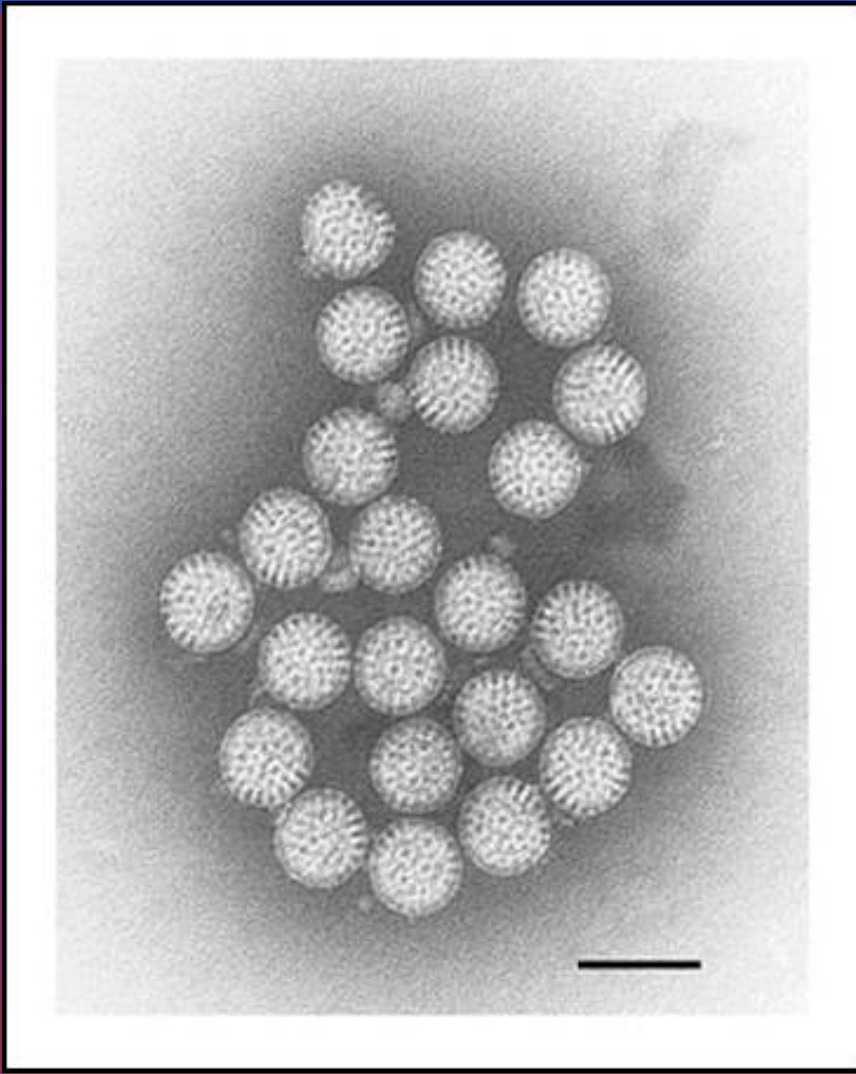


Update on Rotavirus Vaccines in the United States



CDC, NCIRD
Division of Viral Diseases

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October 25, 2012



Today's presentation

- Vaccine effectiveness (VE) results for both licensed vaccines in the United States
 - First US studies assessing both licensed rotavirus vaccines in concurrent use
 - VE against rotavirus hospitalization and emergency department visits
 - Age-specific VE
 - VE by predominant genotype
- Rotavirus strain surveillance, including vaccine-derived strains



2 Rotavirus vaccines used internationally

RotaTeqTM (Merck):

Bovine-human pentavalent

(G1, G2, G3, G4, P[8])

3 doses @ 2, 4, 6 months

Feb 2006 ACIP approval

Rotarix[®] (GlaxoSmithKline):

Human monovalent

(G1, P[8])

