Update on RotaTeq® Vaccine Reports to the Vaccine Adverse Event Reporting System (VAERS), 2/1/06-3/31/08

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Background

- **Rotashield® rotavirus vaccine: withdrawn from US market in 1999 after postlicensure monitoring identified increased risk for intussusception (IS)***
  - **29 fold increase 3-14 days post dose 1**
- **RotaTeq® rotavirus vaccine licensed in 2006****
  - **No increased risk for IS observed in clinical trials**

** Source: Murphy et al. NEJM. 2001. ** Source: Vesikari et al. NEJM 2006.*

Vaccine Adverse Event Reporting System (VAERS)

- National passive surveillance system
  - Identifies potential vaccine safety concerns

➢ Limitations

➢ Underreporting or reporting bias

➢ Lack of denominator data

VAERS Analysis for RotaTeq® *

- Reports received from February 1, 2006 through March 31, 2008
- Reports of intussusception (IS) verified by chart review, using Brighton Collaboration criteria
- Vaccine Safety Datalink (VSD) Project used to calculate expected rates for IS

- Sensitivity analyses

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*** Source: Haber et al. Pediatrics. 2008.**

VAERS Analyses for RotaTeq®: Results

- 14,274,551 doses RotaTeq® vaccine distributed*
- 2,600 RotaTeq® VAERS reports
  - 683 (26%) serious
  - 44% of reports involve 1st dose
  - Most frequently reported adverse events: diarrhea and vomiting

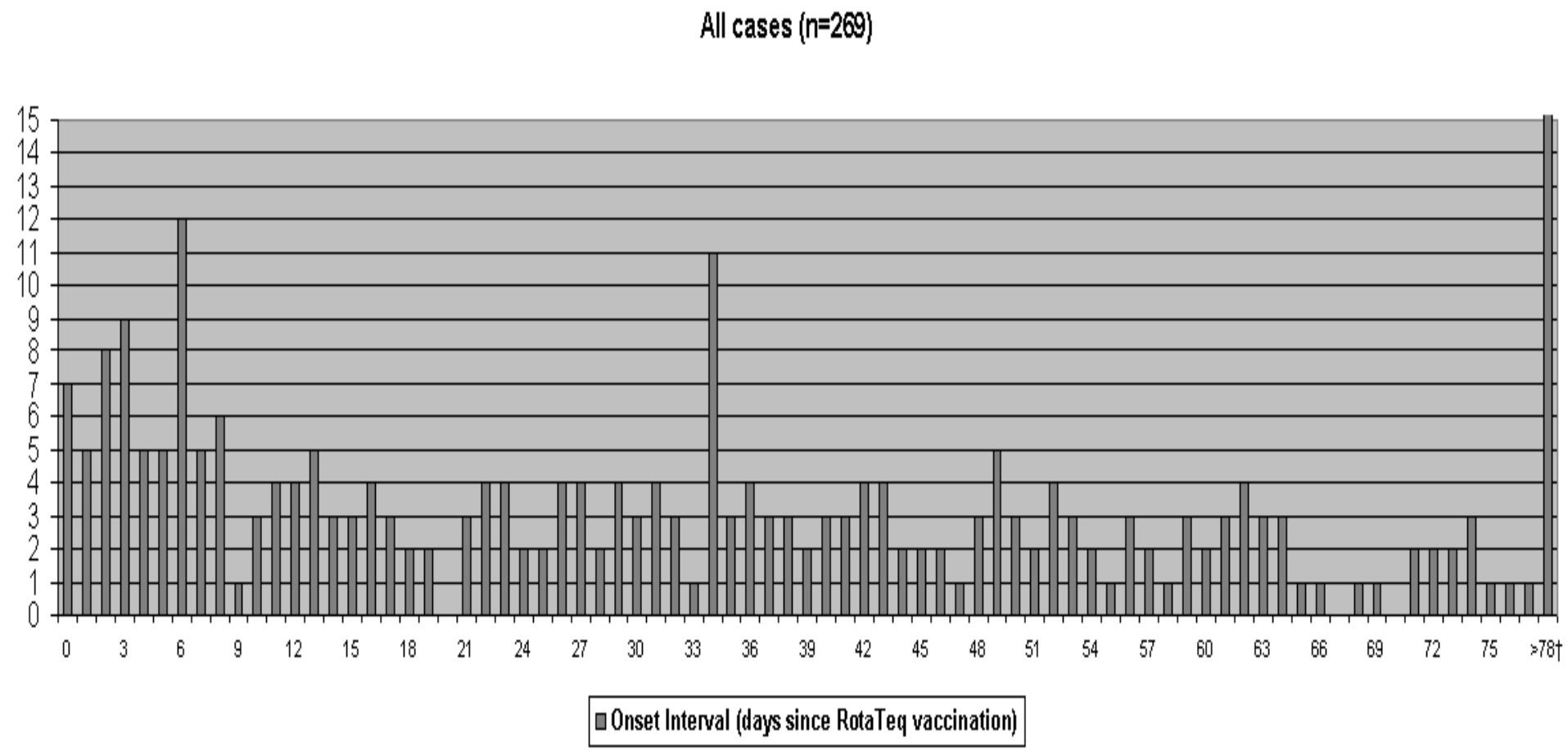
* *Source: Merck, personal communication; February 1, 2006-March 31, 2008*

