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of PUBLIC HEALTH

IVAC

International Vaccine
Access Center

CELEBRATING VACCINE VICTORIES

EPI AT 50 

JOIN THE INTERNATIONAL VACCINE ACCESS CENTER (IVAC) FOR A WEBINAR WITH AN EXPERT PANEL DISCUSSING THE PAST, PRESENT AND FUTURE OF THE **ESSENTIAL PROGRAMME ON IMMUNIZATION (EPI)**. A MODERATED Q&A SESSION WILL FOLLOW.



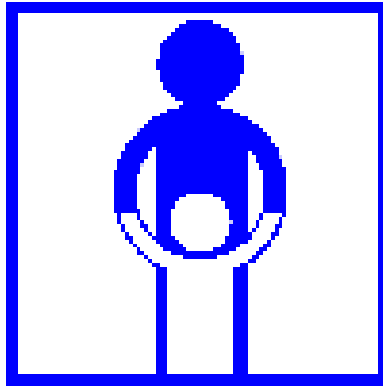
25 April 2024

11am - 12pm ET

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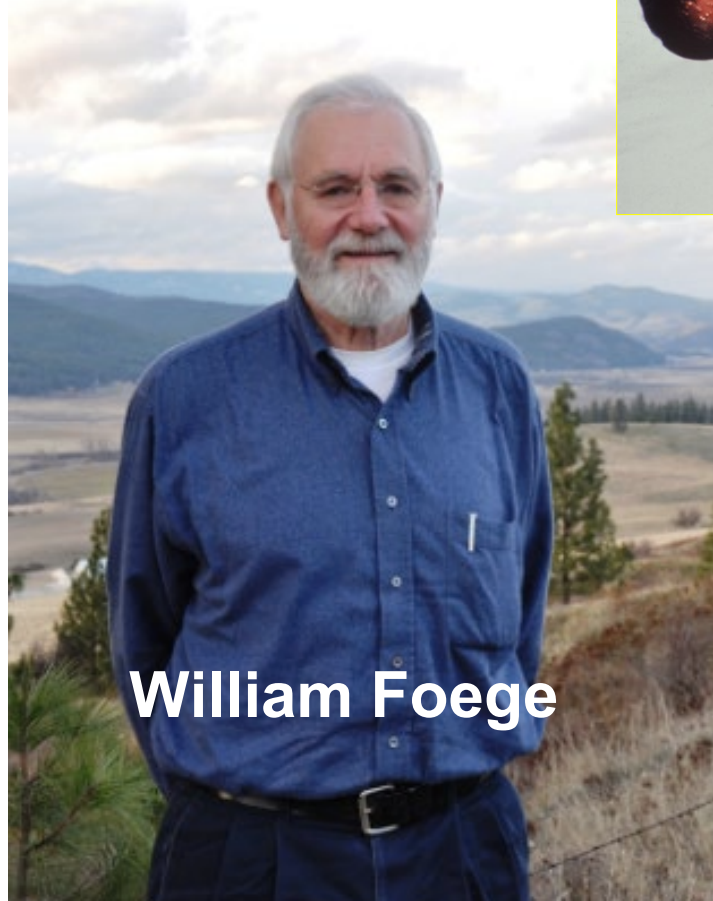
A Brief History of The Expanded Program on Immunization(EPI)*



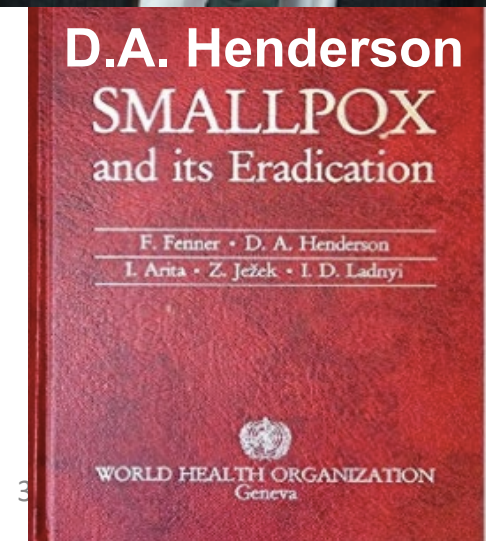
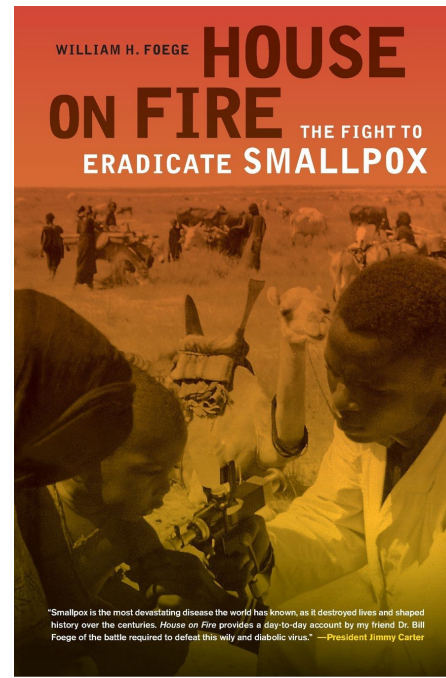
Neal A. Halsey

* 2024: Essential Programme on Immunization

EPI was Established Because of the Successful Smallpox Eradication Program



William Foege



Measles and Smallpox Eradication

Ghana 1970s



AL Rosenbloom. Used with permission.

Ralph(Rafe) Henderson

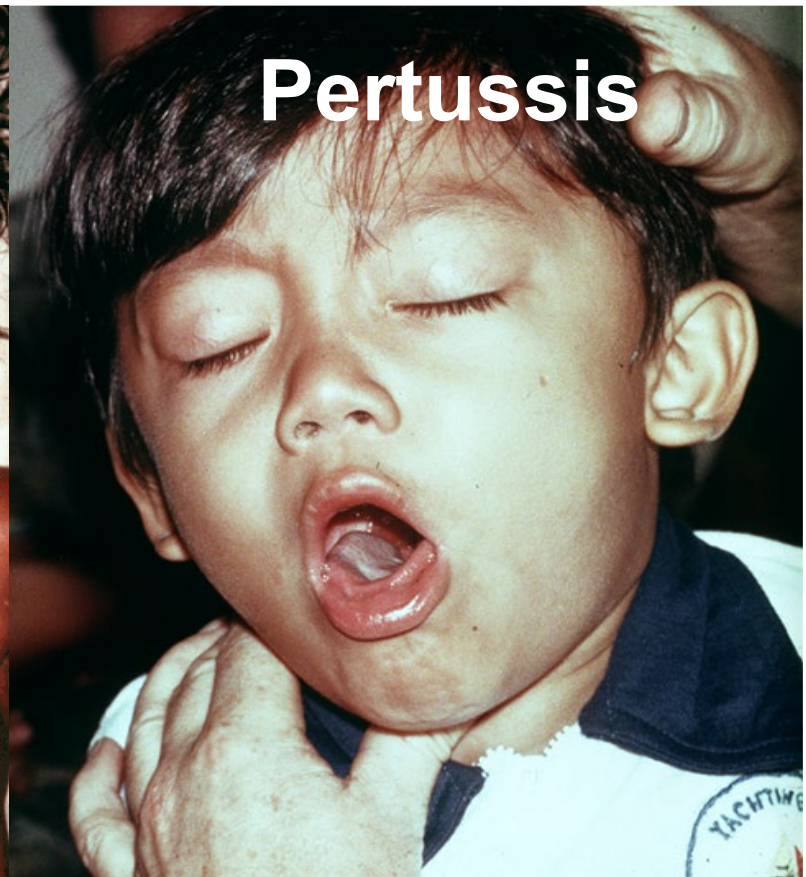
First Director of EPI



- Established:
 - Global management
 - Standardized assessments of coverage
 - Recommended schedule
 - Programs in all countries

Immunizing the children of the world: progress and prospects.
Bull World Health Organ. 1988; 66(5): 535–543.

DTP is the Backbone



EPI Founded in 1974

- WHO initially supported programs and personnel
- Estimated coverage DTP3 by 12 months
 - 1974: no good measure(~5%?)
 - 1980 ~20%
 - 1984 ~41%
 - 1989 ~75%

EPI Immunization Schedule

Established 1984

Birth	BCG, OPV (Endemic countries)
6 wks	DTP, OPV
10 wks	DTP, OPV
14 wks	DTP, OPV
9 months	Measles (Yellow Fever)
Women of Childbearing age	Tetanus Toxoid

Halsey NA, Galazka A. The efficacy of DTP and oral poliomyelitis immunization schedules initiated from birth to 12 weeks of age. Bull Wld Hlth Org; 63:1151-69, 1985.

Logistical issues in establishing EPI Clinics



farm1.static.flickr.com/141/329026396_ad24600

Large Scale Transportation and Storage Issues Overcome



www.msf.ca



WHO EPI

Some Areas are Hard to Reach Himalayan Region Pakistan



Aamir
Khan

Adding Vaccines to EPI Programs

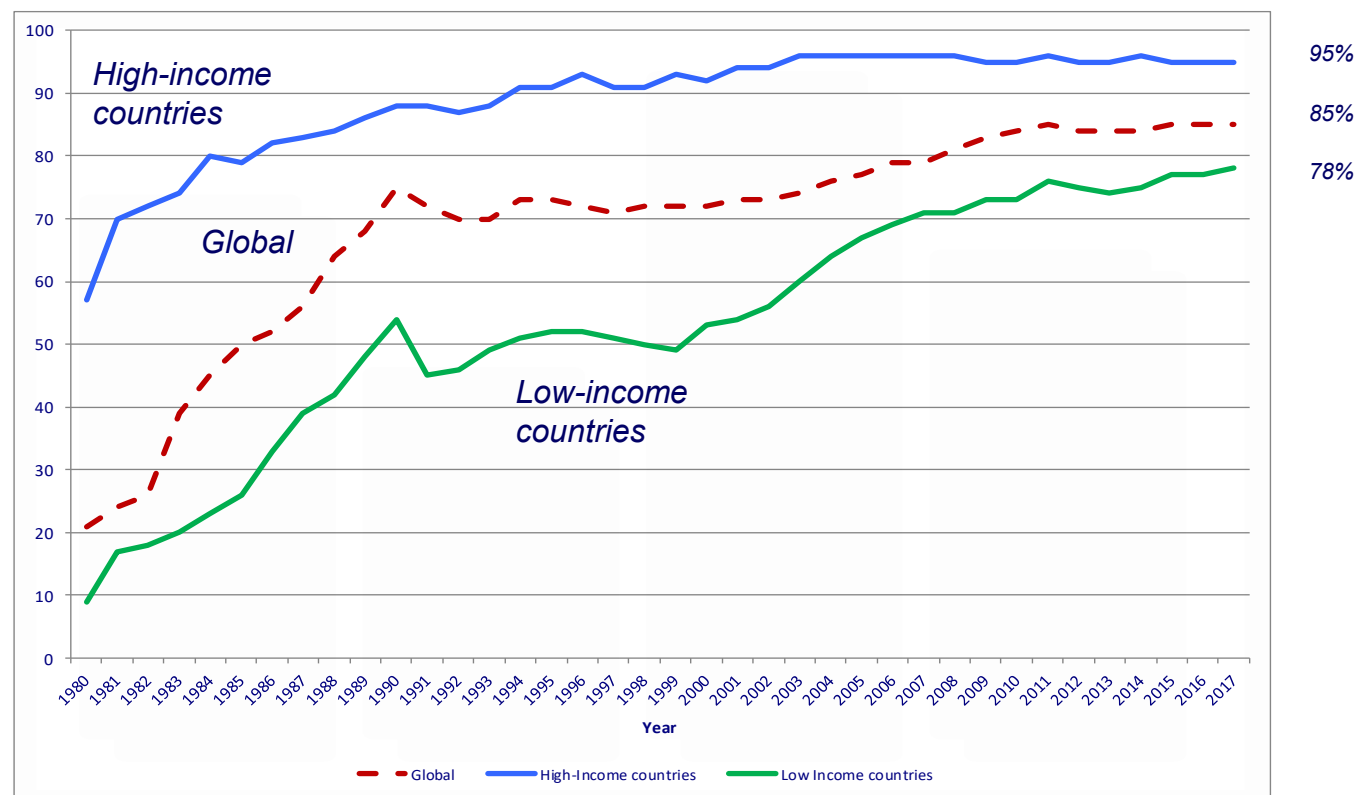
1976

- 1. TB (BCG)**
- 2. Diphtheria**
- 3. Tetanus**
- 4. Pertussis**
- 5. Polio - OPV**
- 6. Measles**
- 7. (Yellow Fever)**

2024

- 1. Hepatitis B**
- 2. *H. influenzae* type b(Hib)**
- 3. Pneumococcal**
- 4. Influenza-pregnant women**
- 5. Polio-IPV**
- 6. Rotavirus**
- 7. HPV**
- 8. Pneumococcal**
- 9. (Rubella,Mumps)**
- 10. (Meningococcal)**
- 11. COVID-19**