2 doses @ 2, 4 months

June 2008 ACIP approval

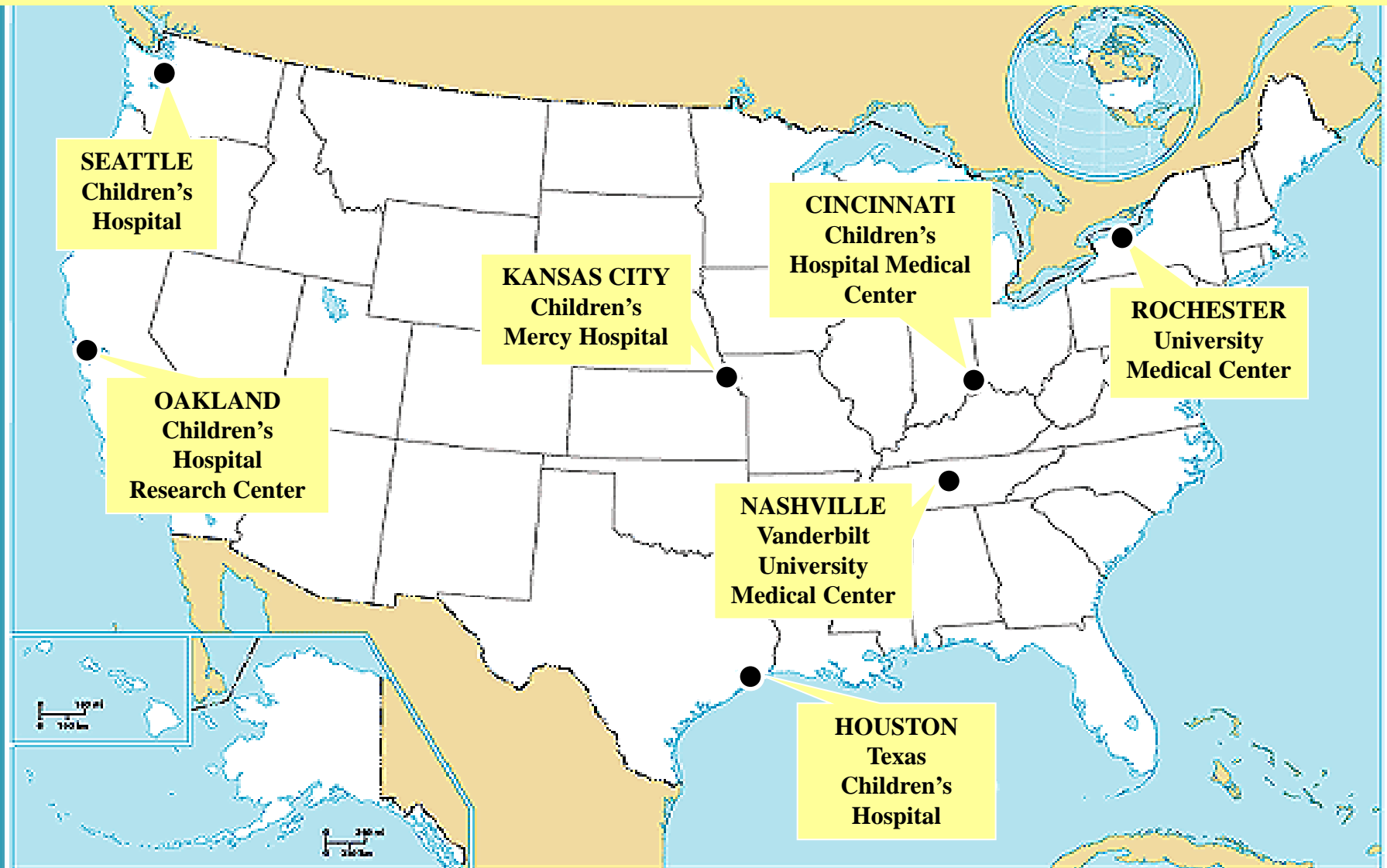
Live, attenuated oral vaccines

Heterotypic immunity against other strains

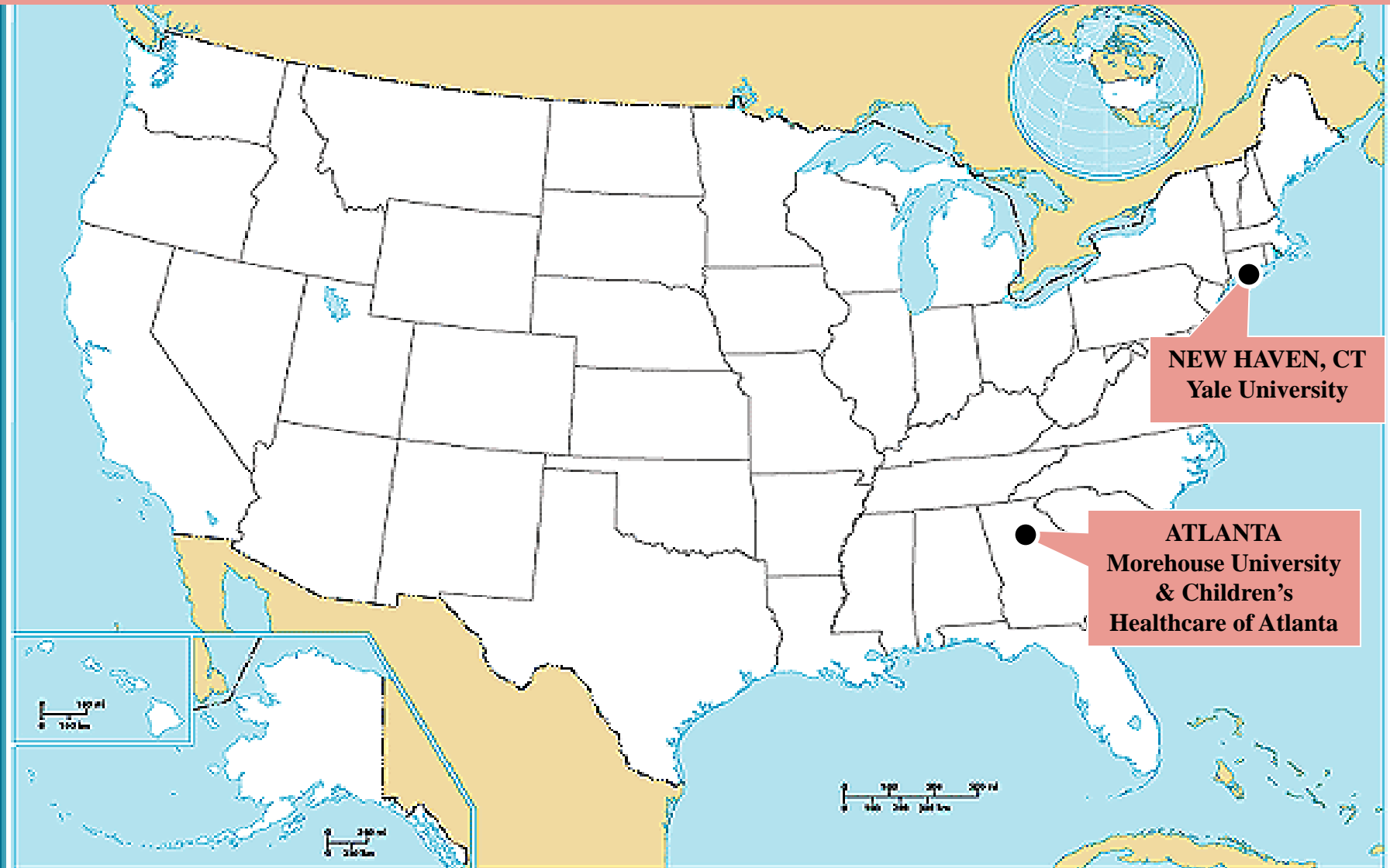
Both vaccines ACIP-recommended for childhood vaccination in U.S. (no preference)



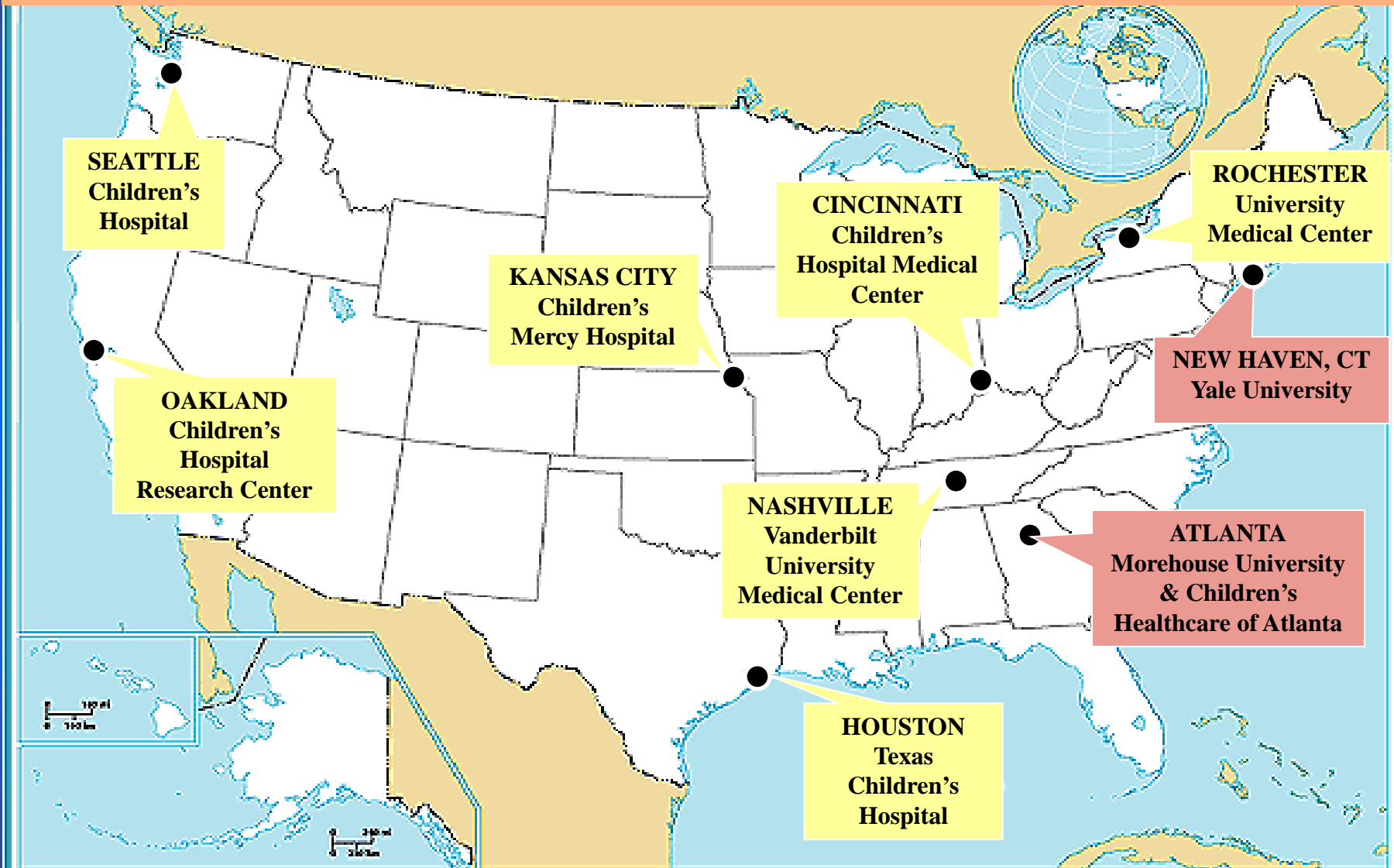
New Vaccine Surveillance Network (NVSN)



