# **Rotavirus vaccines: Issues not fully addressed in efficacy trials**



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### **Two New Rotavirus Vaccines Licensed in 2006**





#### •Trials of 60-70,000 infants each

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

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

## **National RV introductions, 77 countries\***



# How well will vaccines perform in routine use?

### **Rotavirus Vaccines in USA**

- Feb 2006 RotaTeq recommended
- June 2008 Rotarix recommended



### High Effectiveness of RotaTeq against Severe Rotavirus Disease

	Study 1	Study 2	Study 3	Study 4	Study 5
	Boom et al,	Staat et al,	Cortese et al,	Payne et al,	Cortese et al,
	2010	2011	2011	2013	2013
3 doses	<b>89%</b>	<b>87%</b>	<b>90%</b>	<b>84%</b>	<b>92%</b>
	(70, 96)	(71, 94)	(84, 94)	(78, 98)	(75, 97)
2 doses	<b>82%</b>	<b>88%</b>	<b>90%</b>	<b>78%</b>	<b>84%</b>
	(15, 96)	(66, 96)	(75, 96)	(65, 86)	(1, 99)
1 dose	65% (-11, 89)	<b>74%</b> (37, 90)	<b>66%</b> (16, 86)	<b>70%</b> (50, 82)	NA



#### **Sustained RotaTeq Effectiveness Over 4 Years of Life**



Payne DC, et al. Clin Infect Dis 2013

#### All Cause Acute Gastroenteritis (AGE) and Rotavirus AGE Hospitalizations, NVSN 2006-2013



Payne DC, et al. Clin Infect Dis 2011

## Age-Specific Rotavirus Hospitalization Rate Reduction and Vaccine Coverage, USA

Age	Decline in rotavirus hospitalization rate (2008 vs. 2006)	Rotavirus vaccine coverage in 2008 (>=1 dose)	
< 1 year	66%	56%	
1 -< 2 years	95%	44%	
2 -< 3 years	85%	<1%	
This age to rece	e cohort was ineligible eive rotavirus vaccine	Herd Protection	

#### Reduction in Gastroenteritis Hospitalizations in Older Children and Young Adults



Gastanaduy et al JAMA 2013

## Will vaccination save lives?

# First evidence of impact of vaccine on diarrhea mortality in Mexico





#### Effect of Rotavirus Vaccination on Death from Childhood Diarrhea in Mexico



Richardson et al, NEJM 2010

# Mortality decline sustained for four years post vaccine implementation in Mexico



## How well will live 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

### Rotavirus vaccines prevent more disease, despite lower vaccine efficacy, in higher burden settings



Madhi, NEJM 2010

## **GAVI-supported RV introductions, 35 countries**<sup>\*</sup>



## **South Africa**

• Introduced monovalent rotavirus vaccine (Rotarix, RV1) in August 2009



#### Monthly count of diarrhea hospitalizations among children <5 years of age, Soweto, South Africa, 2006-2013





Slide from Michelle Groome

## Rwanda

 Introduced pentavalent rotavirus vaccine (RotaTeq, RV5) in May 2012



Number of Diarrhea Hospitalizations among Children <5 Years of Age, 27 District Hospitals, January 2009 – March 2014, Rwanda Health Management Information System



#### Total Hospital and AGE Admissions among Children <5 Years of Age, 6 Hospitals



#### Rotavirus Positivity by Age Group for Pre-Vaccine Introduction (2011) and Post-Vaccine Introduction (2013)



#### Rotavirus Positivity by Age Group for Pre-Vaccine Introduction (2011) and Post-Vaccine Introduction (2013)



# How well will vaccines protect against range of strains?

### **RotaTeq is Pentavalent & Rotarix is Monovalent**

#### RotaTeq



Five bovine-human rotavirus strains

#### **Rotarix**



## Single human rotavirus strain

## High Rotarix (G1P8) Effectiveness against Non-Vaccine Strains in Several Countries

Country	Post-vaccine	Vaccine Effectiveness
	strains	(95% CI)
Brazil	G2P[4]	85% (54, 95)

## High Rotarix (G1P8) Effectiveness against Non-Vaccine Strains in Several Countries

Country	Post-vaccine strains	Vaccine Effectiveness (95% CI)
Brazil	G2P[4]	85% (54, 95)
Mexico	G9P[4]	94% (16, 100)

## High Rotarix (G1P8) Effectiveness against Non-Vaccine Strains in Several Countries

Country	Post-vaccine strains	Vaccine Effectiveness (95% CI)
Brazil	G2P[4]	85% (54 <i>,</i> 95)
Mexico	G9P[4]	94% (16, 100)
Bolivia	G9P[8]	84% (64 <i>,</i> 92)
	G2P[4]	71% (19 <i>,</i> 90)
	G3P[8]	92% (60, 98)
	G9P[6]	87% (-10, 98)

### **Key Messages**

Marked impact in affluent countries

- Indirect benefits to unvaccinated groups
- Impact on diarrhea mortality
- Efficacy lower in low income settings
  - But impact greater because of high burden
  - Promising early data from African countries
- Both vaccines show broad protection against strains included and not included in vaccine