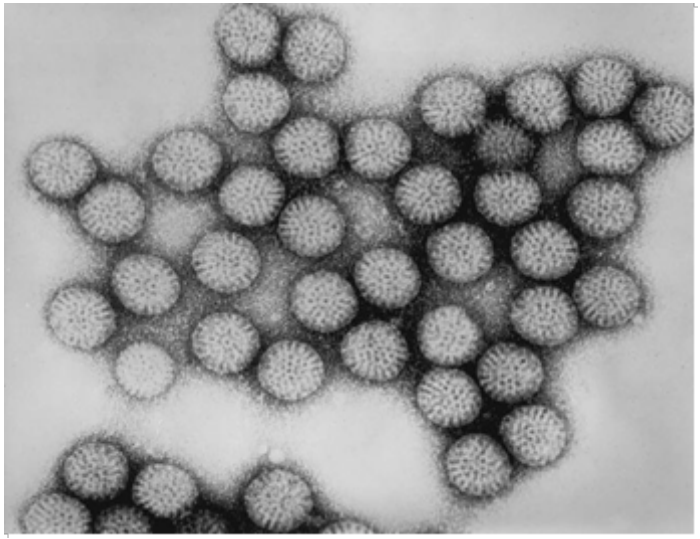
Lessons from Rotavirus Vaccine Implementation in the U.S.



Jeff Duchin, MD
Chief, Communicable Disease Epidemiology & Immunization Section
Public Health - Seattle & King County
Professor in Medicine, Division of Allergy & Infectious Diseases
University of Washington, Seattle

Overview

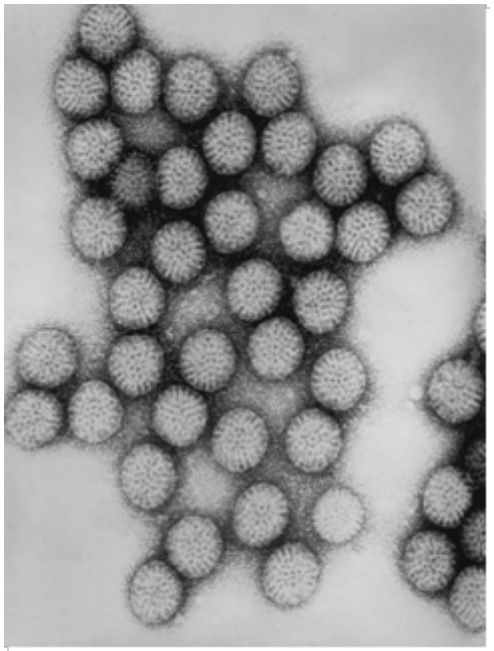
- General experience of introducing the vaccine in the US
- Impact of the vaccine on the epidemiology of rotavirus in the US
- Monitoring rotavirus vaccine safety
- Lessons learned from the implementation of a live attenuated oral vaccine

Rotavirus

- First identified as cause of diarrhea in 1973
- Most common cause of severe diarrhea in infants and children
- Nearly universal infection by 5 years of age
- Responsible for up to 500,000 diarrheal deaths each year worldwide

Rotavirus

- Reovirus (RNA)
- VP7 and VP4 antigens define virus serotype and induce neutralizing antibody
- 5 predominant strains in US (G1-G4, G9) account for 90% of isolates; G1 strain accounts for 75% of infections
- Very stable, may remain viable for weeks or months if not disinfected



Rotavirus Immunity

- Antibody against VP7 and VP4 probably important for protection
- First infection usually does not lead to permanent immunity
- Reinfection can occur at any age
- Subsequent infections generally less severe

Rotavirus Clinical Features

- Short incubation period (usually <48 hours)
- First infection after age 3 months generally most severe
- May be asymptomatic or result in severe dehydrating diarrhea with fever and vomiting
- Gastrointestinal symptoms generally resolve in 3 to 7 days

Rotavirus Complications

- Severe diarrhea
- Dehydration
- Electrolyte imbalance
- Metabolic acidosis
- Immunodeficient children may have more severe or persistent disease

Rotavirus Epidemiology

• Reservoir	Human-GI tract
• Transmission	Fecal-oral, fomites
• Temporal pattern	Fall and winter (temperate areas)
• Communicability	2 days before to 10 days after onset

Rotavirus Disease Burden in the US (Pre-Vaccine)

- Etiology of 5%-10% of all gastroenteritis episodes among children <5 years of age
- 95% of children infected by 5 years of age
- Highest incidence among children 3 to 35 months of age
- The most severe disease among children 3-24 months of age

Rotavirus Disease Burden in the US (Pre-Vaccine)

- Each year rotavirus caused:
  - about 3 million cases of gastroenteritis
  - Over 400,000 physician visits
  - Over 200,000 emergency department visits
  - 55,000-70,000 hospitalizations
  - 20-60 deaths among children <5 years of age
- Annual direct and indirect costs estimated at approximately $1,000,000,000

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- Annual direct and indirect costs estimated at approximately $1,000,000,000
- **Lesson: Impact of rotavirus infection underappreciated**

Rotavirus Vaccines

- RV5 (RotaTeq®)
  - Contains five reassortant rotaviruses developed from human and bovine parent rotavirus strains
  - Vaccine viruses suspended in buffer solution
  - Contains no preservatives or thimerosal

Rotavirus Vaccines

- RV1 (Rotarix®)
  - Contains one strain of live attenuated human rotavirus (type G1P[8])
  - Provided as a lyophilized powder that is reconstituted before administration
  - Contains no preservatives or thimerosal

Rotavirus Vaccines in the US

- Feb. 2006 – RotaTeq® recommended
- June 2008 – Rotarix® recommended
- Both vaccines significantly reduced both physician visits for diarrhea & rotavirus-related hospitalization

Rotavirus Vaccine Efficacy
Clinical Trials RV5

Condition	**Efficacy**
Hospitalizations	**96% (91-98%)**
Reduced ED visits	**94% (89-97%)**
Reduced office visits	**86% (74-93%)**

Rotavirus Vaccine Efficacy
Clinical Trials RV1

Condition	**Efficacy**
Severe rotavirus	**96% (90-99%)**
Rota AGE	**87% (80-82%)**

Rotavirus Vaccine
Recommendations

- For both rotavirus vaccines
  - maximum age for first dose: 14 weeks 6 days
  - minimum interval between doses: 4 weeks
  - maximum age for any dose: 8 months 0 days (no catch-up)

***MMWR* 2009;58:(RR-2)**

TABLE 6. Percentage of infants with solicited adverse events (any intensity and Grade 3*) within 8 days following any dose of Rotarix® (RV1) or placebo†

	RV1 (n = 3,286)		Placebo (n = 2,015)	
Event	% Any intensity	% Grade 3	% Any intensity	% Grade 3
Fever§	39.8	0.9	48.8	1.1
Fussiness/irritability	62.2	6.3	61.6	8.1
Loss of appetite	34.8	1.0	35.2	1.1
Vomiting	17.6	3.4	15.8	2.7
Diarrhea	6.8	1.2	5.7	1.5
Cough/runny nose¶	44.2	3.6**	47.2	3.2

No serious events

Prevention of Rotavirus Gastroenteritis Among Infants and Children. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR February 6, 2009 / Vol. 58 / No. RR-2

Safety Concerns Following Experience with RotaShield

The New York Times
Health

October 16, 1999

Vaccine for Infant Diarrhea Is Withdrawn as Health Risk

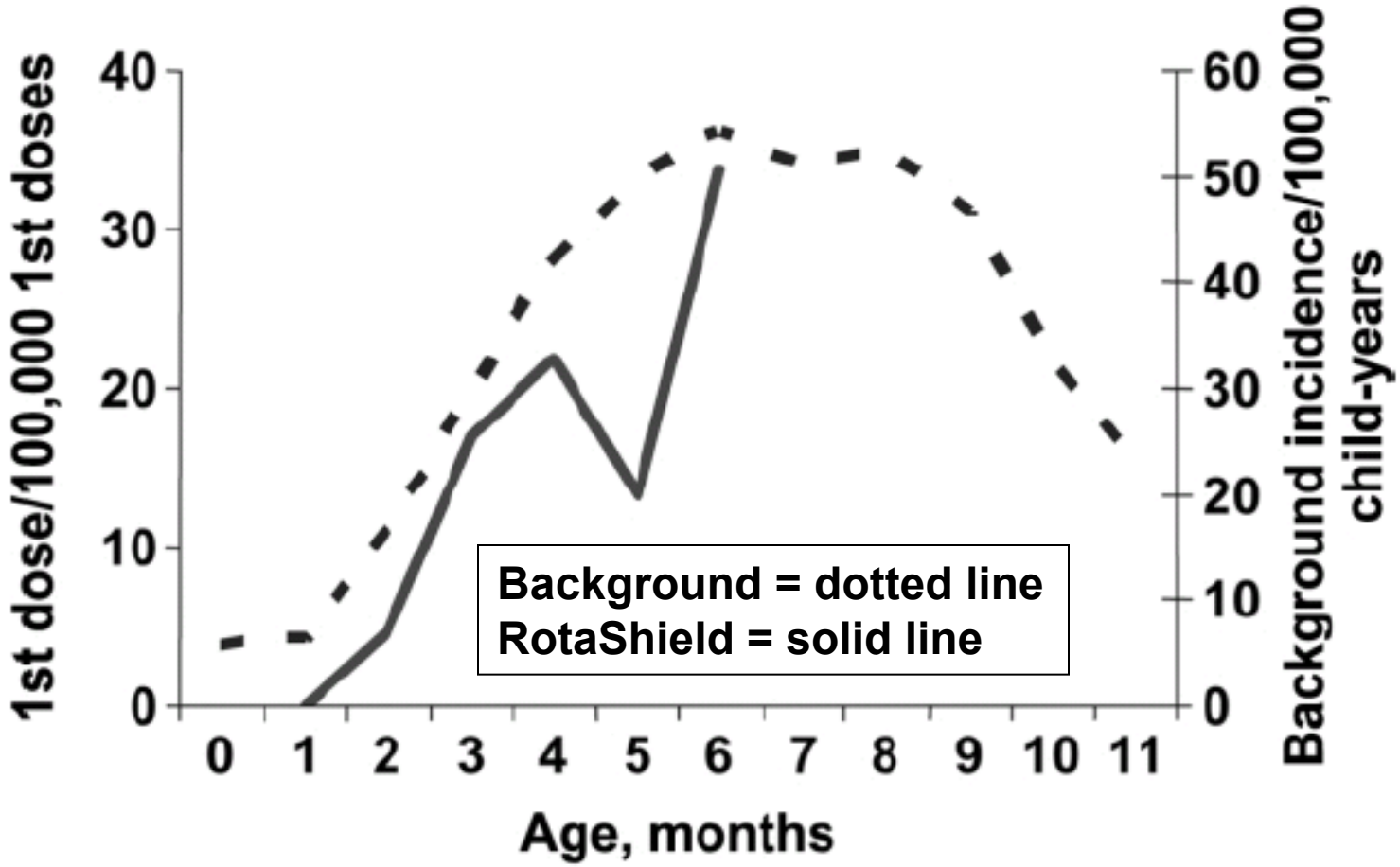
By LAWRENCE K. ALTMAN
Published: October 16, 1999

American Home Products, the manufacturer of the only licensed vaccine to prevent the most common cause of severe diarrhea among infants and children, announced today that it was withdrawing the vaccine from the market because of concerns that it could cause a painful and potentially fatal bowel obstruction.

The diarrhea is caused by the rotavirus, and last year the Government recommended that every infant in the United States get the protective vaccine. One million children swallowed three doses of the vaccine, Rotashield, at 2, 4 and 6 months of age, the company said.