Emerging Infections Program (EIP)



NVSN & EIP

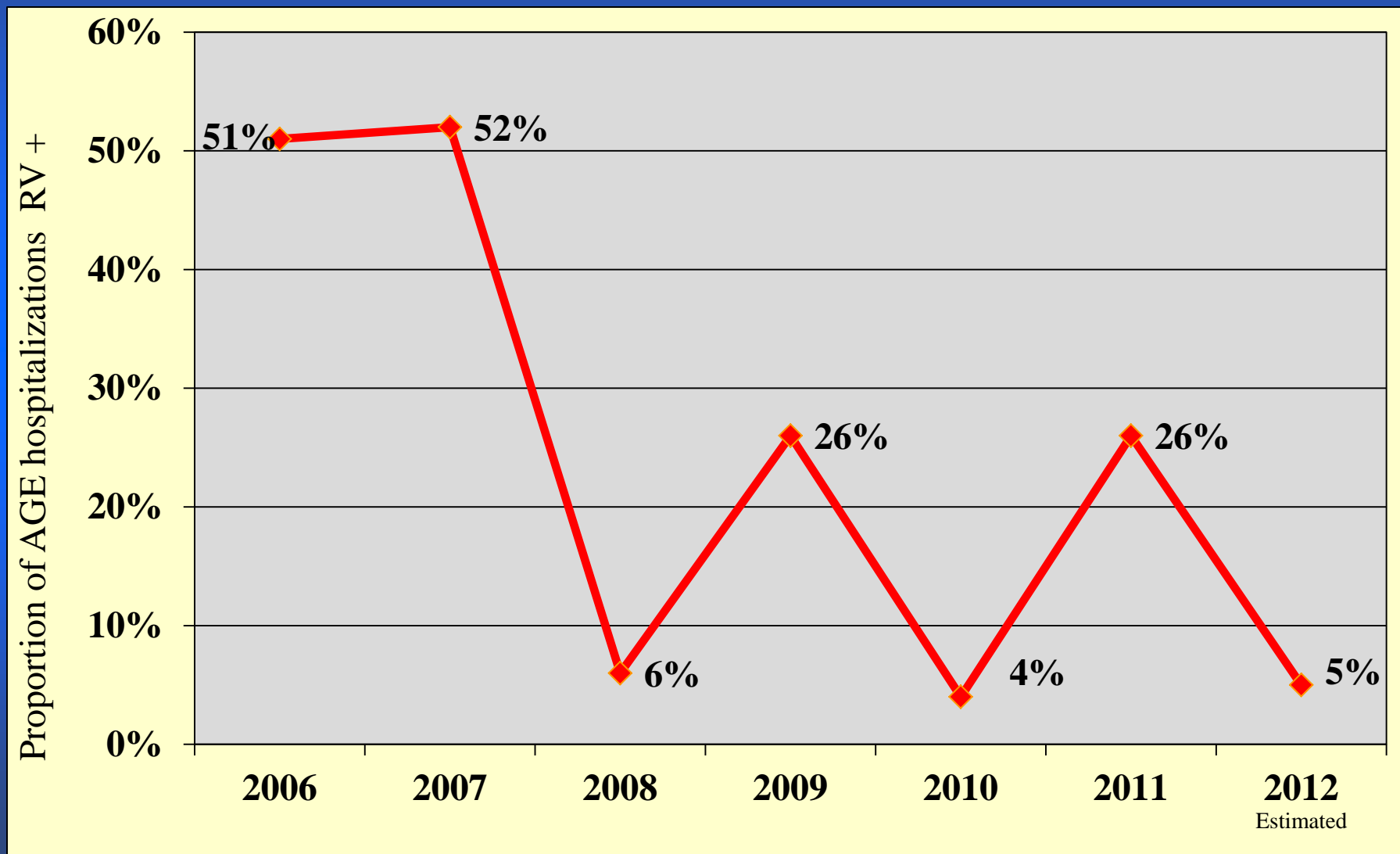


During the post-licensure period,
independent surveillance systems
consistently report:

- a.) continued steep declines in rotavirus incidence
and hospitalizations/ED visits
- b.) the emergence of a biennial peak in rotavirus
activity



NVSN – active surveillance, % rotavirus positive among childhood AGE hospitalizations



New Vaccine Surveillance Network (NVSN)

Effectiveness of pentavalent and monovalent rotavirus vaccines in concurrent use among US children <5 years old, 2009-2011