Coverage with DTP3 containing vaccines, by country income levels, 1980-2017



unicef



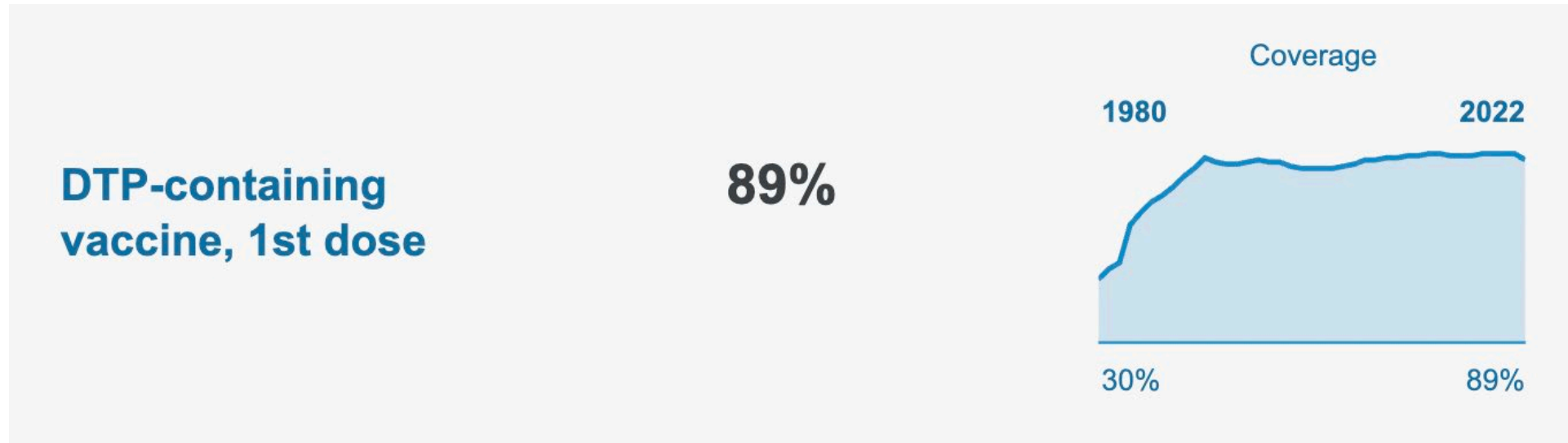
World Health Organization

Gavi

The Vaccine Alliance



Global Vaccination coverage trendline

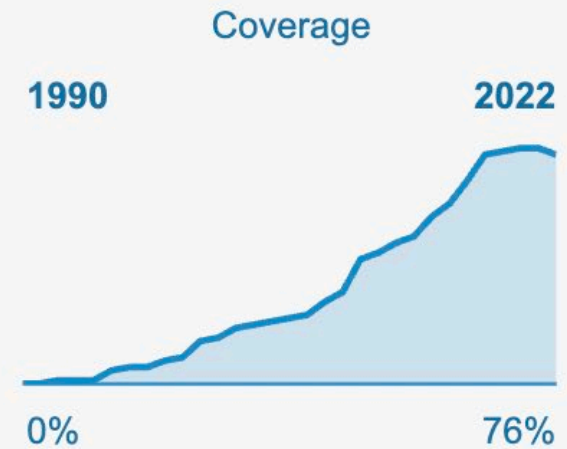


Adding Vaccines Creates New Challenges

H. influenzae type b(Hib)

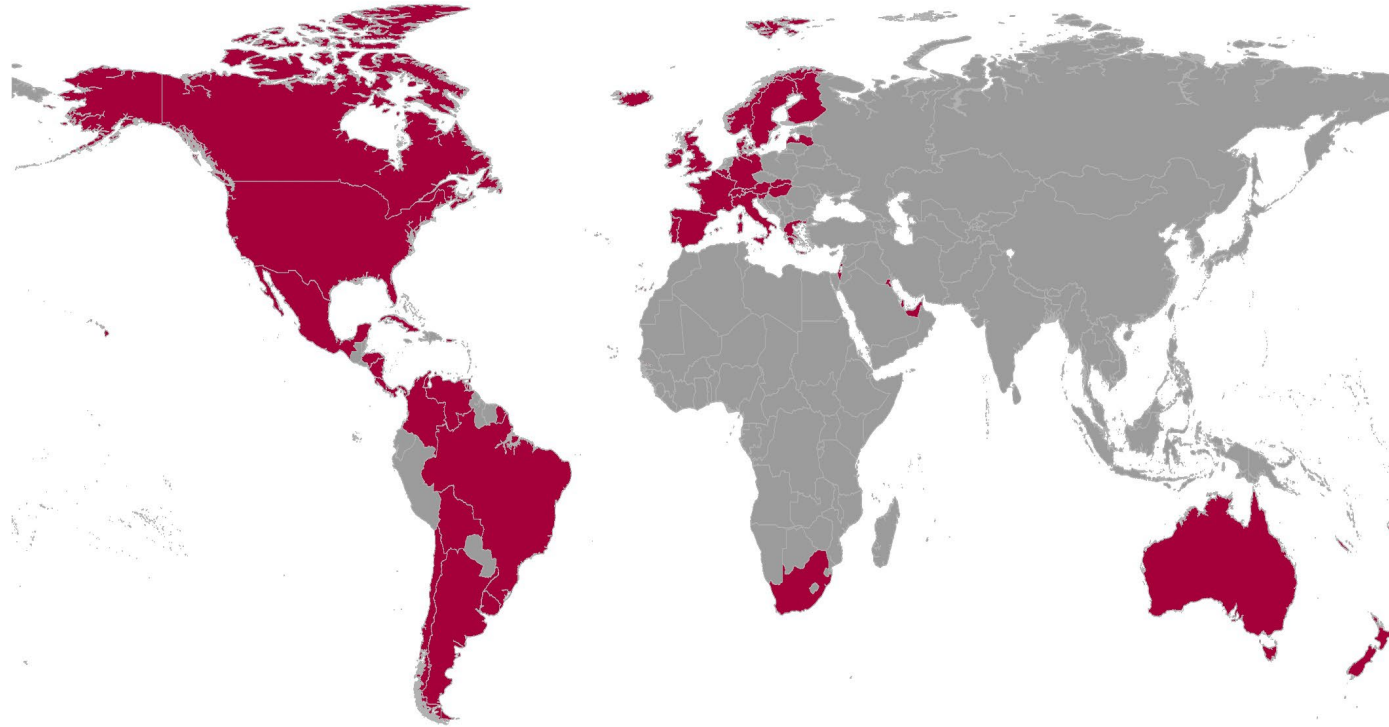
Hib, 3rd dose

76%



IVAC Hib Initiative

Countries Using Hib Vaccine in their National Immunization Program (2000)



Routine Hib Implementation Status, 2000

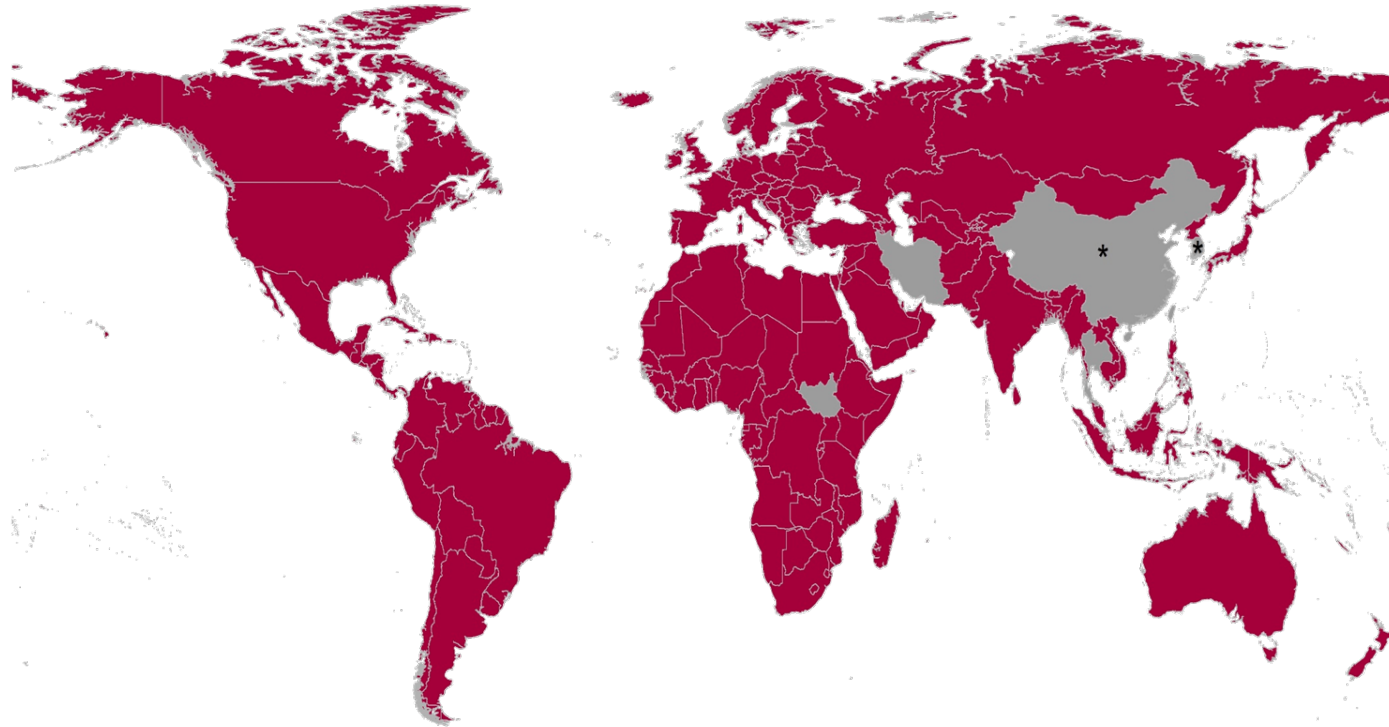


Before Hib Initiative

Source: International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. Vaccine Information Management System (VIMS). April 2014.

IVAC Hib Initiative

Countries Using Hib Vaccine in their National Immunization Program (2014)



Routine Hib Implementation Status, March 2014

 Yes
 No

**Widespread coverage through the private market (≥50%)*

Sources:

International Vaccine Access Center (IVAC), Johns Hopkins Bloomberg School of Public Health. Vaccine Information Management System (VIMS). April 2014.

GAVI Alliance:

<http://www.gavialliance.org/support/nvs/pentavalent/#>

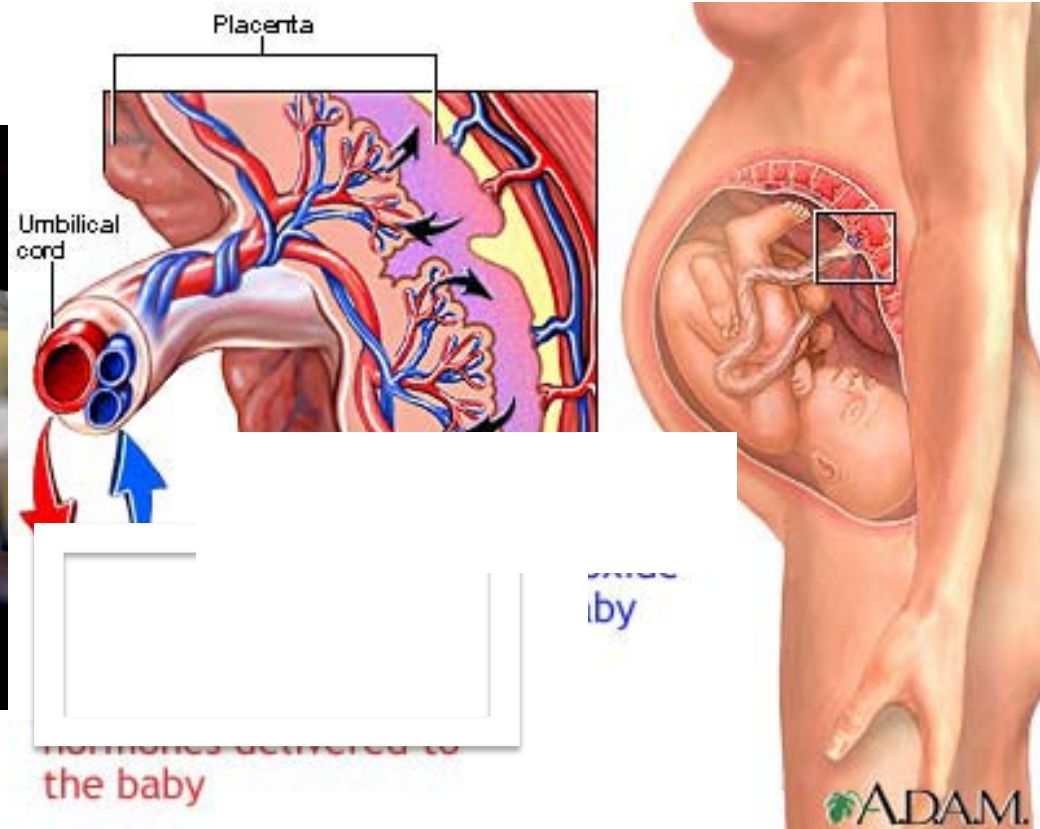
Combination Vaccines Have Helped

- DTP/Hib
- DTP/Hep B/Hib
- DTP/Hib/IPV
- Measles/Rubella
- Measles/Mumps/Rubella

Infants are Protected by Passively Acquired Tetanus Antibodies from Immune Mothers



2 doses TT in pregnancy

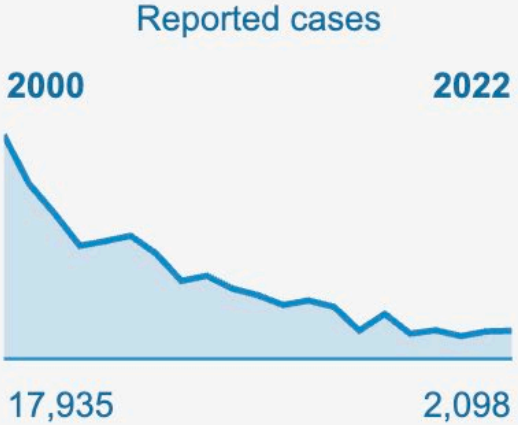


Neonatal Tetanus



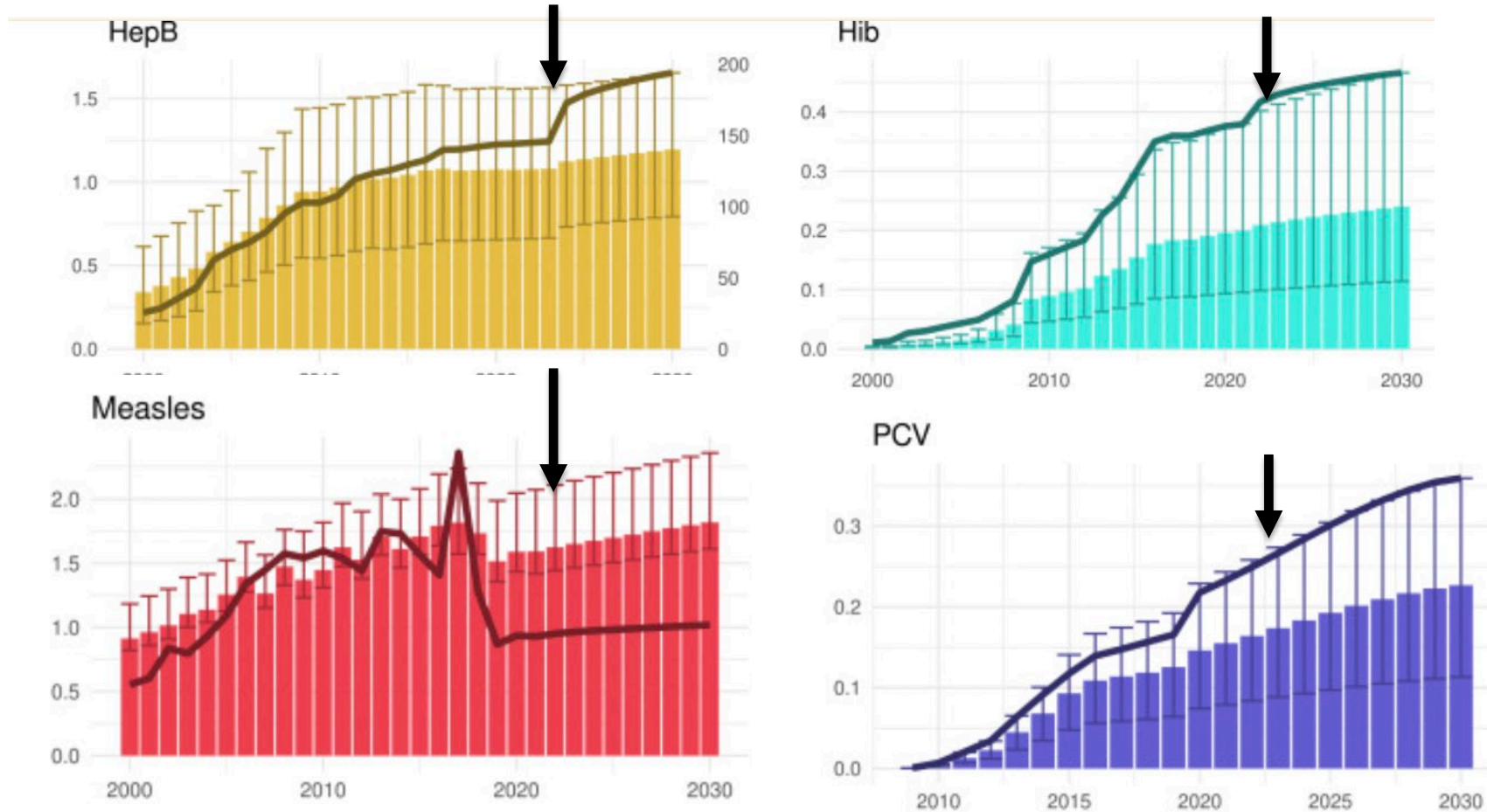
Neonatal tetanus

2,098



All EPI Vaccines Save Lives

- Deaths averted and projected per year



Lives saved with vaccination for 10 pathogens across 112 countries in a pre-COVID-19 world 2021; 10: e67635

Lives Saved From EPI Vaccines 2000–2030 in 112 Countries

- Estimated 50 million deaths averted between 2000 and 2019
- Projected 97 million deaths could be averted 2000–2030

EPI Became a Platform for Delivering Vitamin A Supplementation



Bednets to Prevent malaria



Director of Department of Immunization, Vaccines and Biologicals at WHO

Kate O'Brien Former Executive Director IVAC



DIRECTOR, DEPARTMENT OF IMMUNIZATION, VACCINES AND BIOLOGICALS, WORLD HEALTH ORGANIZATION

Kate O'Brien is the Director of the Department of Immunization, Vaccines and Biologicals at the World Health Organization (WHO). Previously she was the Executive Director of the International Vaccine Access Center (IVAC), and Professor of International Health and Epidemiology, at the Johns Hopkins Bloomberg School of Public Health. Dr O'Brien served on the WHO Strategic Advisory Group of Experts on Immunization (SAGE) committee from 2012 to 2018. Prior to joining IVAC, she served as the Director of Infectious Disease in the Johns Hopkins Center for American Indian Health. She also served as an Epidemic Intelligence Officer, in the Respiratory Diseases Branch, at the CDC, Atlanta (USA).

Dr O'Brien earned her BSc in Chemistry from the University of Toronto (Canada), her MD (Medicinæ Doctorem) from McGill University, Montreal (Canada), and her Master of Public Health from Johns Hopkins Bloomberg School of Public Health, Baltimore (USA). She completed her paediatric and infectious disease clinical training at Johns Hopkins Medical Institutions, Baltimore (USA).



