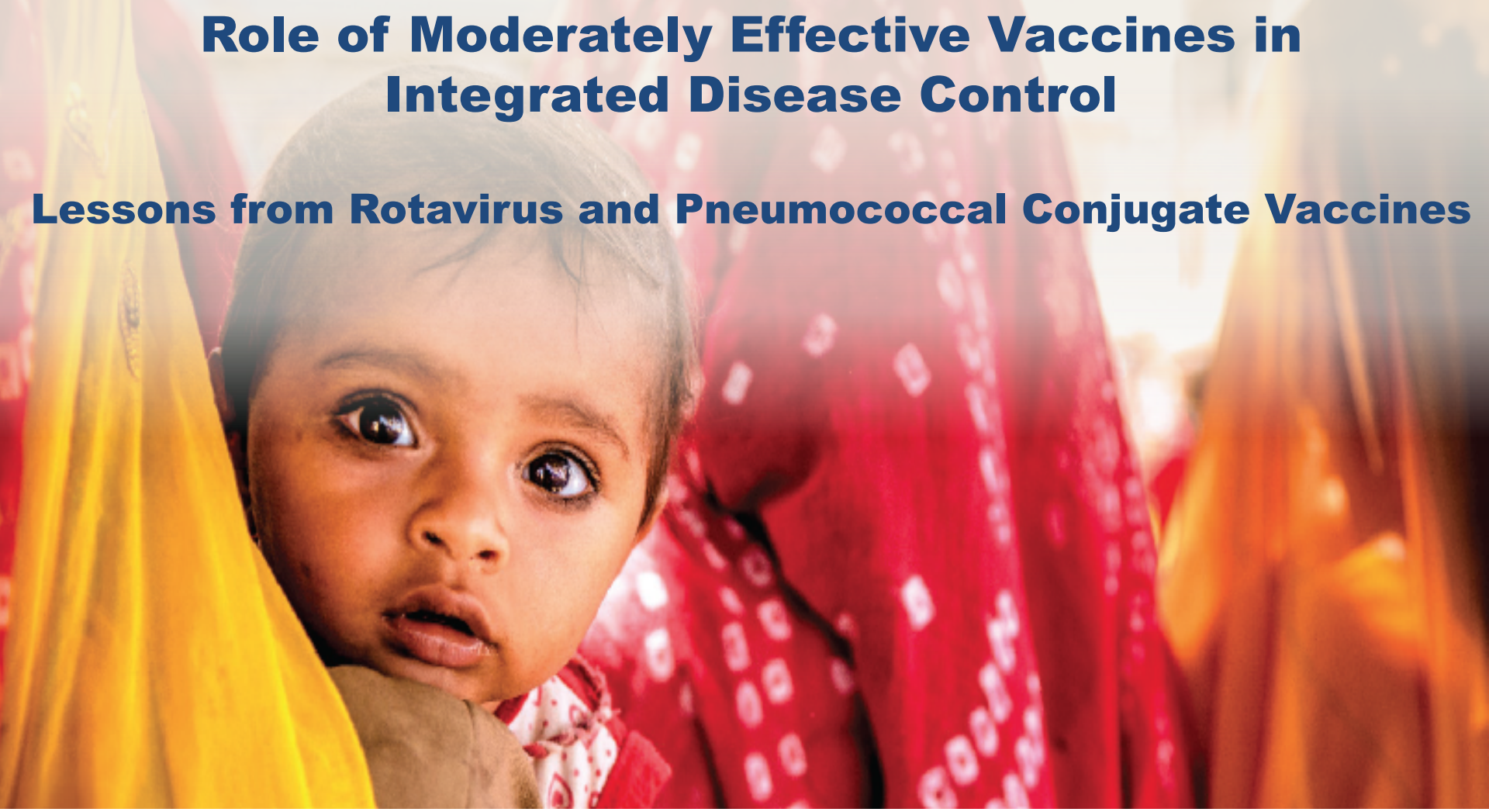
Role of Moderately Effective Vaccines in Integrated Disease Control

Lessons from Rotavirus and Pneumococcal Conjugate Vaccines

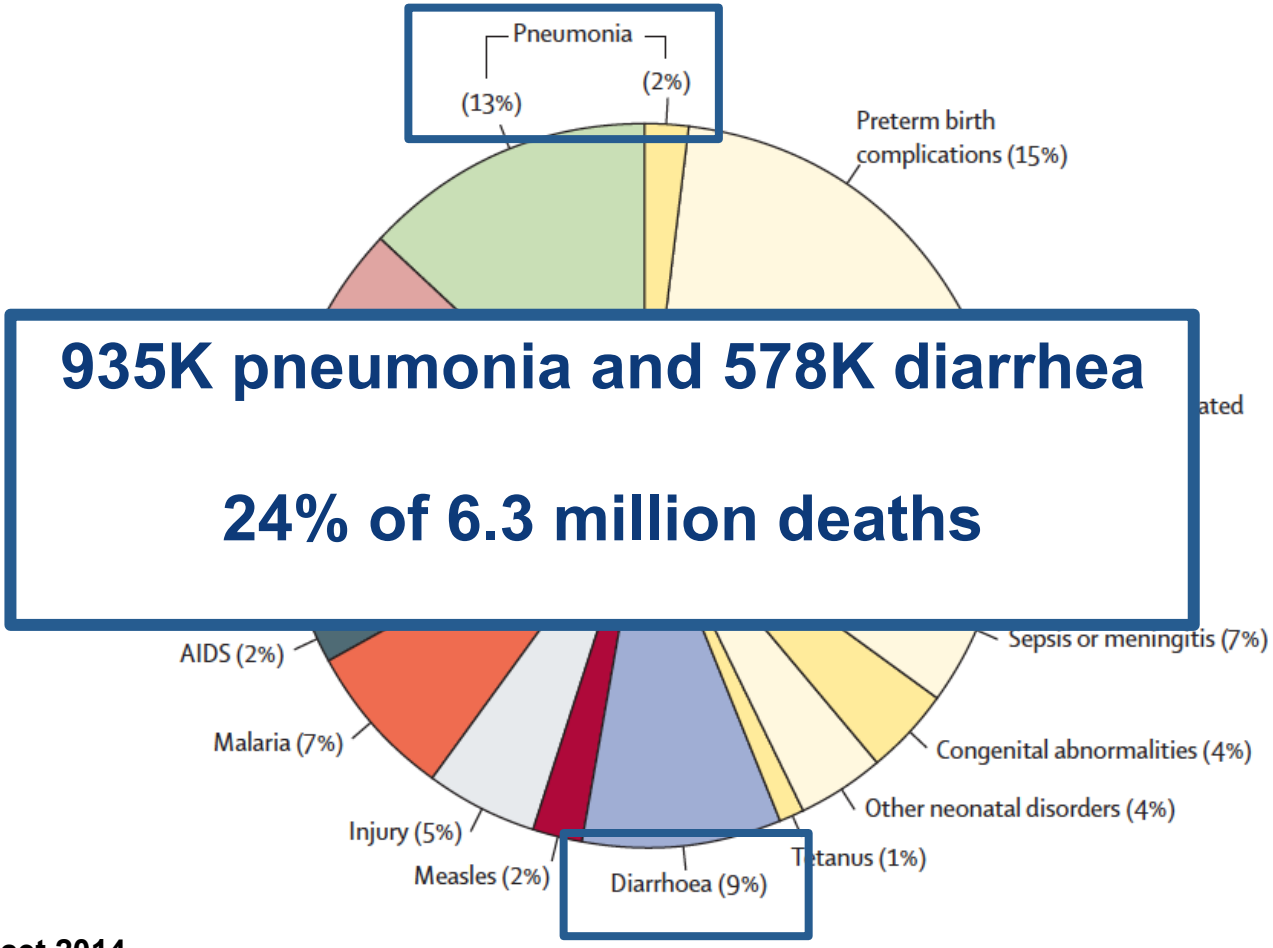


Kate O'Brien, MD, MPH
Professor, Johns Hopkins Bloomberg School of Public Health
International Vaccine Access Center

Global Vaccine and Immunization Research Forum | Johannesburg, South Africa
March 15, 2016

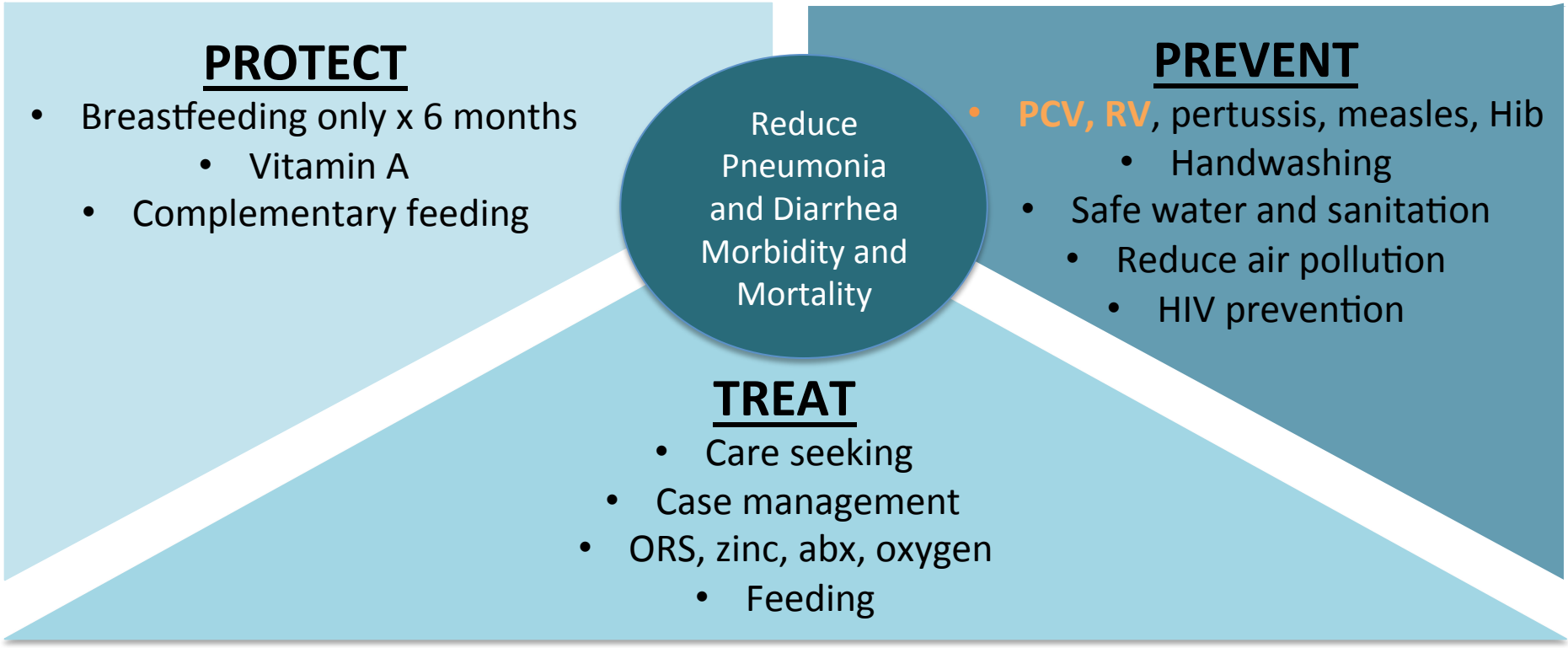
Pneumonia & diarrhea most common causes of death

2013 Causes of Death in Children 0-59 mo.



Liu et al. Lancet 2014

Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea (GAPPD)