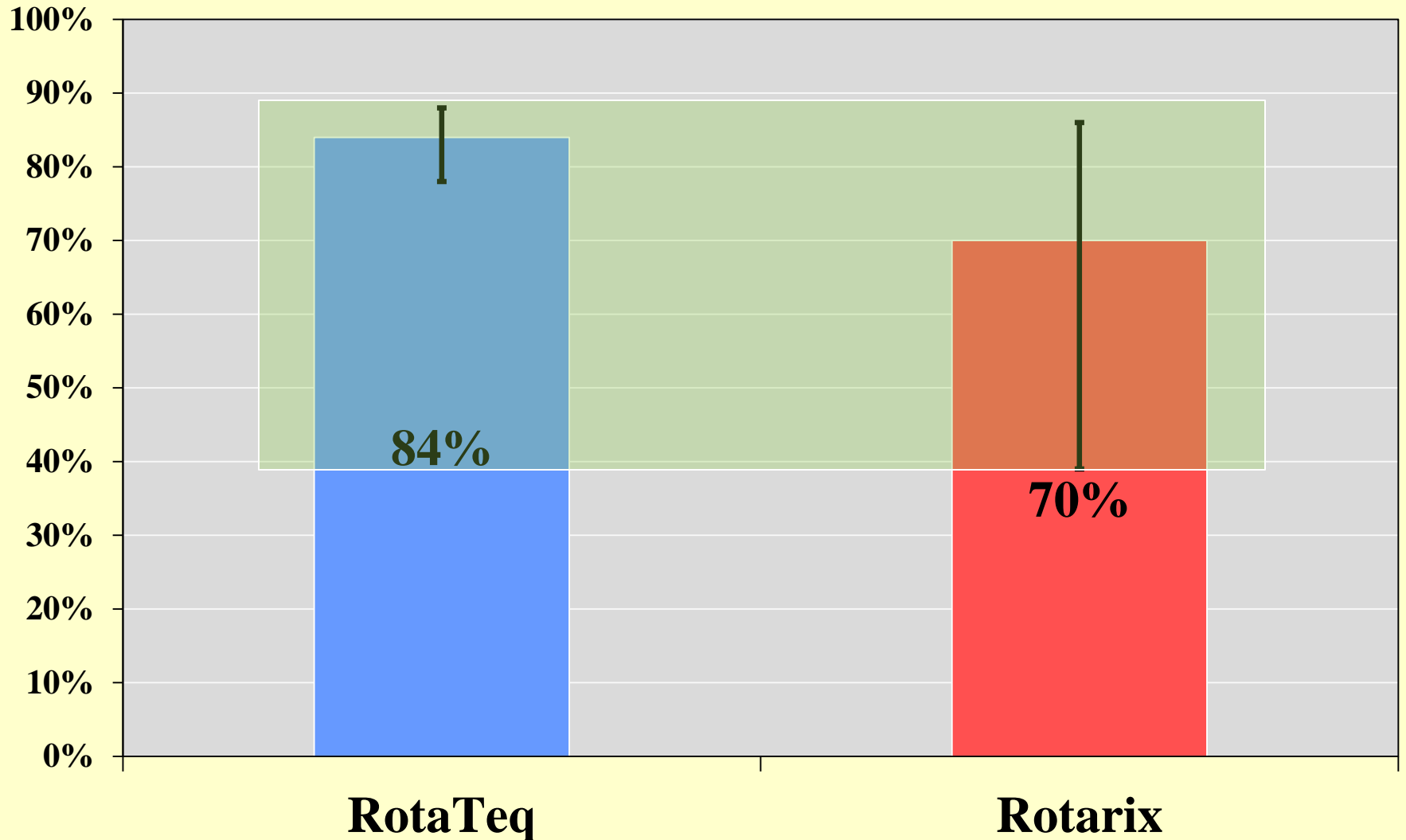
New Vaccine Surveillance Network (NVSN)

- Children <5 years old hospitalized or visiting the ED with AGE (diarrhea and/or vomiting) enrolled through active surveillance, November - June for both seasons.
- All sites were included in RotaTeq-specific analysis. Sites having <5% vaccine coverage with RV1 (Seattle, Houston, Nashville) were not included in Rotarix-specific analyses.
- Case-control logistic regression models: adjusted for month/year of birth, month/year of symptom onset, and surveillance site.
- Rotavirus cases were confirmed by enzyme immunoassay and genotyped.
- Vaccination records confirmed
- Rotavirus-negative control results presented here



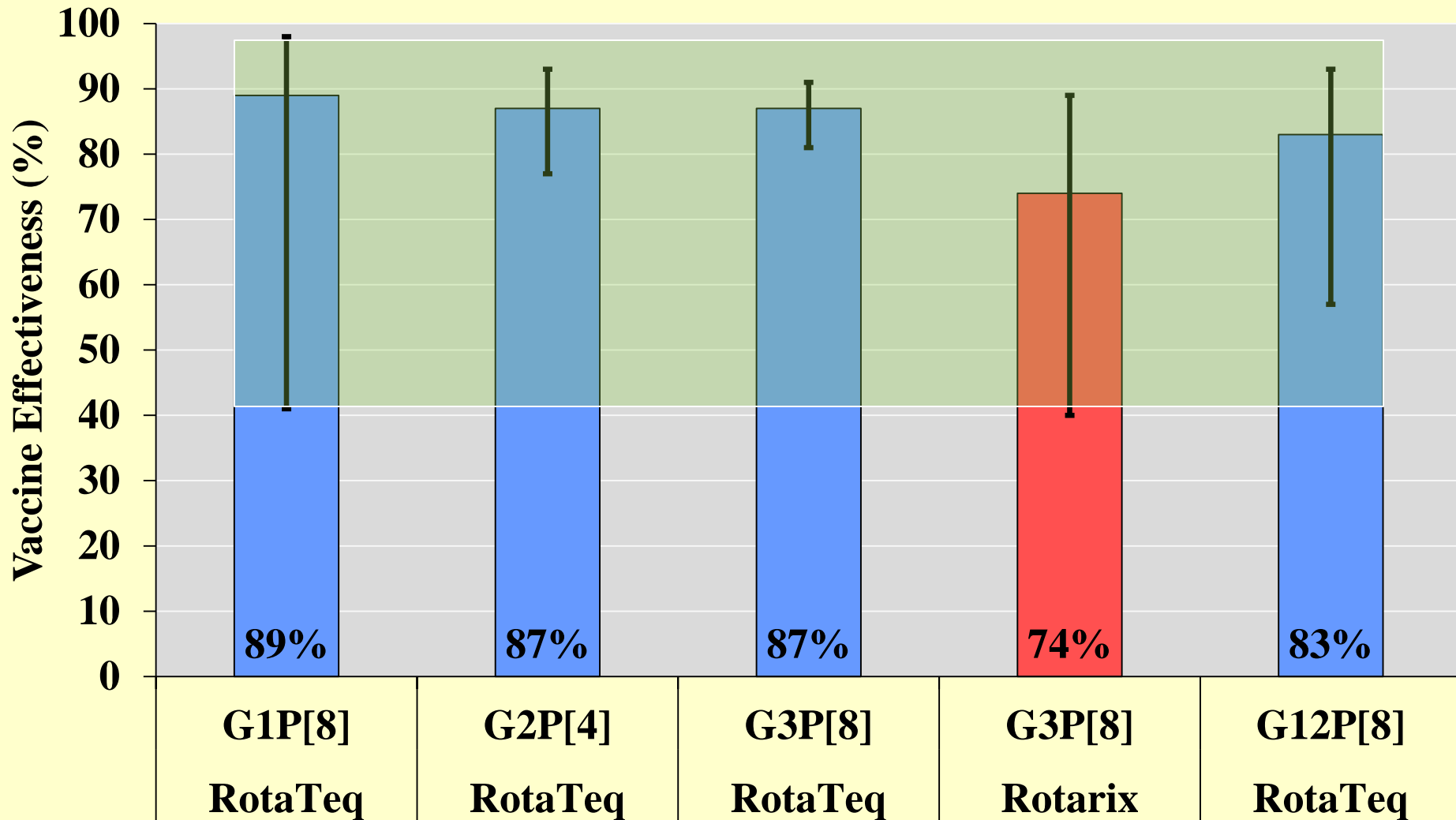
New Vaccine Surveillance Network (NVSN)