25 April 2024 | World Immunization Week

Rotavirus Vaccines

Dr. Mathuram Santosham

Professor, Departments of International Health & Pediatrics
Johns Hopkins University



Etiology of gastroenteritis, Melbourne 1970s

Table 1 Etiological gastroenteritis in children admitted to Royal Children's Hospital, Melbourne

	1972	1974
Total admissions	539	378
<i>Salmonella</i> sp.	39 (7.2%)	40 (10%)
<i>Shigella</i> sp.	2 (0.4%)	5 (1%)
Pathogenic <i>E. coli</i>	23 (4.3%)	7 (2%)
Unknown	475 (88%)	102 (29%)
Rotavirus	not tested	197 (52%)
Enteric adenovirus	not tested	27 (7%)

Bishop R. Discovery of rotavirus: Implications for child health. J Gastroenterol Hepatol. 2009 Oct;24 Suppl 3:S81-5.

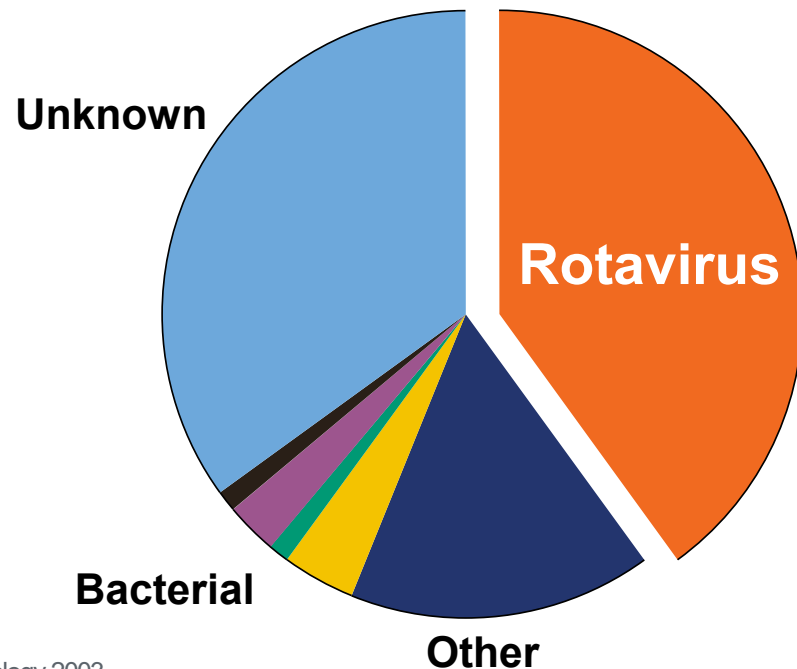


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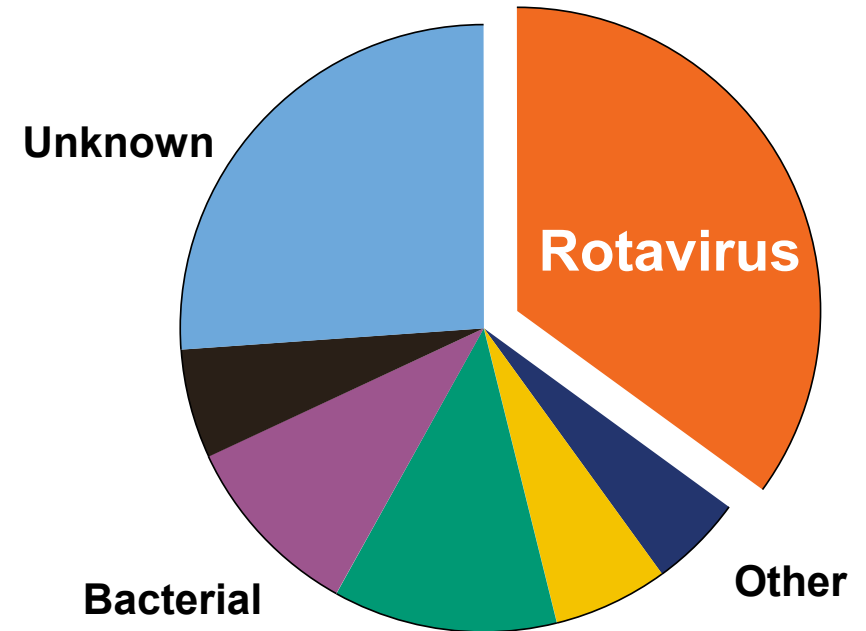
Causes of severe acute gastroenteritis among children <5 years before rotavirus vaccines



Developed Countries



Developing Countries



A. Kapikian, Fields Virology 2003

Timeline of rotavirus vaccine development



Table 2 Development of rotavirus vaccines

1983	RIT	Single bovine strain
1986	RRV	Single simian strain
1991	TRRV	Simian/human reassortant G ₁ G ₂ G ₃ G ₄
1999		Withdrawn
1999	Rotarix	Single human strain G ₁ P(8)
2000	RotaTeq	Bovine/human reassortants G ₁ G ₂ G ₃ G ₄ P(8)

Bishop R. Discovery of rotavirus: Implications for child health. J Gastroenterol Hepatol. 2009 Oct;24 Suppl 3:S81-5.

Health burden of rotavirus



Rotavirus is a leading cause of death due to diarrhea in young children, and the leading cause among infants.

In the absence of vaccination, nearly every child is infected—rotavirus kills ~200,000 children and hospitalizes hundreds of thousands more each year

>500 Number of children dying from rotavirus every day

~37% Percent of under-5 diarrhea hospitalizations due to rotavirus, globally (2013)

>90% Percent of under-5 rotavirus deaths occurring in Gavi-eligible low-income countries (2013)

Tate, CID, 2016. Slide courtesy of Molly Sauer.

Economic burden of rotavirus

Treating rotavirus diarrhea is expensive for families and countries



Uganda

Inpatient admission for one episode of severe rotavirus diarrhea costs **10% of the average family's monthly income**



Bangladesh

Treating one episode of rotavirus diarrhea can amount to **85% of the average family's monthly income**



Malaysia

Rotavirus hospitalization costs more than **25% of the average family's monthly income**

Slide courtesy of ROTA Council. Images courtesy of Photoshare: © 2009 Jessica Alderman, © 2014 SPRING Project, © 2014 Aji Styawan Sigei C, et al., Vaccine. 2015;33 Suppl 1:A109-18; icddr,b. Preliminary analysis, Protocol# 14009; Chai PL, WS. Vaccine. 2009;27(5):F112-F115

Health system burden of rotavirus



Rotavirus hospitalizations can overwhelm health systems and facilities



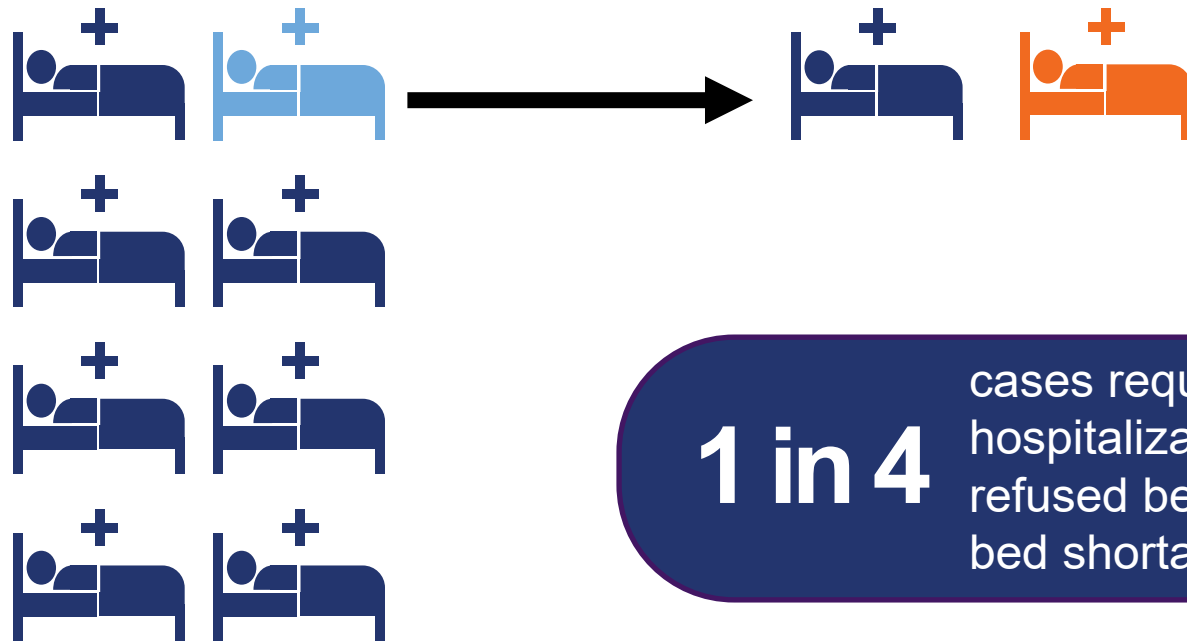
Largest pediatric hospital in Bangladesh

Nov 2015 – Oct 2016

1 in 8

admissions was due to AGE

54% of AGE admissions were due to rotavirus



1 in 4

cases requiring hospitalization was refused because of bed shortages

Rotavirus vaccines



Development of the Tetravalent Rhesus Rotavirus Vaccine

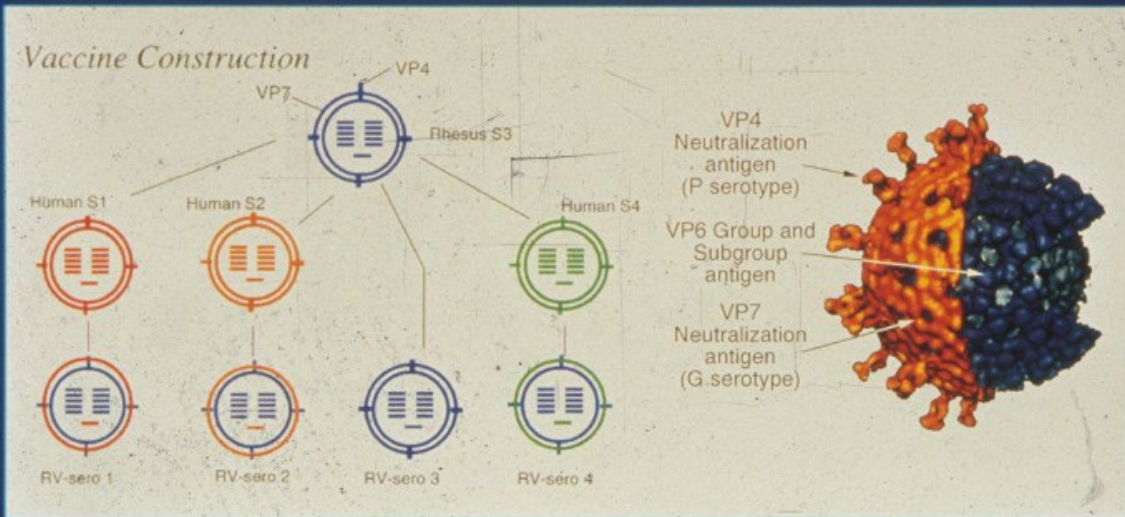


Figure at right reproduced with permission from Estes MK. *J Infect Dis.* 1996;174(Suppl 1):S39.

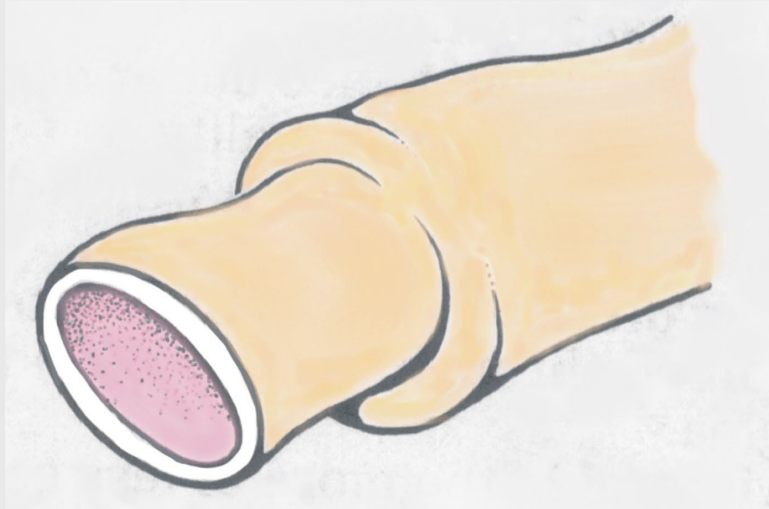
First generation vaccines

- “Jennerian” approach
 - Naturally attenuated animal strains (bovine, rhesus)
- Variable performance
 - 80% efficacy in Finland but 0-30% efficacy in developing countries
- Best efficacy of rhesus vaccine (serotype G3) seen in Venezuela during G3 outbreak

Second generation vaccines

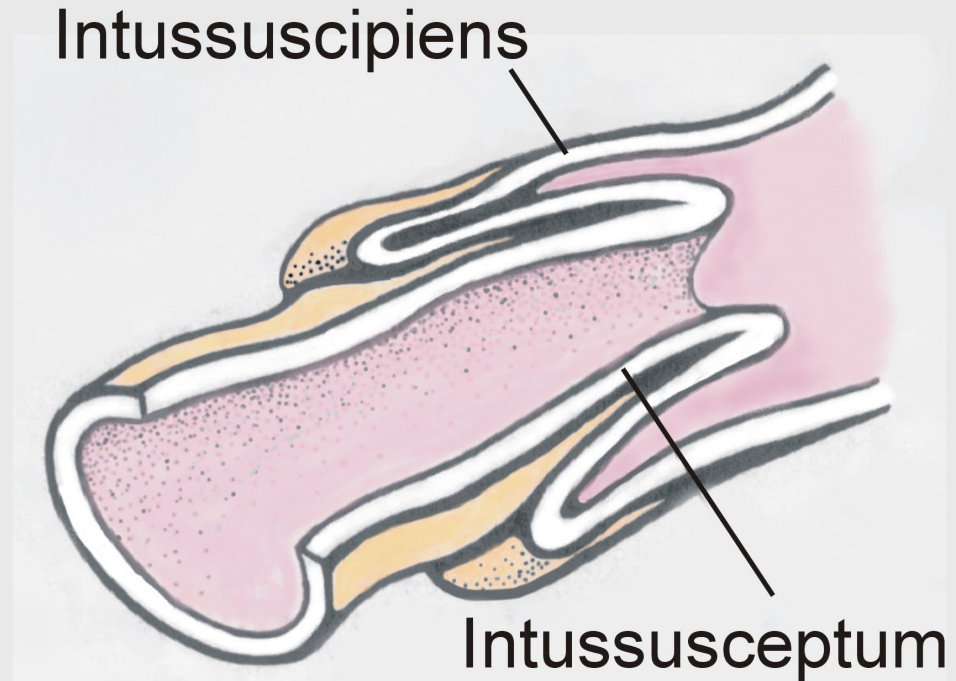
- “Modified Jennerian” approach
- Naturally attenuated animal strain as backbone
- Insertion of genes coding human G types by reassortment in cell culture

Intussusception (IS)



Intussusception

The telescoping of the intestine onto itself usually at the ileal-cecal junction, leading to reversible repair or entrapment with edema, necrosis and perforation

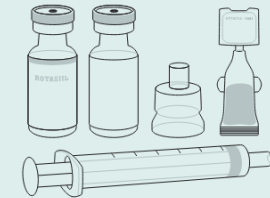
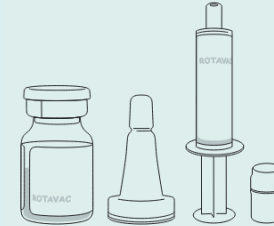
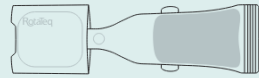


Final chapter for Rotashield[®]



- US Withdrew recommendation
- Without efficacy data from Asia and Africa, clinical trials needed
- Trials considered ethical, but political challenges of testing tainted vaccine
- Vaccine manufacture stopped
- Abrupt demise of first vaccine licensed after 20 years of research