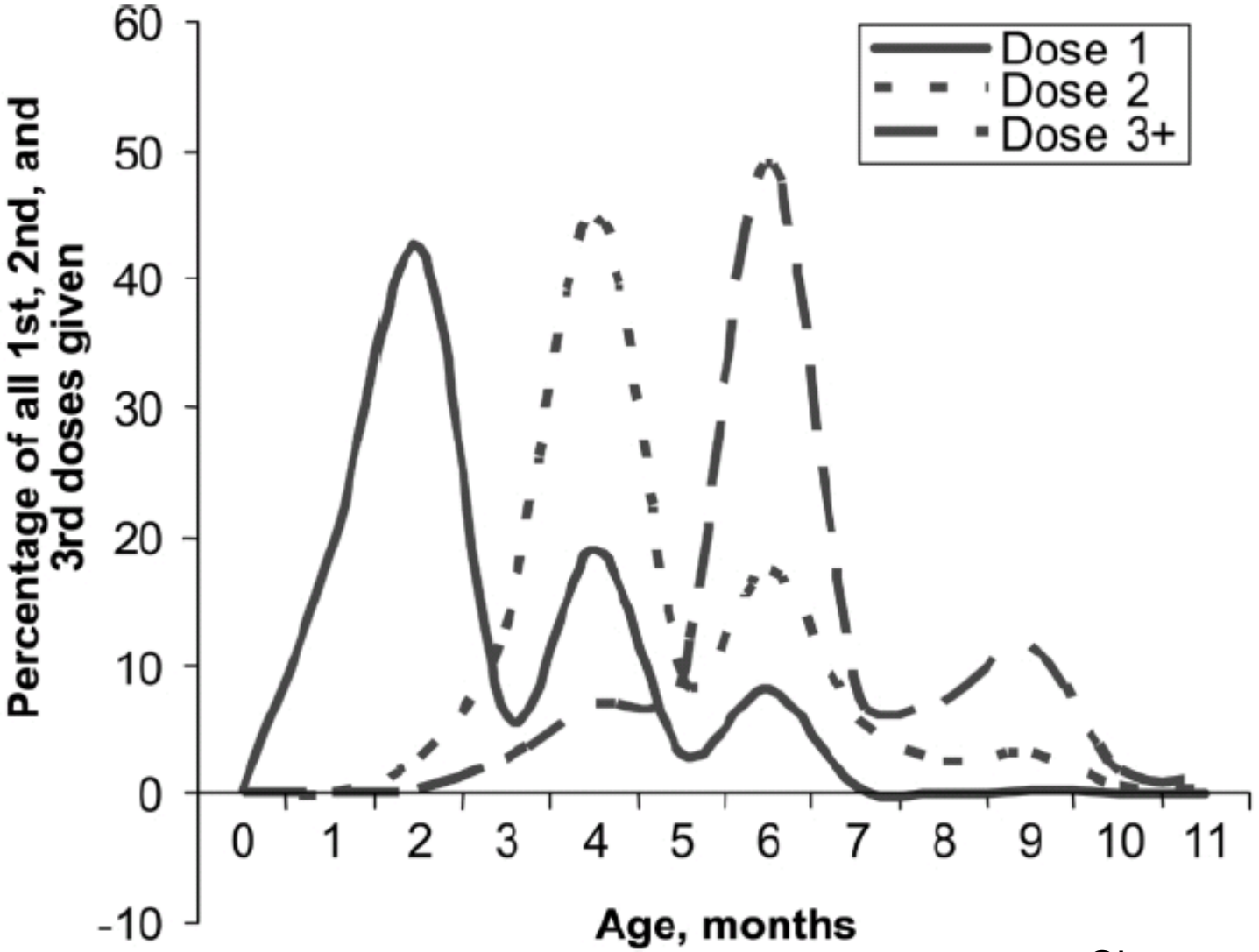
But in July the Centers for Disease Control and Prevention, a Federal agency based here, said no one should get the vaccine because a program that monitors side effects suggested a link between the vaccine and the bowel condition, called intussusception.

Observed age-specific incidence of intussusception associated with use of RotaShield and annual background incidence of intussusception in the U.S. estimated from Healthcare Cost & Utilization Project data.



Simonsen. JID 2005

Age at receipt of 1st, 2nd & 3rd doses of RotaShield among US infants, OCT 1998-July 1999



Simonsen. JID 2005

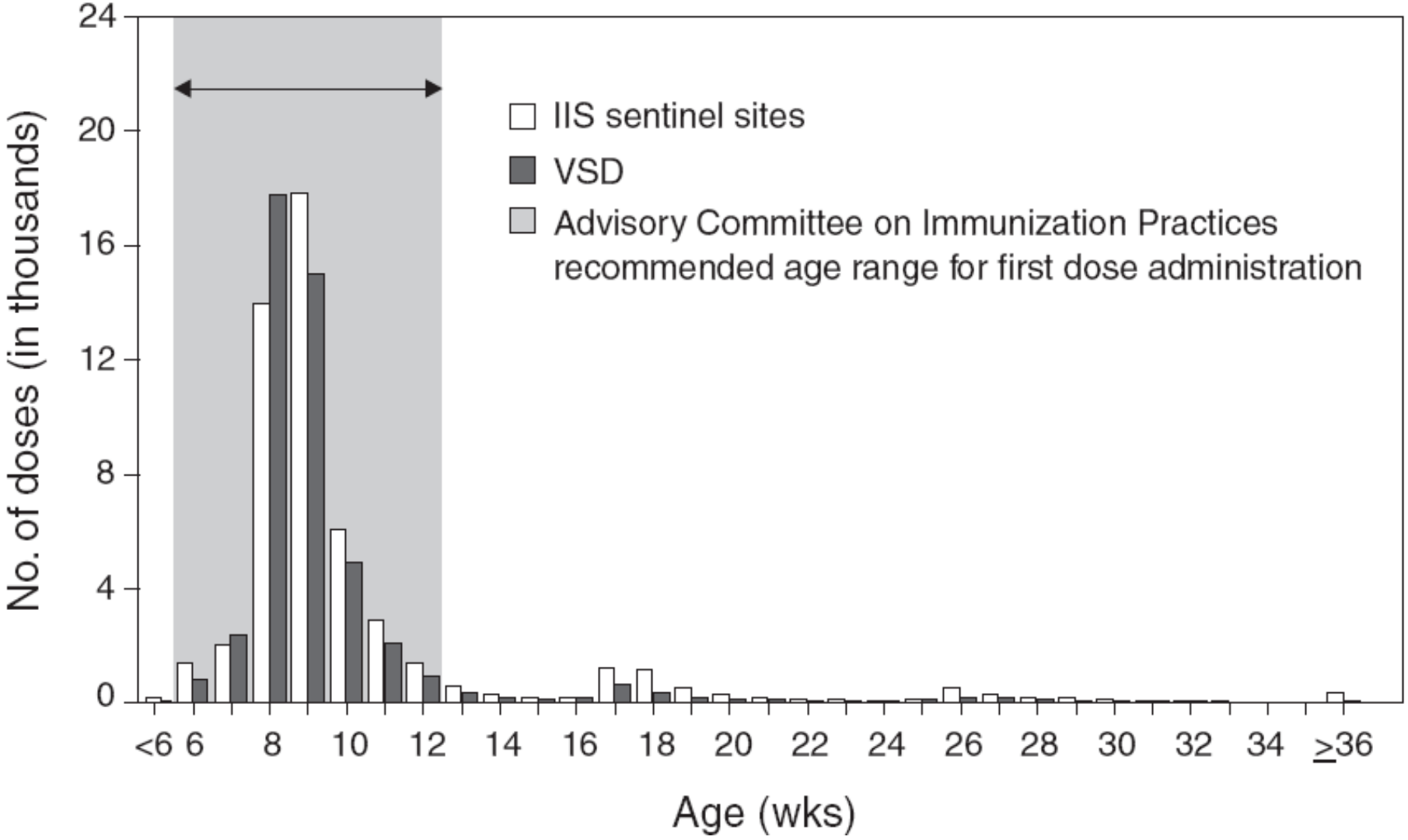
Current Rotavirus Vaccines and Intussusception – Clinical Trials

	No. of Infants	Vaccine Recipients	Placebo Recipients
RV1*	**63,225**	**7 cases**	**7 cases**
RV5*	**69,625**	**6 cases**	**5 cases**

***RV1: 0-30 days after either dose; RV5: 0-42 days after any dose.**
Small increased risk for intussusception not detectable

Prevention of Rotavirus Gastroenteritis Among Infants and Children. Recommendations of the Advisory Committee on Immunization Practices (ACIP) MMWR February 6, 2009 / Vol. 58 / No. RR-2

Administration of first dose of RV5 by age of child—immunization information system (IIS) sentinel sites and Vaccine Safety Datalink (VSD), US, 2006–2007. Data reported through May 31, 2007



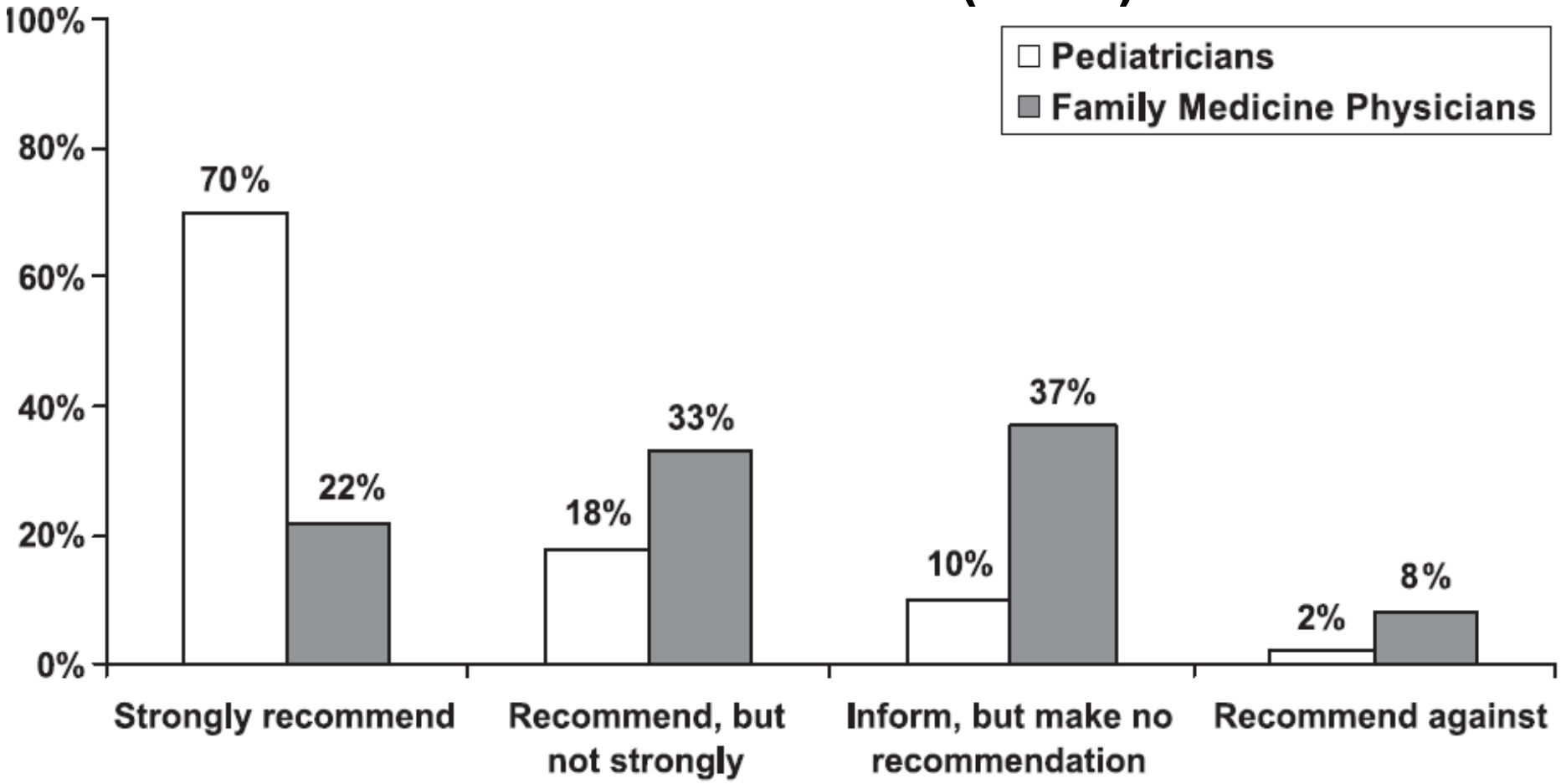
Tate. PIDJ 2010

U.S. Physicians' Attitudes Regarding Rotavirus Vaccine

- 2007 survey using network recruited from random sample of AAP and AAFP members
- Designed to be representative of AAP & AAFP membership:
  - Region of country (NE, S, MW, W)
  - Location (urban, suburban, rural)

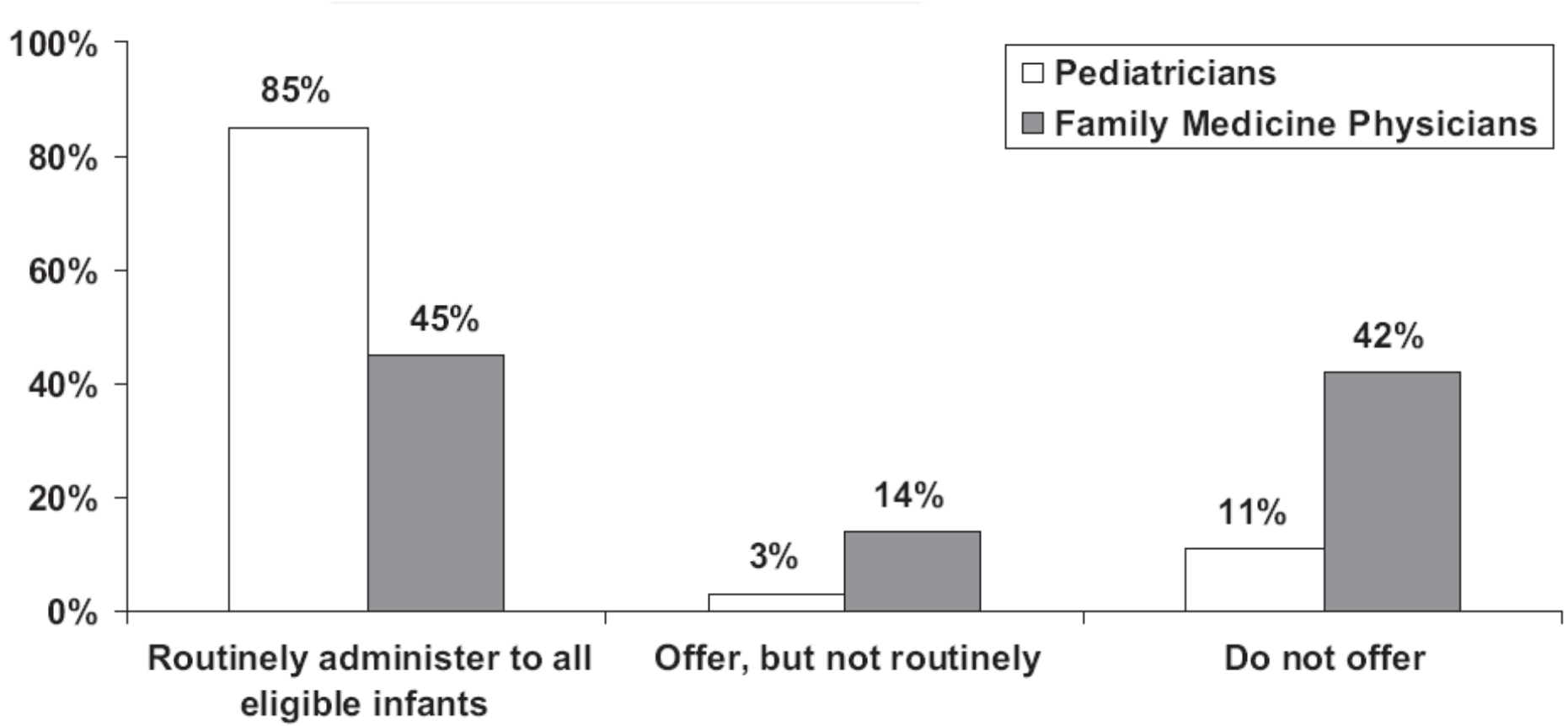
Kempe. Pediatrics 2008

Adoption of Rotavirus Vaccination by Pediatricians and Family Medicine Physicians in the United States (2007)