Full course VE and 95% CI for RotaTeq and Rotarix



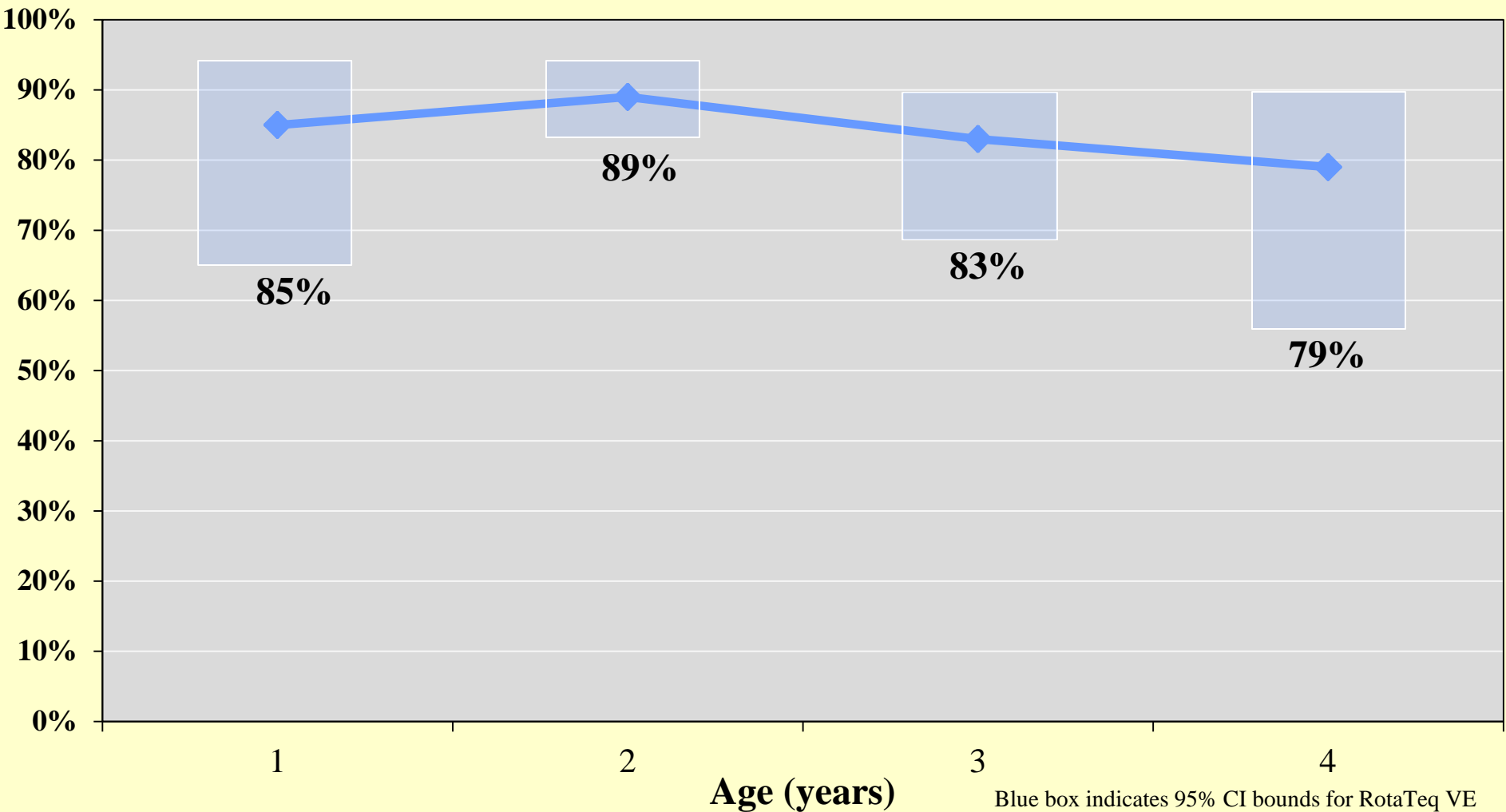
New Vaccine Surveillance Network (NVSN)

Full course VE and 95% CI by Rotavirus Genotype
for RotaTeq and Rotarix



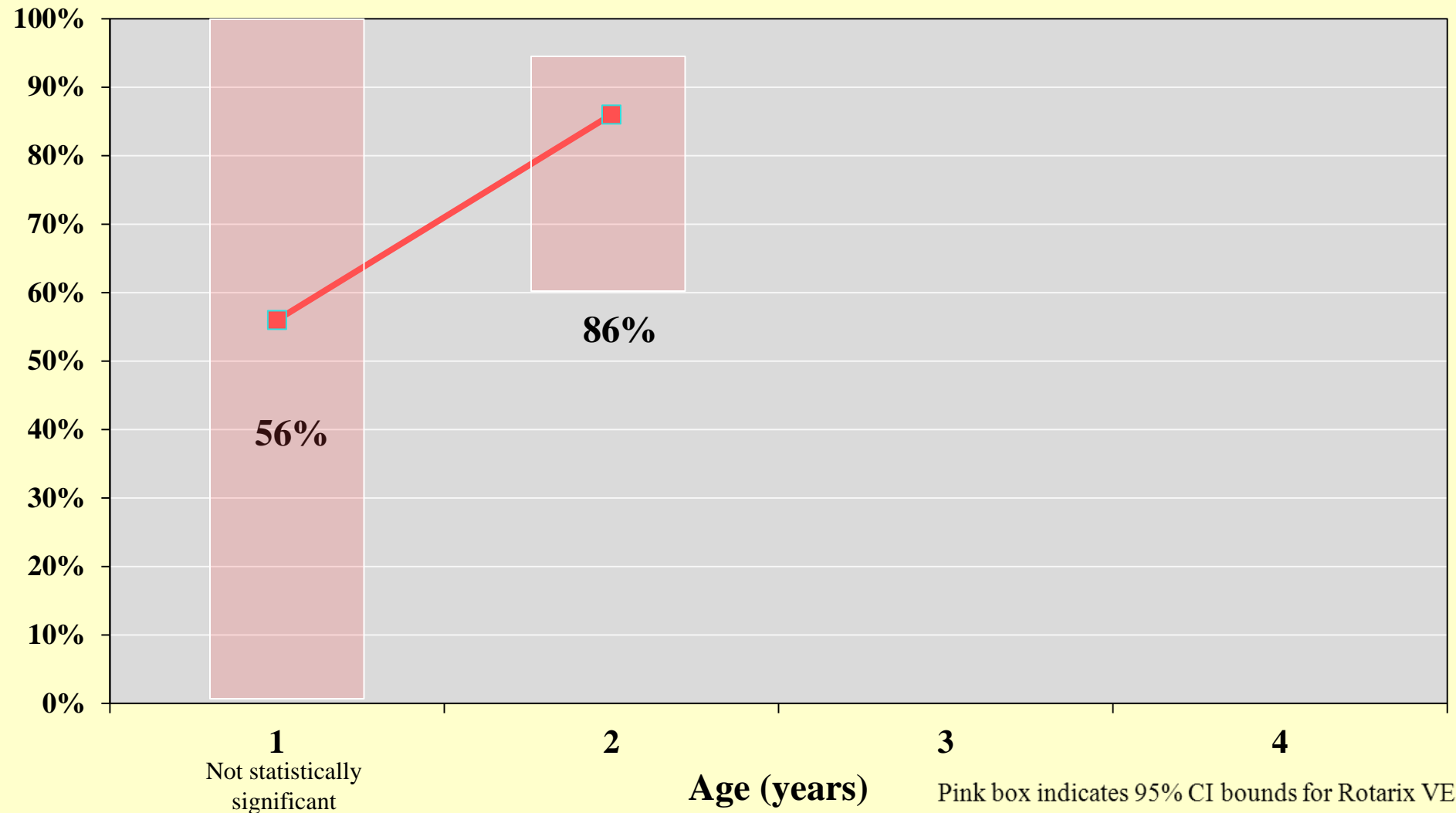
New Vaccine Surveillance Network (NVSN)