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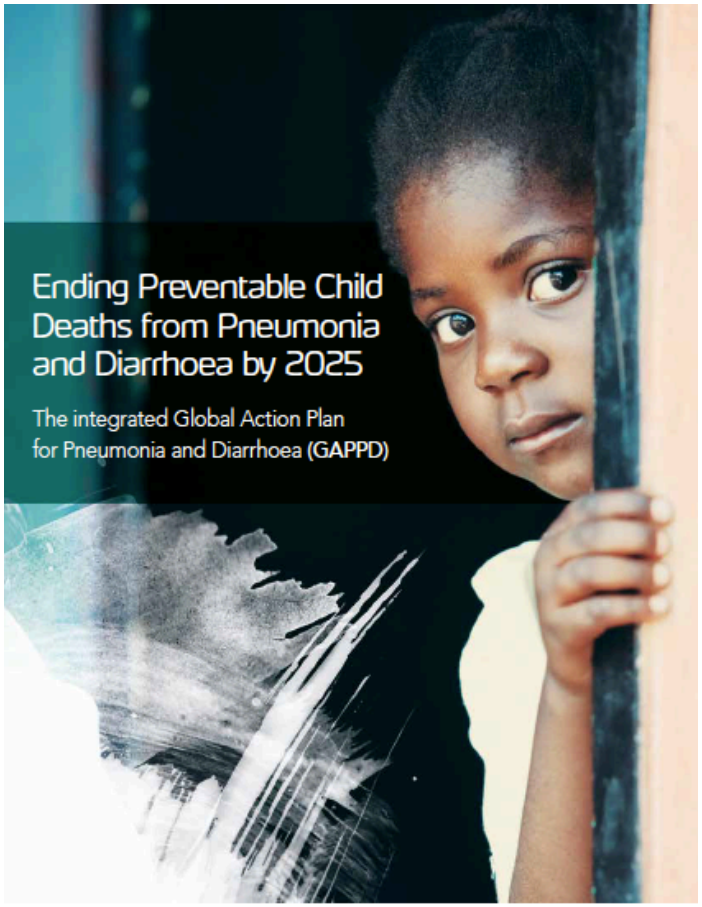
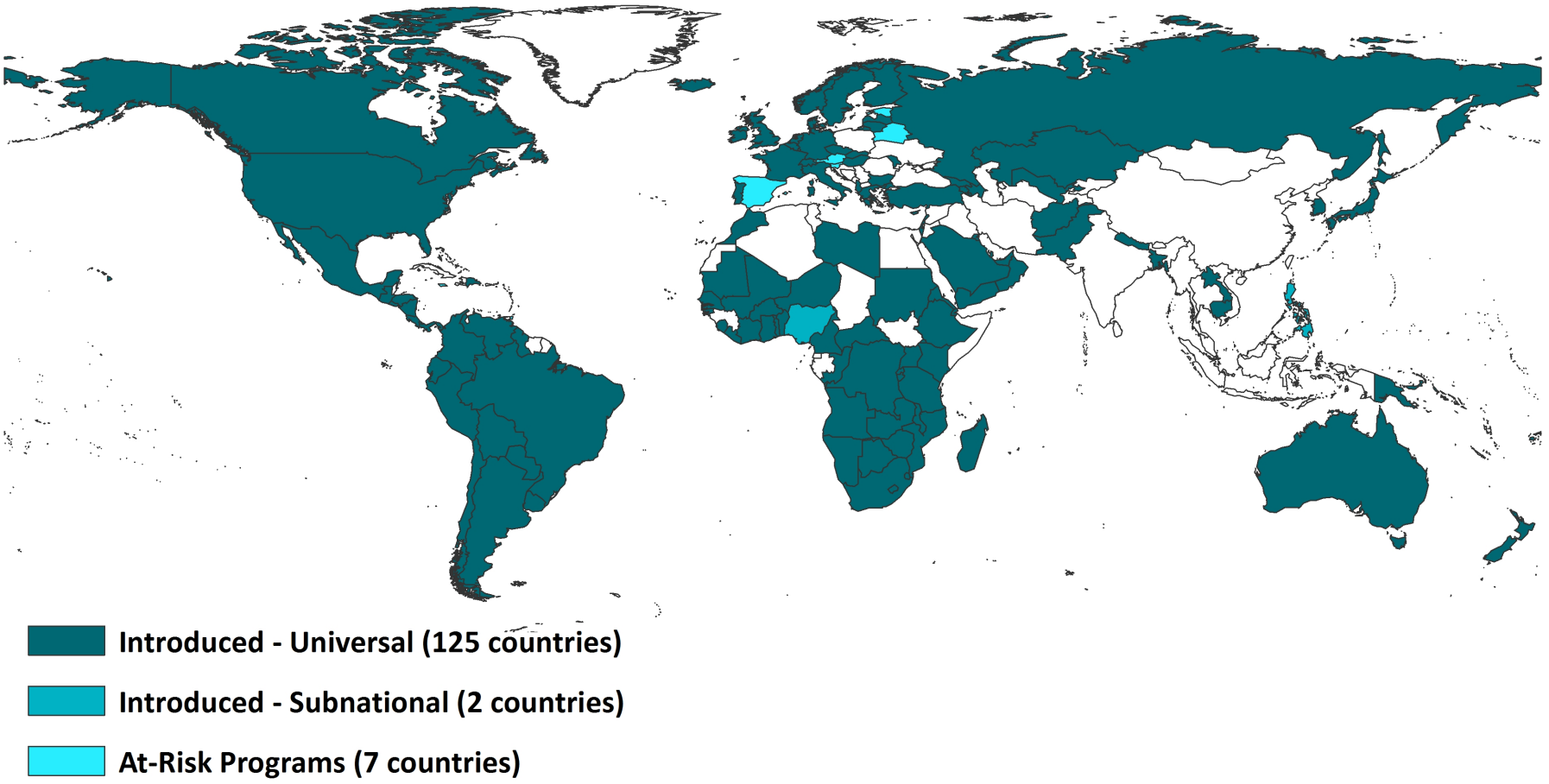


- **By 2025**
  - **Pneumonia mortality <3/1,000 live births**
  - **Diarrhea mortality <1/1,000 live births**
- **To get there**
  - **90% vaccine coverage**
  - **90% care and treatment coverage**
  - **50% exclusive breast feeding to 6 mo.**
  - **Elimination of pediatric HIV**

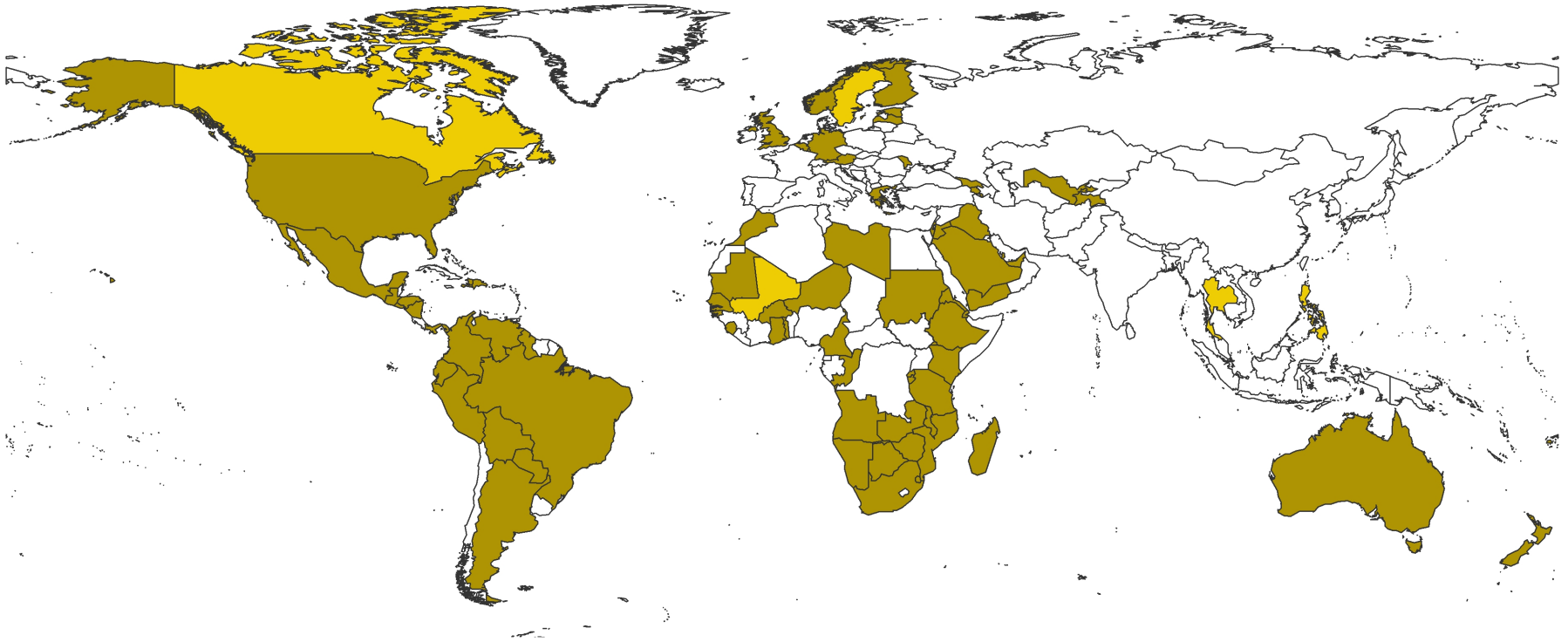
WHO/UNICEF (2013) http://www.who.int/maternal_child_adolescent/documents/global_action_plan_pneumonia_diarrhoea/en/index.html

Substantial Progress on Global PCV Introduction



Source: International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. Vaccine Information Management System (VIMS) Global Vaccine Introduction Report, December 2015.

Progress on Global Introduction of Rotavirus Vaccine

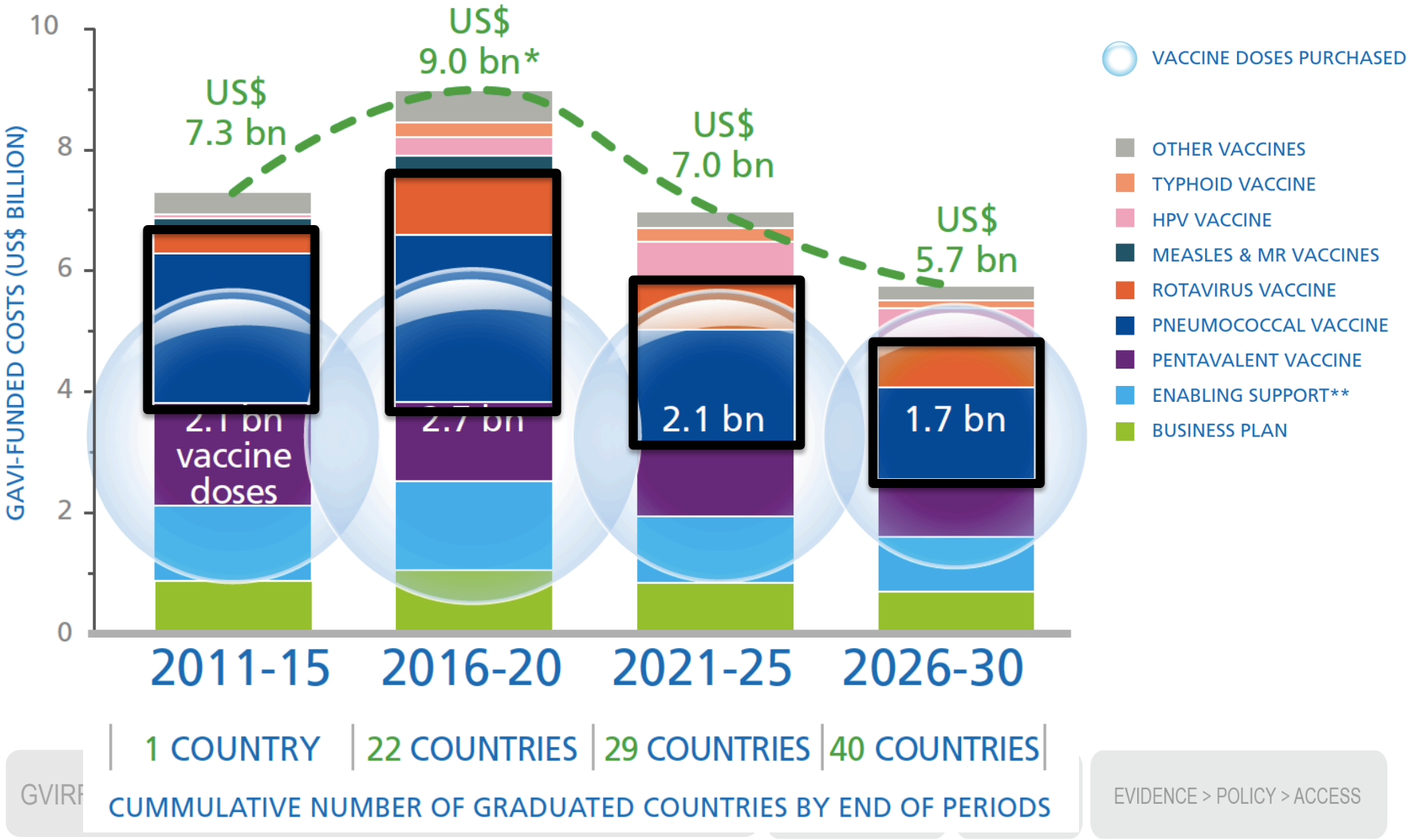


Introduced - Universal (80 countries)

Introduced - Subnational (5 countries)

Source: International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. Vaccine Information Management System (VIMS) Global Vaccine Introduction Report, December 2015.