Today's WHO-prequalified rotavirus vaccines

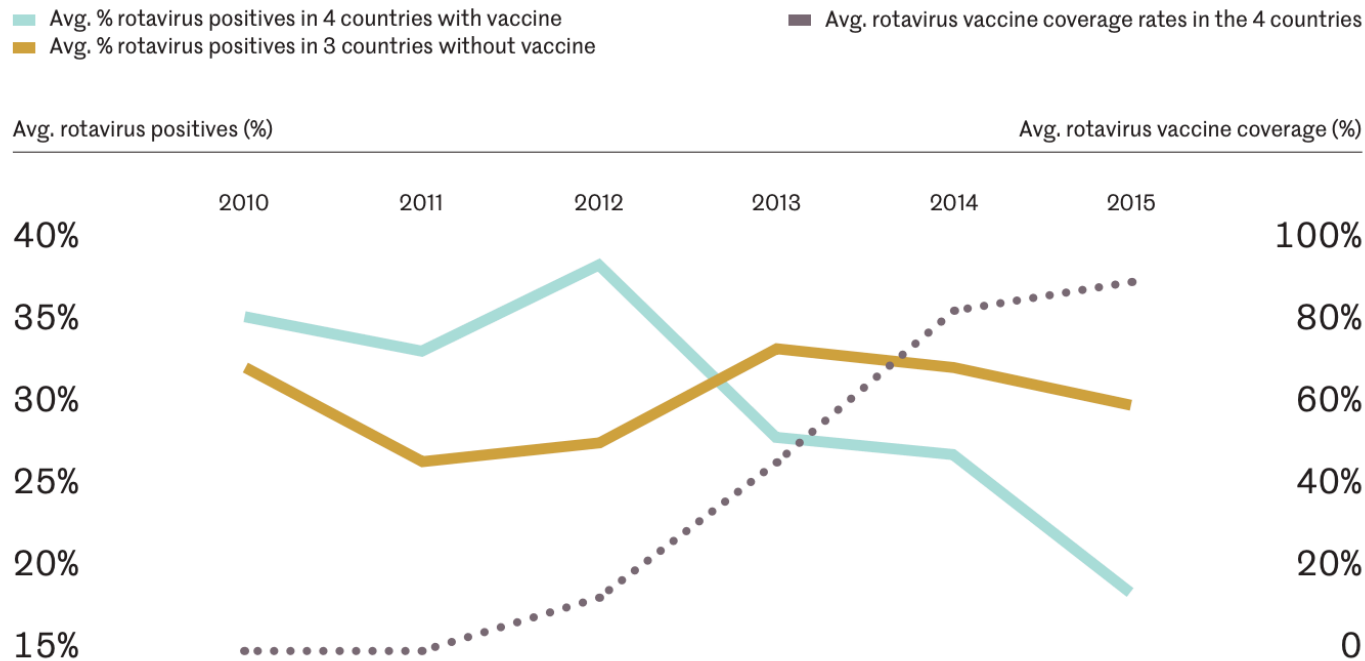


Vaccine name <i>Manufacturer</i>	RotaTeq® <i>Merck & Co.</i>	ROTARIX® <i>GSK</i>	ROTAVAC® / ROTAVAC5D® <i>Bharat Biotech</i>	ROTAIIL® <i>Serum Institute of India</i>
Dosing schedule	3 doses (same as DTP/penta 1, DTP/penta 2, DTP/penta 3)	2 doses (same as DTP/penta 1, DTP/penta 2)	3 doses (same as DTP/penta 1, DTP/penta 2, DTP/penta 3)	3 doses (same as DTP/penta 1, DTP/penta 2, DTP/penta 3)
Formulation options	Liquid ready-to-use	Liquid ready-to-use	(1) Frozen (2) Liquid ready-to-use	(1) Lyophilized (2) Liquid ready-to-use
Efficacy against severe rotavirus gastroenteritis in:	HIC / UMIC	98-100% ^{1,2}	85-96% ^{5,6}	No data
	LMIC / LIC	43-64% ^{3,4}	49-77% ⁷	56% (<i>in India</i>) ^{8,9}
				36% (<i>in India</i>) ¹⁰ 67% (<i>in Niger</i>) ¹¹

Impact of rotavirus vaccines



Rotavirus diarrhea hospitalizations declined with routine rotavirus vaccine use



Country income level	Percent efficacious	Case prevented per 100 vaccinated infants
Low	50%	4 orange circles
Middle	75%	2 blue circles

Vaccines prevent more hospitalizations and deaths per population in low-income countries than they do in middle- and high-income countries

Weldegebriel, G., et al., *Impact of rotavirus vaccine on rotavirus diarrhoea in countries of East and Southern Africa*. 2017.
 Zaman, K., et al., *Efficacy of pentavalent rotavirus vaccine against severe rotavirus gastroenteritis in infants in developing countries in Asia: a randomised, double-blind, placebo-controlled trial*. *The Lancet*, 2010. 376(9741): p. 615-623.

Brazil and Mexico: Vaccination benefit versus risk



	Admissions per year	Deaths per year
Rotavirus events averted by vaccination	- 81,123	- 1,303
Intussusception events caused by vaccination*	+ 118	+ 5
Benefit to risk comparison	687 to 1	261 to 1

** Source of background IS rates: Patel et al. Exp Rev Vacc; 2009; 8(11); assumes Rotarix coverage at current DTP3 rates; risk estimates from current study for week 1 after vaccination; with assumption of 5% case-fatality*

WHO recommendations (2021)



“Rotavirus vaccines should be included in all national immunization programmes and considered a priority, particularly in countries with high rotavirus gastroenteritis-associated fatality rates, such as in South and South-eastern Asia and sub-Saharan Africa. ...

The use of rotavirus vaccines should be part of a comprehensive strategy to control diarrhoeal diseases with the scaling up of both prevention (promotion of early and exclusive breastfeeding, handwashing, improved water supply and sanitation) and treatment packages packages (low osmolarity ORS and zinc).”

Rotavirus Organization of Technical Allies (ROTA Council)



MISSION

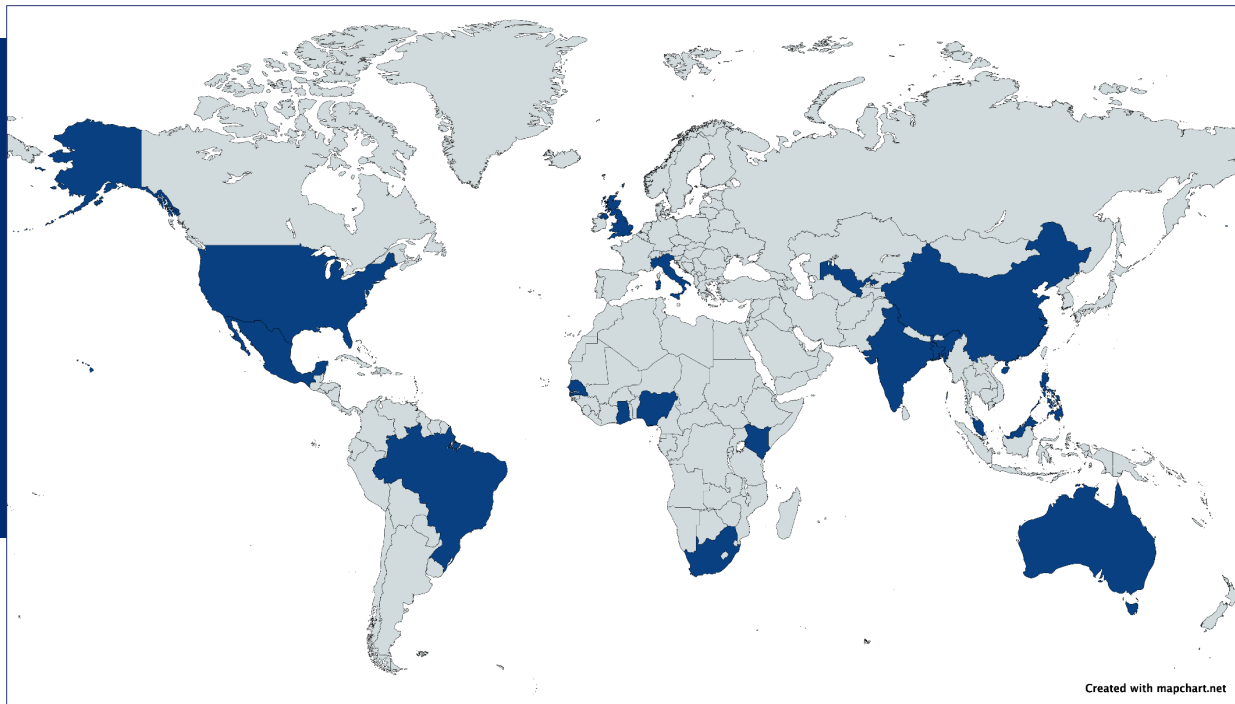
To accelerate the introduction of rotavirus vaccines through the use of evidence and strategic communications targeting policymakers and other key decision makers



Expert members and advisors



24 members from 16+ countries



Created with mapchart.net

Council Chair		Core Partners			
 Mathuram Santosham USA		 Deborah Atherly USA	 Umesh Parashar USA		
 Jon Andrus USA	 George Armah Ghana	 Mamadou Ba Senegal	 Julie Bines Australia	 Lulu Bravo Philippines	
 Nigel Cunliffe UK	 Shams El Arifeen Bangladesh	 Carlo Giaquinto Italy	 Roger Glass USA	 Zulkifli Ismail Malaysia	
 Gagandeep Kang India	 Li Li China	 Alexandre Linhares Brazil	 Erkin Musabaev Uzbekistan	 Tony Nelson Hong Kong	
 Kathleen Neuzil USA	 Vesta Richardson Mexico	 Duncan Steele USA	 Oyewale Tomori Nigeria	 Fred Were Kenya	 K. Zaman Bangladesh

The role of ROTA Council



- **Communicating** the burden of rotavirus and need for prevention
- **Delivering** accurate information on vaccine safety and efficacy, underscoring the availability, affordability and life-saving, health-improving potential of vaccines
- **Serving** as an independent body for the latest evidence on rotavirus vaccines
- **Working** to ensure that vaccines are seen as part of a comprehensive approach to addressing all of diarrhea's causes

ROTAVIRUS DISEASE AND IMMUNIZATION: AN OVERVIEW

This summary highlights select themes and evidence covered in a seven-brief series tailored to support immunization programs and policies.

THE EPIDEMIOLOGY AND BURDEN OF ROTAVIRUS

Common cause
Rotavirus remains among the most common causes of severe diarrhea in children under 5 worldwide and is the leading cause of severe and fatal diarrhea in children under the age of 5 years in developing countries and health care settings participating in a recent prospective study.^{1,2}

Vulnerability
Children under 5 years of age suffer the highest rates of rotavirus diarrhea, and in high-income settings, a substantial proportion of cases occur in children less than 6 months of age.^{3,4} The mortality caused by rotavirus—on the basis of hospitalizations, hospital costs and disability-adjusted life years—underrepresented by poor countries.^{5,6}

Where are children dying of rotavirus?
An estimated 215,000 children died from rotavirus in 2017 worldwide, mostly in the low- and middle-income countries.⁷ In 2018, four countries—Nigeria, Chad, Niger, and Mali—were estimated to account for half of all rotavirus deaths, and about 15% occurred in 14 of global low-income and newly emerging economies.⁸

THE EPIDEMIOLOGY AND DISEASE BURDEN OF ROTAVIRUS

INTRODUCTION

Diarrhea is one of the world's leading killers of children and remains common among the most common causes of severe diarrhea in children under the age of 5 years in developing countries. Rotavirus is a viral disease that causes gastroenteritis as an infection of the stomach and intestines. Rotavirus primarily affects the small intestine, damaging the surface tissue and preventing the absorption of nutrients, causing diarrhea. Typical symptoms can range from severe diarrhea to severe diarrhea with vomiting and fever.

WHO-recommended treatment, such as oral rehydration and zinc supplements, can reduce the severity and duration of rotavirus diarrhea. However, in low-income countries, particularly in the health care settings where children do not have timely access to such medical care, or in disaster settings, mortality can be high. In fact, in 2018, four countries—Nigeria, Chad, Niger, and Mali—were estimated to account for half of all rotavirus deaths, and about 15% occurred in 14 of the places where the greatest number of children deaths occur.⁸

ROTAVIRUS VACCINE INTRODUCTION AND COVERAGE

THE STATUS

Just over half of all countries in the world have introduced rotavirus vaccines into their primary care programs (as of March 2022). Introduction of rotavirus vaccines has been particularly rapid in the Americas, followed by the Eastern Mediterranean, the European Region, and the Western Pacific Region. In the Eastern Mediterranean Region, the number of countries that have introduced rotavirus vaccines has increased from 10 in 2010 to 20 in 2022. In the Americas, the number of countries that have introduced rotavirus vaccines has increased from 10 in 2010 to 20 in 2022.

FIG. 1. PERCENT OF INFANTS WORLDWIDE WHO LIVE IN COUNTRIES THAT HAVE INTRODUCED ROTAVIRUS VACCINES*

57% infants worldwide (7/20/23)

CURRENT AND UPCOMING ROTAVIRUS VACCINES

INTRODUCTION

The rotavirus vaccine landscape, or availability of vaccine products and manufacturers and helps to improve the global supply of rotavirus vaccines to low- and middle-income countries. The expanded number of manufacturers could help to increase the availability of rotavirus vaccines in low- and middle-income countries. In addition, some products in development may have advantages over currently available vaccines. This brief focuses on the currently available vaccines and those most likely to become available in the next several years.

TABLE 1. CURRENT ROTAVIRUS VACCINES AND CANDIDATES IN ADVANCED STAGES OF DEVELOPMENT (MANUFACTURER, COUNTRY)

WHO-prequalified	WHO-prequalified	WHO-prequalified
Rotarix® (GSK, Belgium)	Rotavivax® (Novartis, Switzerland)	R5V-BB (Pfizer, United States)
Rotarix® (GSK, Belgium)	Rotavivax® (Novartis, Switzerland)	LLR-manufactured (LLR, United States)
Rotarix® (GSK, Belgium)	Rotavivax® (Novartis, Switzerland)	Rotavivax® (Novartis, Switzerland)
Rotarix® (GSK, Belgium)	Rotavivax® (Novartis, Switzerland)	Rotavivax® (Novartis, Switzerland)
Rotarix® (GSK, Belgium)	Rotavivax® (Novartis, Switzerland)	Rotavivax® (Novartis, Switzerland)

THE BROADER IMPACT OF EARLY CHILDHOOD DIARRHEA

INTRODUCTION

Diarrheal disease in infancy and early childhood—especially severe, prolonged episodes—can have long-term consequences on a child's growth, cognitive development, and ability to go to school. There is also a growing body of research linking diarrhea in early childhood to increased risk factors for non-communicable diseases, such as diabetes, cardiovascular disease, and obesity. In this brief, we discuss the long-term impact of childhood diarrhea in general—not specifically rotavirus gastroenteritis.



Childhood diarrhea, especially repeated and prolonged bouts, can have a long-term impact on growth and development.

THE IMPACT OF ROTAVIRUS VACCINATION

INTRODUCTION

The oral, live attenuated rotavirus vaccine (the live-attenuated rotavirus vaccine) is the only vaccine against severe rotavirus diarrhea (RRV) in the United States and 70% in the United States. The live-attenuated rotavirus vaccine (RRV) is the only vaccine against severe rotavirus diarrhea (RRV) in the United States and 70% in the United States. The live-attenuated rotavirus vaccine (RRV) is the only vaccine against severe rotavirus diarrhea (RRV) in the United States and 70% in the United States.

ROTAVIRUS VACCINE SAFETY

INTRODUCTION

Rotavirus vaccines currently available on the international market have been shown to be safe. The most widely concerns has been a very small increased risk of an intestinal bleed syndrome called intussusception. Intussusception occurs frequently in infants under 18 months of age in the absence of any rotavirus vaccine. However, a very small increased risk has been found in some countries following the introduction of rotavirus vaccines, especially within the first week after the first dose is given.