Kempe *Pediatrics* 2009;124;e809

Early Practices Regarding Rotavirus Vaccine Administration by Pediatricians and Family Medicine Physicians in the United States (2007)



Kempe *Pediatrics* 2009;124;e809

Barriers to Giving Rotavirus Vaccine

Definitely a Barrier	PEDS (n=359)	FM (n=264)
Respondent's concern about the safety of rotavirus vaccine	**9%**	**25%**
Addition of another vaccine to the schedule	**5%**	**22%**
Failure of some insurance companies to cover vaccination	19%	22%
The "up-front" costs to purchase the vaccine	17%	22%
Lack of adequate reimbursement	15%	18%

Kempe *Pediatrics* 2009;124;e809

Complex age of administration guidelines

Survey of pediatricians & family medicine physicians

- 31% of pediatricians (PED) and 70% of family practice providers (FP) did NOT know the age by which the first dose of RV5 should be administered

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- 38% PED and 68% FP did NOT know the age by which all 3 doses should be administered

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- 12% of PED and 20% of FP reported that they frequently or sometimes gave the *first dose* of RV5 to infants 12 months of age

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- 31% of pediatricians (PED) and 70% of family practice providers (FP) did NOT know the age by which the first dose of RV5 should be administered
- 38% PED and 68% FP did NOT know the age by which all 3 doses should be administered
- 12% of PED and 20% of FP reported that they frequently or sometimes gave the *first dose* of RV5 to infants 12 months of age
- 7% of PED and 10% FP reported frequently or sometimes administering the *third dose* to infants >32 weeks of age

Kempe *Pediatrics* 2009;124;e809

Clinical Issues
Administration of oral vaccines

- April, 2007: Washington State began ordering and distributing Rotavirus vaccine.
  - Licensed Health Care Assistants (HCA) NOT authorized to administer oral vaccines
  - New legislation (2008) required to expand scope of practice for HCAs to allow administration of all FDA approved vaccines given by "injection, orally, or topically, including nasal administration".

A Few Clinical Issues

What if baby spits out or regurgitates the dose?

A Few Clinical Issues

What if baby spits out or regurgitates the dose?

- **RotaTeq:** Replacement dose is not recommended, not studied in the clinical trials.
- **RotaRix:** If the infant spits out or regurgitates *most of* the vaccine dose, a single replacement dose may be considered at the same vaccination visit.
- **ACIP:** Do not re-administer a dose of rotavirus vaccine to an infant who regurgitates, spits out, or vomits during or after administration of vaccine.
  - No data exist on the benefits or risks associated with re-administering a dose.
  - The infant should receive the remaining recommended doses of rotavirus vaccine following the routine schedule (with a 4-week minimum interval between doses).

Clinical Issues

Dosing/Administration Schedule

- **RotaTeq**: Administer starting at 6 to 12 weeks of age, with the subsequent doses at 4- to 10-week intervals. The third dose should not be given after 32 weeks of age
- **ROTARIX** (diluent): Administer first dose beginning at 6 weeks of age. Administer second dose after an interval of at least 4 weeks and prior to 24 weeks of age
  - Inadvertent IM injection
- **ACIP:**
  - The maximum age for dose 1 of rotavirus vaccine is 14 weeks and 6 days.
  - The maximum age for the last dose of rotavirus vaccine is 8 months and 0 days .
  - The minimum interval between doses of rotavirus vaccine is 4 weeks; no maximum interval is set.

Monitoring Rotavirus Vaccine Safety

- VAERS (As of AUG 2010, 32 million doses of RotaTeq and 2.8 million doses of Rotarix distributed in US)
- Vaccine Safety Datalink (VSD): primary system used for post marketing safety surveillance
  - Data from 10 managed care organizations: No safety signals
  - Excludes risk greater than 1 case per 25,000 infants vaccinated
- Post-marketing surveillance by manufacturer
  - Small increase in intussusception risk in Mexico & Brazil (1 per 51,000 & 68,000 infants vaccinated, respectively) with 96 cases and 5 deaths
  - Vaccination prevents 80,000 hospitalizations and 1300 deaths in these countries each year; Benefit>>>Risk
  - Compensatory decrease in later intussesception in vaccinees by preventing wild-type infection?

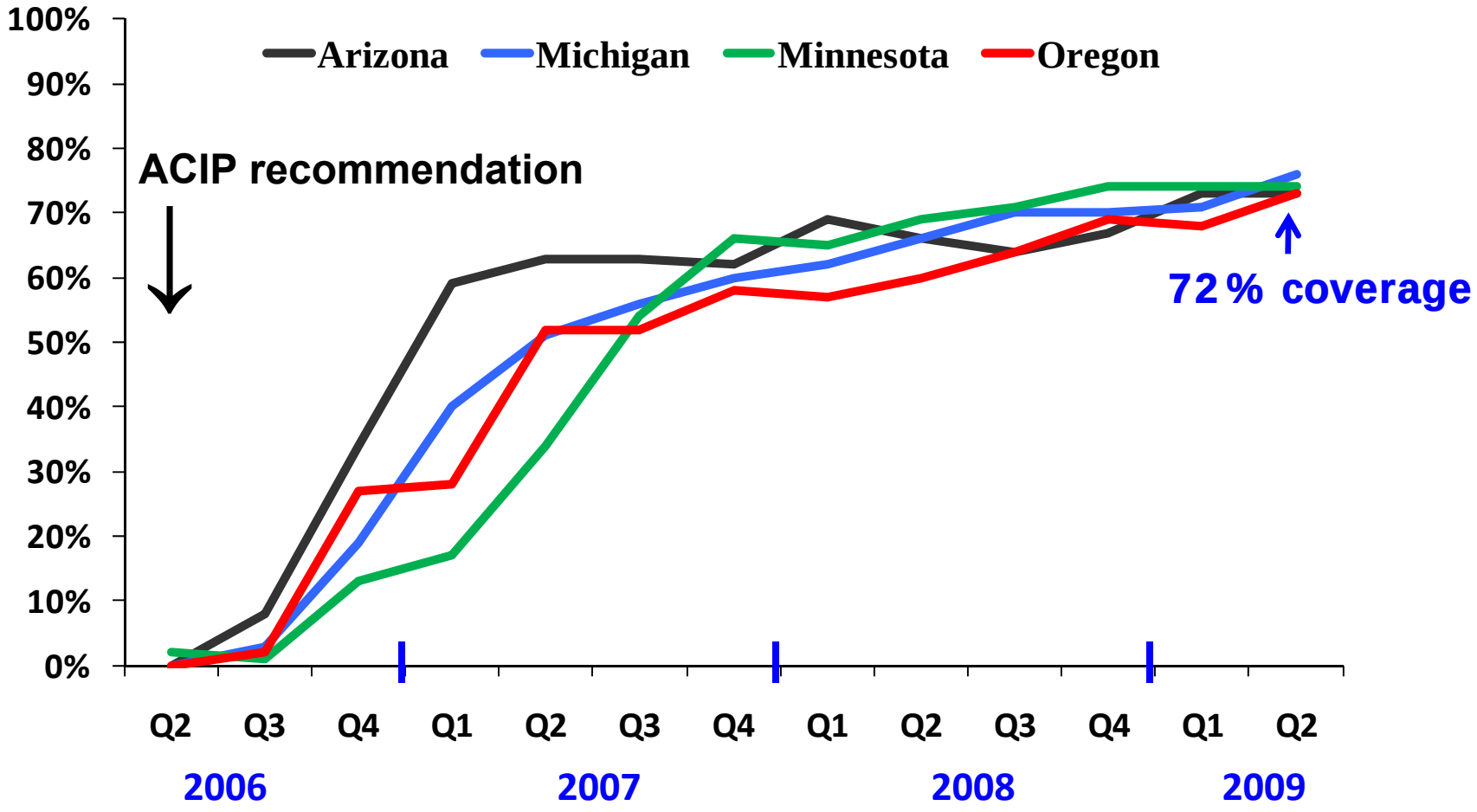
Monitoring Rotavirus Vaccine Safety

- *If* risk observed in Mexico present in US, would result in approximately:
  - Risk: 0-4 excess cases per 100,000 infants vaccinated (50-60 cases of intussusception)
  - Benefit: Over 50,000 hospitalizations prevented

Rotavirus Vaccine Safety

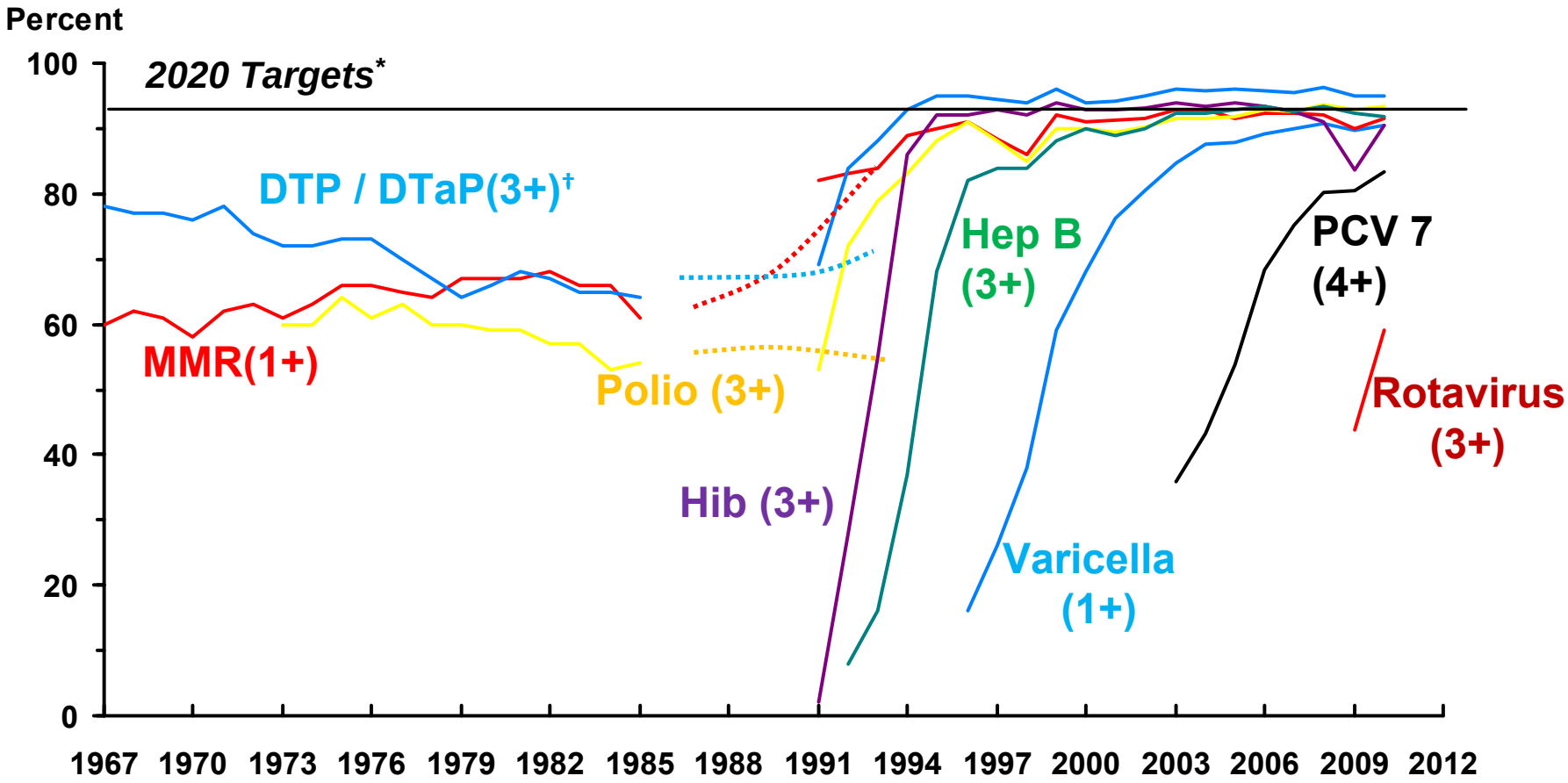
- 2010: Porcine Circovirus (PCV) DNA found in Rotarix and RotaTeq using metagenomic and panmicrobial microarray techniques (Delwart, BSRI, San Francisco)
- Common swine virus
- Human exposures likely common, PCV found in human stool, no antibody response
- Not associated with illness in pigs or humans
- FDA: Hypothetical risks do not outweigh benefits
- Advised companies to produce PCV-free vaccines