PCV and Rota Vaccine Substantial "Spends" for Gavi



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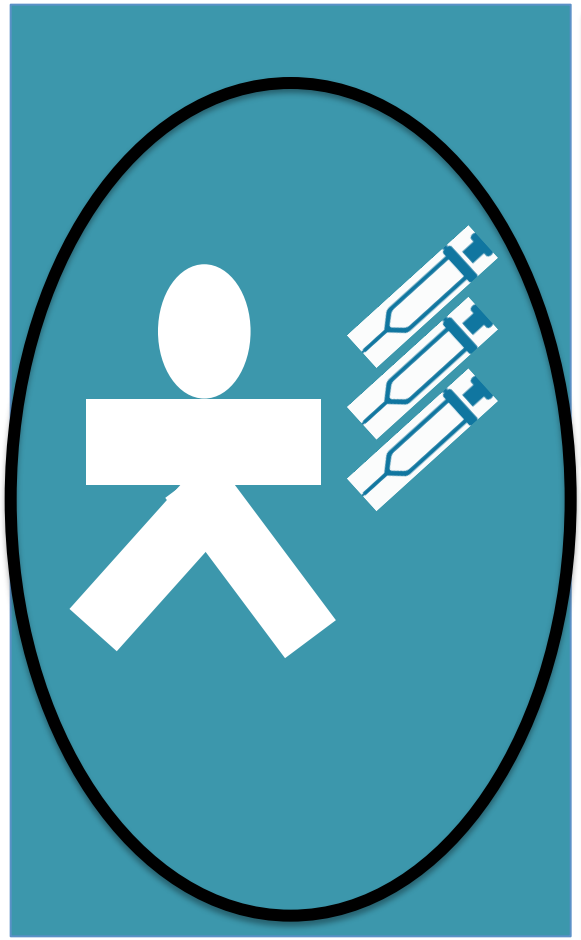
Vaccine Efficacy (%) led to Licensure



VE= % reduction

PCV: 96%
VT- IPD

RV: 85-98%
Rotavirus hosp. diarrhea

Safety=Benefit/Risk

PCV: % IPD that is VT

Rota : Intussusception

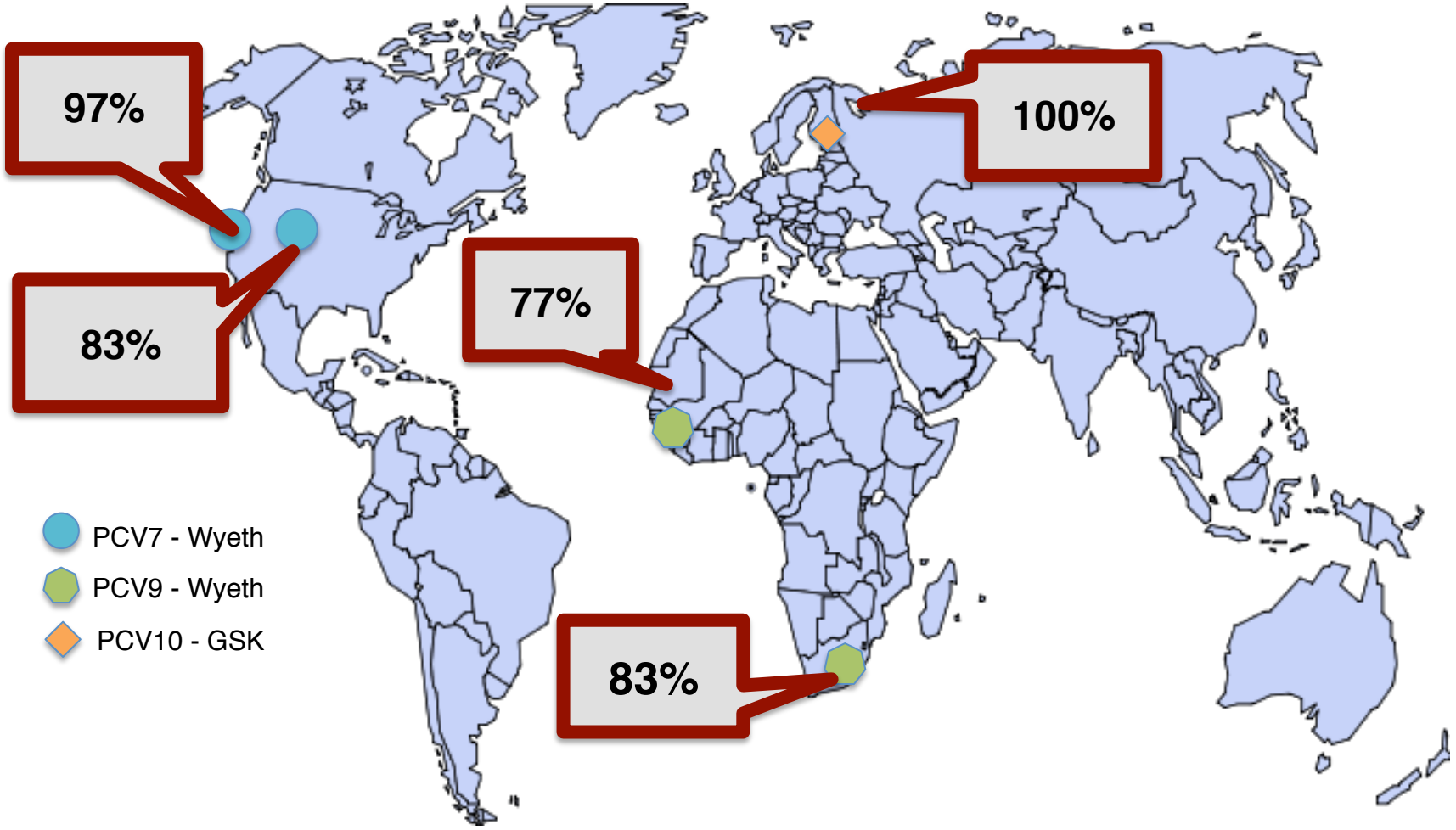
High Efficacy of Rotavirus Vaccines in High/Middle Income Country Trials

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

Vesikari et al and Ruiz-Palacios et al, NEJM 2006
Vesikari et al, Lancet, 2007.

High PCV Efficacy Against VT- Invasive Pneumococcal Disease

Multiple clinical trials

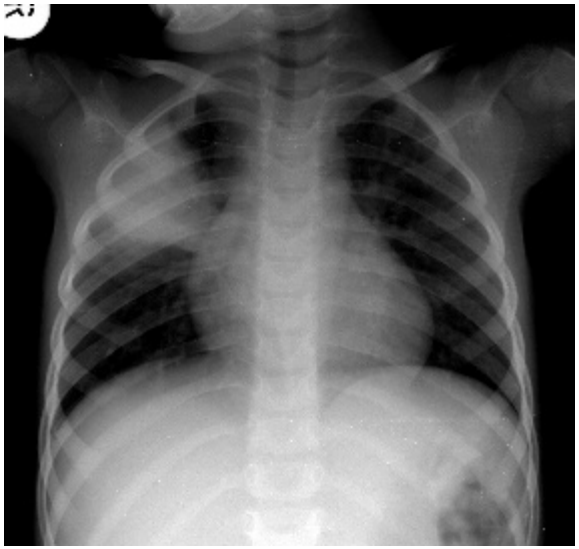


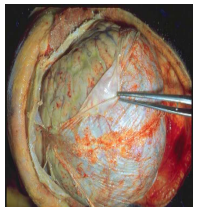
Moderate Efficacy of Rotavirus Vaccines in Africa & Asia

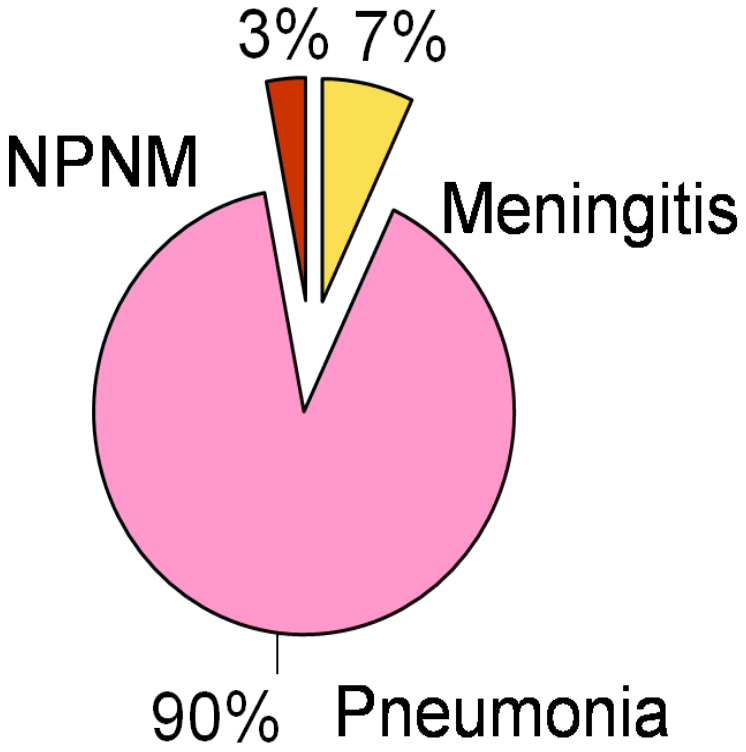
Vaccine	Region	Countries	Efficacy (95%CI)
Rotarix	Africa	South Africa, Malawi	62% (44%-73%)
RotaTeq	Africa	Ghana, Kenya, Mali	64% (40%-79%)
RotaTeq	Asia	Bangladesh, Vietnam	51% (13%-73%)

