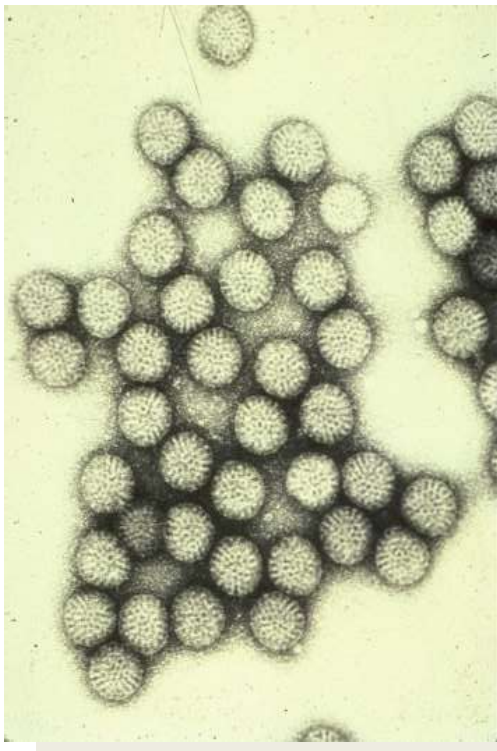


Current Rotavirus Vaccines – Achievements & Challenges

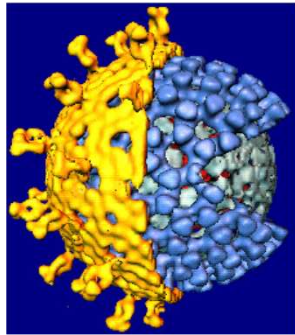


Umesh D. Parashar
Lead, Viral Gastroenteritis Epidemiology Team
Centers for Disease Control Prevention
Atlanta, GA



Human Rotavirus Vaccine (Rotarix, GSK)

Human rotavirus



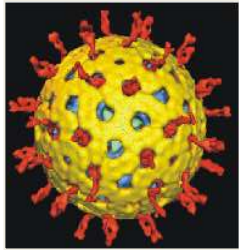
G1P[8]



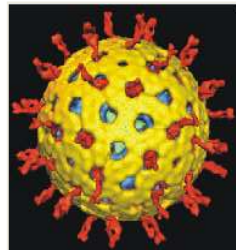
2 doses

Human-Bovine Rotavirus Vaccine (RotaTeq, Merck & Co.)

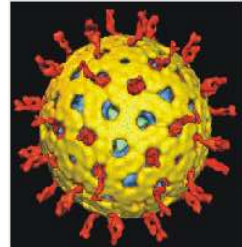
Bovine rotavirus with single human rotavirus gene substitution



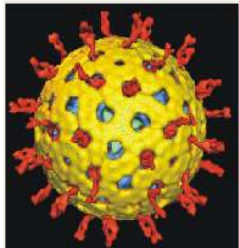
G1



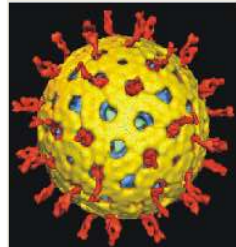
G3



P[8]