Coverage With ≥1 dose of Rotavirus Vaccine Among Infants Aged 5 Months, June 2006 - June, 2009



MMWR 2010

Vaccine-Specific Coverage Rates Among Preschool-Aged U.S. Children: 1967 - 2010



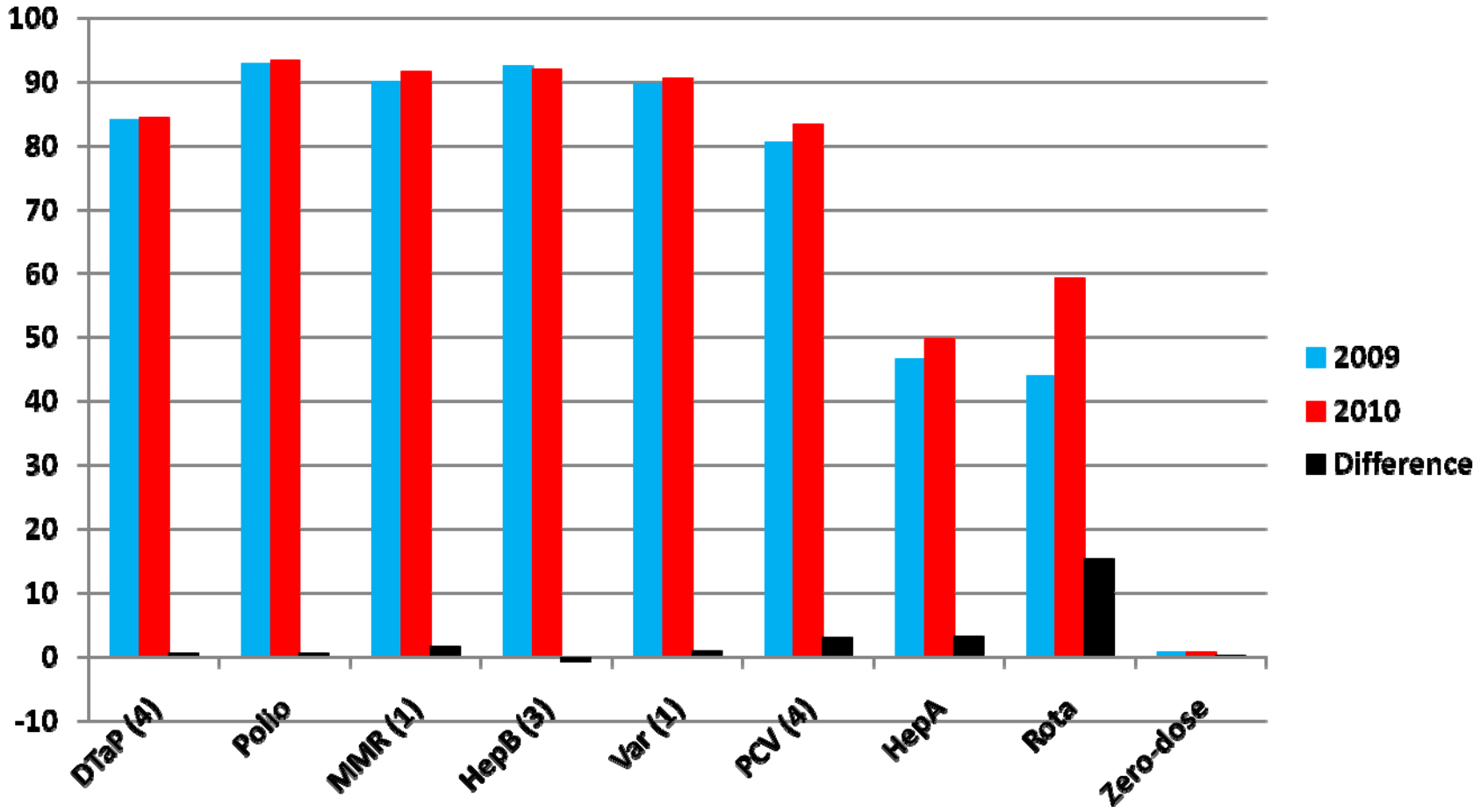
† DTP(3+) is not a Healthy People 2010 objective. DTaP(4) is used to assess Healthy People 2010 objectives.

Note: Children in the USIS and NHIS were 24-35 months of age. Children in the NIS were 19-35 months of age.

Source: USIS (1967-1985), NHIS (1991-1993) CDC, NCHS, and NIS (1994-2010), CDC, NIP and NCHS; No data from 1986-1990 due to cancellation of USIS because of budget reductions.

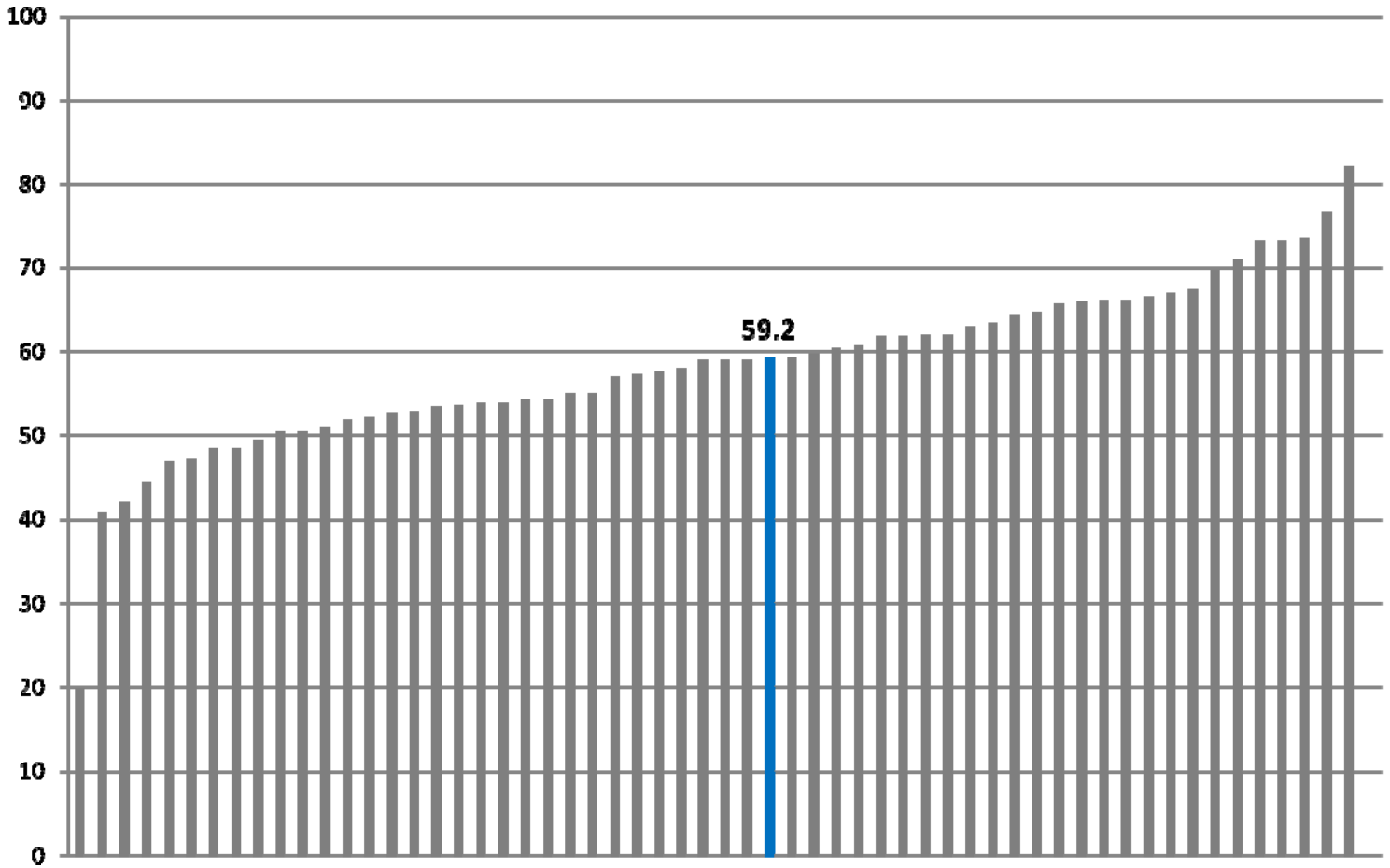
* Healthy People 2020 targets are 90% except for rotavirus vaccine, which is 80%

Comparison Between 2009 and 2010 NIS 19-35 Month Old Coverage Levels



Source: NIS at www.cdc.gov/vaccines

Rotavirus Series; 19-35 Months of Age; 2010 National Immunization Survey



U.S. National Average

Blue

Source: www.cdc.gov/vaccines

So, How's It Working?
Real World Effectiveness Studies

Effectiveness of Pentavalent Rotavirus Vaccine in a Large Urban Population in the U.S.

- Case-Control study Texas Children's Hospital, February-June 2008
- Cases: Children 15 days - 23 months with lab-confirmed rotavirus AGE
- Controls:
  - children with rotavirus-negative AGE
  - children with acute respiratory infection (ARI)

Boom et al. Pediatrics 2010

Effectiveness of Pentavalent Rotavirus Vaccine in a Large Urban Population in the U.S.

	Vaccine Effectiveness (by control type)	
	RV-negative AGE	**ARI**
1 dose	**65%**	**65%**
2 doses	**82%**	**72%**
3 doses	**89%**	**85%**

Boom et al. Pediatrics 2010

Effectiveness of Pentavalent Rotavirus Vaccine in a Large Urban Population in the U.S.

- Complete series:
  - **100% protection (95% CI: 71–100%) against severe rotavirus disease requiring hospitalization**
  - **96% protection (95%CI: 72%–99%) against disease requiring intravenous hydration**
- Vaccine effectiveness of partial series against severe disease (hospitalization or ED visits):
  - **1 dose 69% (95% CI: 13%–89%)**
  - **2 doses 81% (95% CI:13%–96%)**

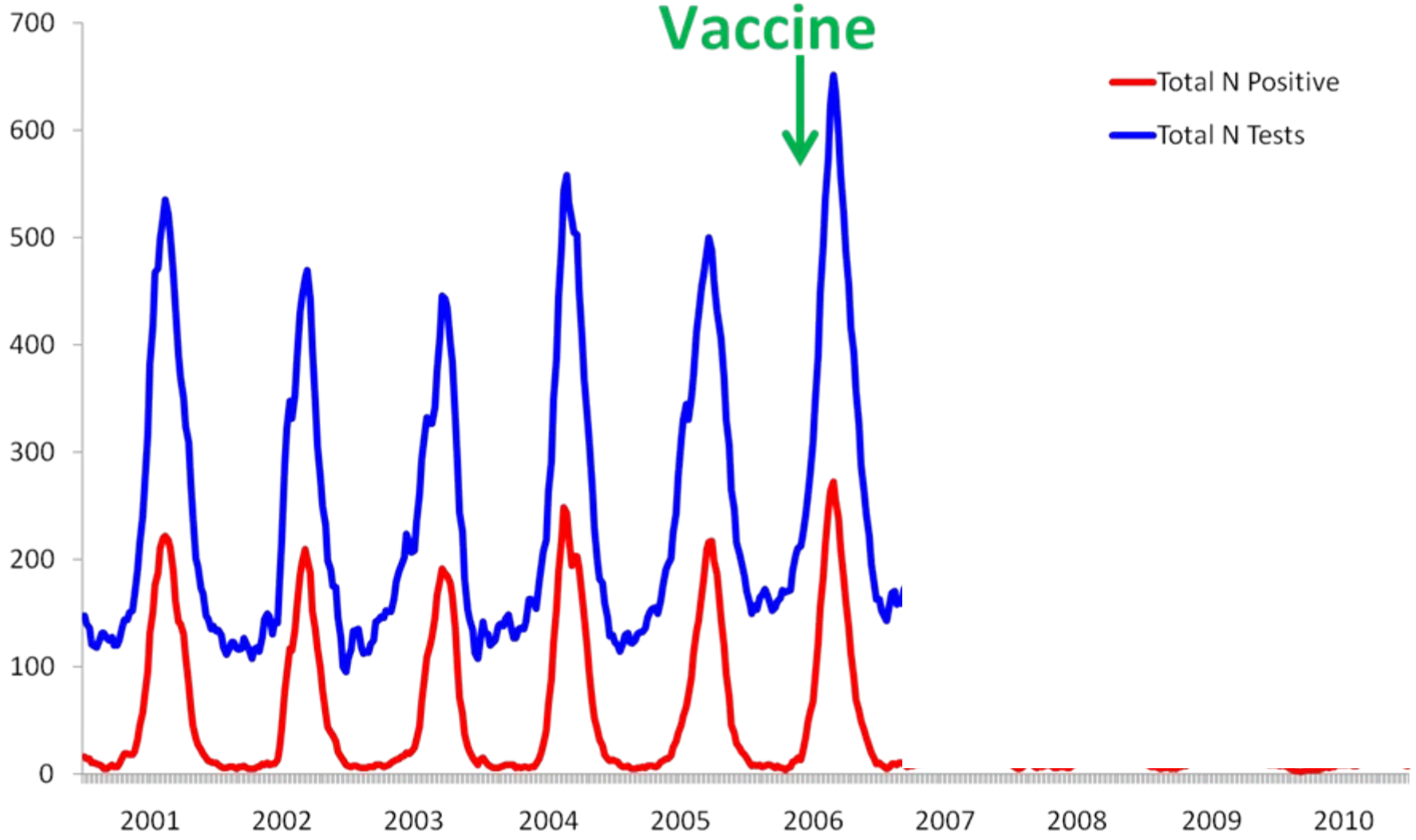
Boom et al. Pediatrics 2010

U.S. National Respiratory and Enteric Virus Surveillance System (NREVSS)