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

Pneumococcal Deaths by Syndrome



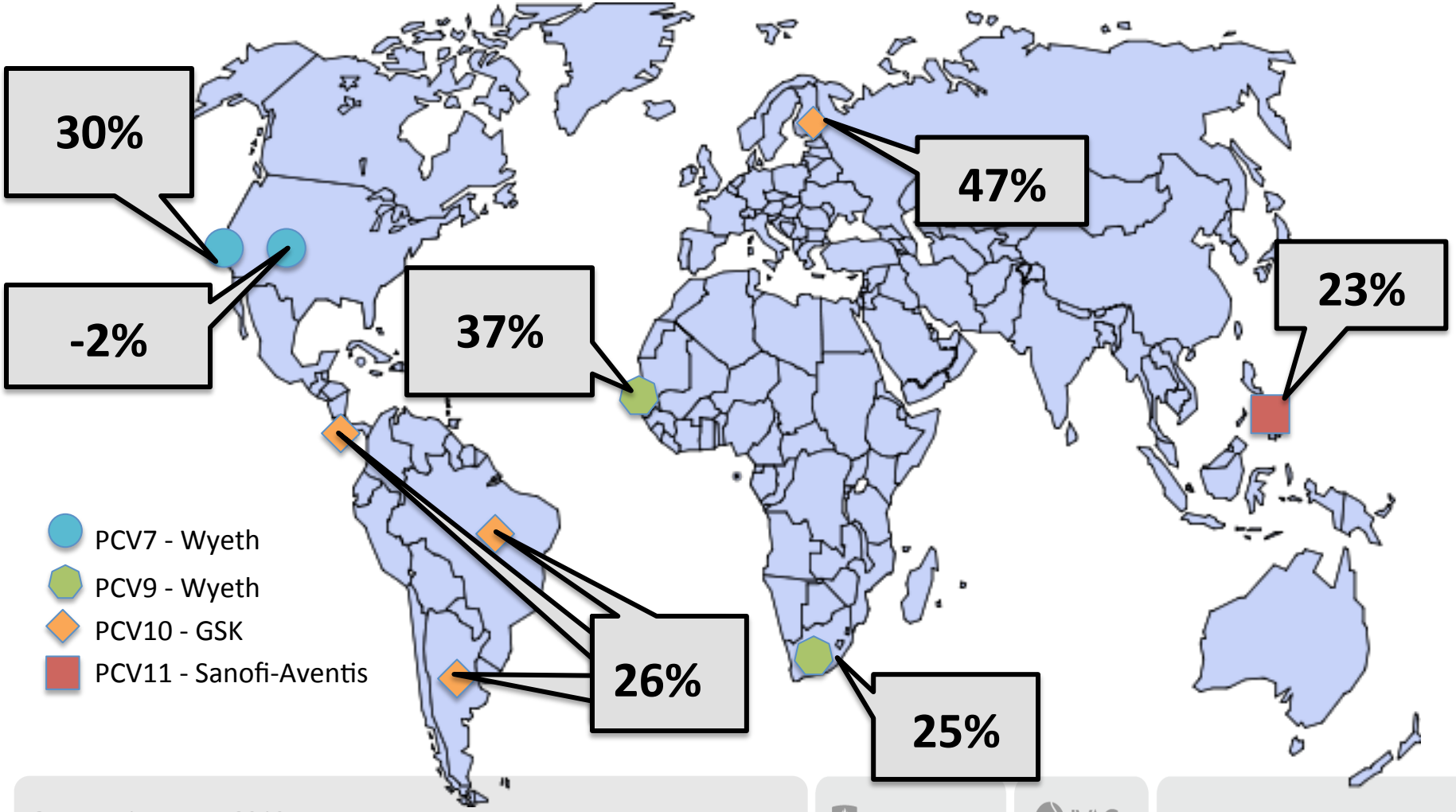




HIV (+) deaths included

O'Brien KL Lancet 2009

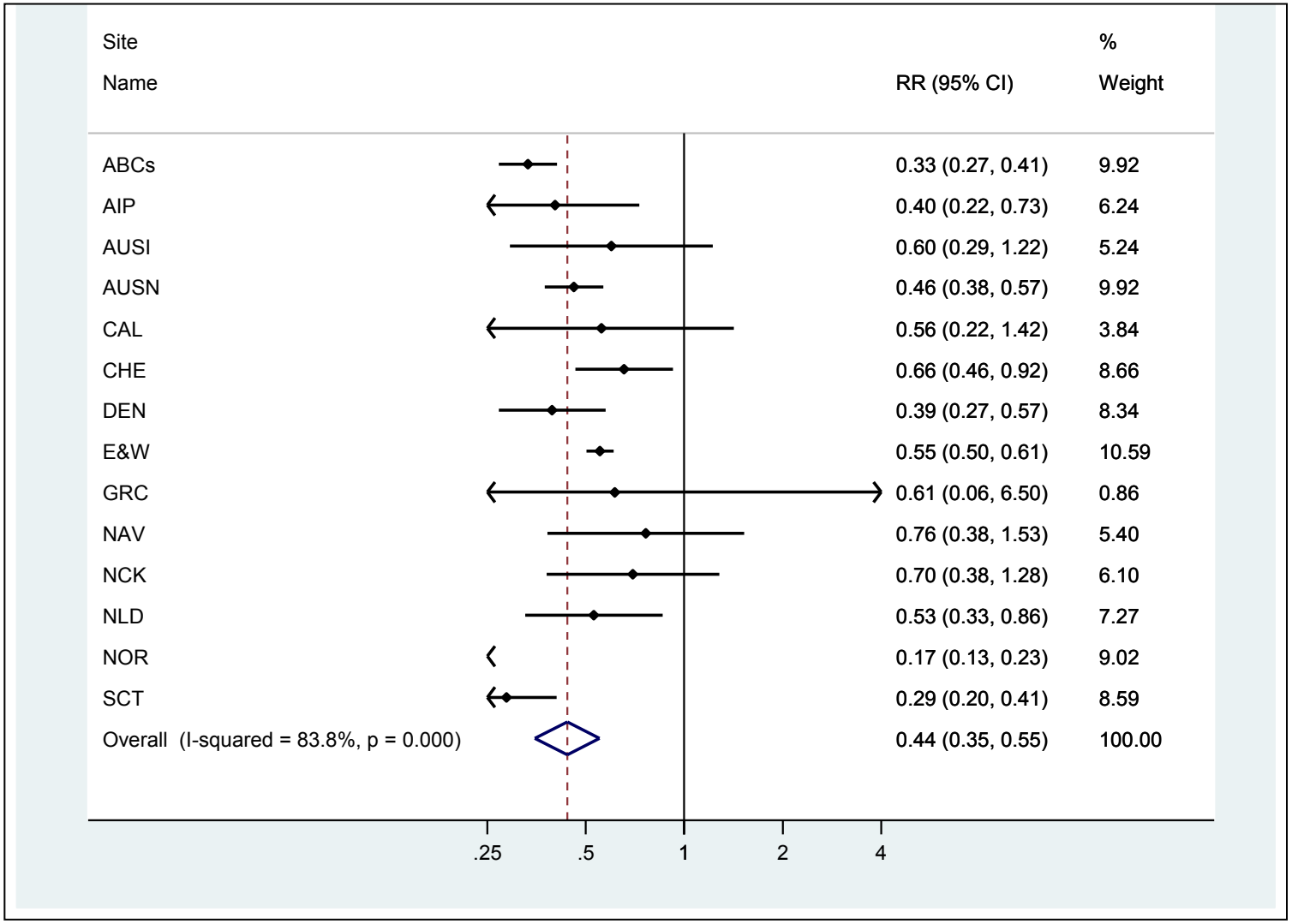
Moderate PCV Efficacy Against CXR (+) Pneumonia



60% Effectiveness of PCV against All-Serotype IPD

Meta-analysis of all serotype RRs

Children <5 years old, Year 3 post-PCV7 introduction



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2. What role should vaccine preventable disease incidence (VPDI), transmission and indirect impact play in valuation of vaccines ?

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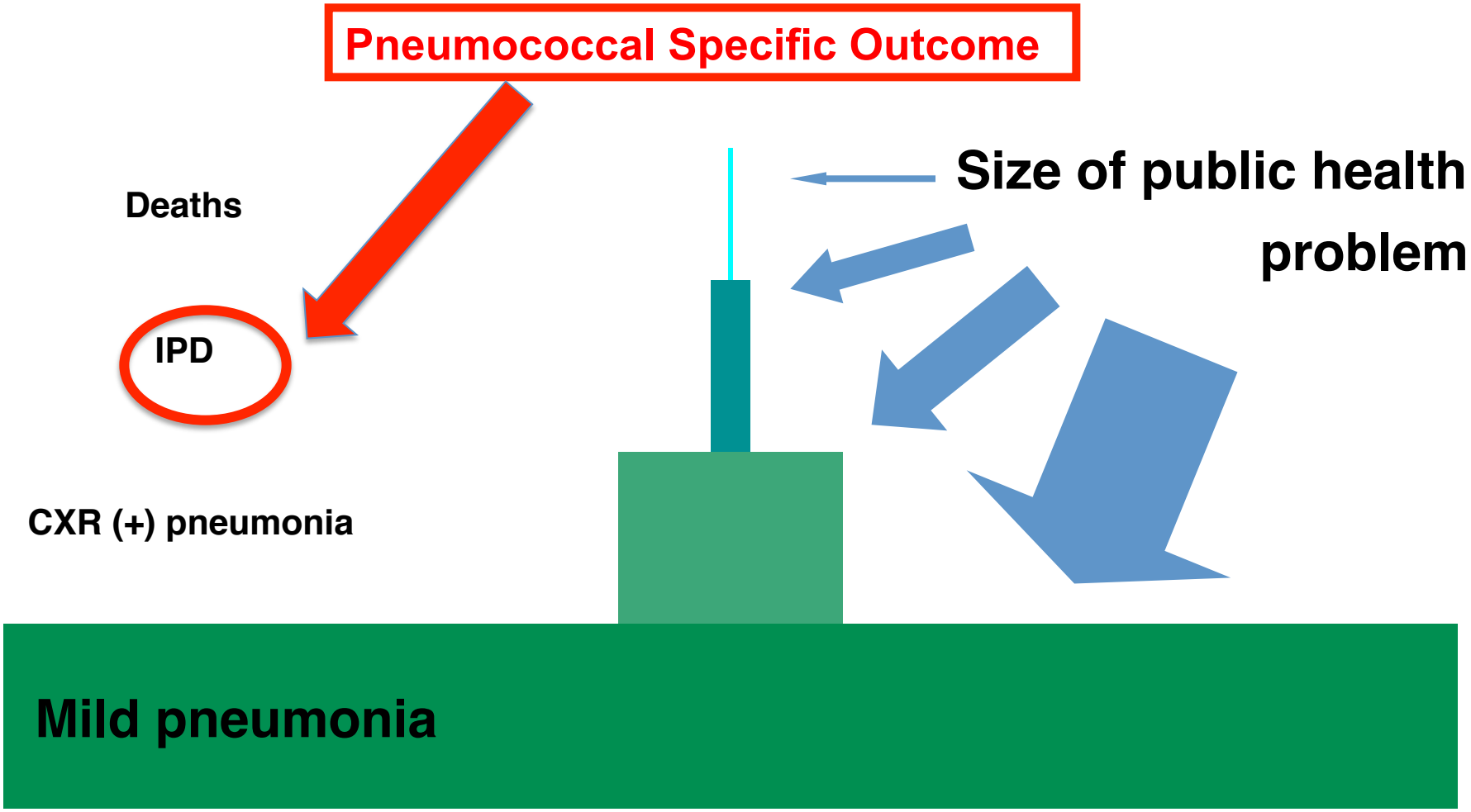
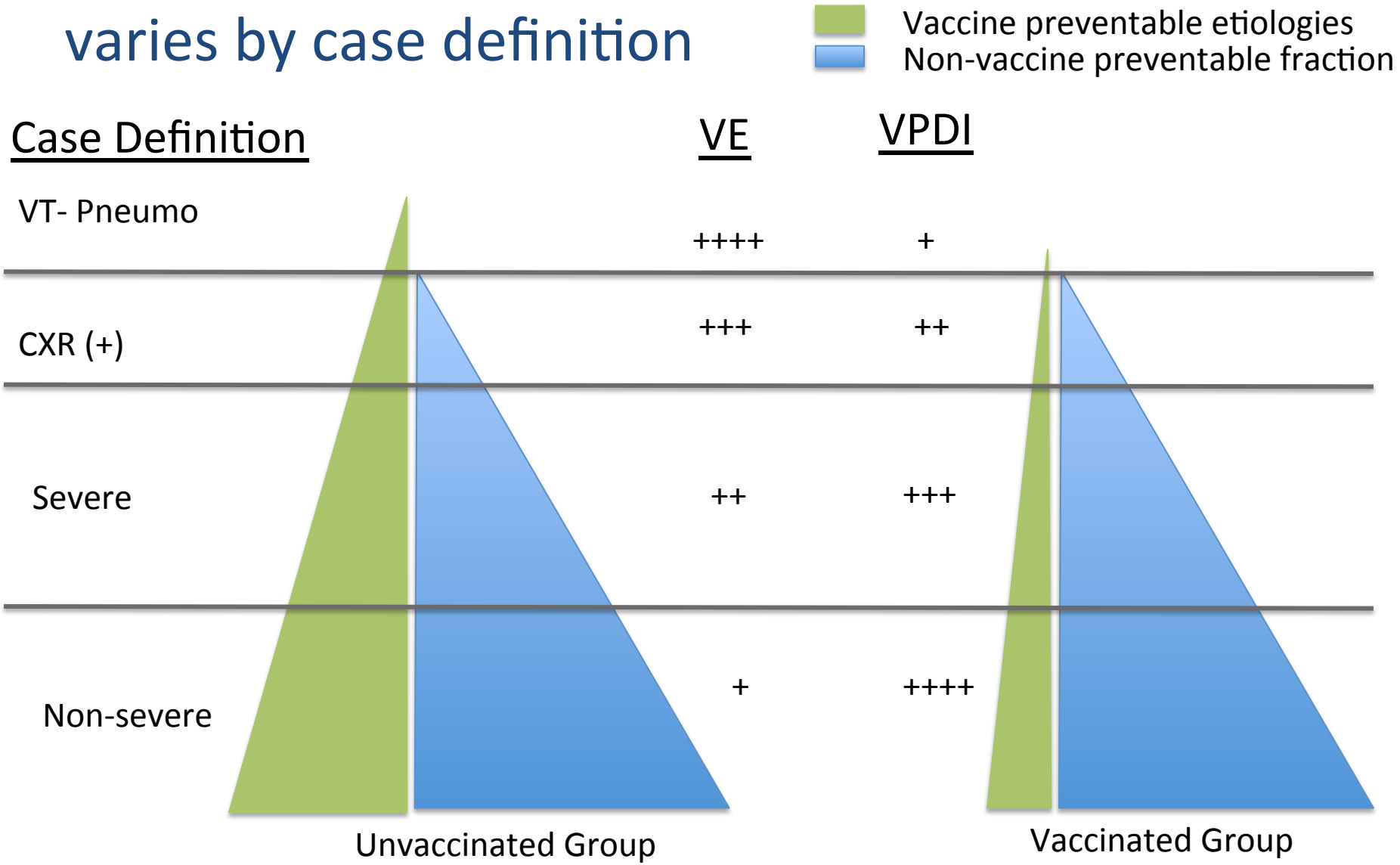
What disease outcomes can be measured for PCV impact?