G2



G4

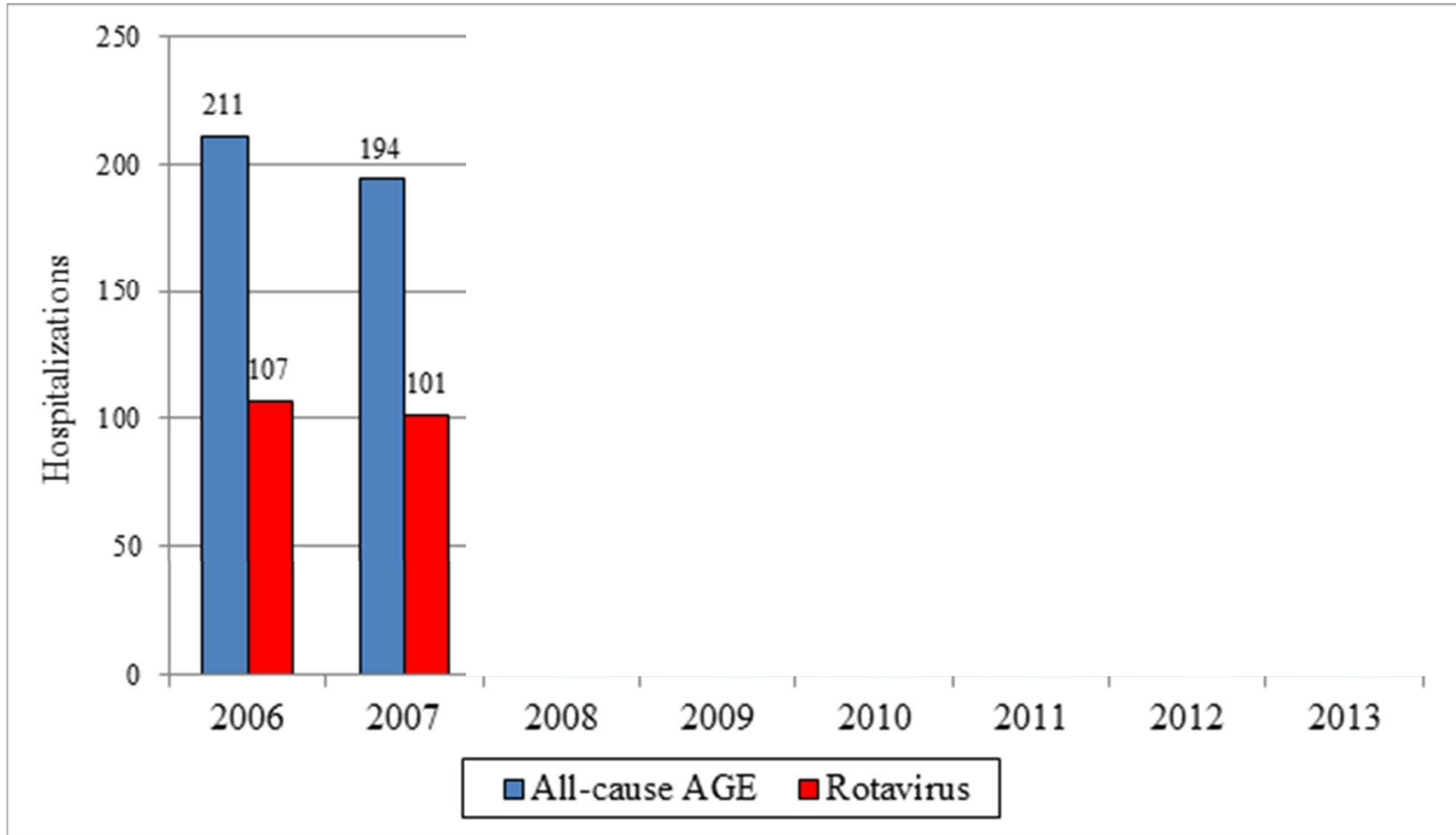


3 doses

High Efficacy of Both Vaccines in Trials in High/Middle Income Countries

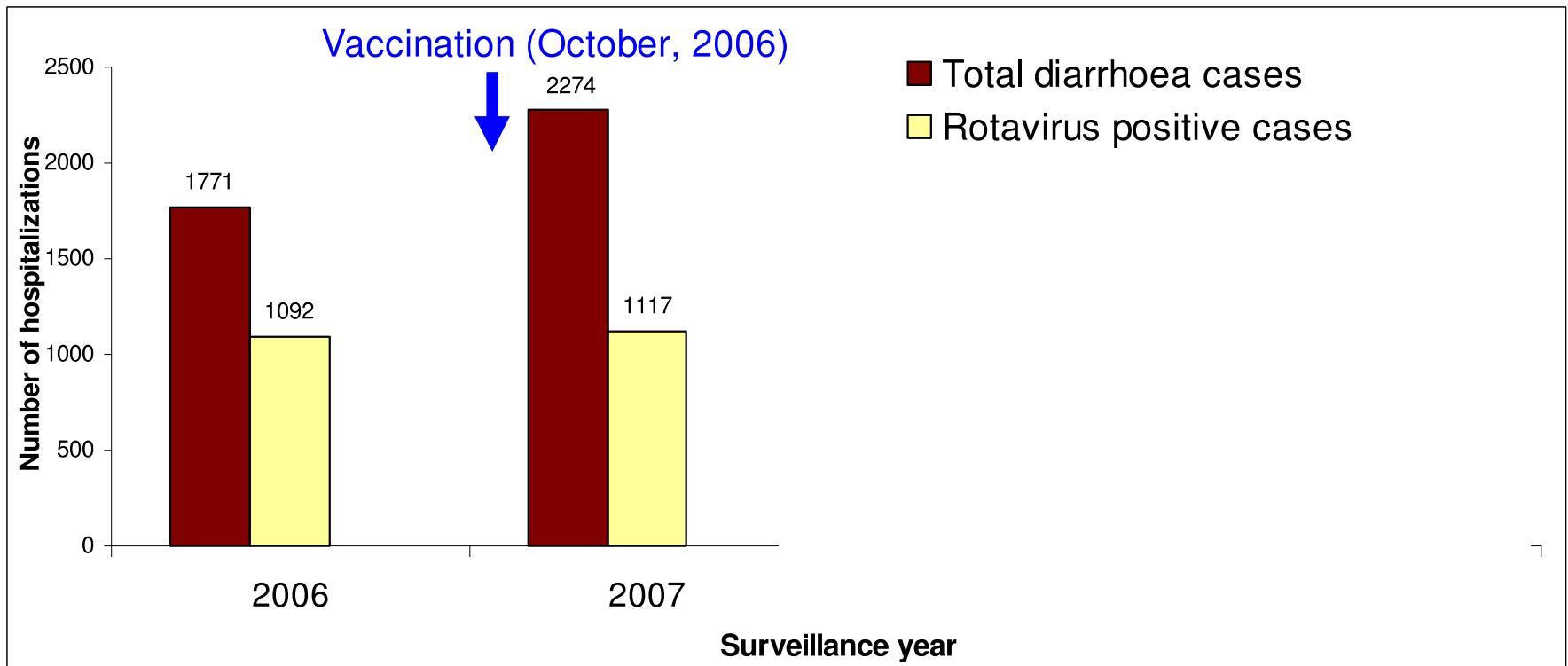
Vaccine	Region	Efficacy (95%CI)
Rotarix	Europe	96% (90%-99%)
Rotarix	Latin America	85% (72%-92%)
RotaTeq	Europe/US	98% (88%-100%)

Impact on All-Cause and Rotavirus-Specific Gastroenteritis Hospitalizations in USA