- **Network of 67 laboratories reporting since 2000**
- **Weekly reporting: # stool specimens tested for rotavirus (EIA) and # positive tests**

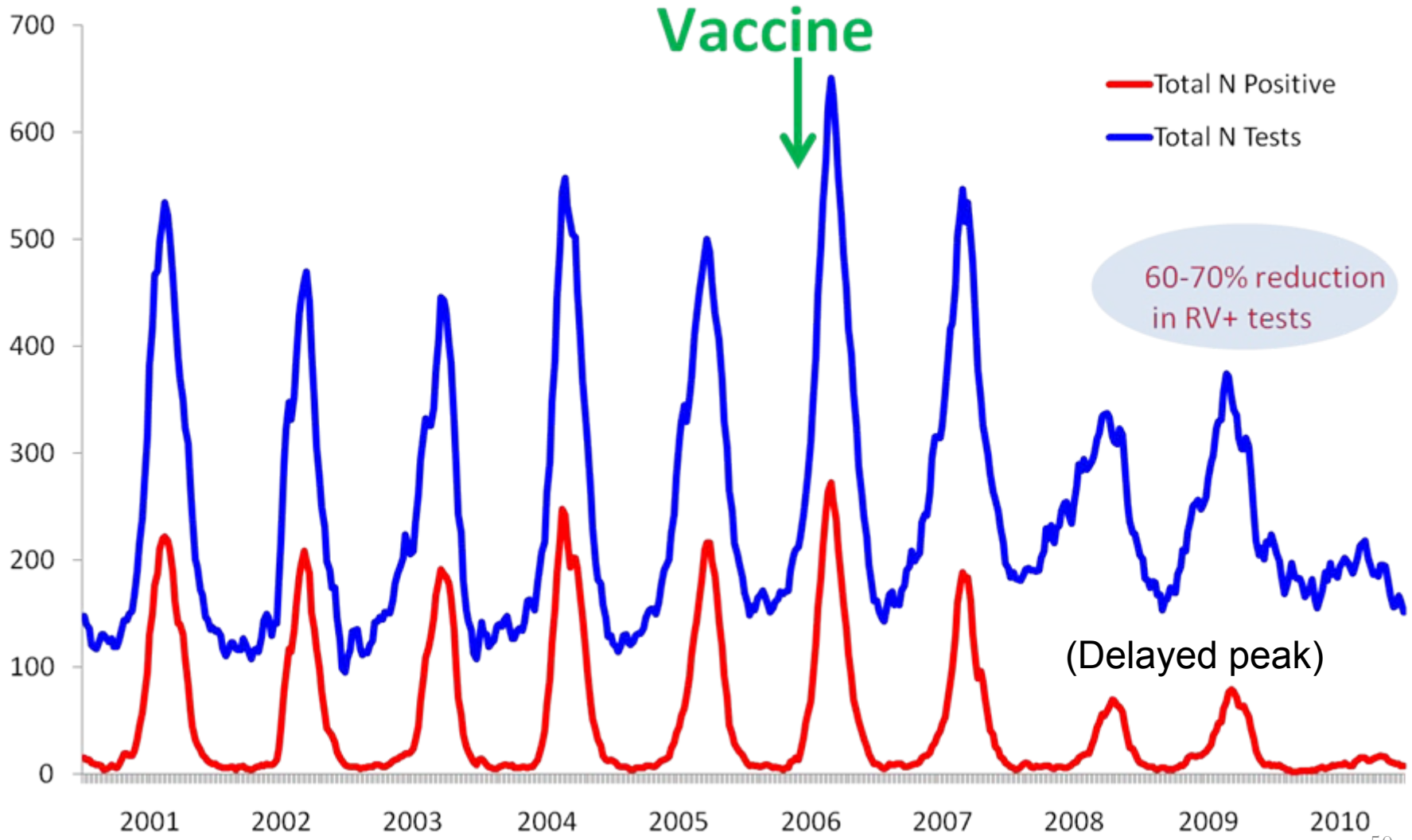
Tate et al. Pediatrics 2009 and unpublished CDC data

NREVSS Total & Positive Rotavirus Tests 2000-2010



Tate et al. Pediatrics 2009 and unpublished CDC data

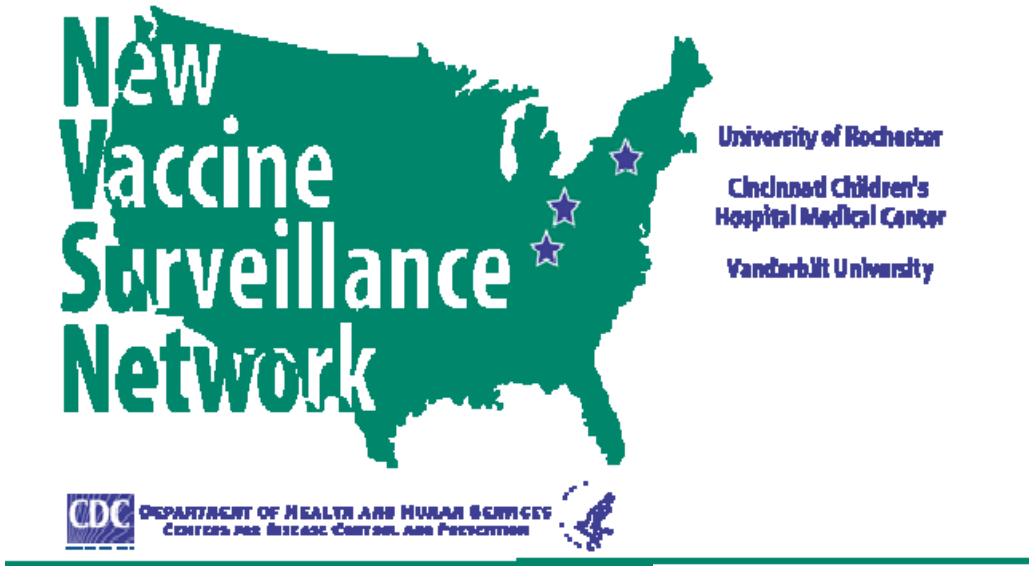
NREVSS Total & Positive Rotavirus Tests 2000-2010



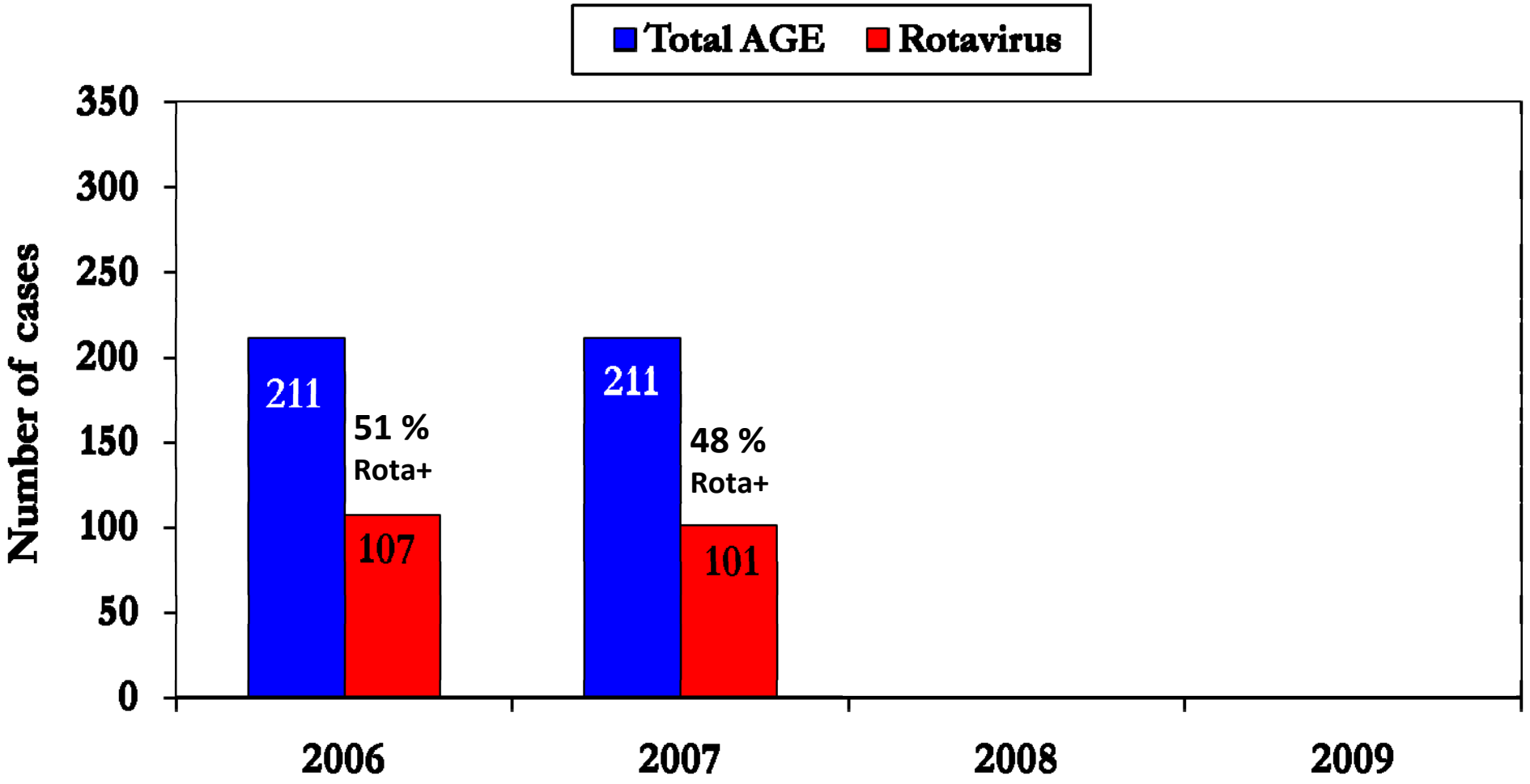
Tate et al. Pediatrics 2009 and unpublished CDC data

Active Rotavirus Surveillance - NVSN

- Capture >95% of all pediatric infectious hospital admissions in 3 US counties
- Enrollment of inpatients, emergency room patients, and outpatients with AGE
- Fecal specimens obtained and tested for rotavirus

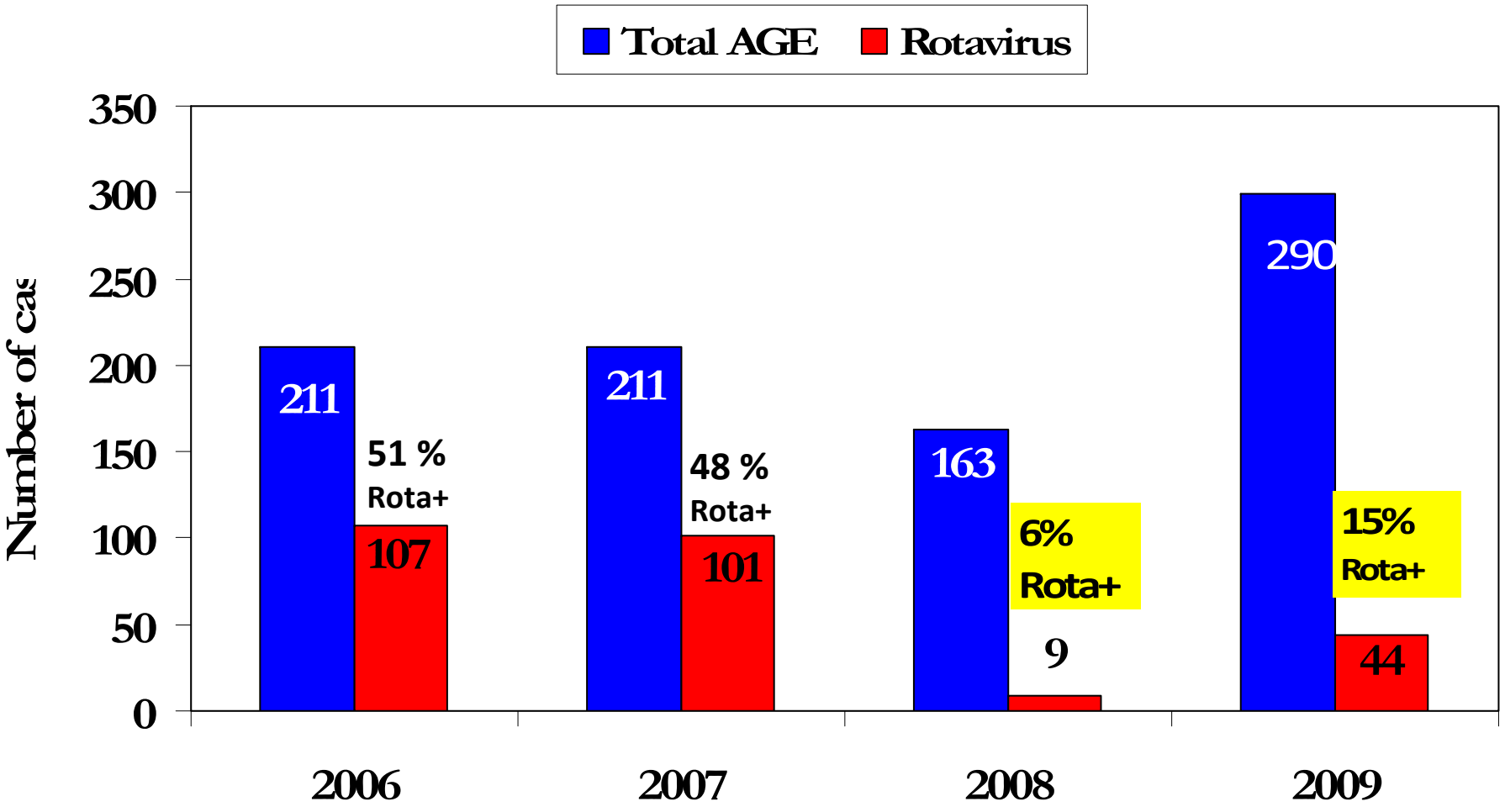


Total Acute Gastroenteritis and Rotavirus Hospitalizations, NVSN 2006-2009



Payne D et al CID, 2011 and unpublished data

Total Acute Gastroenteritis and Rotavirus Hospitalizations, NVSN 2006-2009



Payne D et al CID, 2011 and unpublished data

Age-Specific Rotavirus Hospitalization Rate Reduction and Vaccine Coverage, NVSN

Age	Rotavirus vaccine coverage in 2008 (≥1 dose)	Decline in rotavirus hospitalization rate (2008 vs. 2006)
< 1 year	56%	66%
1 to < 2 years	44%	95%
2 to < 3 years	<1%	85%

Herd immunity?