Full course VE and 95% CI by Age for RotaTeq



New Vaccine Surveillance Network (NVSN)

VE and 95% CI by Age for a full course of Rotarix



Emerging Infections Program (EIP)

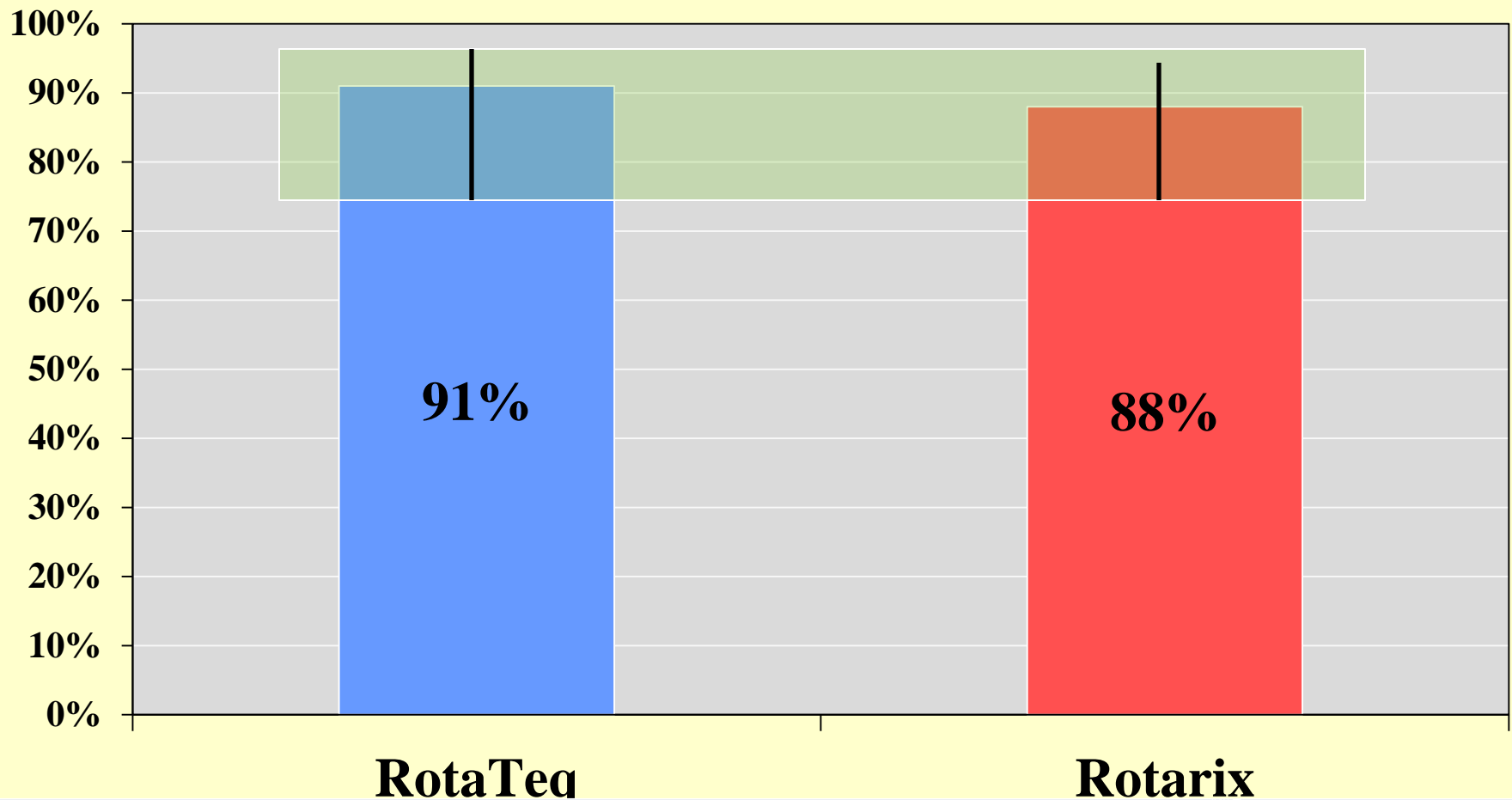
January – June 2010 & 2011

- Two EIP sites: Georgia (3 hospitals) & Connecticut (2 hospitals)
- Children age-eligible to have received Rotarix, hospitalized or visiting the ED with diarrhea enrolled through active surveillance
- Rotavirus cases were confirmed by enzyme immunoassay and genotyped.
- Vaccination records confirmed
- Case–control logistic regression models
- Rotavirus-negative control results presented here



Emerging Infections Program (EIP)

Full course VE and 95% CI among children aged ≥ 8 months



(Boom JA, et al. *Pediatrics* 2010)

3 dose RotaTeq

VE = 89%

(70%, 96%)

(Staat MA, et al. *Pediatrics* 2011)

3 dose RotaTeq

VE = 87%

(71%, 94%)

(Cortese MM, et al. *Pediatrics* 2011)

3 dose RotaTeq

VE = 89%

(81%, 94%)

N
V
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N

RotaTeq

(Payne DC, et al. *PRELIMINARY*)

3 dose RotaTeq VE = 84% (78%, 88%)