Intussusception in infants
Intussusception is the most common naturally occurring cause of bowel obstruction in infants, although it is well-recognized, with incidence rates in infants of less than 100 per 100,000 live births per year in a birth cohort of 1 million in a recent study.¹ In the United States, there are an estimated 100,000 cases of intussusception each year, with an incidence rate of approximately 100 per 100,000 live births per year. However, there are large differences in incidence rates of intussusception by region and country, with the incidence rate as high as 400 per 100,000 live births in the United States and as low as 10 per 100,000 live births in the United Kingdom.²

What is intussusception?
Intussusception is a rare but serious condition in which a segment of the intestine folds into another segment, causing an obstruction. Symptoms include severe abdominal pain, vomiting, and stool bleeding. If not treated, it can lead to intussusception of the gut and even death.³

Intussusception in more common in infants between the ages of 6 and 24 months, from one case every 100,000 live births per year in the United States to one case every 100,000 live births per year in the United Kingdom.²

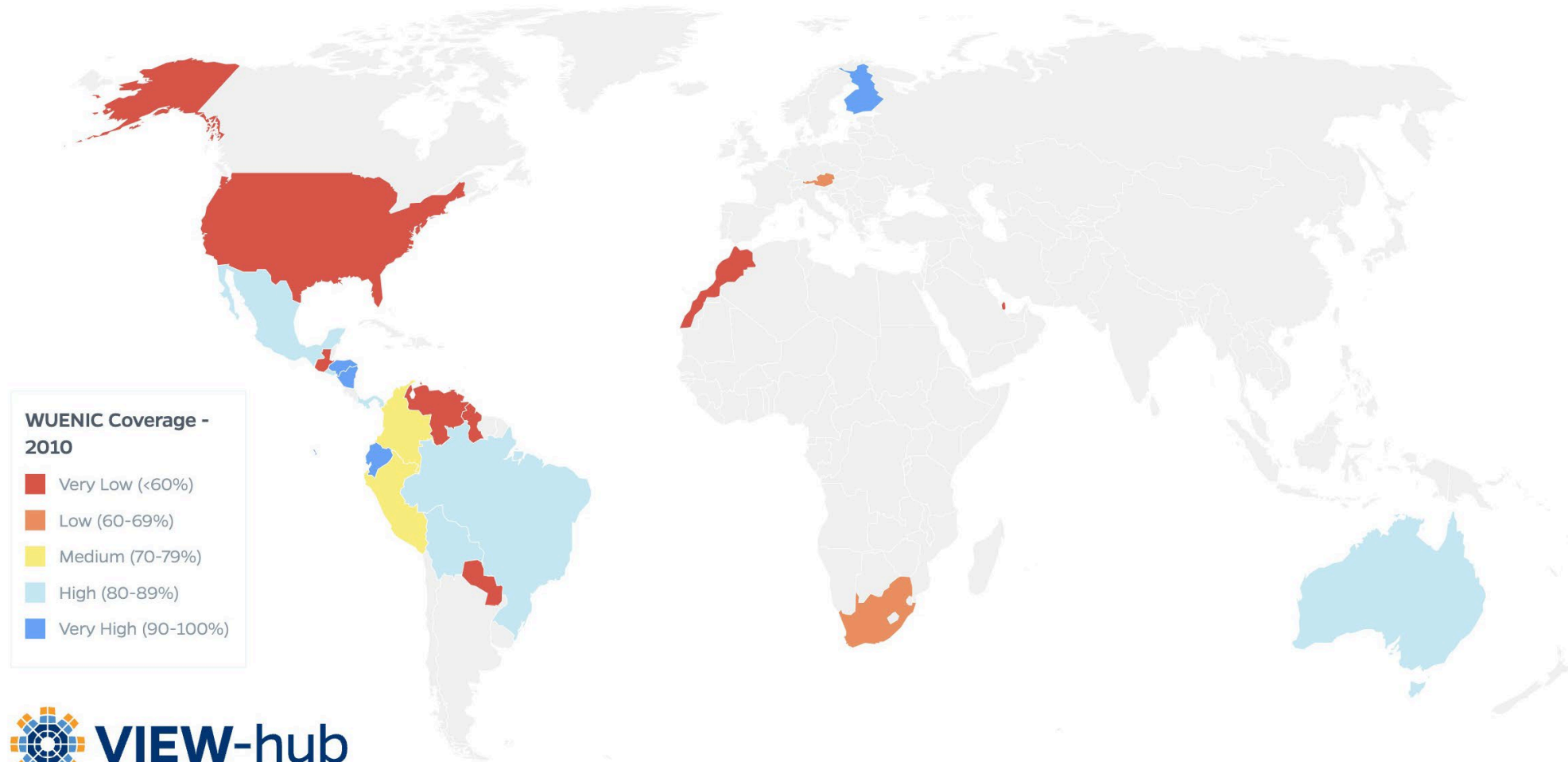
ECONOMIC COSTS OF ROTAVIRUS DISEASE AND THE VALUE OF VACCINES

COSTS TO GOVERNMENTS AND HEALTH SYSTEMS

The cost of treating rotavirus illness can be substantial to governments and health care systems in countries at all levels of development. India spent an estimated \$1.5 billion on treating rotavirus in 2010, or about \$1.5 million per 100,000 live births per year. In the United States, the cost of treating rotavirus illness can be substantial to governments and health care systems in countries at all levels of development. India spent an estimated \$1.5 billion on treating rotavirus in 2010, or about \$1.5 million per 100,000 live births per year. In the United States, the cost of treating rotavirus illness can be substantial to governments and health care systems in countries at all levels of development. India spent an estimated \$1.5 billion on treating rotavirus in 2010, or about \$1.5 million per 100,000 live births per year.

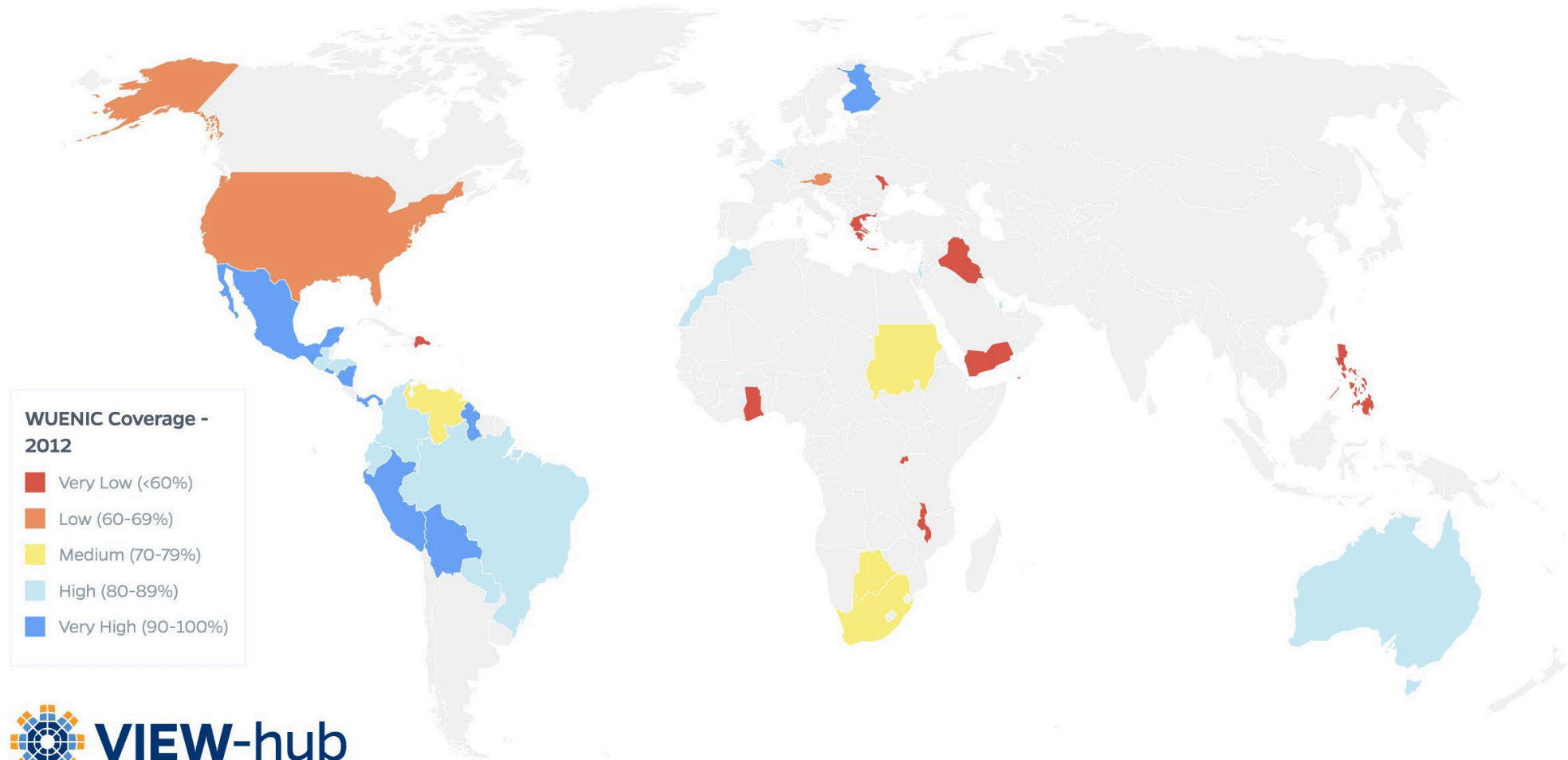


Rotavirus vaccine coverage (2010)



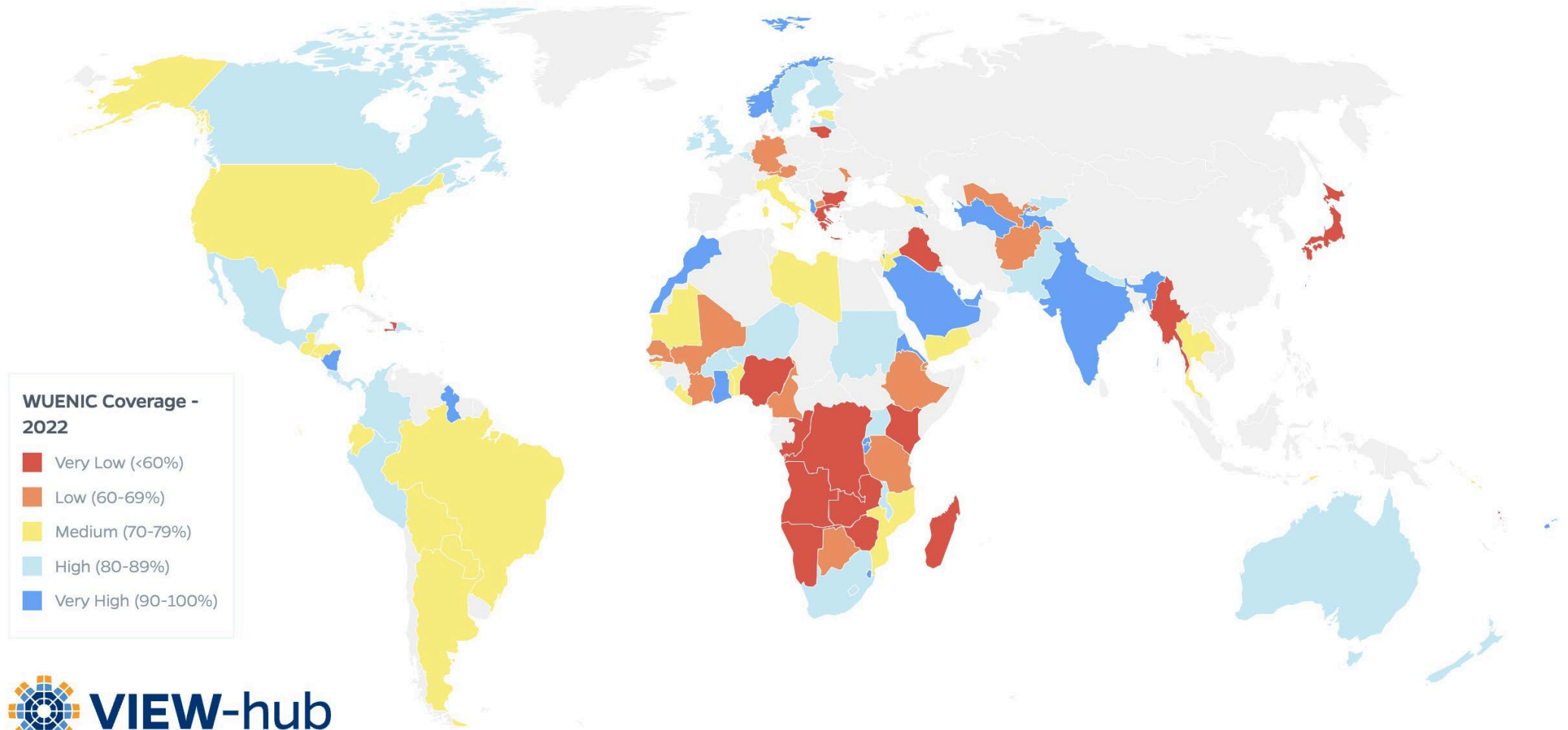
April 17, 2024 © The International Vaccine Access Center (IVAC)

Rotavirus vaccine coverage (2012)



April 17, 2024 © The International Vaccine Access Center (IVAC)

Rotavirus vaccine coverage (2022)



WUENIC Coverage - 2022

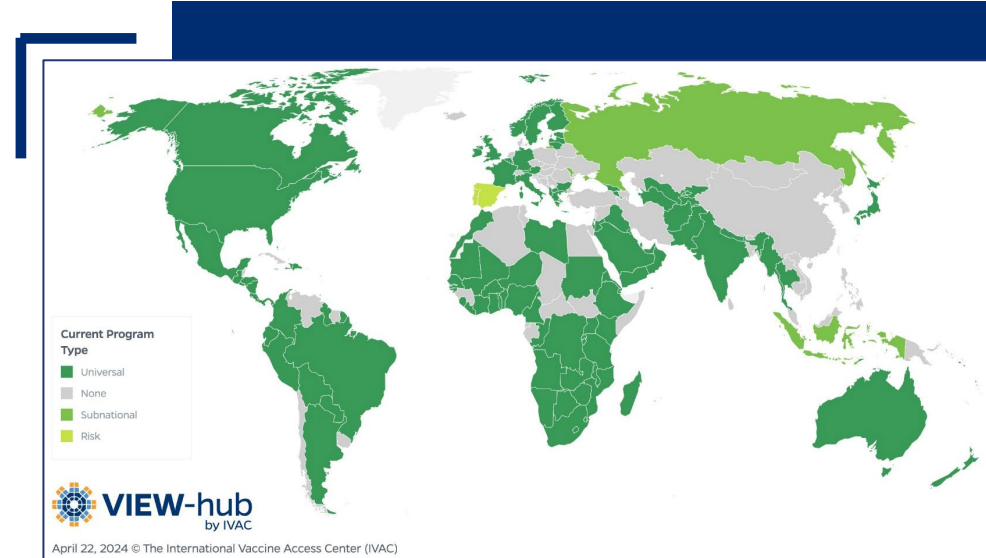
- Very Low (<60%)
- Low (60-69%)
- Medium (70-79%)
- High (80-89%)
- Very High (90-100%)



April 17, 2024 © The International Vaccine Access Center (IVAC)

Progress, challenges, and opportunities

- RVV landscape has drastically expanded from just 7 years ago when just two vaccines were available to countries
- Interchangeability and vaccine switches
 - Elective switches may improve suitability for a specific context and reduce costs
 - Compulsory switches can interrupt RVV programs, strain resources, and may not necessarily be best-suited options for the specific setting
- **120+ countries use RVV** in their national immunization programs **yet 36.2 million children still lack access to RVV**
- **140,000 deaths prevented from 2006 to 2019**
- Global supply challenges and withdrawals lead to stockouts, missed doses, and coverage gaps disproportionately affecting Gavi-eligible countries
- Prioritizing rotavirus vaccines in the remaining countries — and sustaining existing programs — remains critical



Rota team over the years



Tyler Best, Amelia Gerste, Kelly Healy, Kirthini Muralidharan,
Nicole Obe, Debora Sandiford, **Molly Sauer**, Rose Weeks

April 25, 2024

Success Story: Pneumococcal Conjugate Vaccines

Maria Deloria Knoll, PhD
Research Professor



Pneumococcal Disease

Pneumococcus causes severe pneumonia, meningitis and sepsis

Responsible for 37% of child pneumonia deaths (pre-vaccine era)

Annually >600,000 deaths and >5 million cases in children <5 years of age globally (pre-vaccine)

100+ different strains (serotypes) but most (~80%) severe disease is caused by <20 serotypes