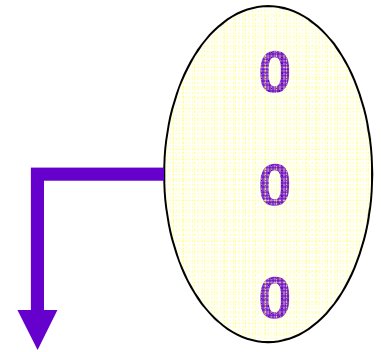
Impact on All-Cause and Rotavirus-Specific Gastroenteritis Hospitalizations in El Salvador

70-80% reduction in rotavirus hospitalizations children < 5 years



Herd Protection: Reduction in Rotavirus among UNVACCINATED Age Groups in El Salvador

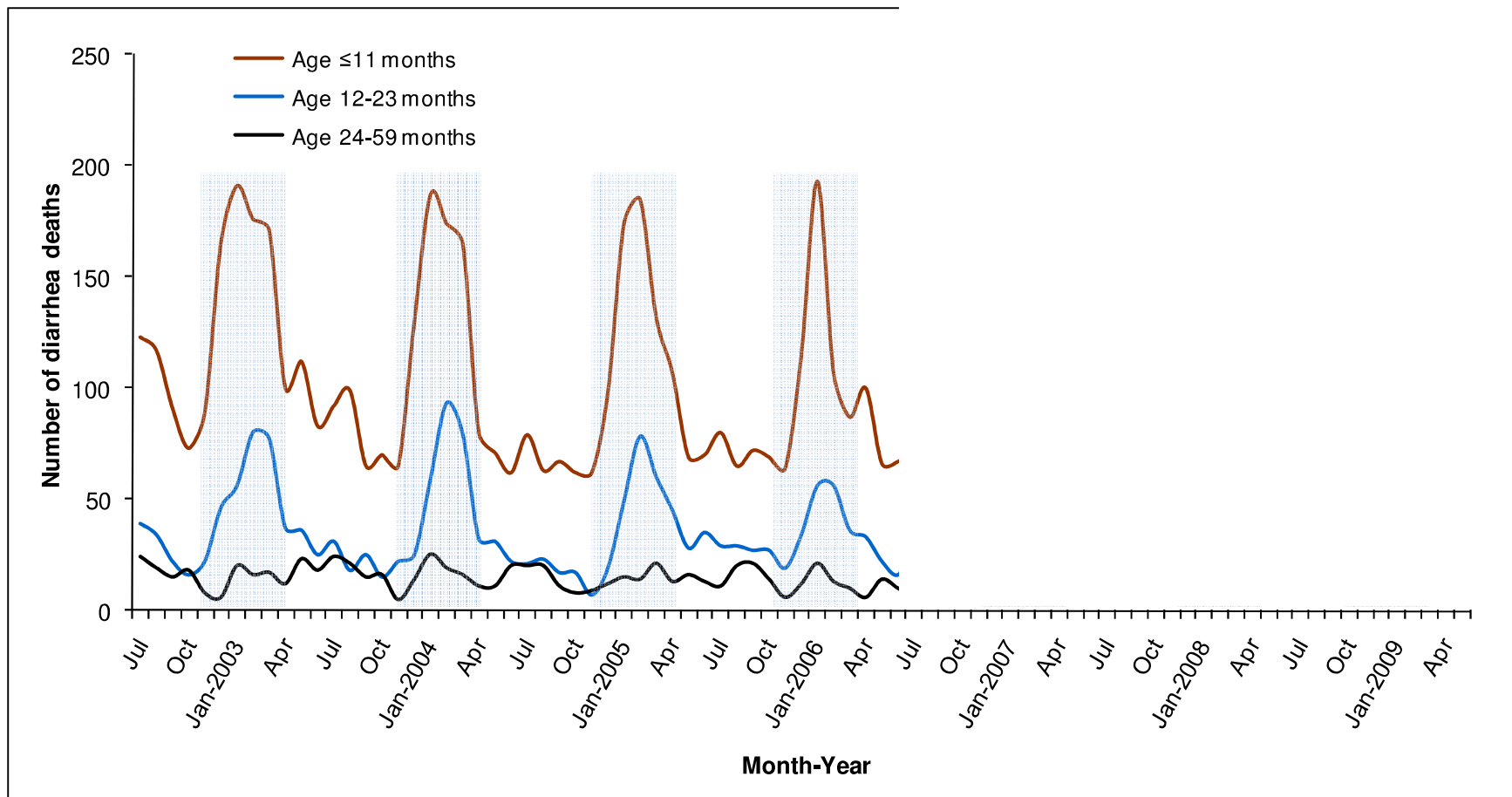
Age	Decline in rotavirus hospitalization rate (2008 vs. 2006)	Rotavirus vaccine coverage in 2008 (>=1 dose)
< 1 year	84% (80 to 88)	76%
1 year	86% (82 to 89)	84%
2 years	65% (50 to 75)	0
3 years	41% (-7 to 68)	0
4 years	68% (29 to 85)	0



These age cohorts were ineligible to receive rotavirus vaccine

ORIGINAL ARTICLE

Effect of Rotavirus Vaccination on Death from Childhood Diarrhea in Mexico



Early Experience with Rotavirus Vaccines



Borrowed from: http://dannybrown.me/wp-content/uploads/2011/01/success_baby.jpg

Challenge 1

How well will oral rotavirus vaccines work in the developing world?