E
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RotaTeq

(Cortese MM, et al. *PRELIMINARY*)

3 dose RotaTeq VE = 91% (73%, 97%)



N
V
S
N

Rotarix

(Payne DC, et al. *PRELIMINARY*)

2 dose Rotarix VE = 70% (39%, 86%)

E
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P

Rotarix

(Cortese MM, et al. *PRELIMINARY*)

2 dose Rotarix VE = 88% (74%, 94%)



Effectiveness of rotavirus vaccines in preventing cases and hospitalizations due to rotavirus gastroenteritis in Navarre, Spain

Jesús Castilla^{a,b,*}, Xabier Beristain^c, Víctor Martínez-Artola^c, Ana Navascués^d, Manuel García Cenoz^{a,b}, Nerea Álvarez^e, Isabel Polo^c, Ana Mazón^c, Alberto Gil-Setas^c, Aurelio Barricarte^{a,b}

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^e Servicio Navarro de Salud-Osasunbidea, Pamplona, Spain

RotaTeq = 81% (95% CI=68–89%)

Rotarix = 75% (95% CI=60–85%)



Summary of VE results

- ✓ High effectiveness observed for both rotavirus vaccines
- ✓ Rotarix VE - requires further monitoring
- ✓ No evidence of waning immunity at the limits of observed study power for either vaccine
- ✓ No difference in VE by genotype