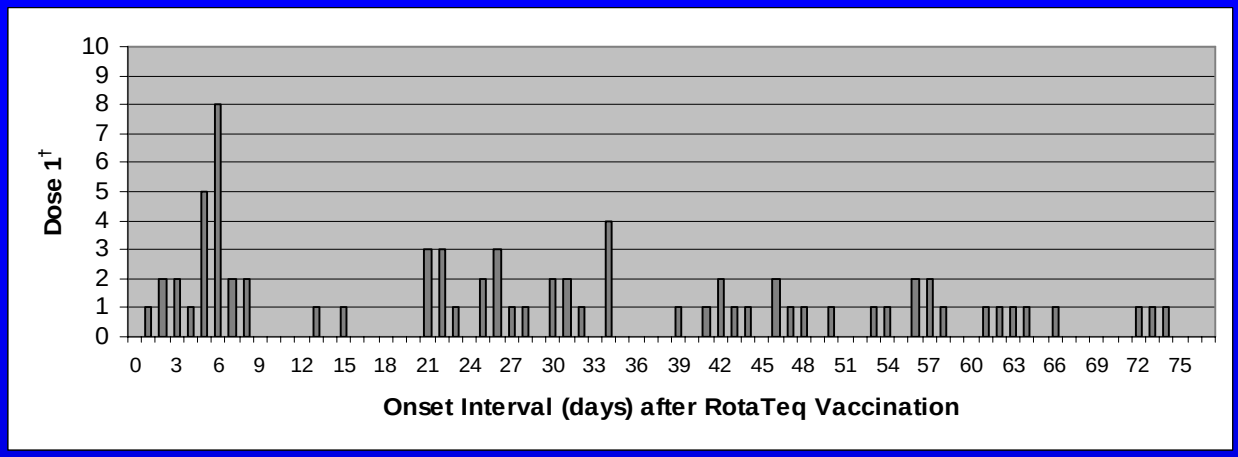
Summary of Intussusceptions (IS) Reported to VAERS

- 267 IS confirmed reports through 3/31/08
  - 91 reports within 1-21 days following vaccine
  - 48 (53%) of 91 were within 1-7 days

- One death report: following dose 2, 18 days post-vaccination

RotaTeq®
IS Reports to VAERS by Onset Interval (N=267)*





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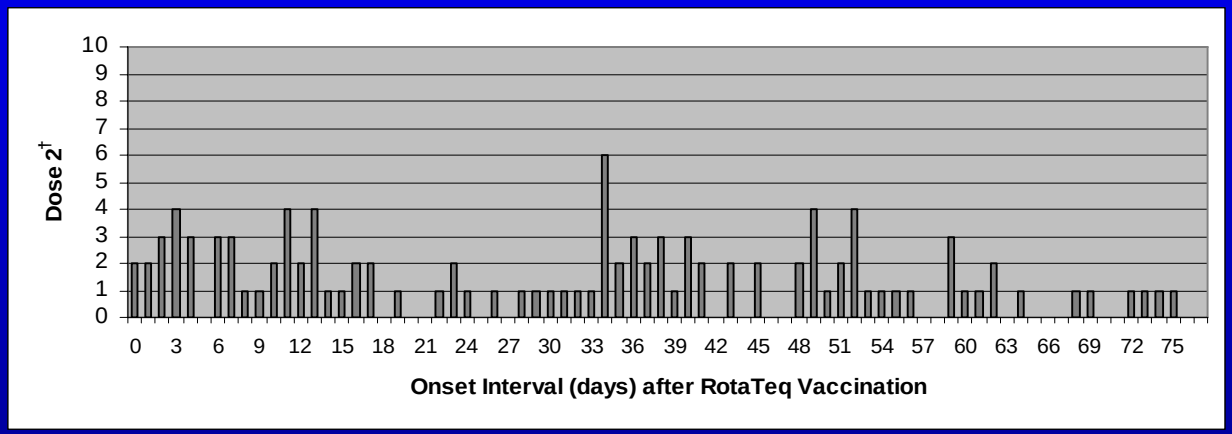