Impact of PCV against pneumonia varies by case definition



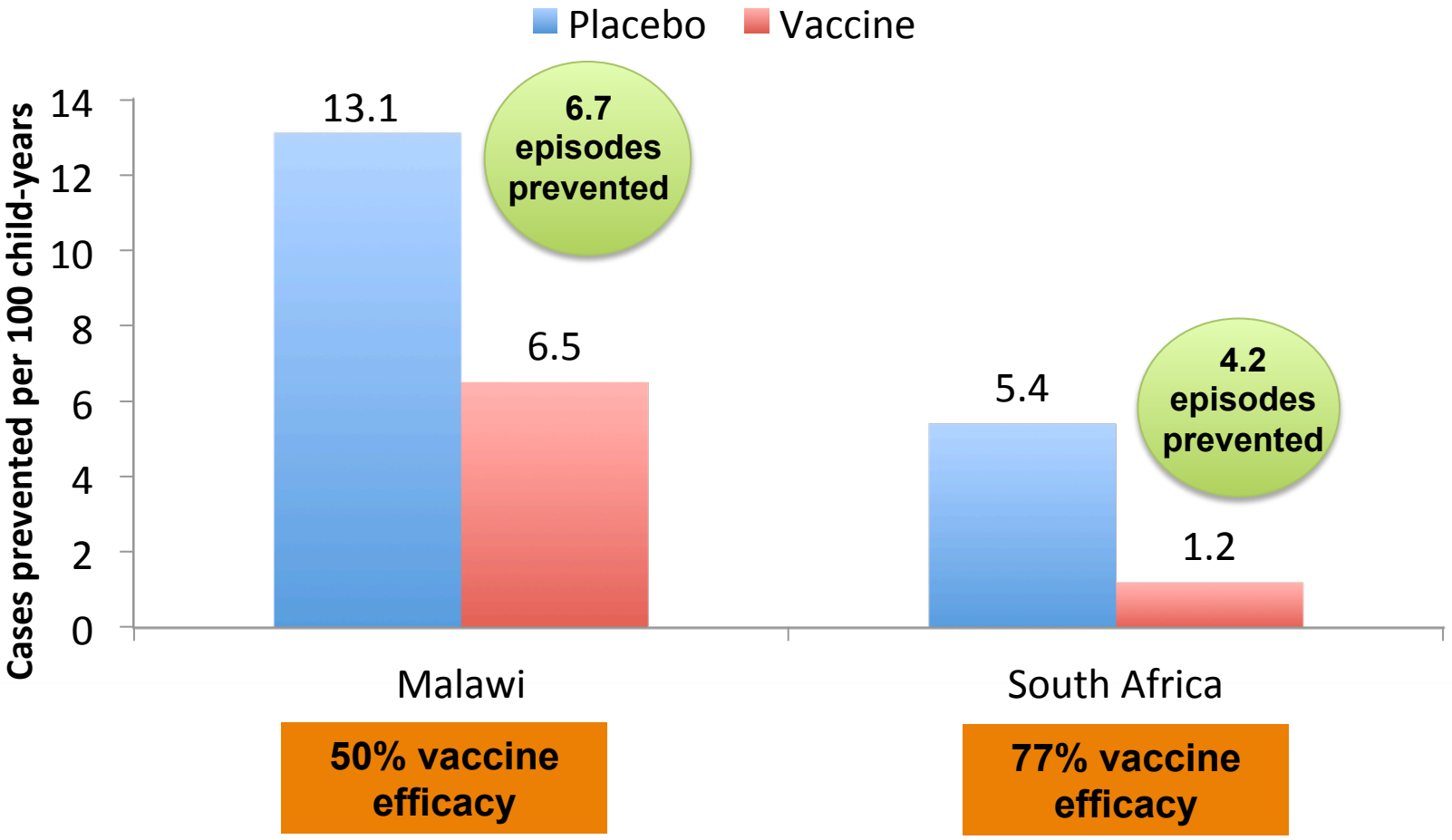
 Gessner, Feikin, Scott (Lancet 2014;383)

Vaccine Preventable Disease Incidence (VPDI) expresses the absolute impact of vaccine

	Syndrome	Etiology Confirmed		Clinical Dx Only	
		VE (%)	VPDI Case/1000 CYO	VE (%)	VPDI Case/1000 CYO
Gambia/PCV	CXR (+) pneumonia	70%	1.4	37%	13
Kenya/RV	AGE	84%	33	34%	190

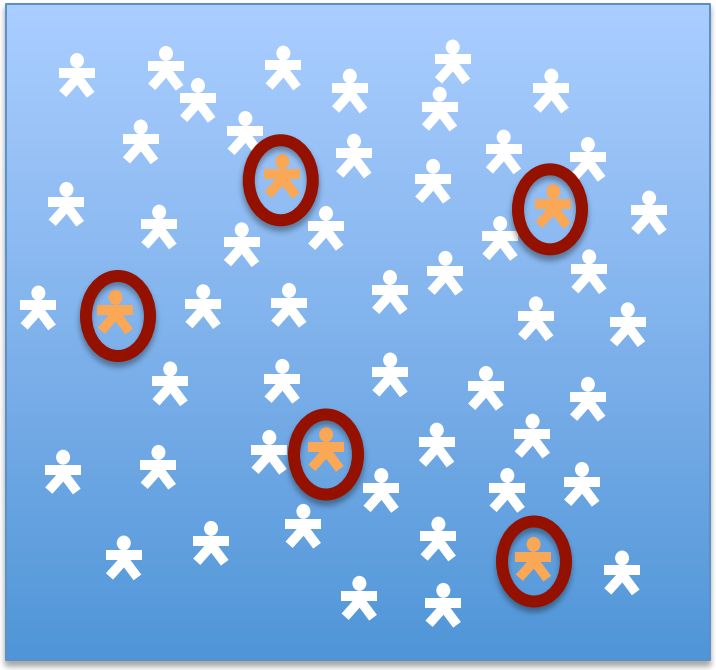
Lancet 2005;365 and Vaccine 2012;30 (Suppl 1)

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

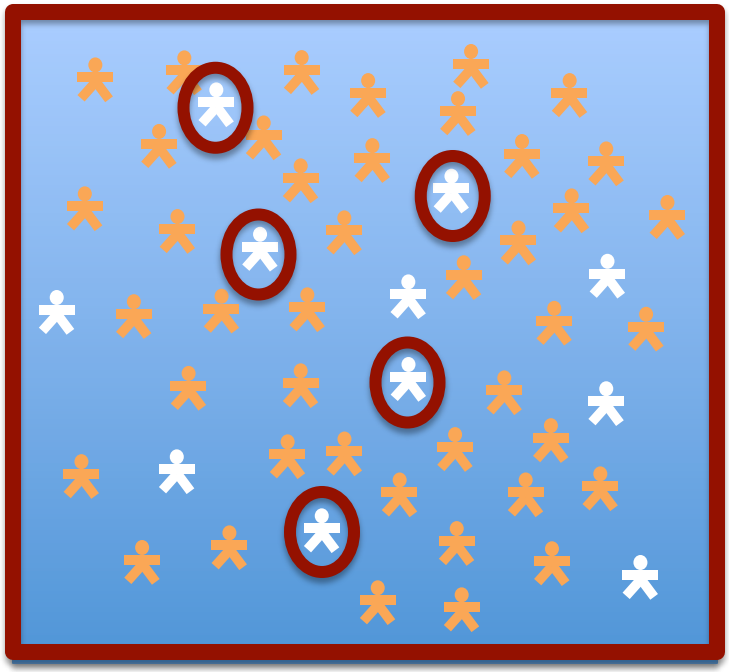


Madhi, NEJM 2010

Population level effects



Vaccine Efficacy Trial



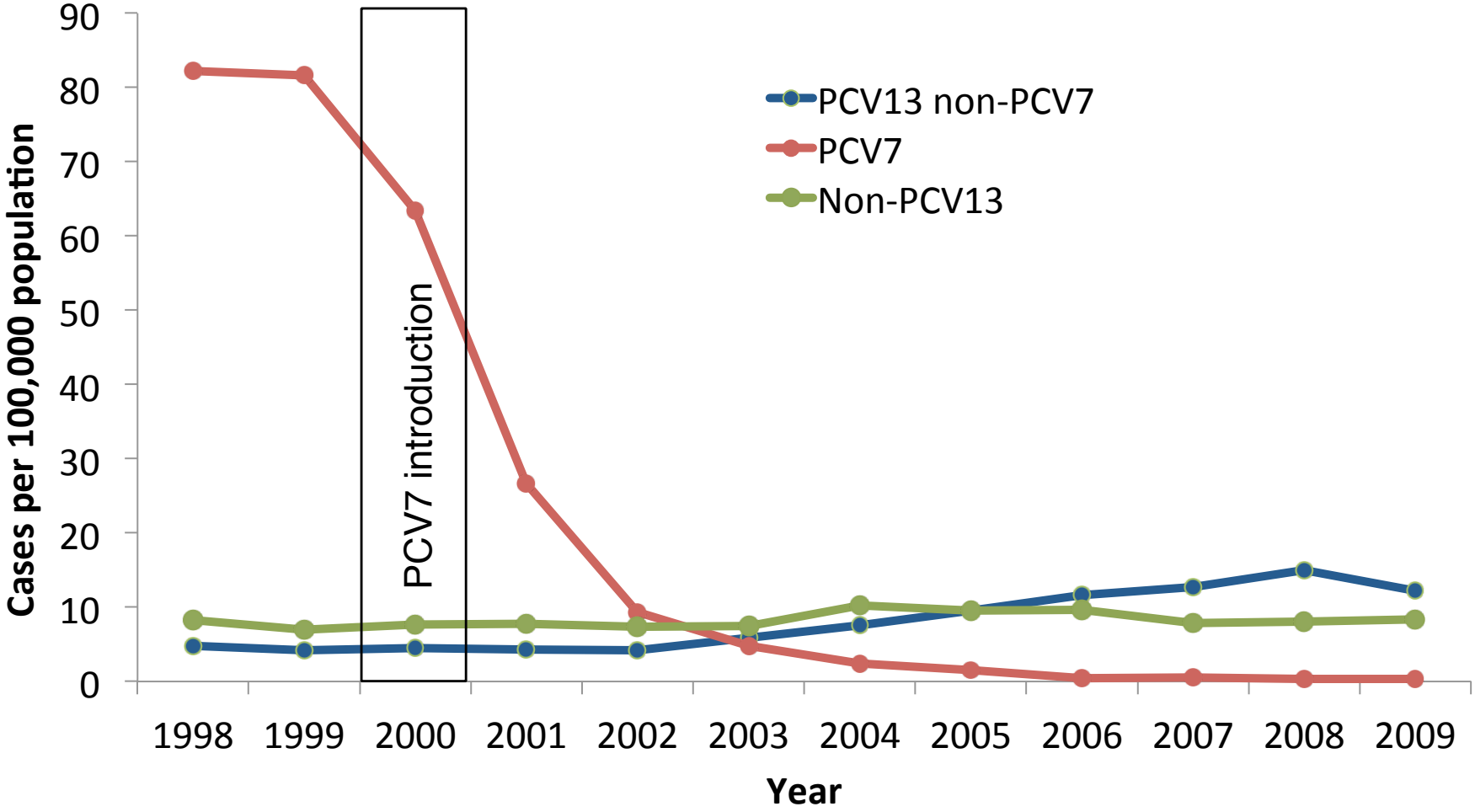
Routine Use Setting

Transmission from Infants Household and Community Contacts

+

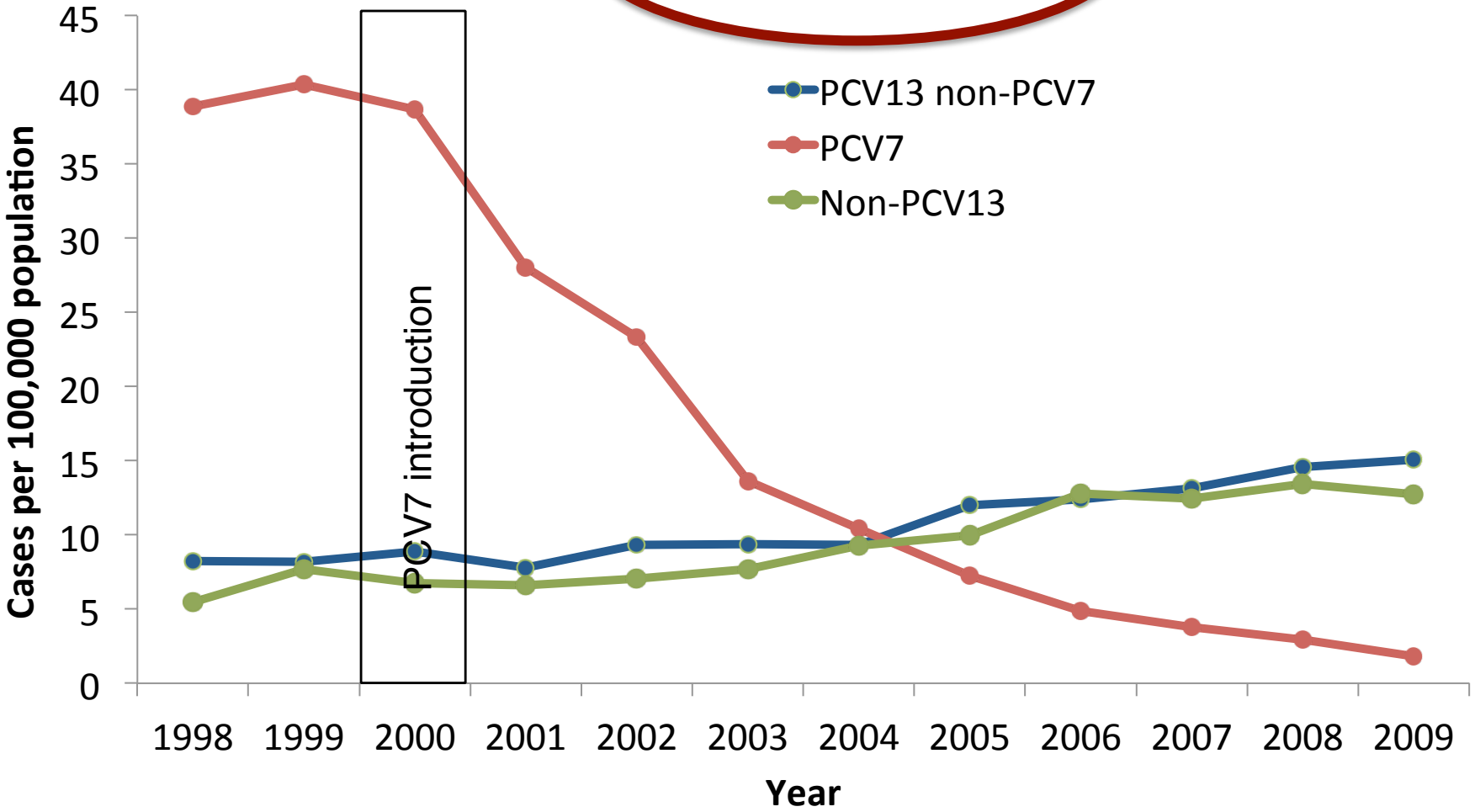
Adapted from C. Whitney (CDC)