Payne D et al CID, 2011 and unpublished data

MAJOR ARTICLE

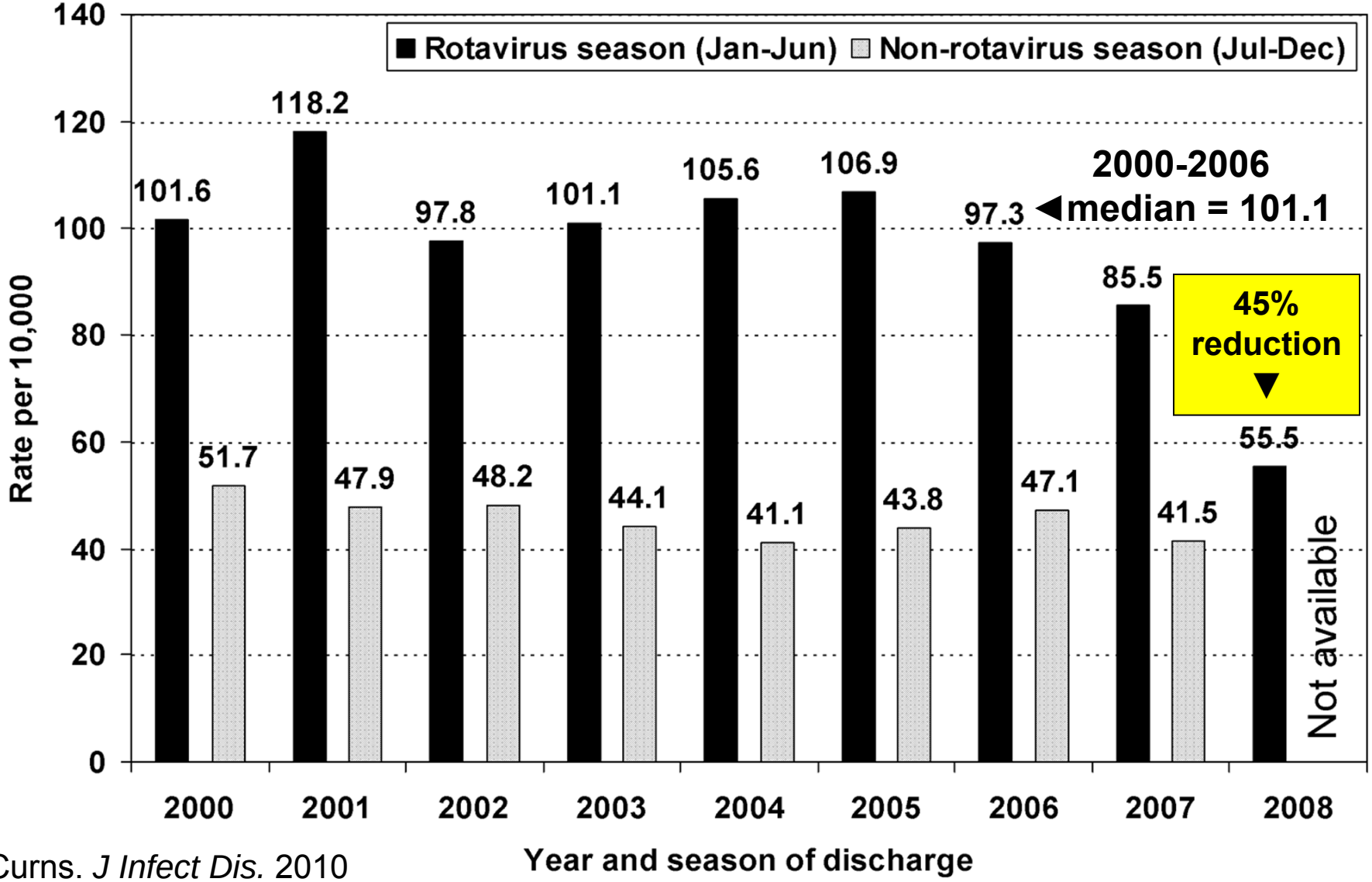
Reduction in Acute Gastroenteritis Hospitalizations among US Children After Introduction of Rotavirus Vaccine: Analysis of Hospital Discharge Data from 18 US States

Aaron T. Curns,[1] Claudia A. Steiner,[2] Marguerite Barrett,[3] Katherine Hunter,[4] Emily Wilson,[4] and Umesh D. Parashar[1]

[1]National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; [2]Healthcare Cost and Utilization Project, Center for Delivery, Organization and Markets, Agency for Healthcare Research and Quality, Rockville, Maryland; [3]M.L. Barrett, Del Mar, and [4]Thomson Reuters, Santa Barbara, California

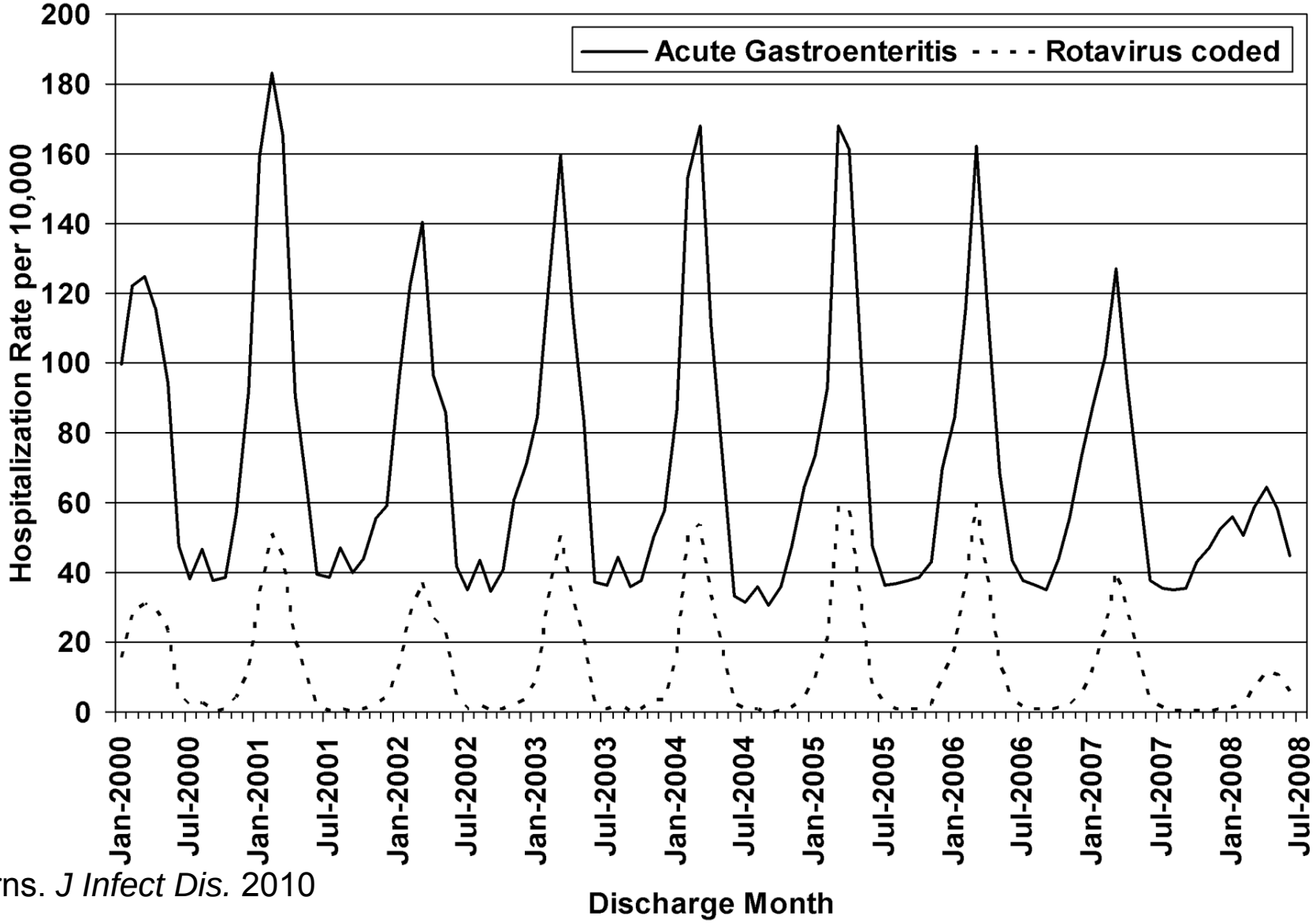
Curns. *J Infect Dis.* 2010

Rates of AGE hospitalization by year and rotavirus season among children 5 years of age, 18 states, January 2000 - June 2008



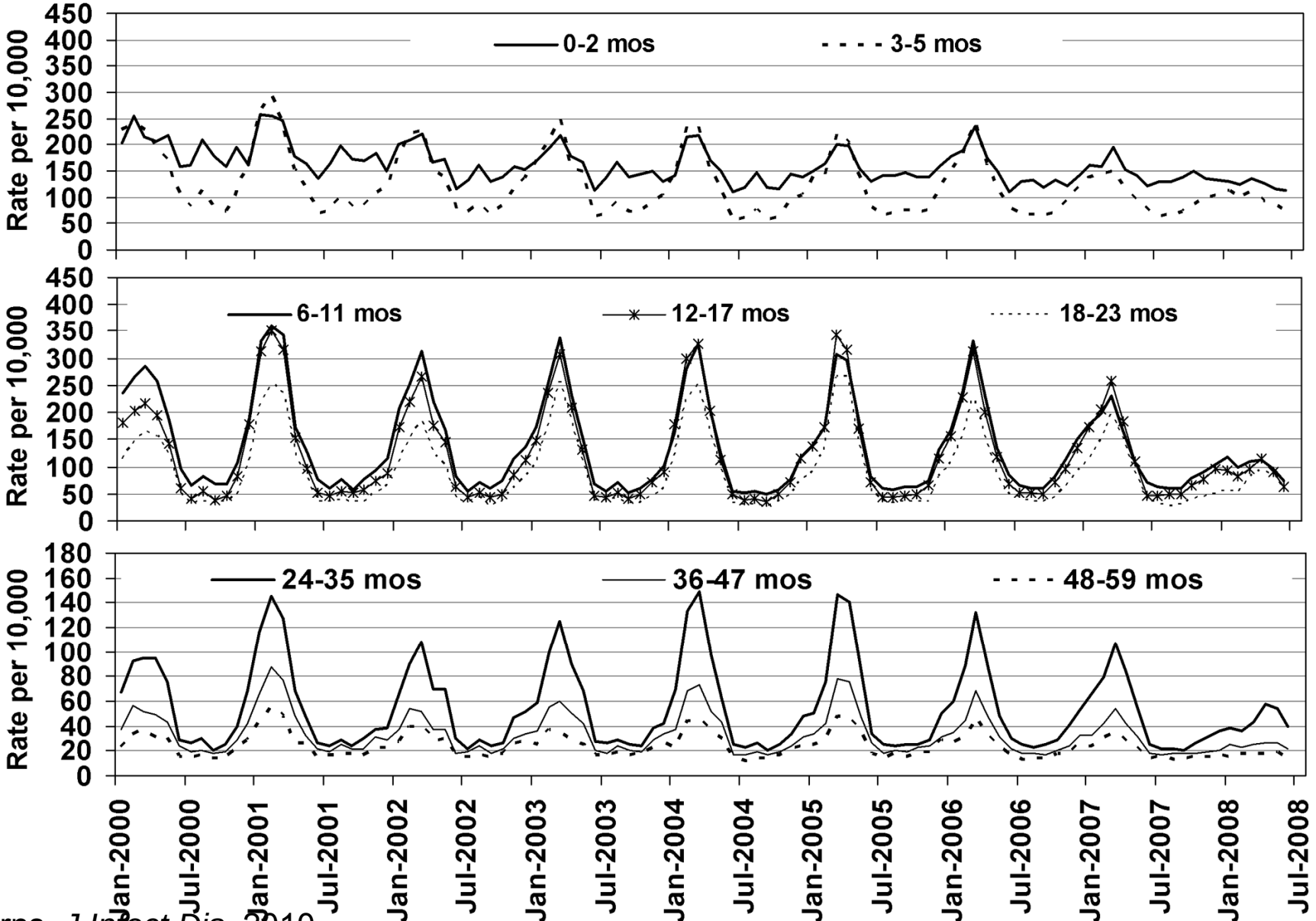
Curns. *J Infect Dis.* 2010

Monthly AGI and rotavirus *ICD-9*–coded hospitalization rates among children aged <5 years from January 2000 through June 2008, in 18 states



Curns. *J Infect Dis.* 2010

Monthly AGI hospitalization rates by age group in 18 states January 2000 - through June 2008



Curns. *J Infect Dis.* 2010

Reduction in Acute Gastroenteritis Hospitalizations among US Children After Introduction of Rotavirus Vaccine: Analysis of Hospital Discharge Data from 18 US States: National Estimate of Reduction

- Approximately 55,000 acute gastroenteritis hospitalizations prevented during the 2008 rotavirus season
- Elimination of 1 in 20 hospitalizations among US children aged <5 years
- Substantial decreases among those too young or old to be vaccinated

Curns. *J Infect Dis.* 2010

Impact of Rotavirus Vaccination on Hospital-Acquired Rotavirus Gastroenteritis in Children

WHAT'S KNOWN ON THIS SUBJECT: Approximately 27% of children with rotavirus in the hospital acquire it while hospitalized for another condition. Pediatric rotavirus vaccination greatly decreased the number of children hospitalized with rotavirus from 2007 to 2008.