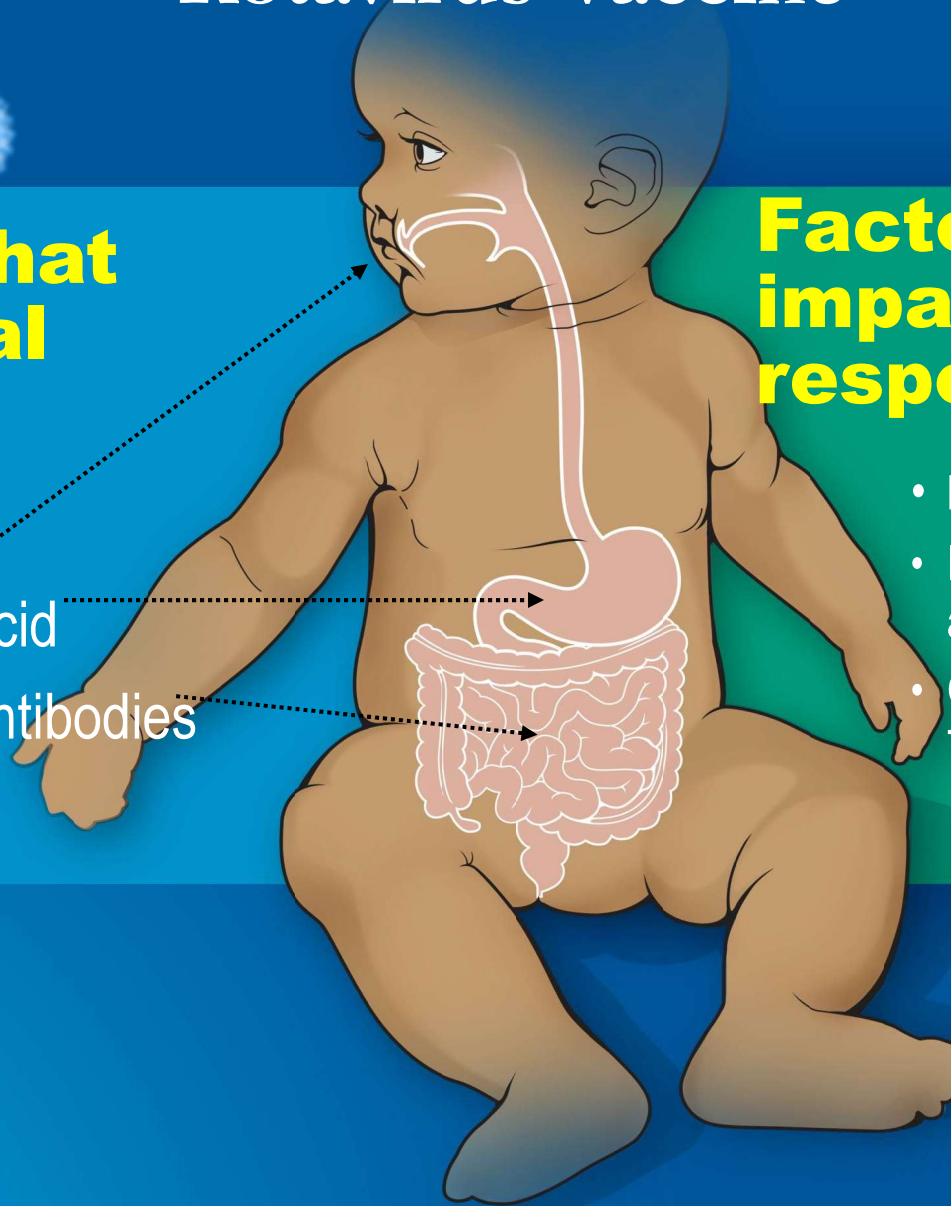
Hurdles to Immunization for a Live Oral Rotavirus Vaccine

Factors that lower viral titer

- Breast milk
- Stomach acid
- Maternal antibodies
- OPV

Factors that impair immune response

- Malnutrition - Zn, Vit A
- Interfering microbes- viruses and bacteria
- Other infections- HIV, malaria, TBC