Rates of IPD caused by PCV7 serotypes and additional serotypes in PCV13, children <5 years, 1998–2009



Moore M, CDC

Rates of IPD caused by PCV7 serotypes and additional serotypes in PCV13, adults ≥65 years, 1998–2009

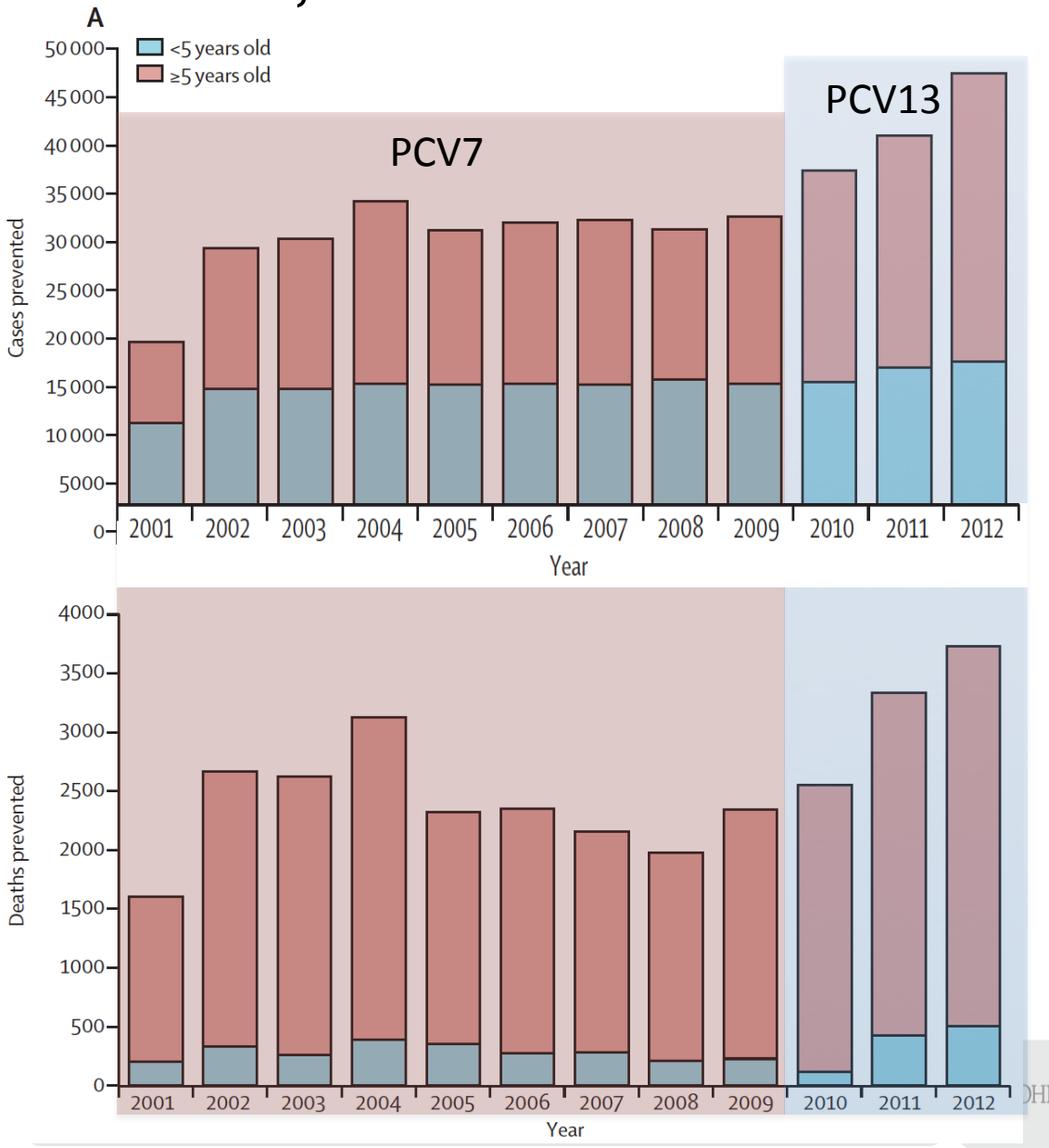


Moore M, CDC

Absolute Impact of PCV7/ PCV13, USA 2001-2012

Effect of use of 13-valent pneumococcal conjugate vaccine in children on invasive pneumococcal disease in children and adults in the USA: analysis of multisite, population-based surveillance

Matthew R Moore, Ruth Link-Gelles, William Schaffner, Ruth Lynfield, Catherine Lexau, Nancy M Bennett, Susan Petit, Shelley M Zansky, Lee H Harrison, Arthur Reingold, Lisa Miller, Karen Scherzinger, Ann Thomas, Monica M Farley, Elizabeth R Zell, Thomas H Taylor Jr, Tracy Pondo, Laura Rodgers, Lesley McGee, Bernard Beall, James H Jorgensen, Cynthia G Whitney



400,000 Cases Averted

- 50% in adults

30,000 Deaths Averted

- 90% in adults

JOHNS HOPKINS IVAC EVIDENCE > POLICY > ACCESS

Lancet Infect Dis 2015;15: 301-309

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%

Vaccine ineligible

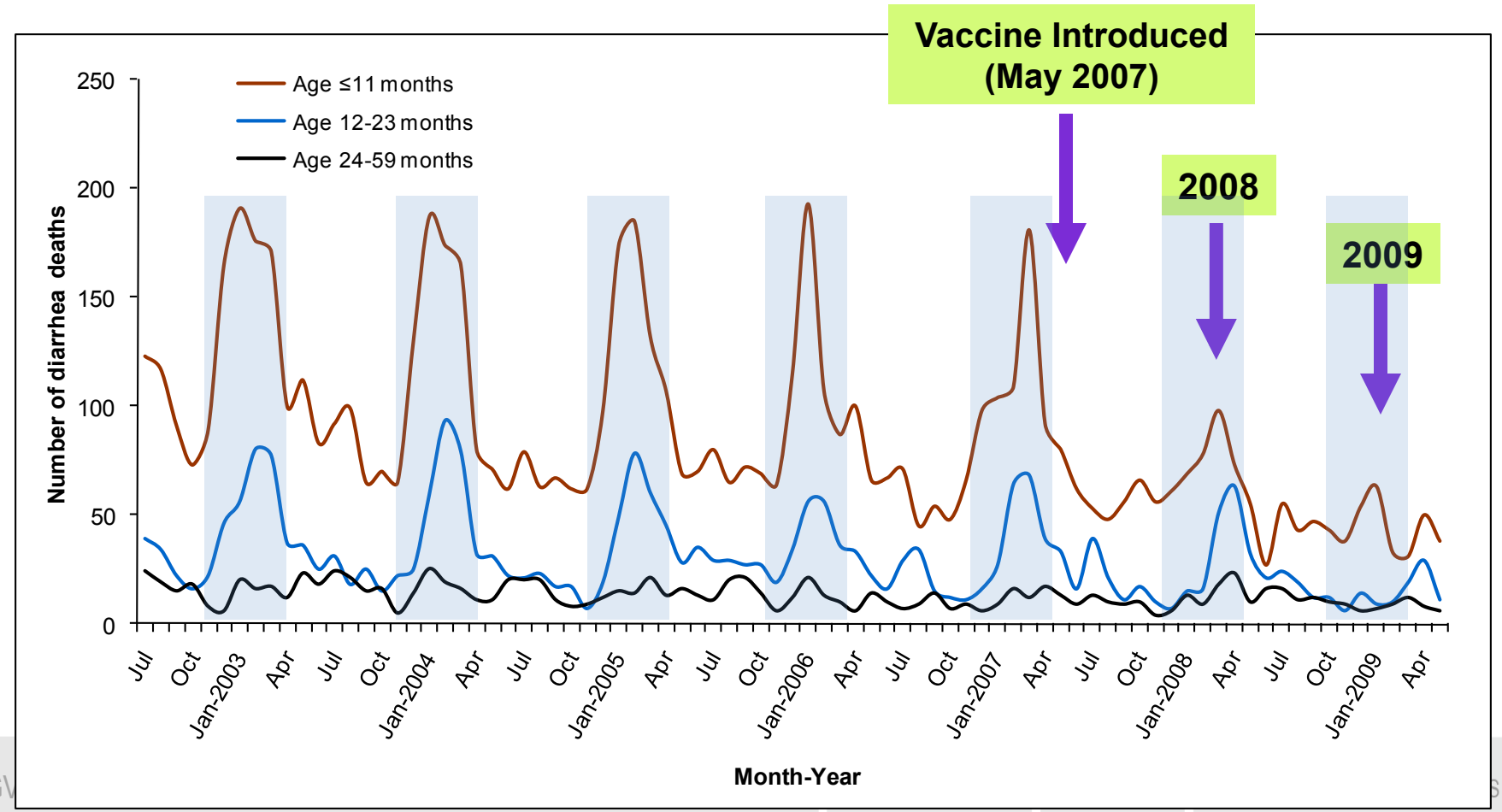
Herd Protection?