WHAT THIS STUDY ADDS: Routine community-based rotavirus infant vaccination protects hospitalized children from acquiring rotavirus. Thus, community-based vaccination efforts should be encouraged as a strategy to decrease hospital-acquired rotavirus.

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KEY WORDS
rotavirus, RSV, influenza, nosocomial infections, vaccines

ABBREVIATIONS
HA—hospital-acquired
CA—community-acquired
CMH—Children's Memorial Hospital
RSV—respiratory syncytial virus

These data were presented in part (as poster 1148) at the 47th annual meeting of the Infectious Diseases Society of America; October 29–November 1, 2009; Philadelphia, PA.

www.pediatrics.org/cgi/doi/10.1542/peds.2010-1830

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

FINANCIAL DISCLOSURE: *Dr Anderson has served on the speaker's bureau for Merck, has consulted for both Merck and GlaxoSmithKline, and has received research support from Merck, Meridian Bioscience, Inc, and Clearview and financial compensation for writing a review article for Medscape CME; Dr Shulman has served on the speaker's bureau for both Merck and GlaxoSmithKline and has served on an advisory board for Merck vaccines and Novartis vaccines; and Dr Noskin is on the*

abstract

FREE

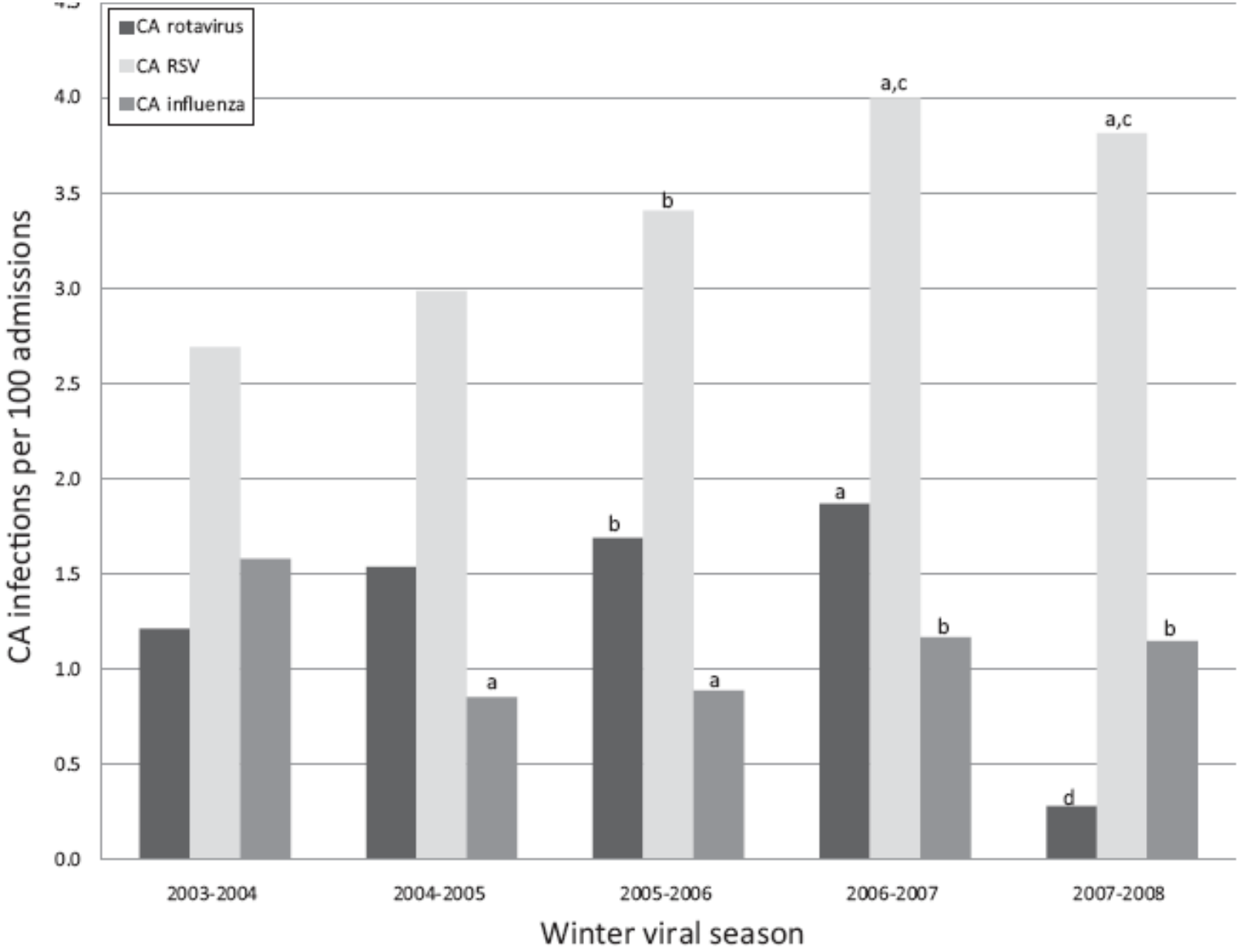
OBJECTIVE: Data show that after the implementation of routine rotavirus vaccination for infants in the United States, community-acquired (CA) rotavirus cases declined substantially in the 2007–2008 season. The impact of community-based rotavirus vaccination on the substantial burden of hospital-acquired (HA) rotavirus has not been documented.

PATIENTS AND METHODS: We assessed CA and HA rotavirus, respiratory syncytial virus, and influenza infections at Children's Memorial Hospital for 5 winter seasons (defined as occurring from September through May) from 2003 to 2008. We also report rotavirus data from the 2008–2009 season.

RESULTS: A similar dramatic decline (>60% compared with the median of previous seasons) occurred in the rates of cases of both CA ($P < .0001$) rotavirus hospitalizations and HA ($P < .01$) rotavirus infec-

Anderson. Pediatrics 2011;127:e264–e270

Community-Acquired Infections per 100,000 Admissions



Anderson. Pediatrics, 2011

FIGURE 1

CA viral infection admissions per 100 admissions. [a] $P \leq .003$ versus the 2003–2004 season; [b] $P < .04$ versus the 2003–2004 season; [c] $P \leq .007$ versus the 2004–2005 season; [d] $P \leq .0001$ versus previous seasons. For exact P values, see the text.

Hospital-Acquired Infections per 100,000 Patient-Days

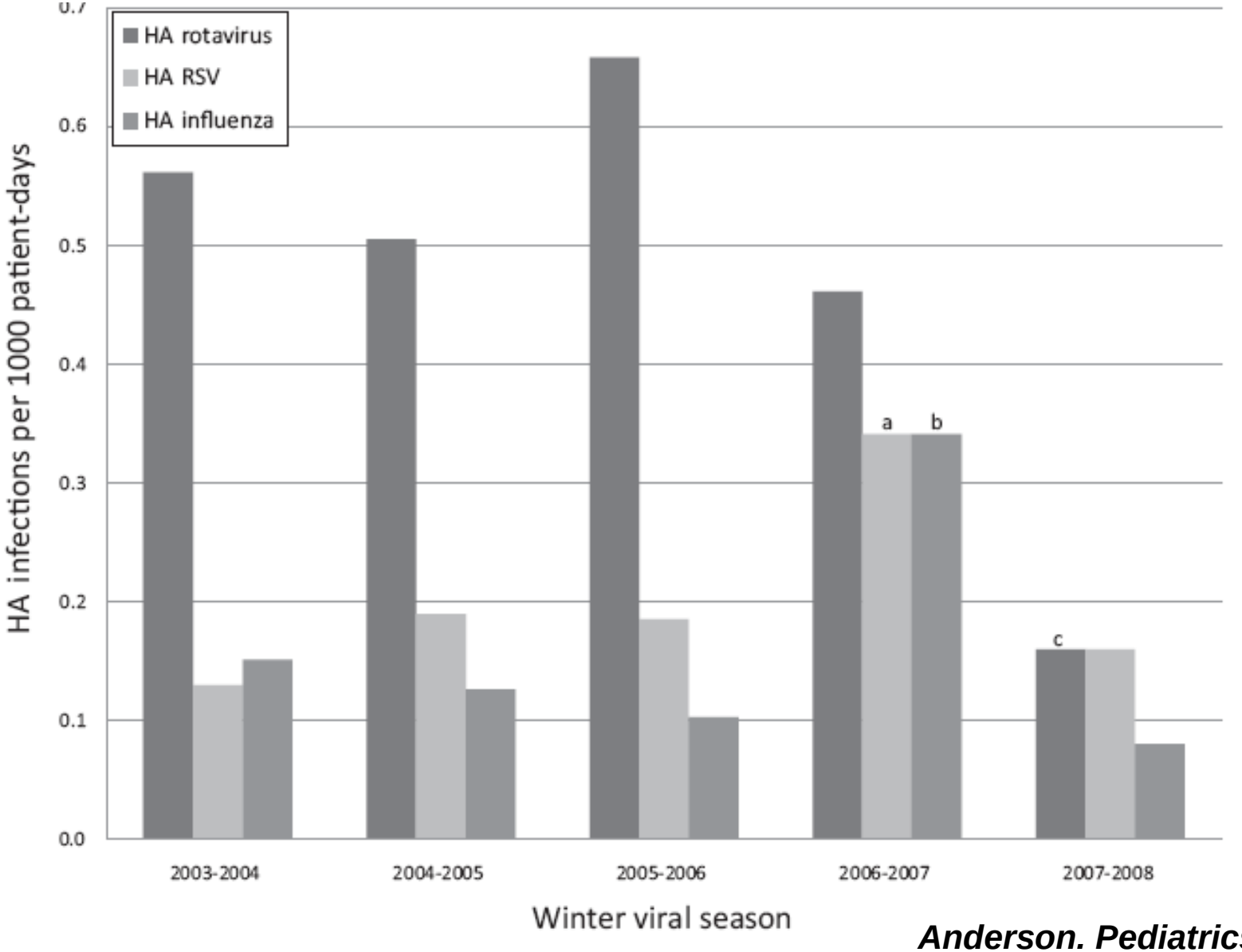


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FIGURE 2

HA viral infections per 1 000 patient-days. [a] $P < .05$ versus the 2003–2004 season; [b] $P < .04$ versus the 2004–2005, 2005–2006, and 2007–2008 seasons; [c] $P < .01$ versus all previous years. For exact P values, see the text.