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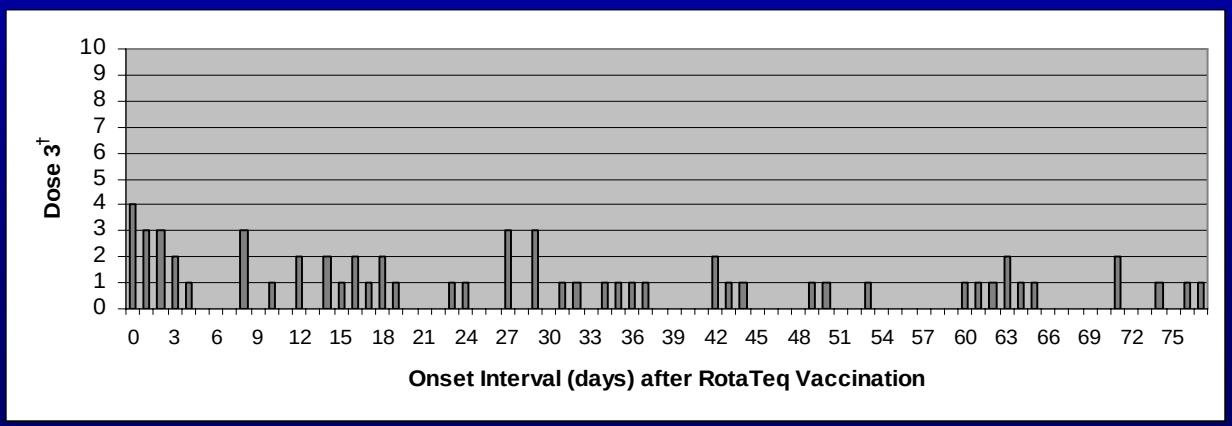

N=74

RotaTeq® IS Reports by Dose and Onset Interval (N=267)

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Observed versus expected calculations

- Age-stratified analysis important since baseline intussusception rate varies 10-fold during 1st six months of life
- 3 doses of vaccine are administered during this time period

- **Data assumptions**
  - Reporting completeness to VAERS
  - Number of vaccine doses administered

Observed versus Expected Cases after RotaTeq®
1 to 21 Days (any dose)*

% reporting	% doses given	VAERS cases	Expected cases	RR (95% CI)
100	100	92	242	0.37 (0.27-0.50)
75	75	123	181	0.65 (0.49-0.88)
50	50	184	121	1.45 (1.11 – 1.92)

**Sources: Vaccine Safety Datalink (VSD) for background and age of vaccine administration and Merck distribution data; analyses adjusted for age*

Observed versus Expected Cases after RotaTeq® 1 to 7 Days (any dose)*

% reporting	% doses given	VAERS cases	Expected cases	RR (95% CI)
100	100	49	81	0.58 (0.39-0.84)
75	75	66	60	1.02 (0.73-1.44)
50	50	98	40	2.25 (1.65 – 3.07)

** Source: VSD for background and age of vaccine administration; Merck distribution data *adjusted for age*

Observed versus Expected Cases after RotaTeq® 1 to 7 Days (dose 1)*

% reporting	% doses given	VAERS cases	Expected cases	RR (95% CI)
100	100	22	22	1.03 (0.53-1.98)
75	75	29	16	1.81 (0.98-3.34)
50	50	44	11	4.14 (2.40- 7.19)

•*Source: VSD for background and age of vaccine administration; Merck distribution data* **adjusted for age*