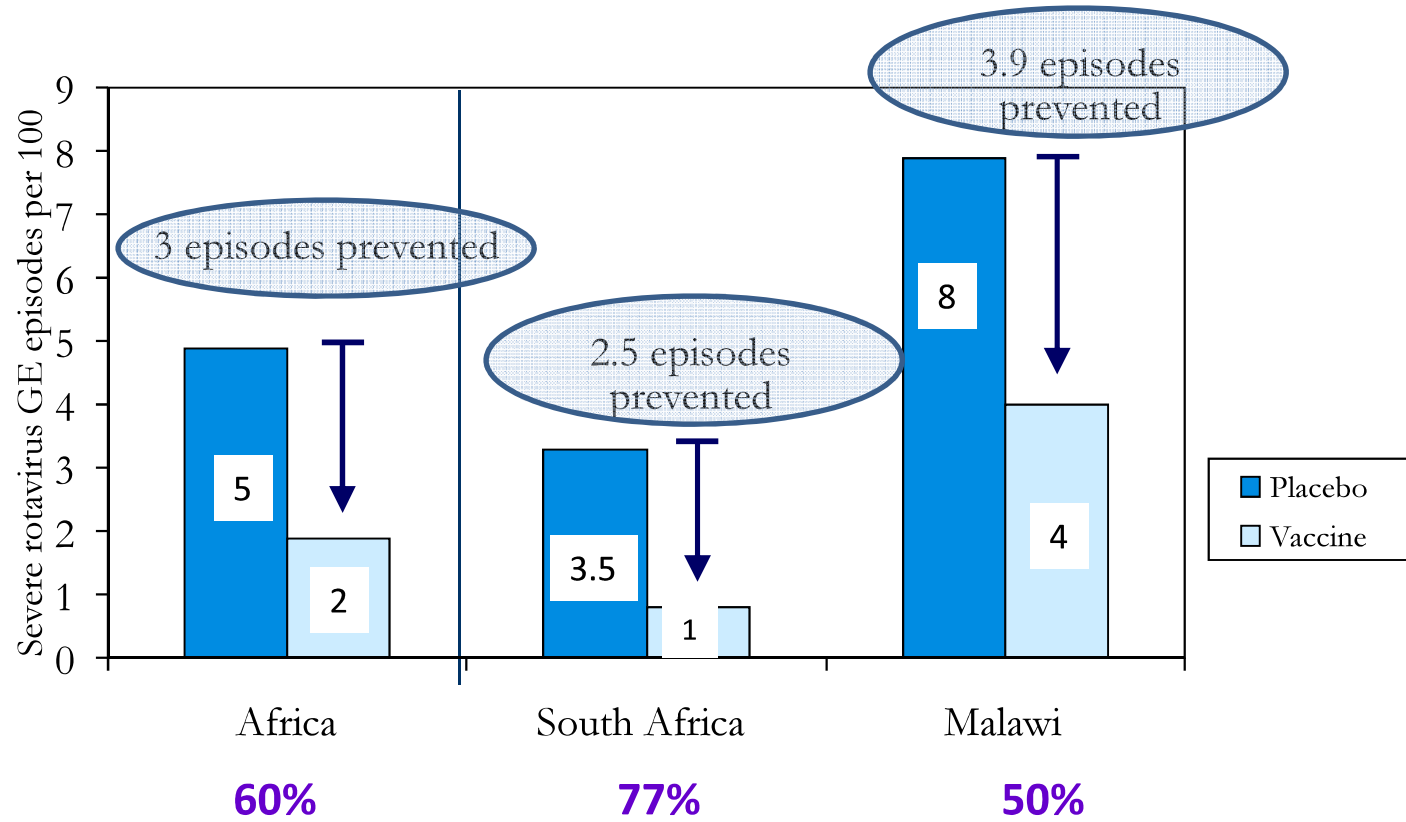


Moderate Efficacy of Rotavirus Vaccines in Africa and Asia

Vaccine	Region	Countries	Efficacy (95%CI)
RotaTeq	Africa	Ghana, Kenya, Mali	64% (40%-79%)
RotaTeq	Asia	Bangladesh, Vietnam	51% (13%-73%)
Rotarix	Africa	South Africa, Malawi	62% (44%-73%)

Armah et al. Lancet 2010
Zaman et al. Lancet 2010
Madhi et al NEJM 2010

Despite lower efficacy, Rotarix prevented more severe rotavirus disease per 100 vaccinated children in Malawi because of higher baseline incidence