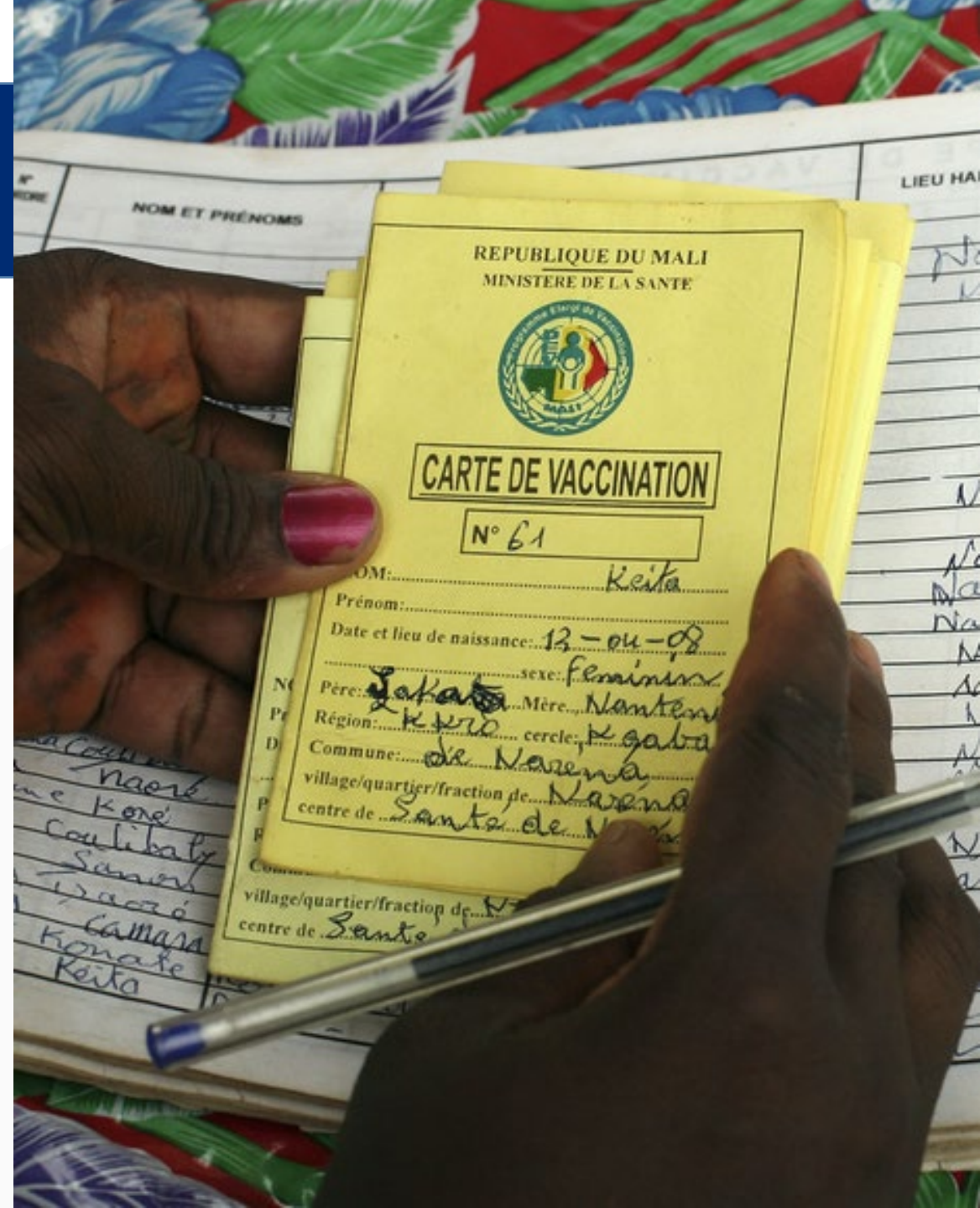
Pneumococcal Conjugate Vaccine (PCV)

First PCVs licensed in high-income country in 2000 - highly effective & very safe

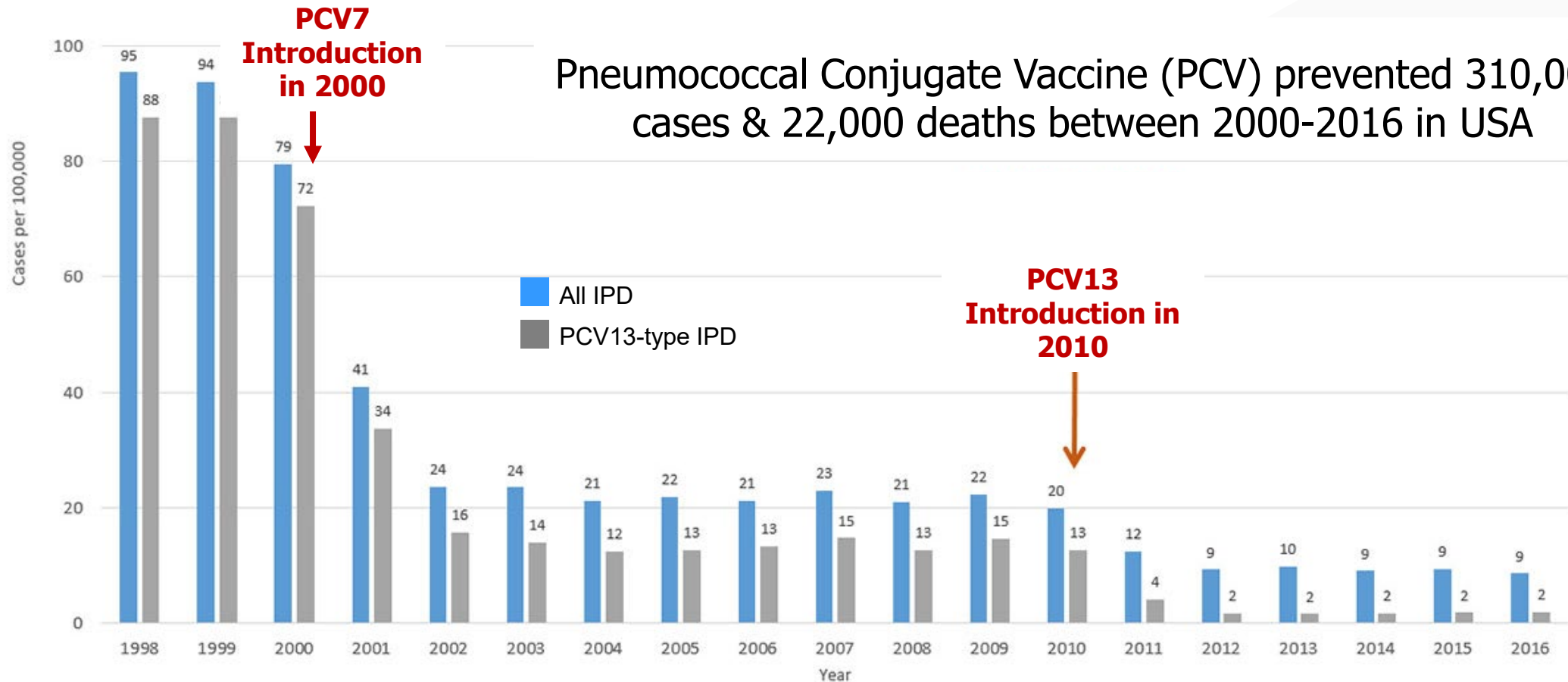
Protected against 7 of 100+ serotypes responsible for 50-80% of severe disease

10- and 13-valent PCVs licensed in 2009/10 (protect against 70-90% of disease)

15- and 20-valent PCVs licensed in 2023/24



PCVs prevented 90% of invasive pneumococcal disease (IPD) in children <5 years old, USA

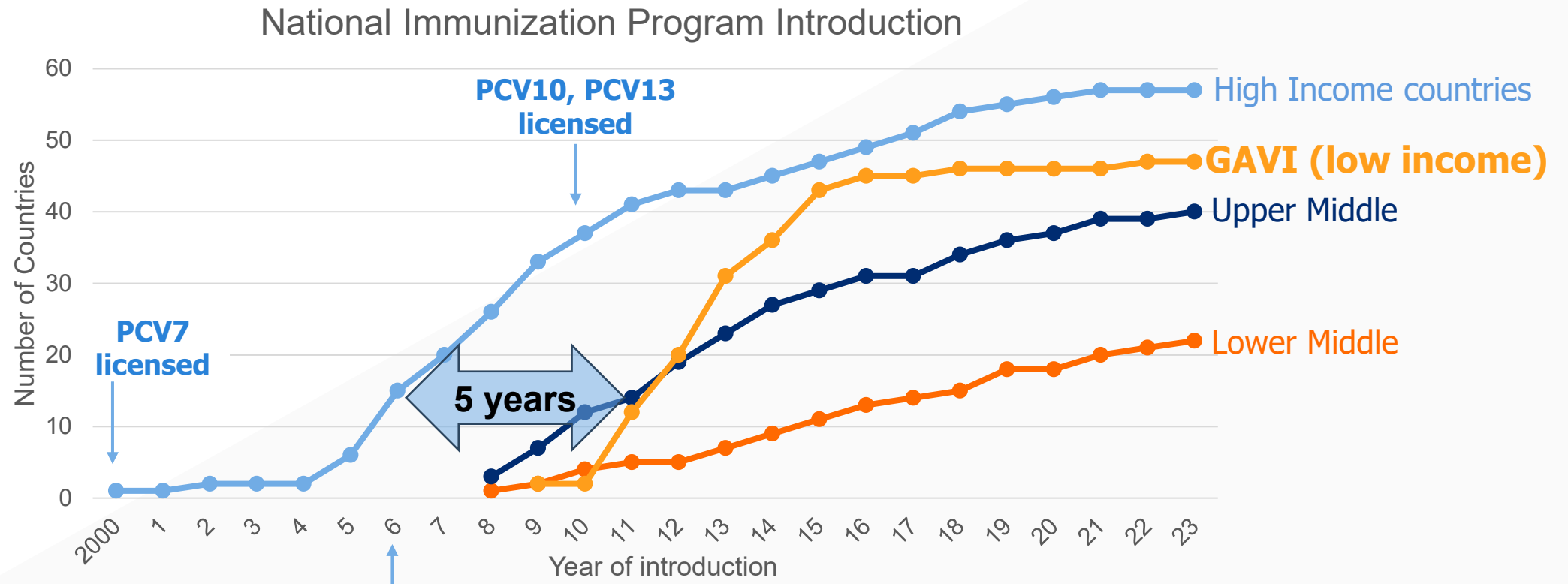


*PCV13 serotype: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F

Source: CDC, Emerging Infections Program, Active Bacterial Core surveillance, <https://www.cdc.gov/pneumococcal/surveillance.html>

Low-income countries had access to PCV decades sooner

IVAC's PneumoADIP project (funded by Gavi) accelerated access to PCV in low-income countries

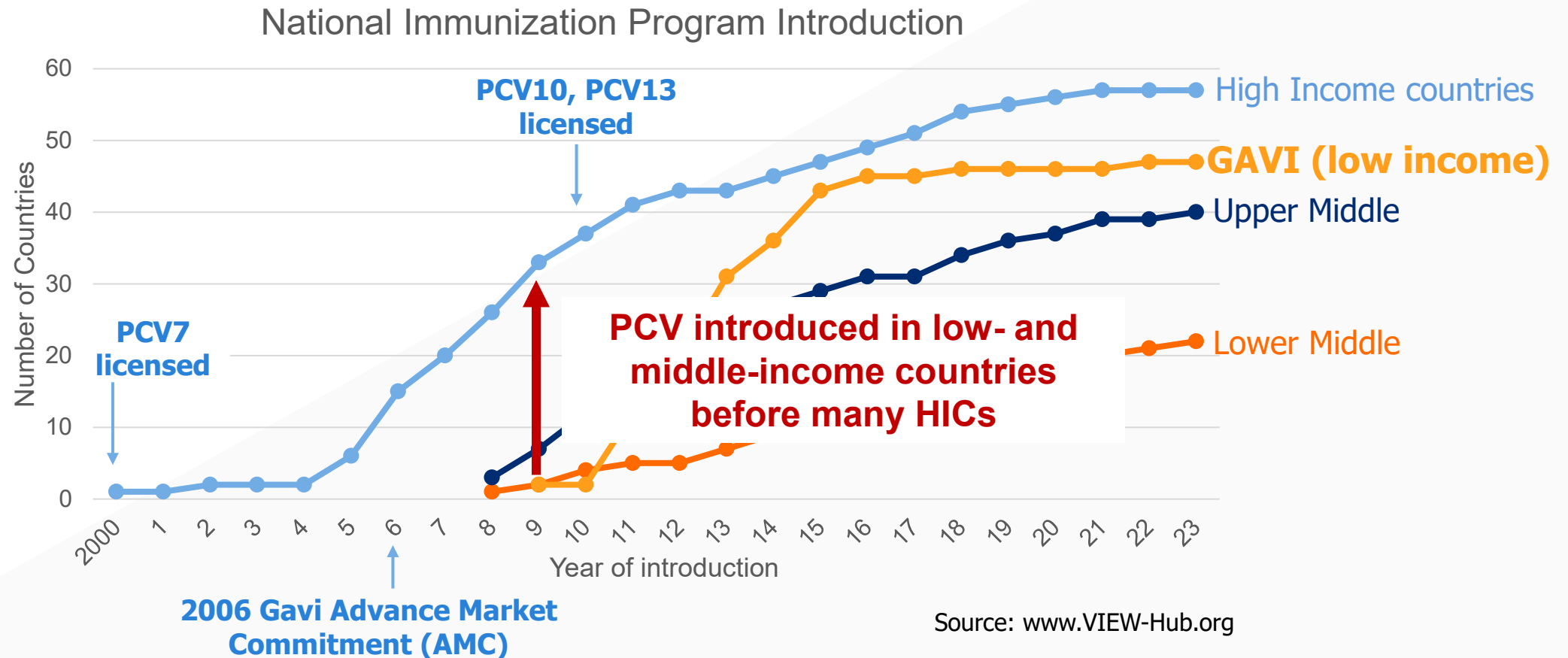


2006 Gavi Advance Market Commitment (AMC)

Source: www.VIEW-Hub.org

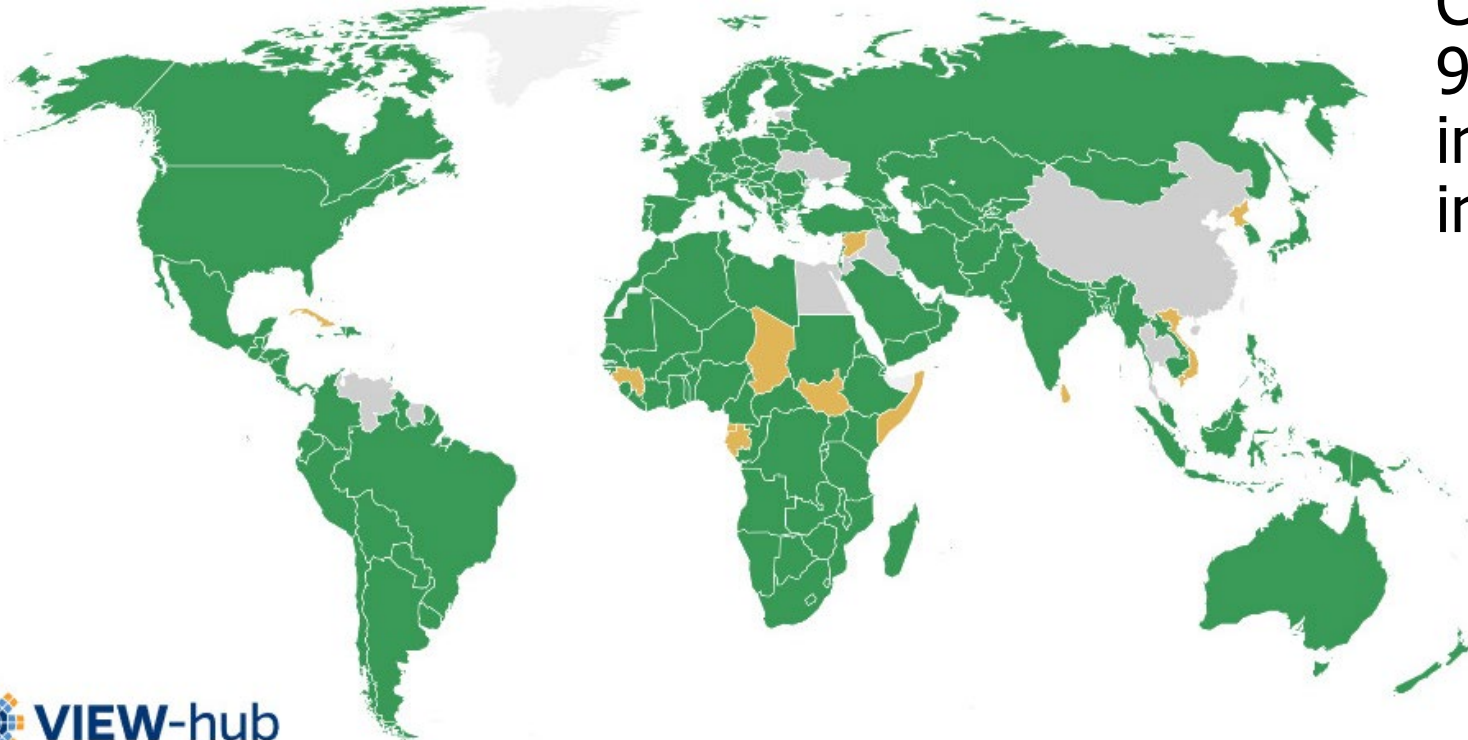
Low-income countries had access to PCV before some high-income countries