Slide courtesy U. Parashar

The NEW ENGLAND JOURNAL of MEDICINE

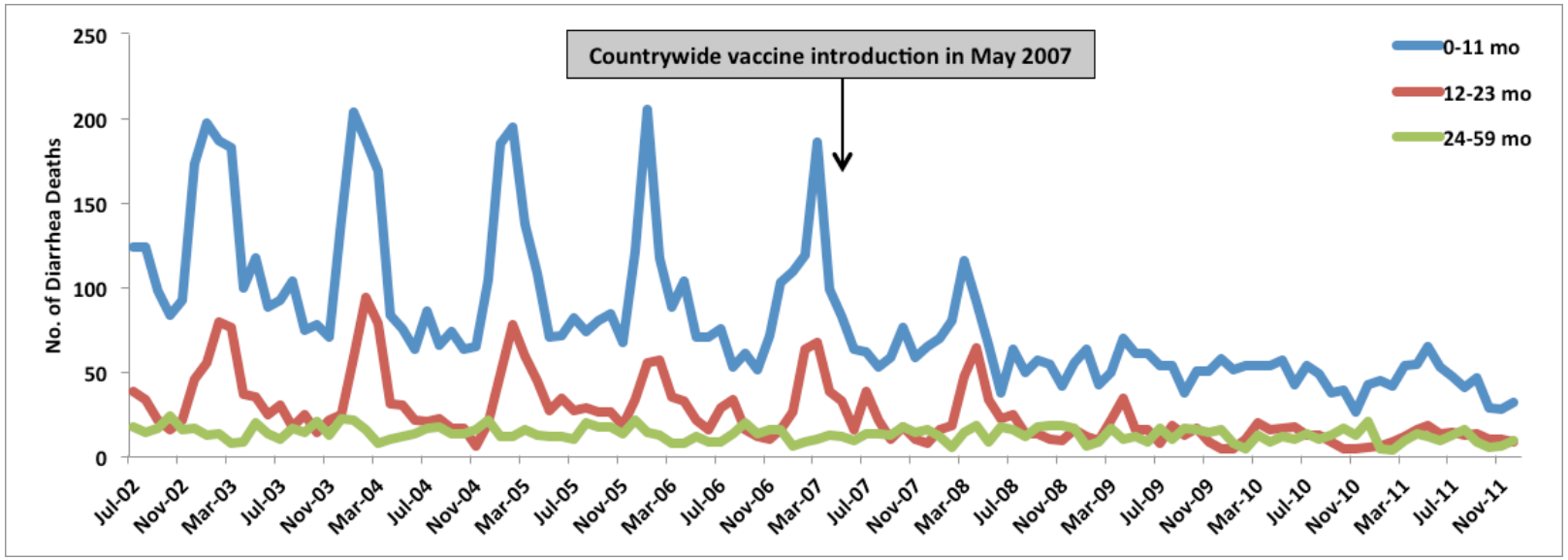
ORIGINAL ARTICLE

Effect of Rotavirus Vaccination on Death from Childhood Diarrhea in Mexico

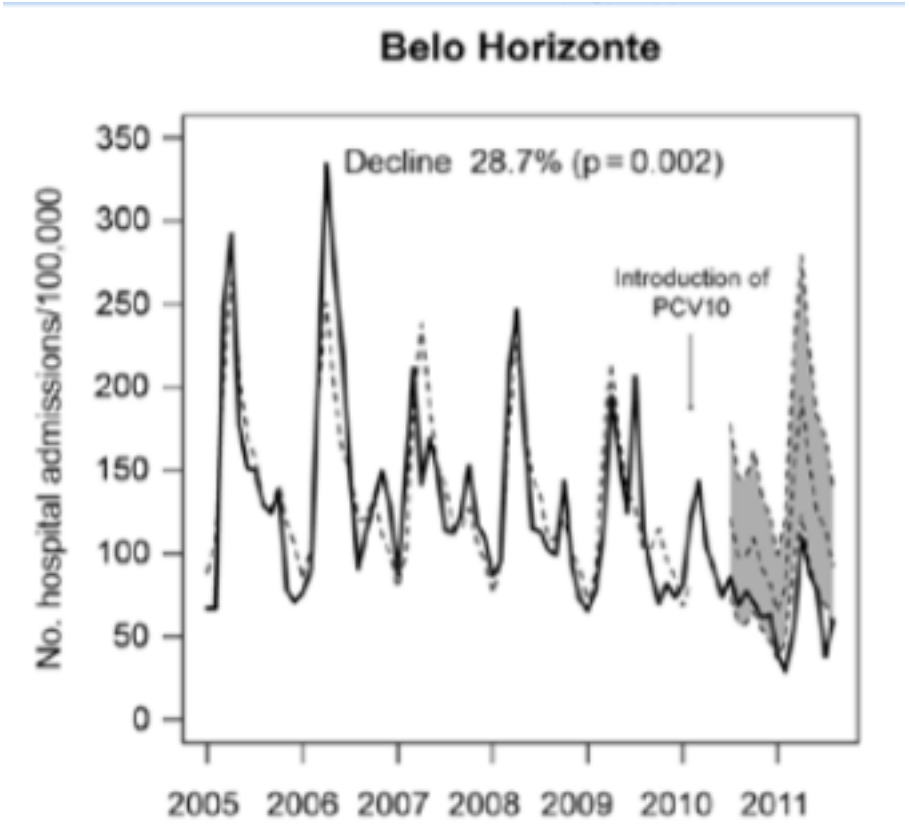


Richardson et al, NEJM 2010

Mortality decline sustained for four years post vaccine implementation in Mexico



PCV10 Effectiveness Against Hospitalized Pneumonia, Brazil



Afonso ET, Emerg Infect Dis 2013

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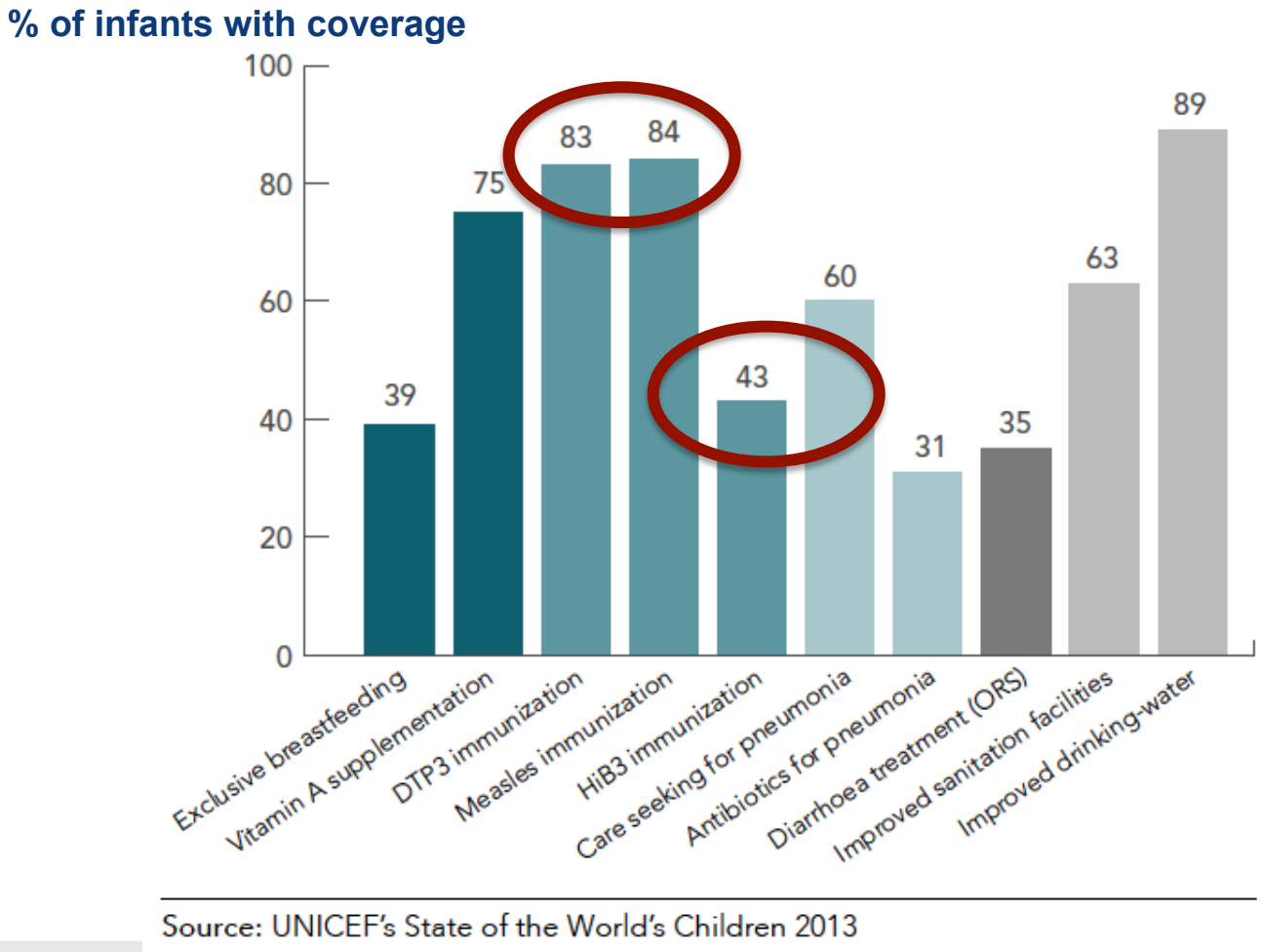
3. Are we at risk for "letting the perfect be the enemy of the good"?

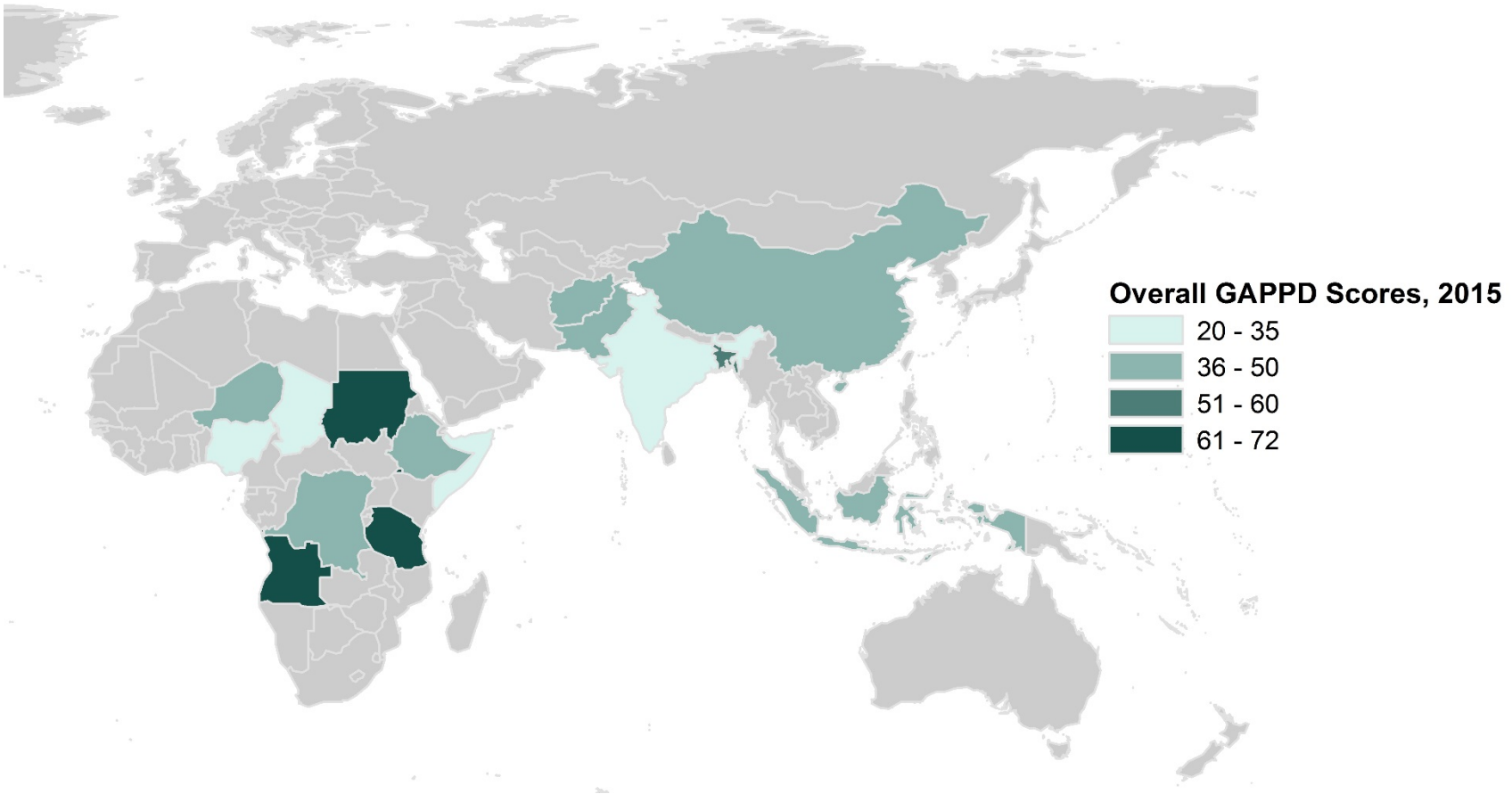
Global Action Plan for the Prevention and Control of Pneumonia and Diarrhea (GAPPD)

Score	DTP3	MCV1	Hib3	PCV3	RV (last dose)	Pneumonia Treatments		Diarrhea Treatments		Exclusive breastfeeding in first 6 months
						Care by an appropriate health care provider	Antibiotics	ORS	Zinc supplements	
Overall GAPPD score	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
GAPPD-Pneumonia score	✓	✓	✓	✓		✓	✓		✓	✓
GAPPD-Diarrhea score		✓			✓			✓	✓	✓

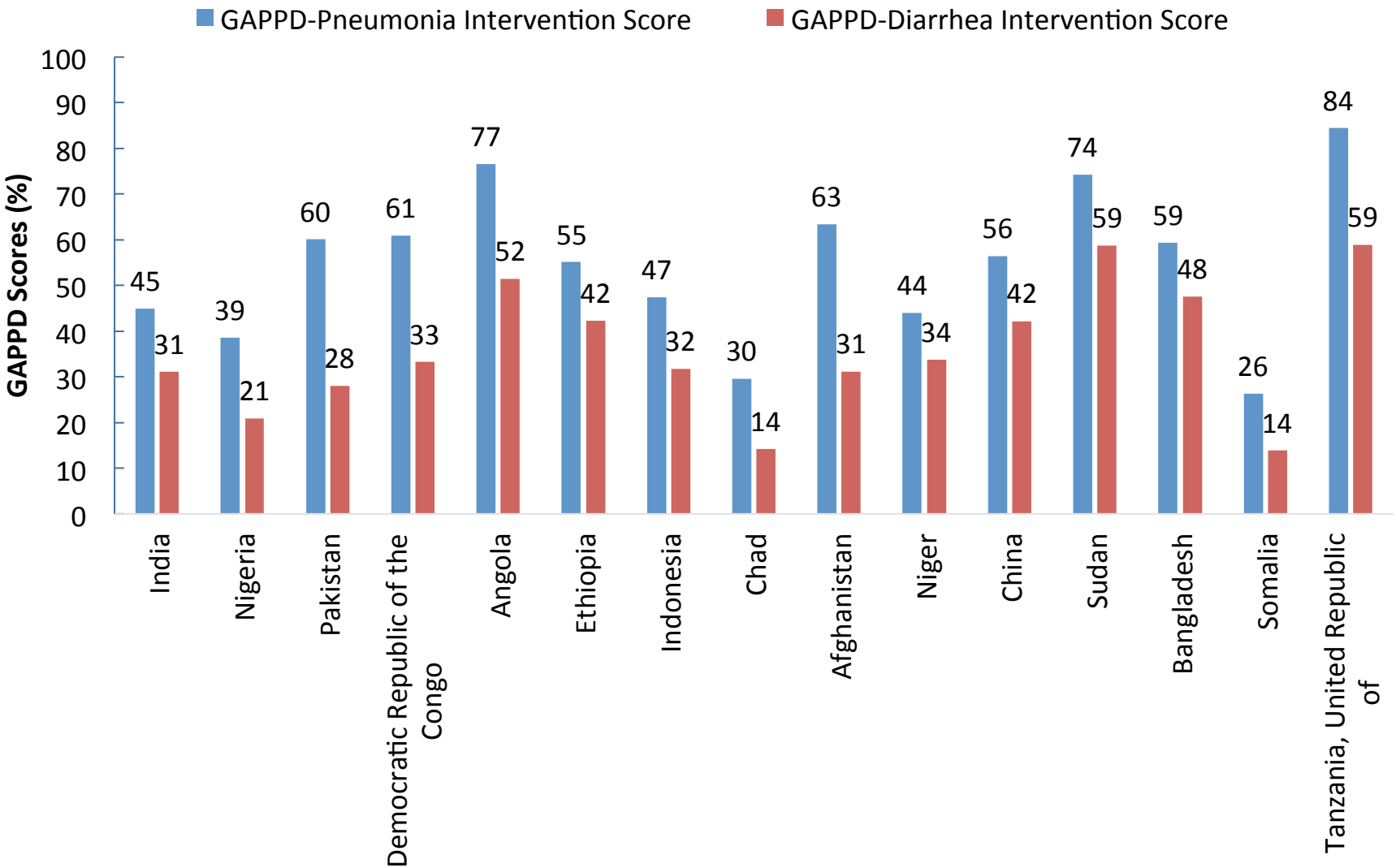
Existing GAPPD interventions are inadequately deployed
Vaccines are one, but not only, component