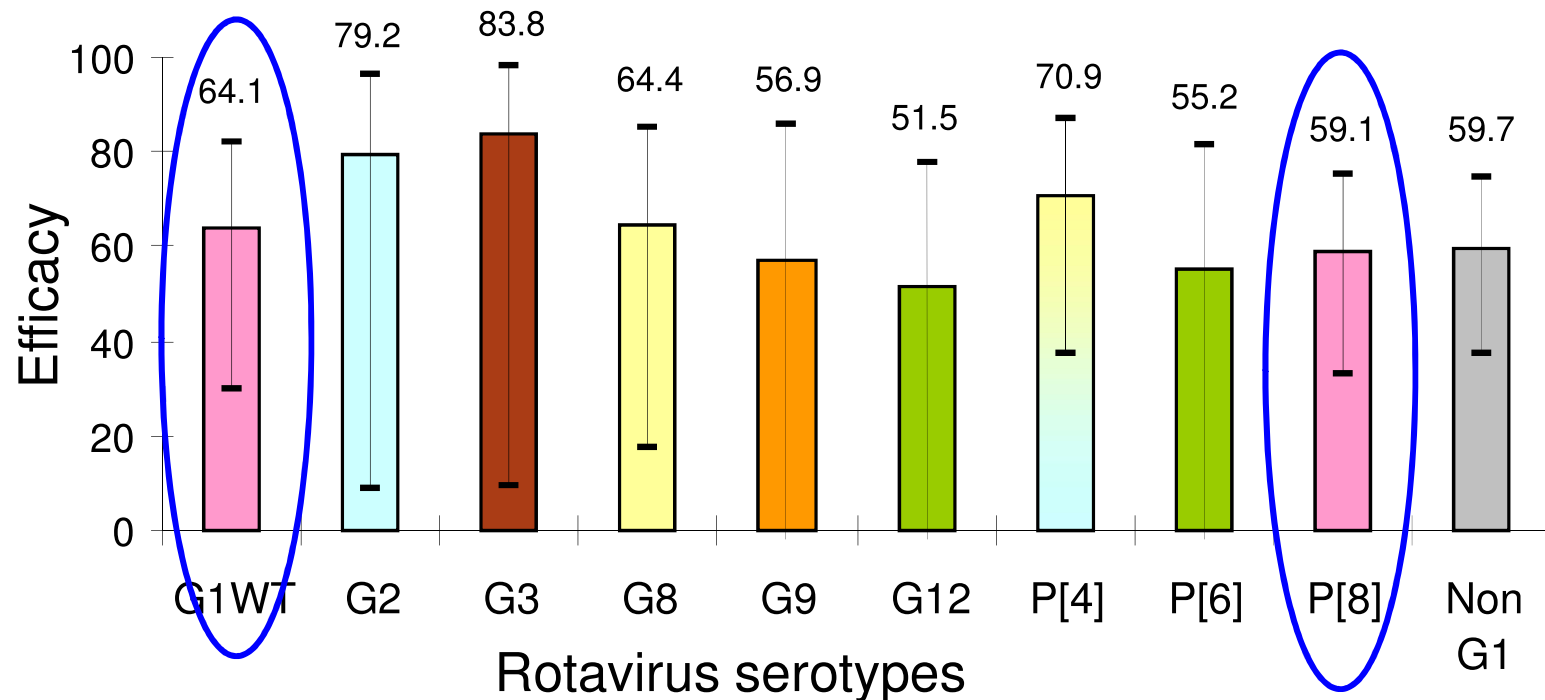


Challenge 2

**How well will vaccines protect
against range of strains?**

Rotarix (G1P8) efficacy similar against rotavirus GE due to vaccine & non-vaccine types in Africa