Proportion* of IS reports to VAERS after RotaTeq® and RotaShield®* Vaccines

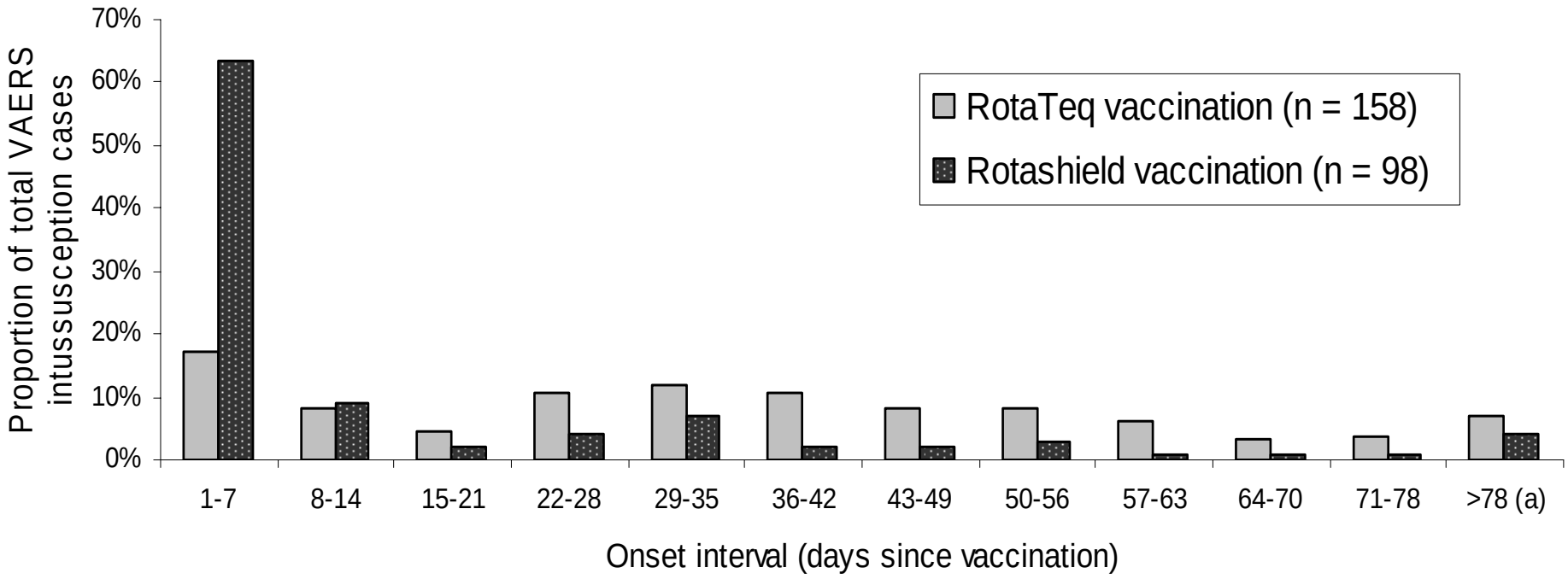

*Figure2: Pediatrics June 2008 (Haber et al)

***RotaShield® was withdrawn from the US market in 1999: 37 fold elevated risk 3-7 days after dose1**

Summary

- **After 2 years of monitoring, VAERS did not identify a safety concern for intussusception (IS) within 21 days after RotaTeq® for any dose**
  - **Because of VAERS underreporting, use of doses distributed instead of doses administered, VAERS can not rule out increased risk of IS after dose 1 within 1-7 days of RotaTeq® vaccination compared to week 2 & 3**
  - **Safety monitoring is ongoing**
- **Evaluation conducted in the Vaccine Safety Datalink (VSD) Project**

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Acknowledgement

- **Co-investigators:**
  - Margaret Cortese (CDC/NCIRD)
  - Karen Broder (CDC/ISO)
  - Wei Hua (FDA/CBER)
    Robert Ball (FDA/CBER)
  - John Iskander (CDC/ISO)
  - Elaine Miller (CDC/ISO)
  - Jacquelyn Tate (CDC/NCIRD)
  - Jon Gentsch (CDC/NCIRD)
  - Sherif Zaki (CDC/NCZVED)
  - Wun-Ju, Shieh (CDC/NCZVED)
  - Edward Belongia (Marshfield clinic)
  - VSD investigators

References

- Haber P, Patel M, Izurieta HS et al. Postlicensure monitoring of intussusception after RotaTeq vaccination in the United States, February 1, 2006, to September 25, 2007. *Pediatrics*. 2008;121:1206-1212.

- CDC. Postmarketing Monitoring of Intussusception After RotaTeq™ Vaccination --- United States, February 1, 2006--February 15, 2007. *MMWR*. 200756(10):218-222.

Thank you