IVAC's PneumoADIP project (funded by Gavi) accelerated access to PCV in low-income countries



Source: www.VIEW-Hub.org

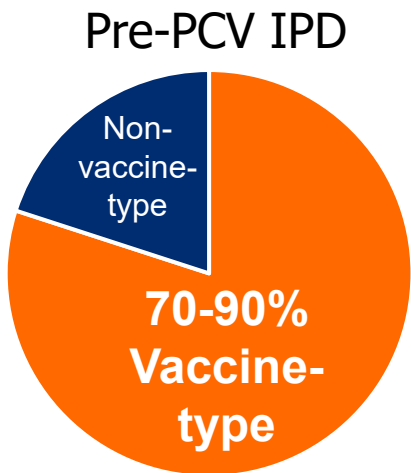
Global Introduction Status of PCV, April 2024



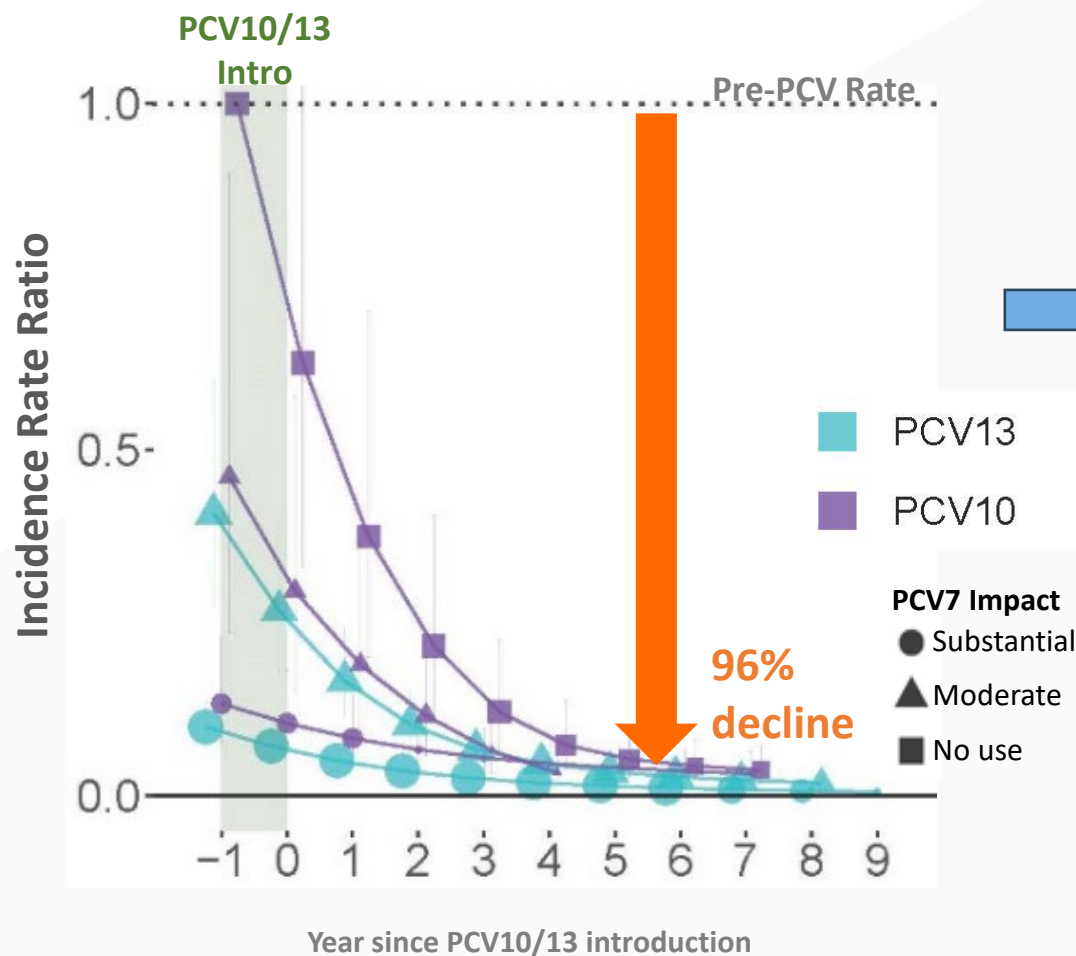
Currently all Gavi countries and 93% of countries worldwide have introduced PCV or are planning introduction

	Global Gavi	
Introduced	166	47
Planning	14	7
Not Introduced	10	0
Program Suspended	4	0

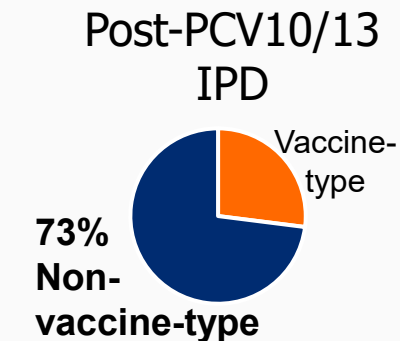
Global impact of PCV on invasive pneumococcal disease (IPD)



PCV10-type IPD in Children <5 years



All IPD declined 58-74%

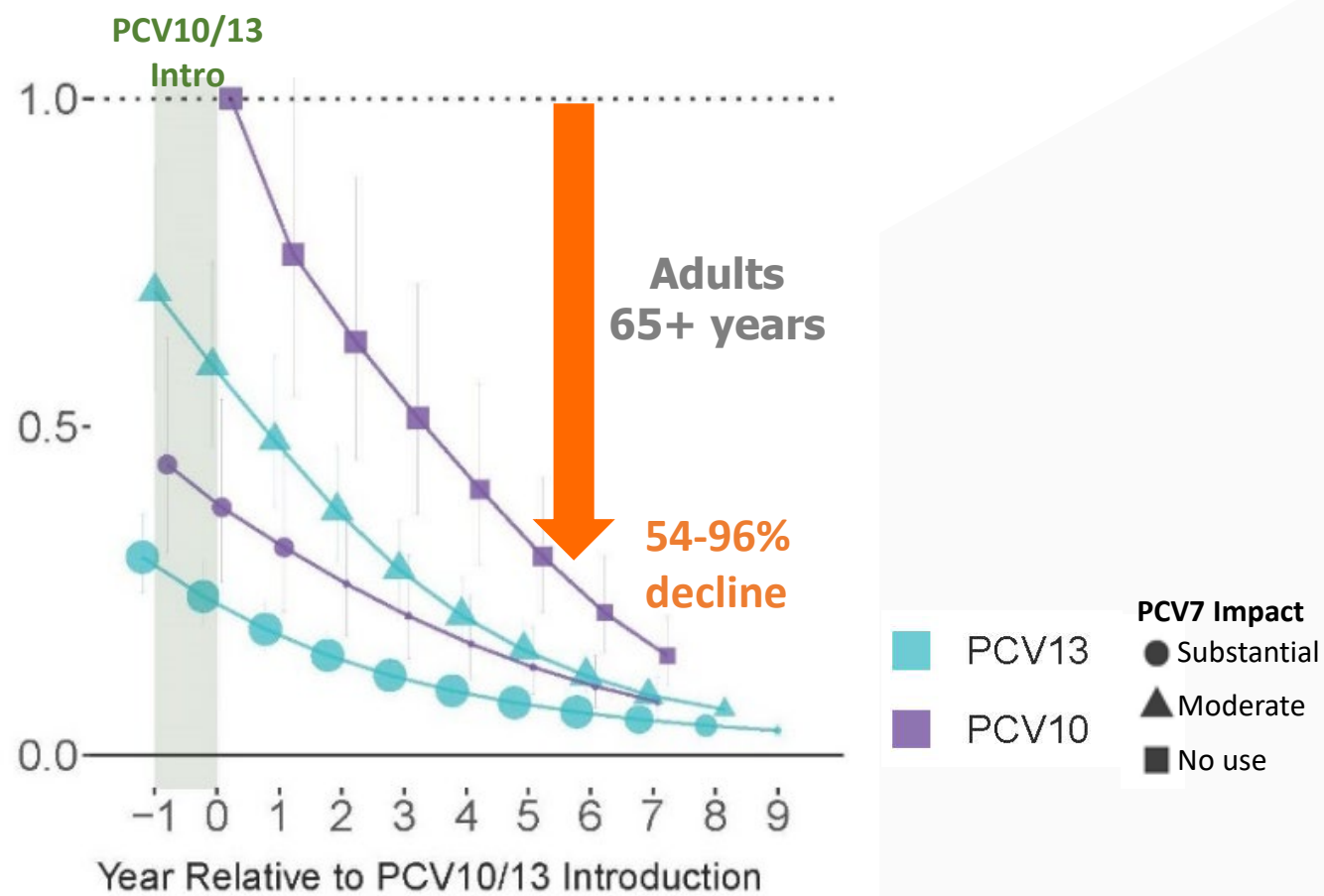


Source: PSERENADE
40 country study
Bennett & Deloria
Knoll, et al. *Lancet*
PREPRINT 2024



Infant PCV program reduced invasive pneumococcal disease (IPD) in all ages

PCV10-type IPD in Adults 65+ Years

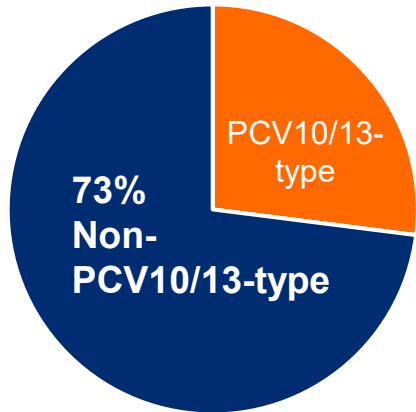


Source: PSERENADE
40 country study
Bennett & Deloria
Knoll, et al. *Lancet*
PREPRINT 2024



New PCVs coming to address much remaining pneumococcal disease

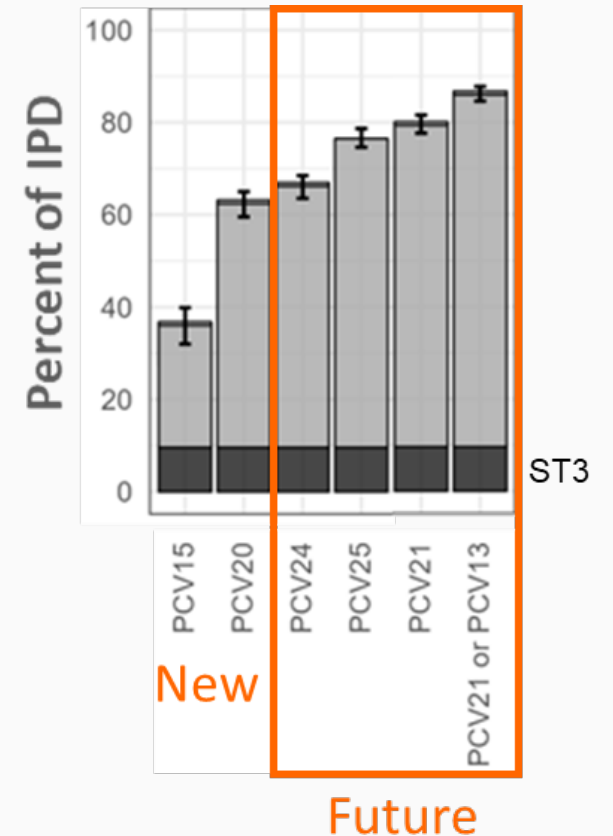
Post-PCV10/13 IPD



Serotypes covered by current and anticipated new PCVs

	PRODUCT	SEROTYPE																																		
		4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	6C	22F	33F	8	10A	11A	12F	15BC	2	9N	17F	20	15A	16F	23A	23B	24F	31	35B			
Discontinued	PCV7 (Pfizer)	<i>PCV7 replaced by PCV13</i>																																		
Licensed for children and adults	Licensed PCV10 (GSK)	[Orange]											[Orange]																							
	Licensed PCV10 (SII)	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]
	Licensed PCV13 (Pfizer)	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]	[Orange]
	Licensed PCV15 (Merck)	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]
	Licensed PCV20 (Pfizer)	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]	[Dark Orange]
Coming	Investigational PCV24 (Merck)	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	[Blue]	
	Investigational PCV25 (Inventrise)	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	[Dark Blue]	
	Investigational PCV21 (Merck)											[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	[Yellow]	

Remaining IPD covered by current and anticipated new PCVs in children <5 years



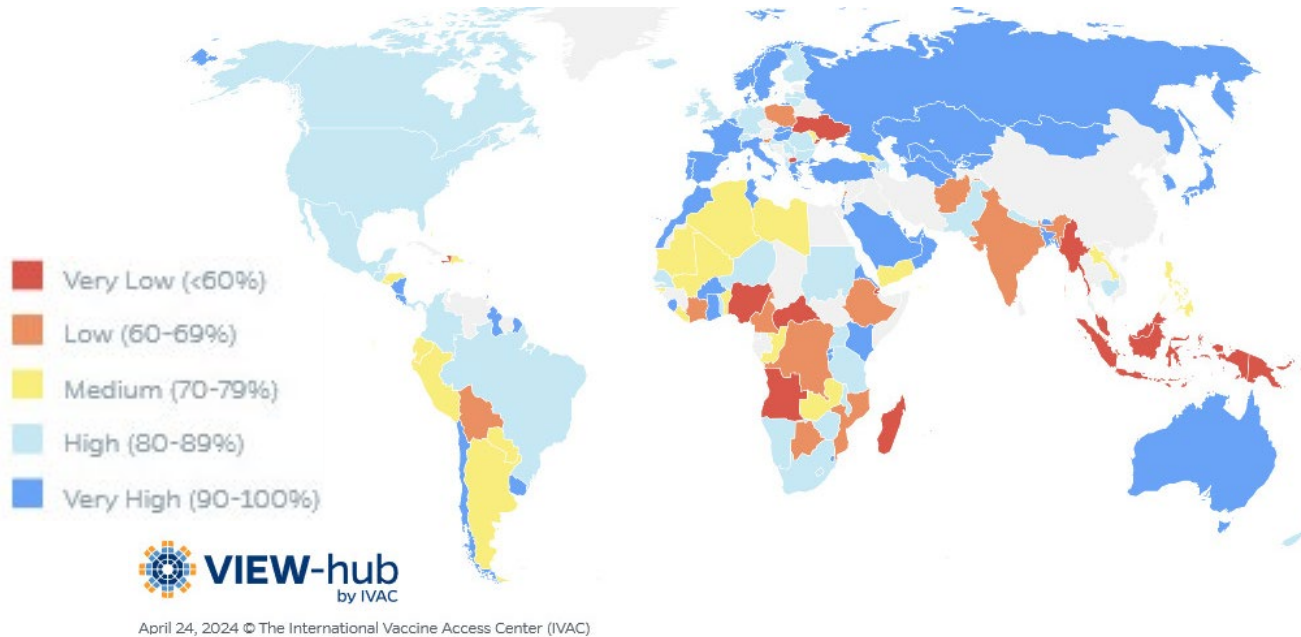
Source: PSERENADE 40 country study



Garcia Quesada, et al. *Lancet* PREPRINT 2024

Remaining challenges

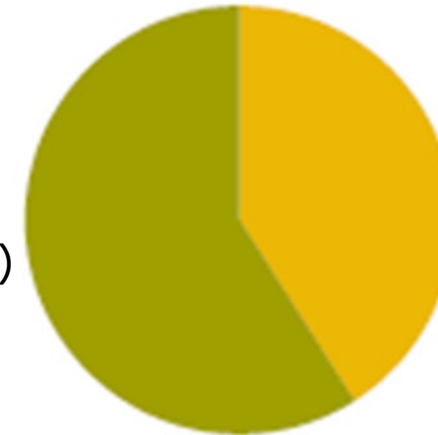
Global WUENIC coverage 2022



<https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage> Update of 18 Jul 2023