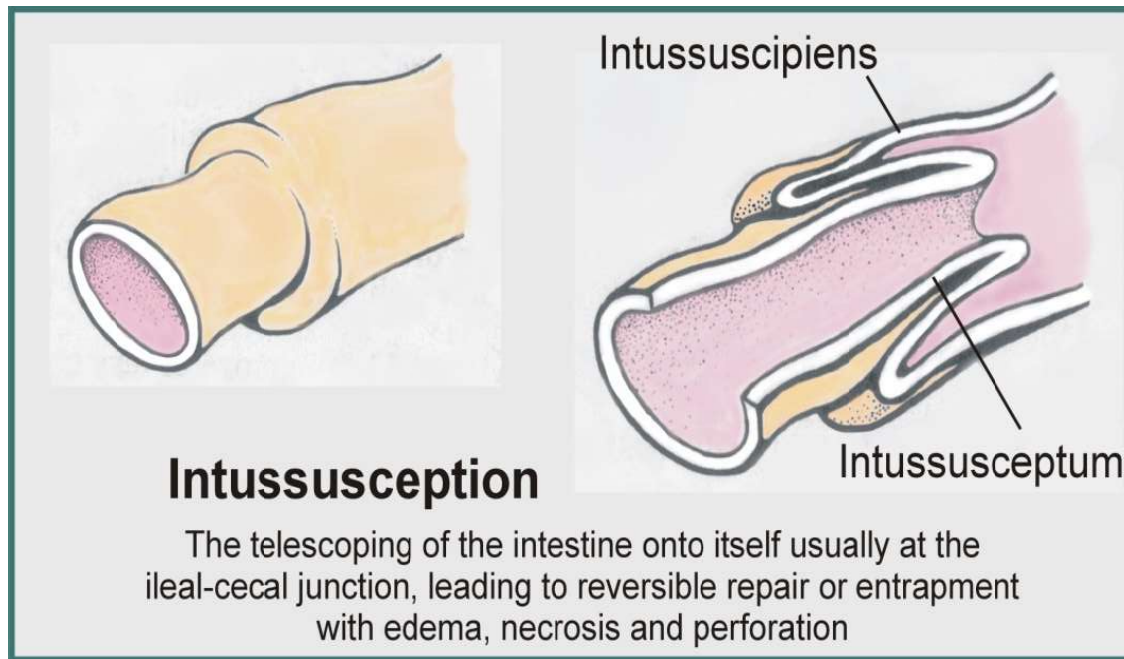
N = 2974 (Vaccine)
N = 1143 (Placebo)



Challenge 3

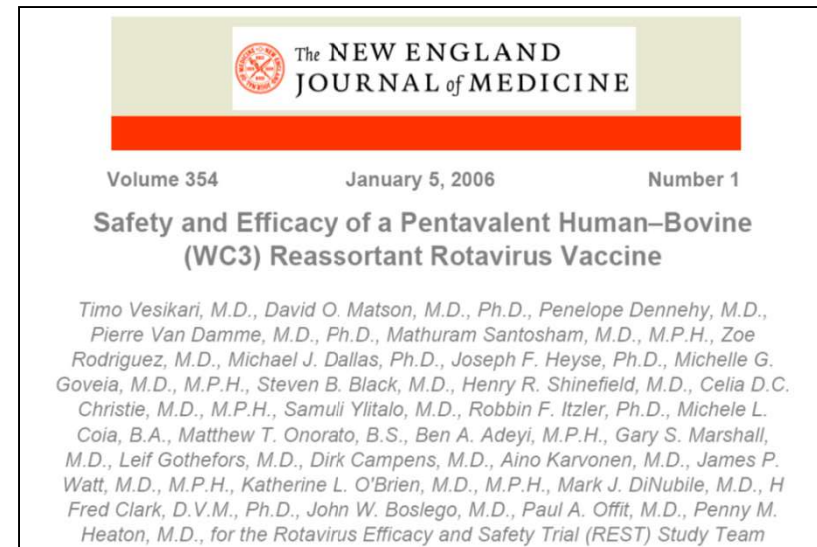
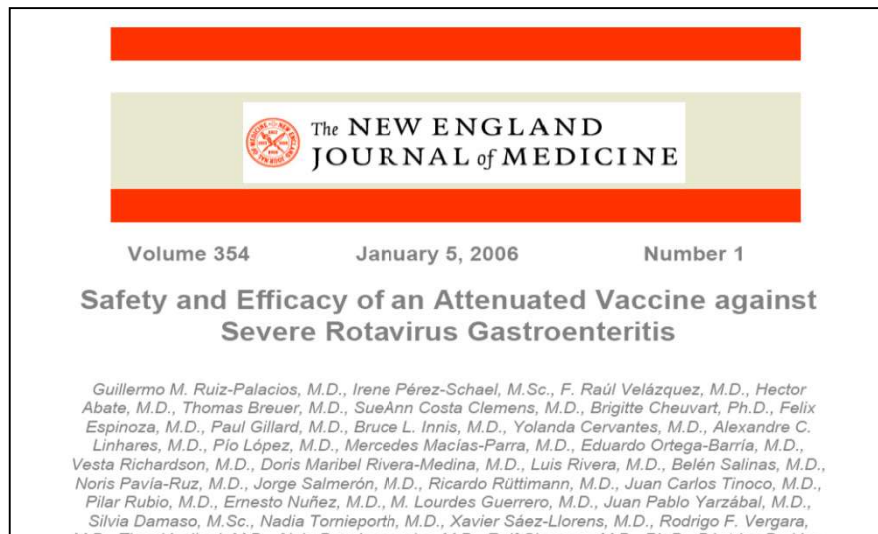
**Will new Rotavirus Vaccines
cause Intussusception?**

