate rotavirus VE**

# Acknowledgments

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