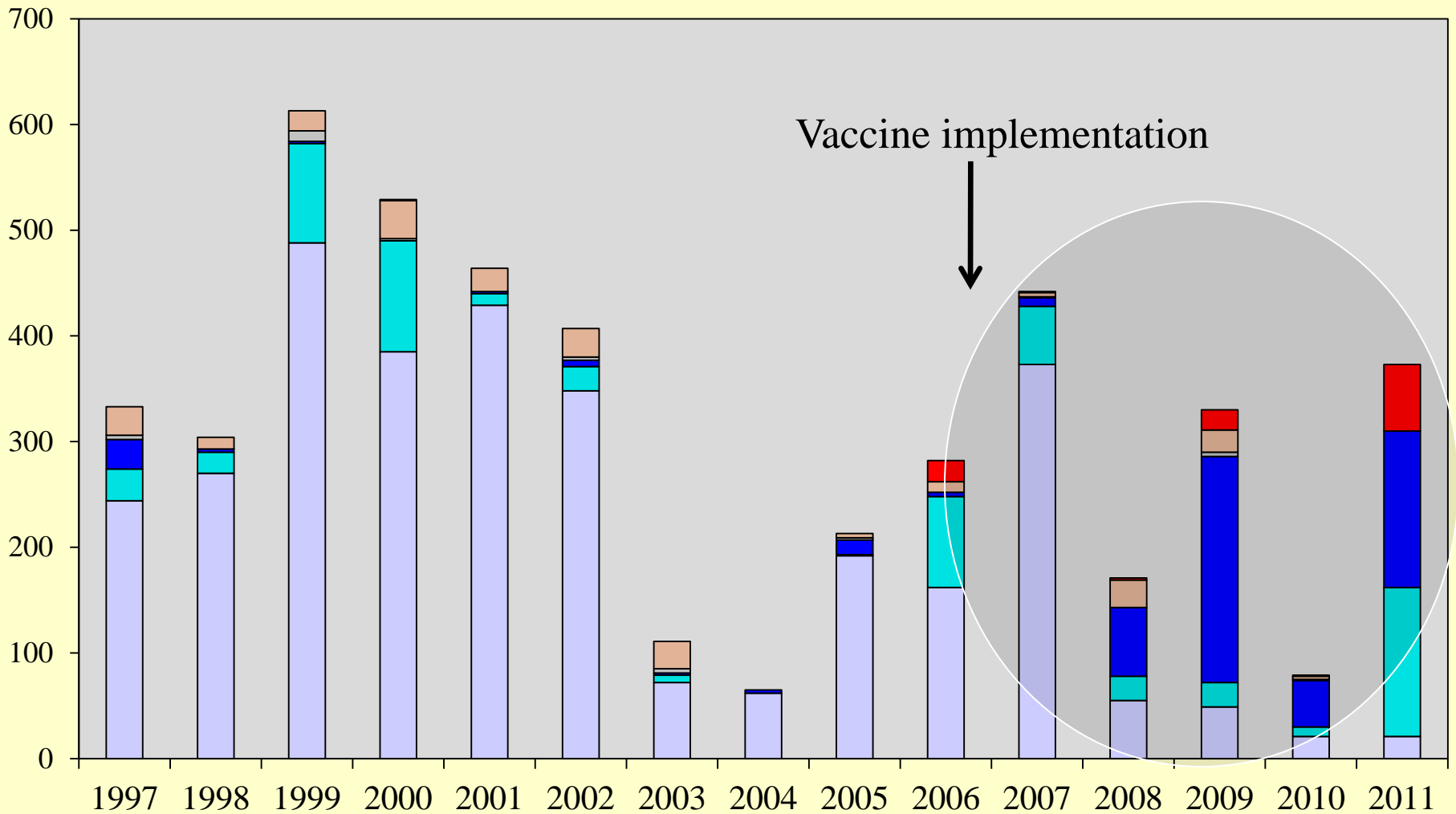


Rotavirus strain monitoring & vaccine-derived strains

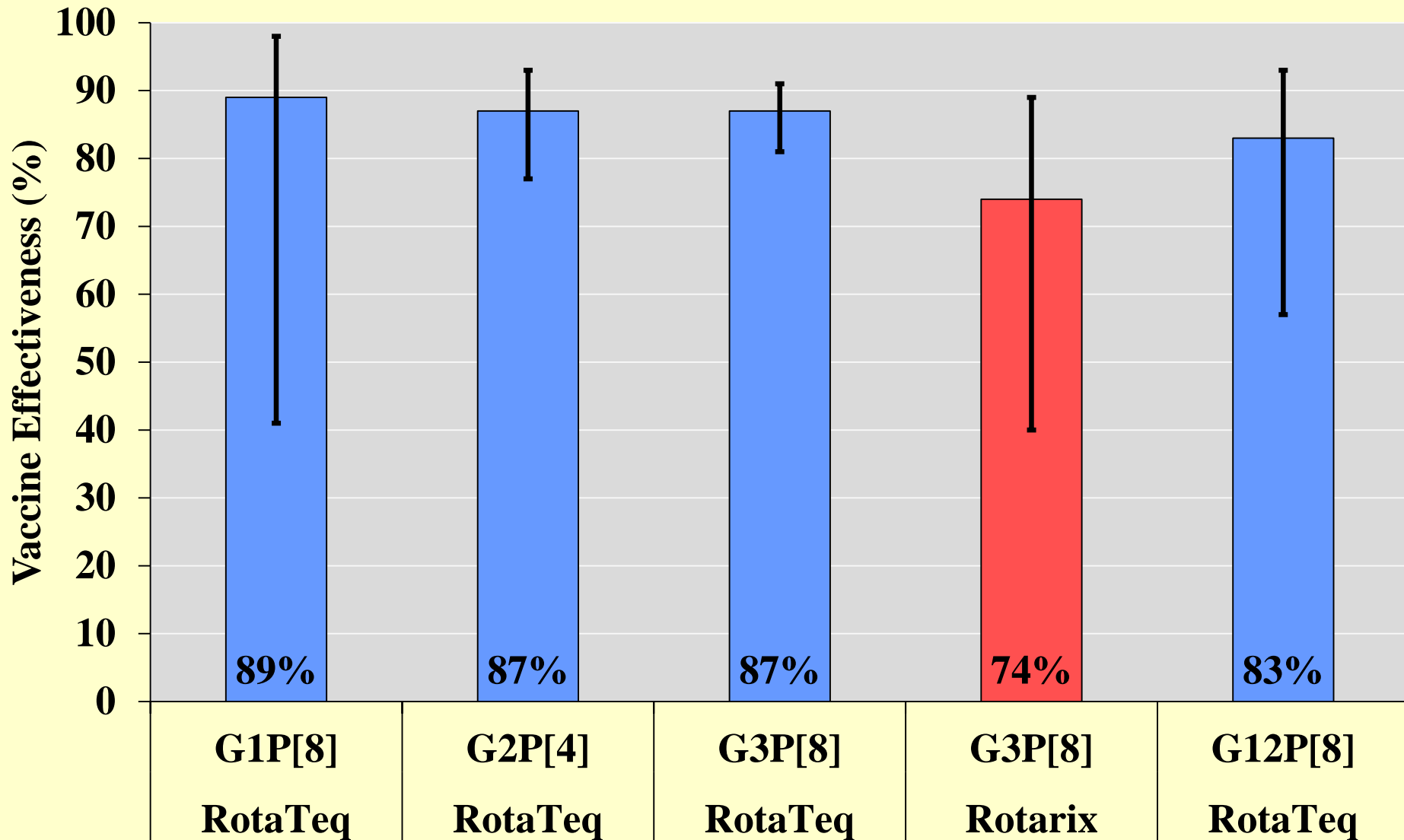


Longitudinal Variation of Rotavirus G Types in the United States, 1996-2011

Legend: G1 (light blue), G2 (cyan), G3 (dark blue), G4 (grey), G9 (tan), G12 (red)



Recall... no difference in VE was observed by predominant genotype



Shedding Rotavirus Vaccine Virus

Shedding of a live, attenuated vaccine virus is the product of the intended *in vivo* replication of the vaccine

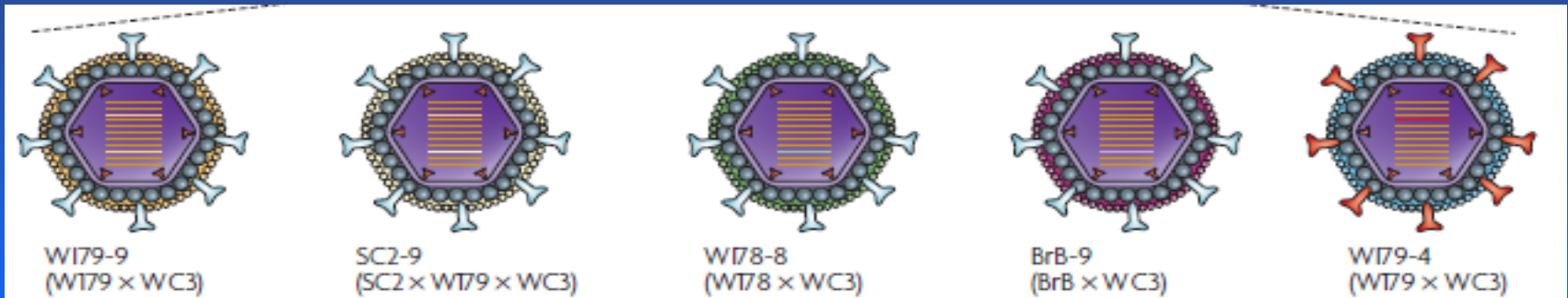
Shed rotavirus vaccine virus has been observed in approximately 9-21% (RotaTeq) and 35-80% (Rotarix) infants within ~2 weeks of vaccination, respectively

ACIP 2009:

“...the protection of the immunocompromised household member afforded by vaccinating the infant in the household and preventing wild-type rotavirus disease outweighs the small risk for transmitting vaccine virus to the immunocompromised household member and any subsequent theoretic risk for vaccine virus-associated disease.”



Reassortment *in vivo* between RotaTeq vaccine strains



P[5]G1

P[5]G2

P[5]G3

P[5]G4

P[8]G6

G1 VP7 gene

P[8] VP4 gene

Reassortant strain =
vdG1P[8]

Transmission appears possible and
may cause AGE symptoms



Detection of RotaTeq reassortants among NVSN subjects enrolled with acute gastroenteritis

<u>Season</u>	<u>Reassortants</u>	<u>NVSN AGE subjects*</u>
2007-08	0	1,041
2008-09	1 § Payne et al., Pediatrics 2009.	1,305
2009-10	3 Boom et al. J Infect Dis 2012.	958
2010-11	4	775

(Note: no reassortants detected among any healthy control subjects)

* subjects with AGE symptoms receiving inpatient/ED medical care – each tested for rotavirus and positive specimens analyzed for reassortant

§ from a catchment area of >141,000 children



Summary of rotavirus strain reports

- a) G3 P[8] observed as the predominant strain in the post-licensure era
- b) G12 P[8] no longer considered an “emerging” strain, and VE is high
- c) RotaTeq reassortants observed at low frequencies in several vaccinated populations
- d) human-to-human transmission of the RotaTeq reassortant appears possible and may cause AGE symptoms, although causality is not clear in all published reports
- e) evidence regarding Rotarix vaccine strain is limited, but some transmission to unvaccinated subjects may occur
- d) further monitoring of circulating serotypes with corresponding epidemiological and clinical data is needed



Acknowledgements:

- Michael Bowen
- Jon Gentsch
- Mathew Esona
- George Gallucci
- Rashi Gautam
- Tara Kerin
- Jamie Lewis
- Freda Lyde
- Osbourne Quaye
- Slavica Rustempasic
- Kim Foytich
- Nicole Gregoricus
- Baoming Jiang
- David Lee
- Jan Vinje
- Charles Humphrey
- NVSN & EIP surveillance staff
- Umesh Parashar
- Margaret Cortese
- Jackie Tate
- Mary Wikswo
- Aaron Curns
- Idris Sulemana
- Benjamin Lopman
- Aron Hall
- Manish Patel
- Marietta Vazquez
- Lilly Cheng Immergluck
- Mary Allen Staat
- Peter Szilagyi
- Kathryn Edwards
- Julie Boom
- Raj Selvarangan
- Eileen Klein
- Parvin Azimi