An Earlier Vaccine (Rotashield) Withdrawn in US in 1999 Because of Association with Intussusception



1 intussusception per 10,000 vaccinated infants

Current Vaccines Not Associated with Intussusception in Large Pre-Licensure Trials



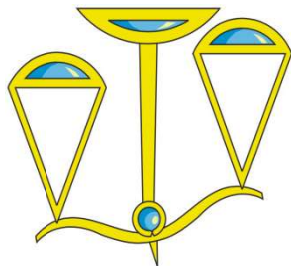
- Trials of 60-70,000 infants designed to assess intussusception risk
- No risk identified with either vaccine
- Low risk could not be excluded

Post-Licensure Intussusception Data

- Mexico, Brazil, Australia, and US have identified a low-level risk of intussusception after both vaccines
 - ~1-5 cases per 100,000 vaccinated
- *Key Question – How does this level of risk compare with the observed benefits?*

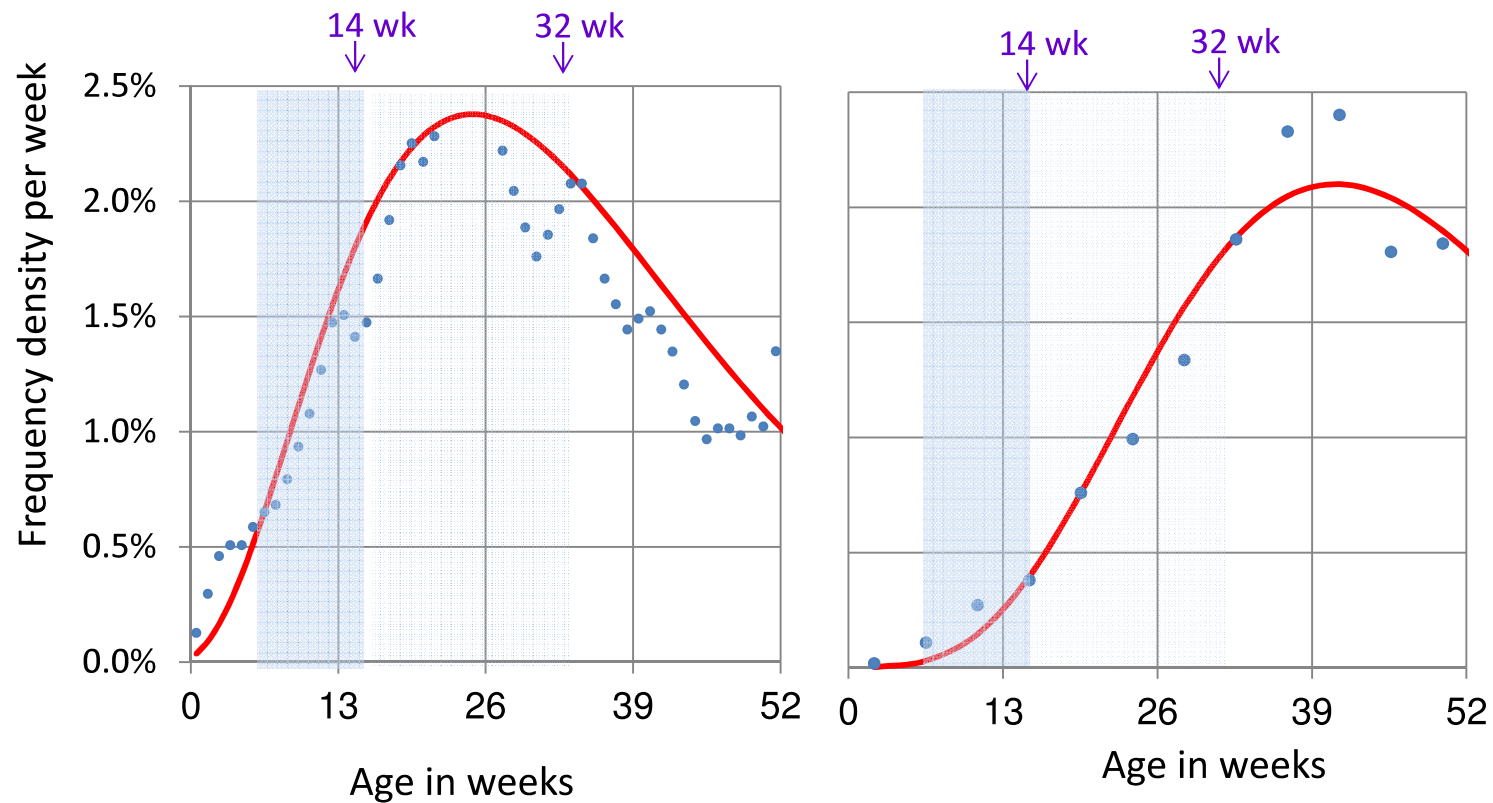
Mexico: Vaccination Benefit versus Risk

	Admissions	Deaths
Rotavirus events averted by vaccination	-12,000	-700
Intussusception events caused by vaccination	+43	+2
Rotavirus events averted vs. Intussusception caused	300 to 1	350 to 1



Challenge 4 -- Protecting Children in Early Infancy

Age Distribution of Rotavirus Hospitalizations in First Year of Life

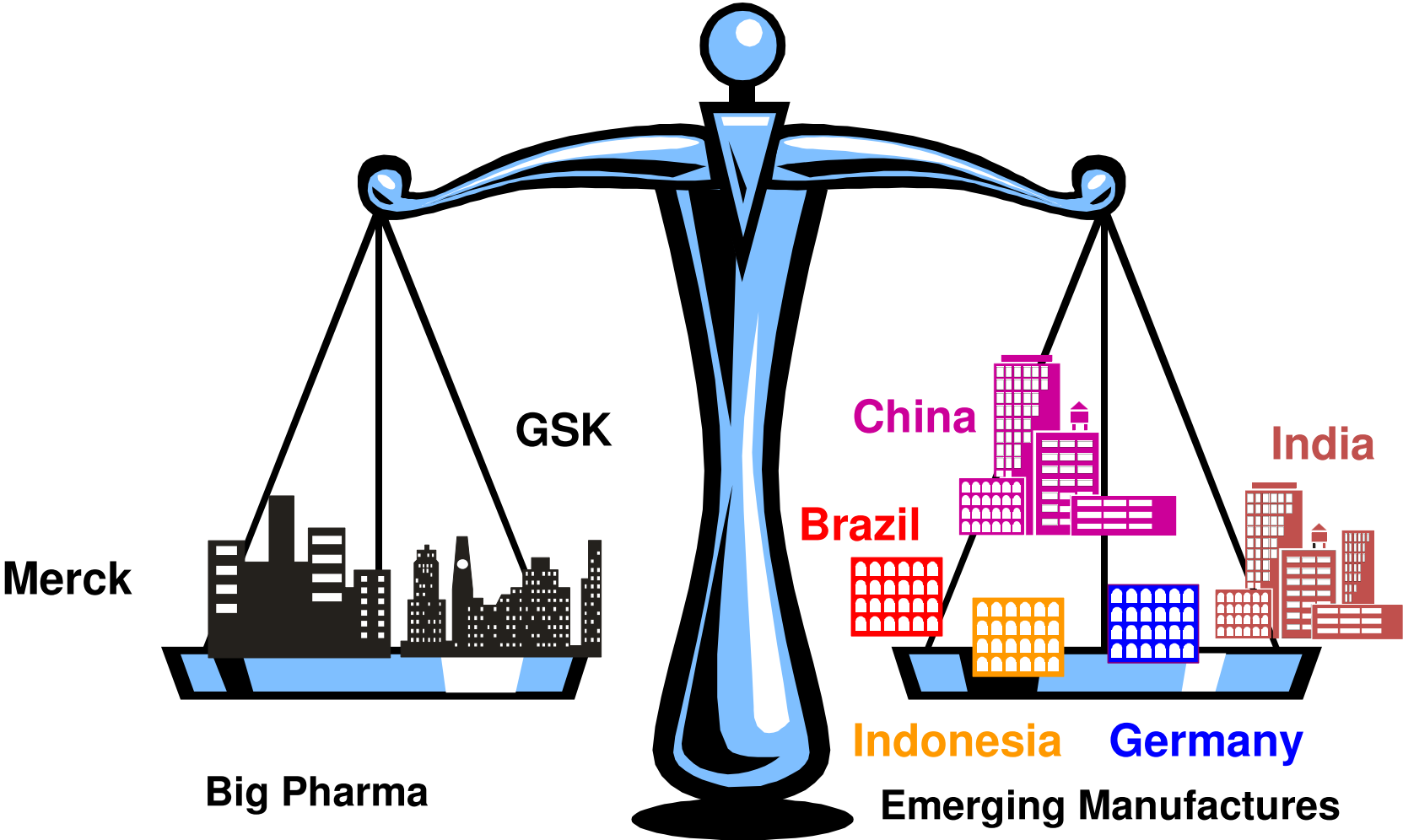


WHO

Blantyre, Malawi

Matlab, Bangladesh

Challenge 5 – Vaccine Supply



Challenge 6 -- Financing



Rotarix -- \$2.50 per dose
RotaTeq -- \$3.50 per dose