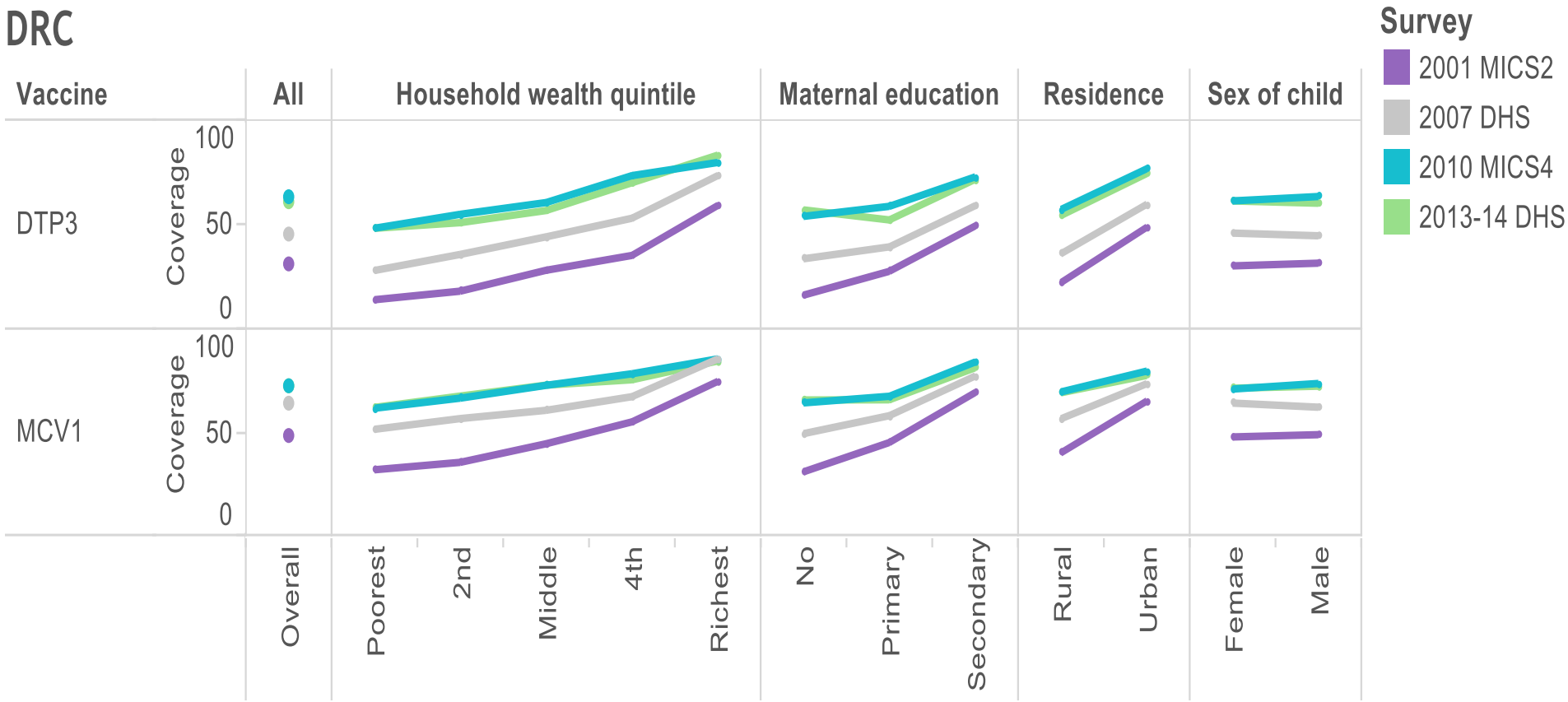
GAPPD scores in the 15 countries with the greatest burden of pneumonia and diarrhea deaths in U5



GAPPD Intervention Scores, 2015



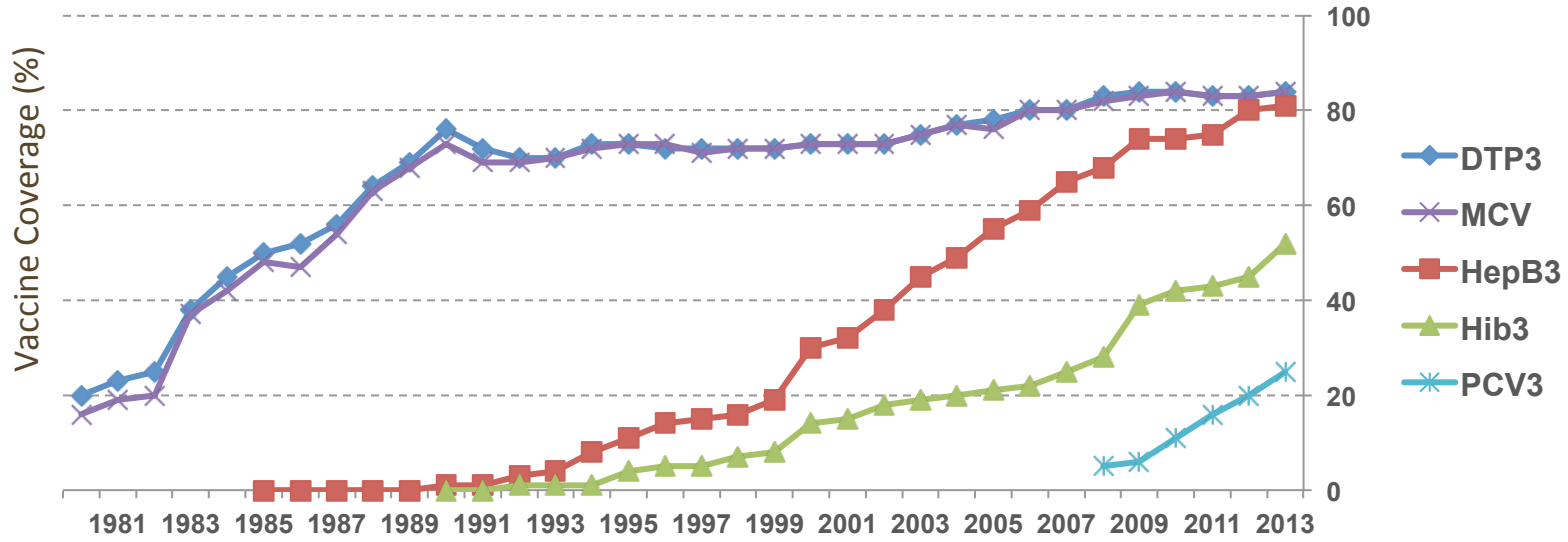
Vaccine Coverage Inequity within Countries – *Example: DRC*



Source: WUENIC 2014 estimates

Global Trends in Vaccine Coverage

WHO-UNICEF Immunization Coverage (WUENIC) 2013 update



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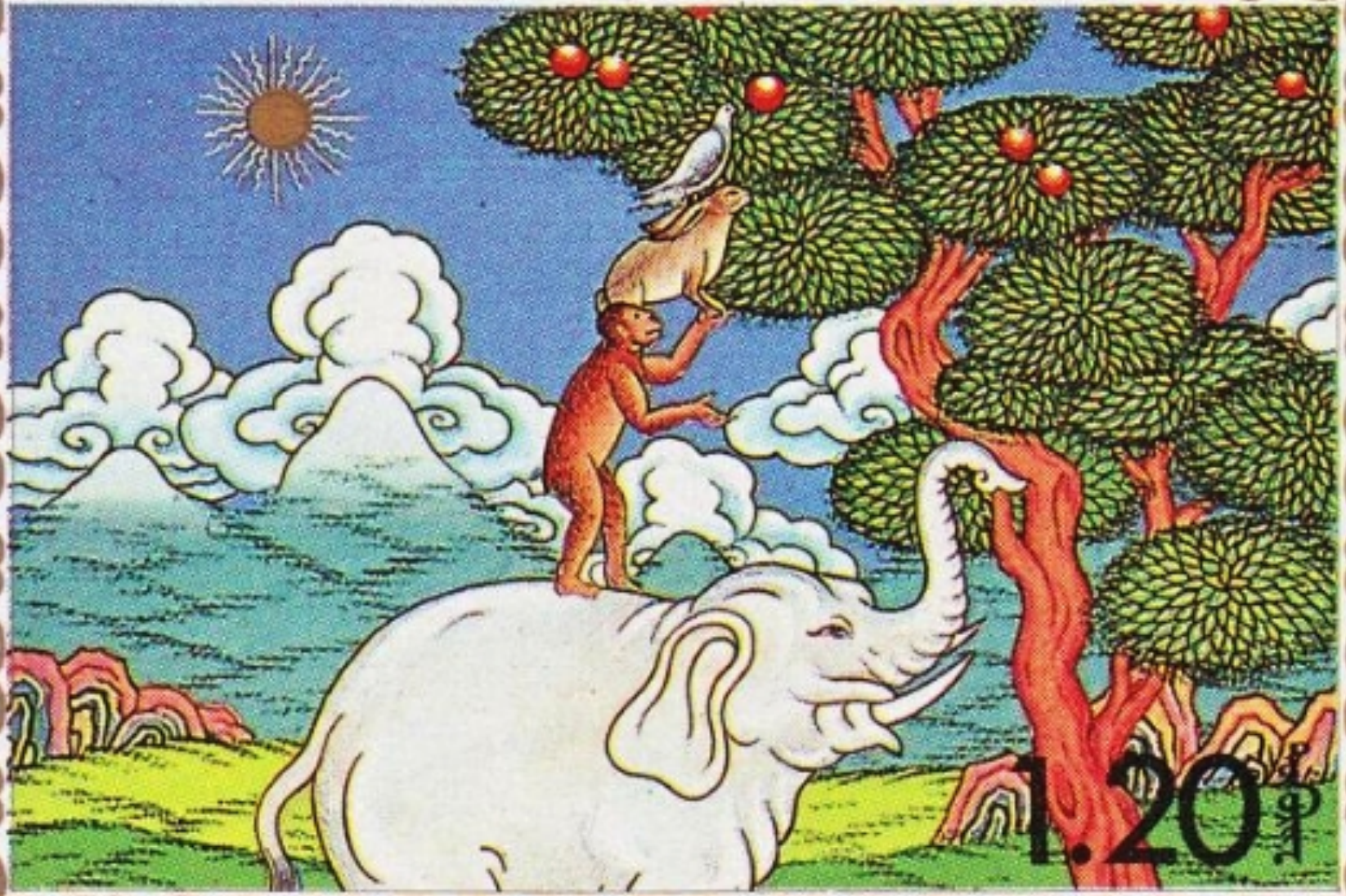
3. Are we at risk for "letting the perfect be the enemy of the good"? Vaccines, even of moderate efficacy, play key role along with other interventions

MONGOLIA · МОНГОЛ ШУУДАН



1984

1. Magnitude of efficacy is not fixed vaccine characteristic

2. There are many more policy relevant outcomes than just individual disease vaccine efficacy

3. Vaccines don't reduce disease, vaccinated people reduce disease; improvements in vaccine coverage, equity and timeliness are at least as important as advancing toward higher efficacy vaccines.