Effectiveness of Pentavalent Rotavirus Vaccine Against Severe Disease

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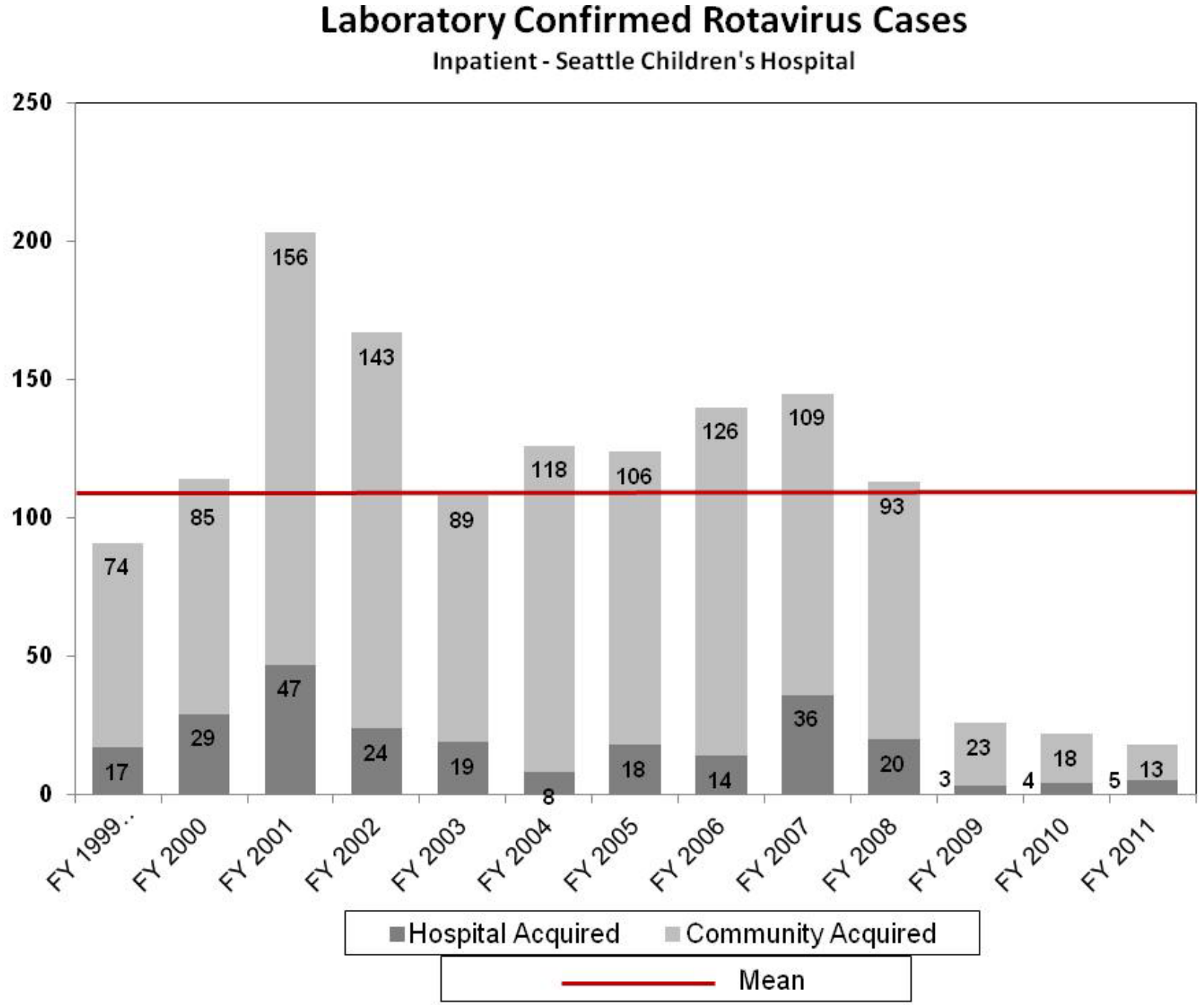
WHAT'S KNOWN ON THIS SUBJECT: The pentavalent rotavirus vaccine RV5 was licensed and recommended for routine immunization in US infants in 2006. Results of studies performed before licensure demonstrated this vaccine to be highly efficacious against rotavirus-associated hospitalizations and emergency department visits.

WHAT THIS STUDY ADDS: In this case-control study the effectiveness of RV5 under field conditions was examined. Both full and partial immunization with RV5 were found to be highly effective against rotavirus-associated hospitalizations and emergency department visits, and effectiveness in children persisted during the second year of life.

NVSN population-based study, 2006-2009
Effectiveness against hospitalization or ED visits

- **1 dose = 74% (37-90%)**
- **2 doses = 88% (66-96%)**
- **3 doses = 87% (71-94%)**

Staat. Pediatrics 2011



* FY = October 1 thru September 30

J Heath, D. Zerr; personal communication

BRIEF REPORT

Infant Rotavirus Vaccination May Provide Indirect Protection to Older Children and Adults in the United States

Ben A. Lopman, Aaron T. Curns, Catherine Yen, and Umesh D. Parashar

Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia

(See the editorial commentary by Glass, on pages 975–7.)

Following the introduction of rotavirus vaccination in the United States, rotavirus and cause-unspecified gastroenteritis discharges significantly decreased in 2008 in the 0–4, 5–14, and 15–24-year age groups, with significant reductions observed in March, the historic peak rotavirus month, in all

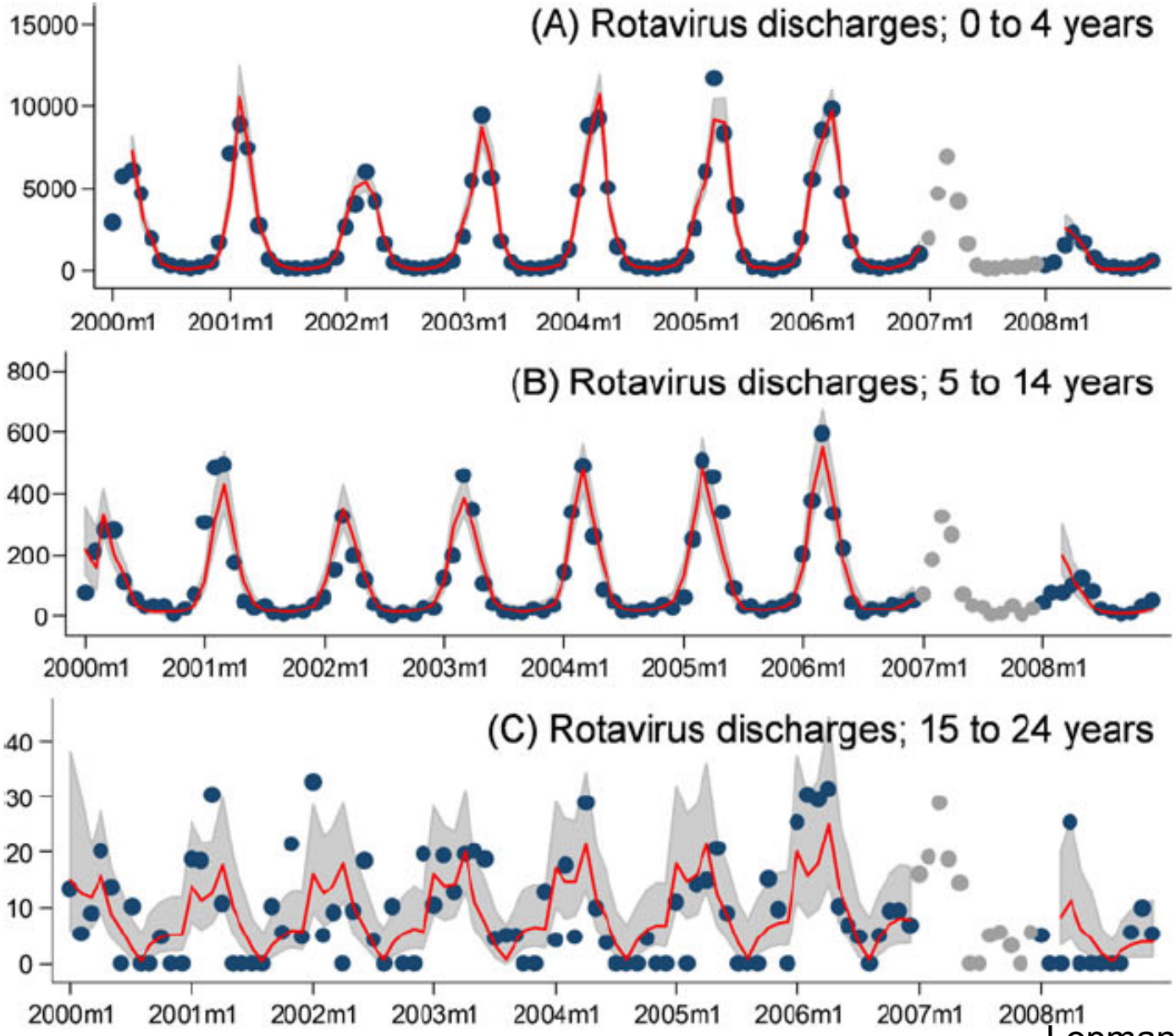
Lopman. JID 2011;204:980–6

Infant Rotavirus Vaccination May Provide Indirect Protection to Older Children and Adults in the United States

- Database covering 20% of all US hospital admissions (Nationwide Inpatient Sample)
- Over 1000 hospitals in 42 states
- ICD-9CM codes for rotavirus and cause – unspecified gastroenteritis-associated hospital discharges 2000-2008
- Regression model to control for seasonal effects and secular trends

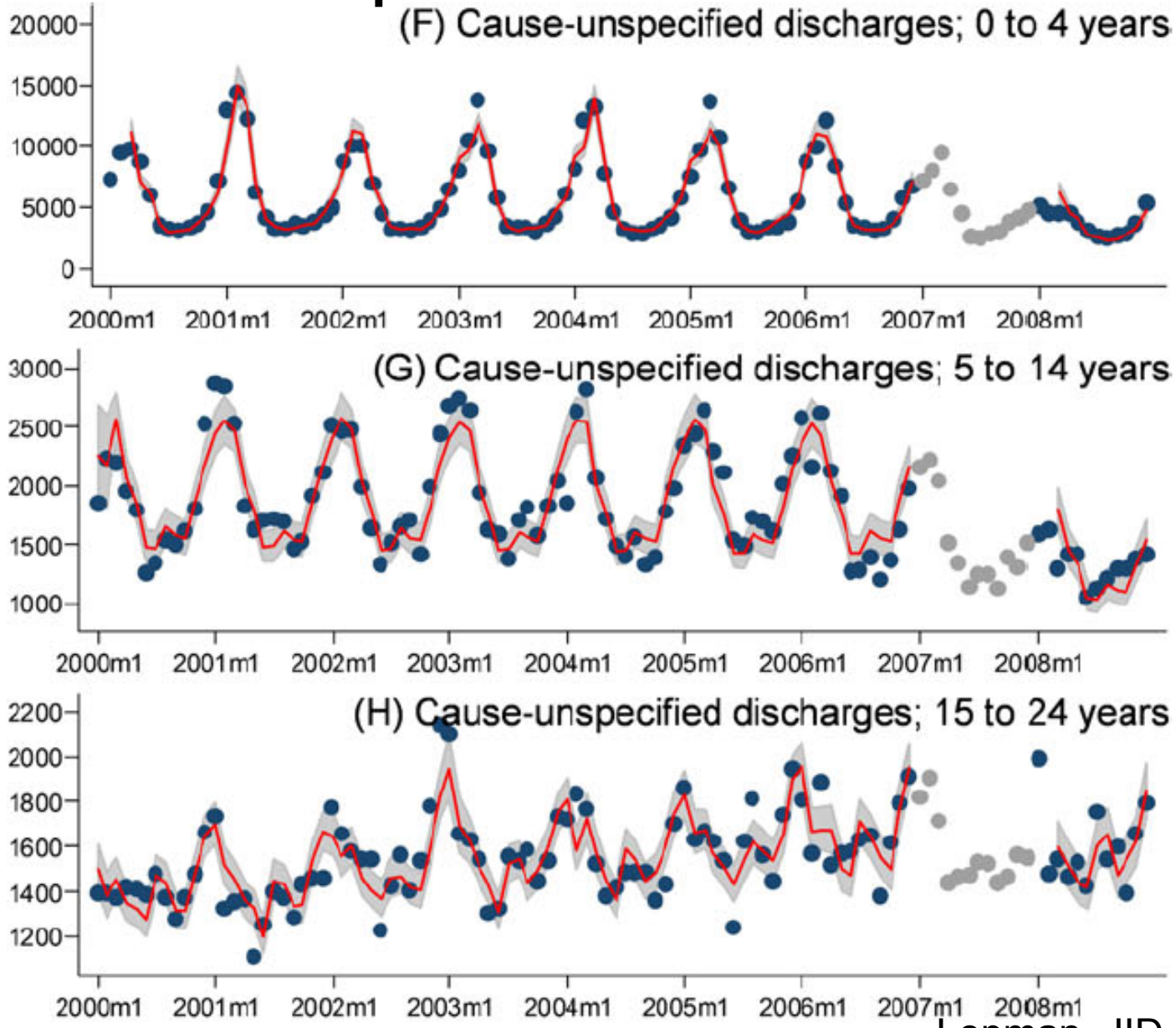
Lopman. JID 2011;204:980–6

Observed and Model-Predicted Monthly Rotavirus and Cause-Unspecified Gastroenteritis Discharges



Lopman. JID 2011;204:980–6

Observed and Model-Predicted Monthly Rotavirus and Cause-Unspecified Gastroenteritis Discharges



Lopman. JID 2011;204:980–6

Infant Rotavirus Vaccination May Provide Indirect Protection to Older Children and Adults in the United States - Results

- Significant reductions in rotavirus and cause-unspecified gastroenteritis hospital discharges in the 0-4, 5-14, & 15-24 year age groups in 2008
- Estimated 66,030 hospitalizations prevented; 15% in the 5-24 year age group
- Approx. $204 million in averted hospitalization costs with 21% in the 5-24 year age group
  - Studies supporting introduction of rotavirus vaccine in US estimated potential cost savings from averted hospitalizations at $130 million

Lopman. JID 2011;204:980–6

Conclusions

- Introduction of rotavirus vaccine has had an immediate and dramatic impact on the epidemiology and burden of rotavirus disease in the U.S.
- Marked indirect benefits among unvaccinated not anticipated and greatly enhanced impact of vaccination in initial assessment of vaccination program

Summary

- Uptake of new rotavirus vaccines improving steadily but lags behind other vaccines
- Value of monitoring the public health impact and safety of new vaccination programs using surveillance systems and epidemiological studies
  - Ongoing monitoring needed to determine if early effects will be sustained
  - Awaiting more data on duration of protection

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Questions?