Global coverage

59%
Vaccinated
(75.7 million)



41%
Unvaccinated
(55.3 million)

Other challenges:

- 20% of children in countries without access
- Remaining non-vaccine type IPD, which increased (“replacement disease”)
- Limited suppliers for low-income markets
- Some higher valency PCVs not affordable for LMICs

Summary

Most countries have introduced PCVs
→ disease declining

PCVs reduce transmission → prevent
disease in unvaccinated children &
adults

Multiple vaccine manufacturers,
including DCVM → good supply

New PCVs could prevent even more
disease, but increasing coverage
more impactful

LMICs need access to higher valency
PCVs



HPV vaccines and impact (introduction into the EPI schedule, and IVAC's role)



Presented by Dr. Chizoba Wonodi, MBBS, MPH, DrPH,

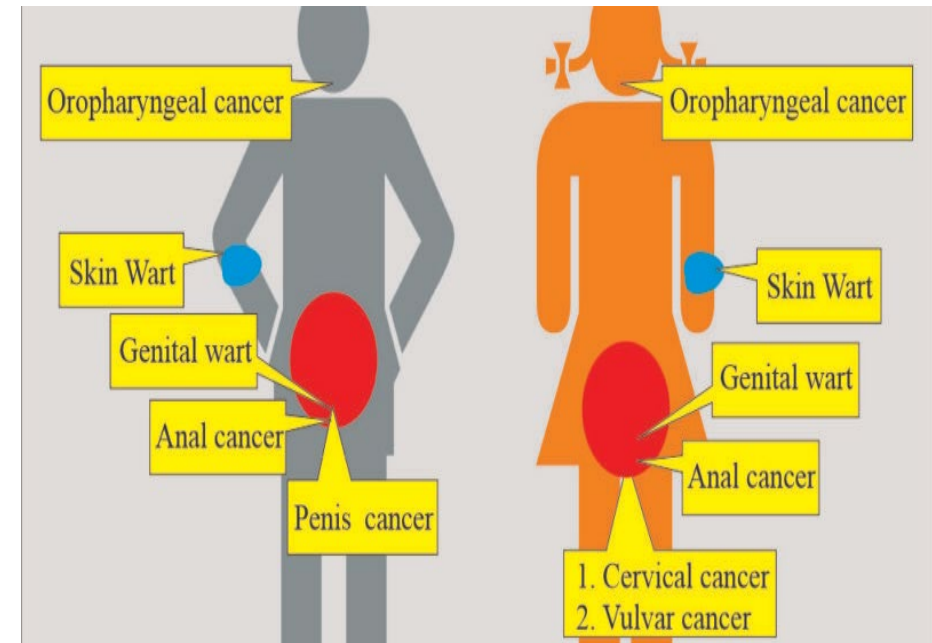
April 25, 2024

The Human Papillomavirus (HPV)

- HPV infection is a common sexually transmitted infection in men and women
- There are over 100 types of HPV, 12 of these are high risk (cancer causing)
- HPV infection resolves spontaneously in most people
- However, in some people, persistent infection can lead to skin and oral warts and oro-genital cancers in both men and women
- HPV causes nearly all cervical cancers

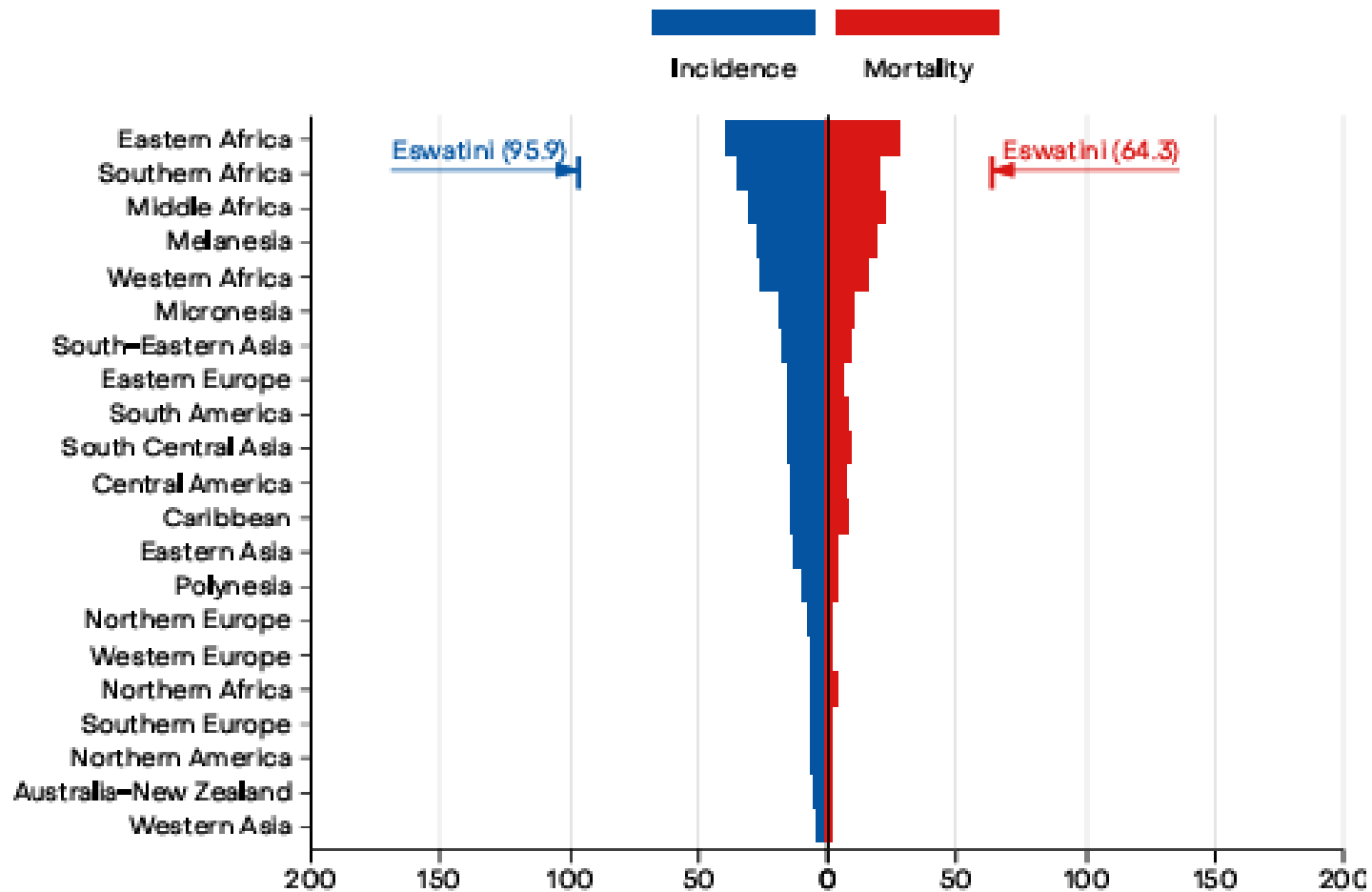


Skin and oral warts



Cervical cancers is a major public health and equity challenge

Age-standardized (World) incidence and mortality rates of cervical cancer, both sexes, per region



<https://gco.iarc.who.int/media/globocan/factsheets/cancers/23-cervix-uteri-fact-sheet.pdf>

- Huge regional disparity in burden
 - (>40 per 100,000)
 - Vrs
 - (<3 per 100,000)

About 4.5% of all cancers worldwide (630,000 new cancer cases per year) are attributable to HPV: 8.6% in women and 0.8% in men

- About 90% of deaths from cervical cancer occurred in low- and middle-income countries [1].

The WHO Strategy for cervical cancer elimination



By 2030, 90% of girls should be fully vaccinated with HPV vaccine at 15 years of age



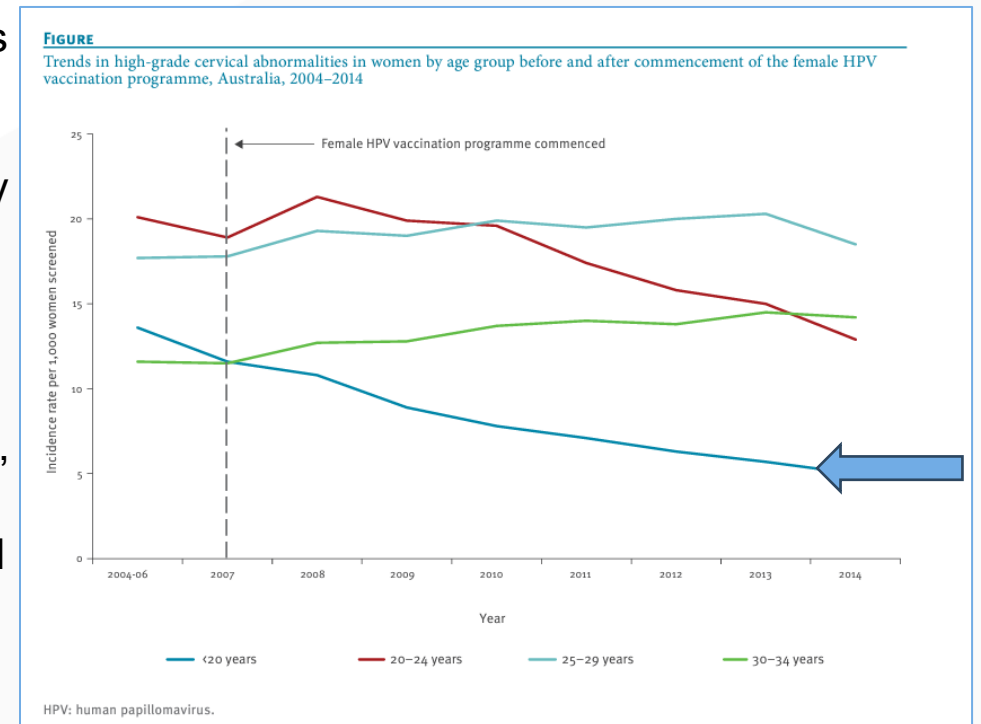
70% of women should be screened using a high-performance test by age 35, and again by age 45



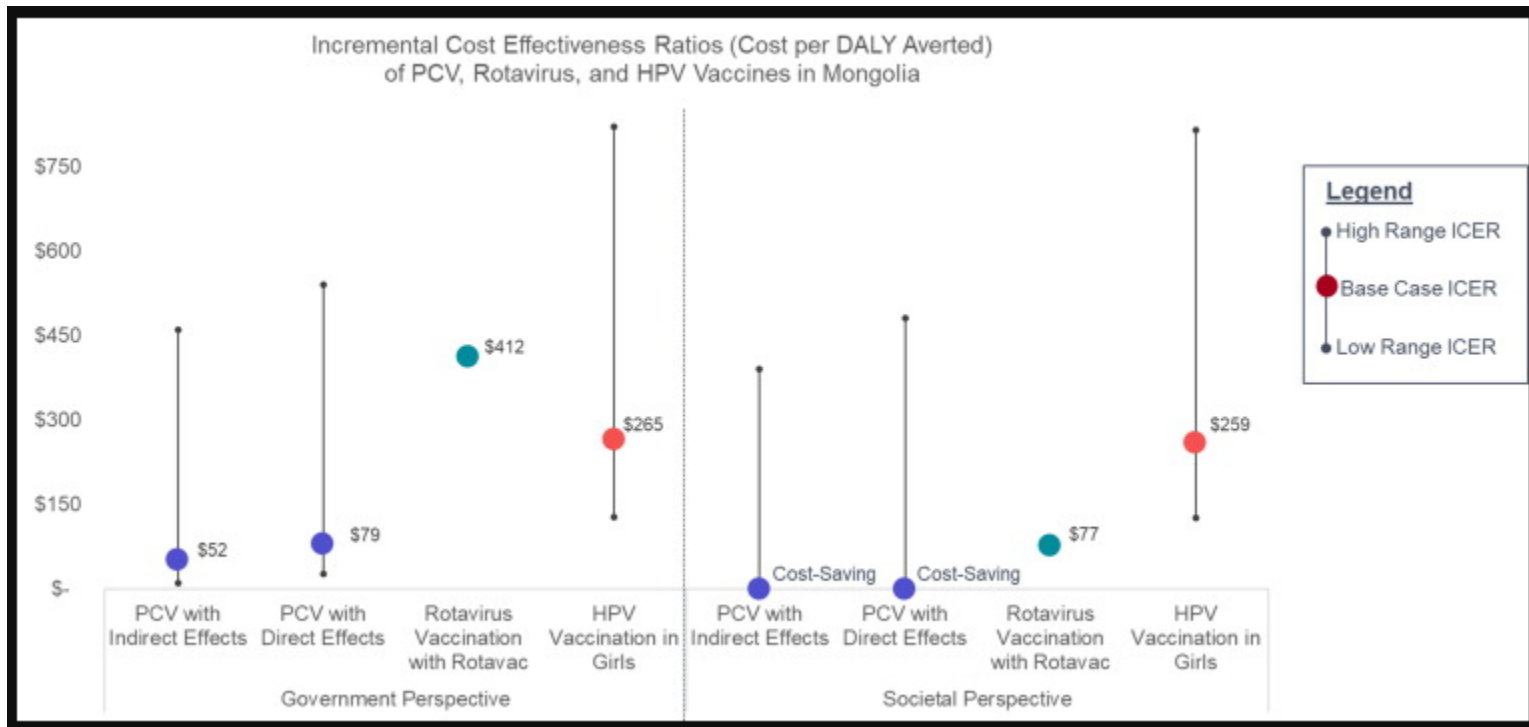
90% of those identified with cervical disease should receive appropriate treatment.

WHO position paper on HPV vaccinations

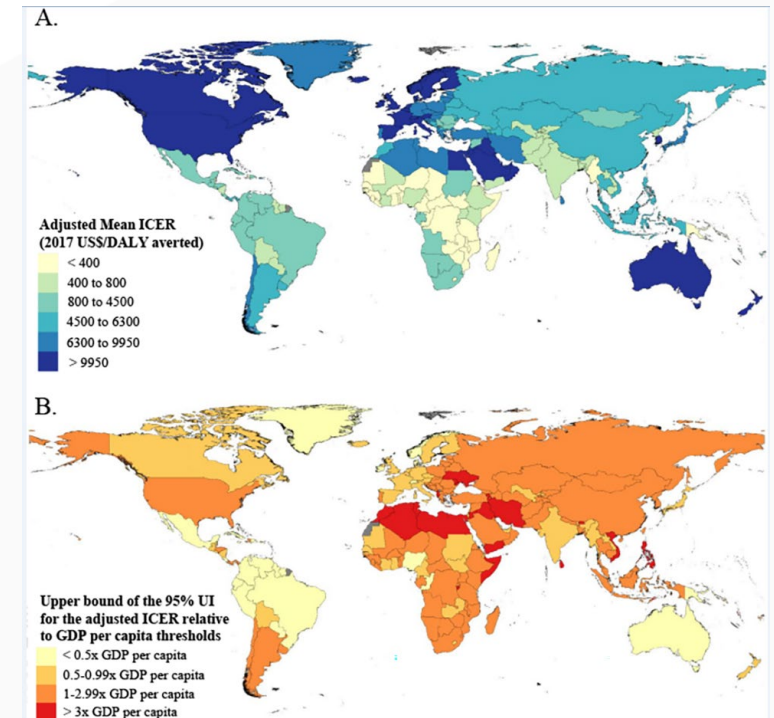
- Six licensed HPV vaccines: three bivalent, two quadrivalent, and one nonavalent vaccine.
- All vaccines are highly efficacious in preventing infection with virus types 16 and 18, which are together responsible for approximately 70% of cervical cancer cases globally.
- Highly efficacious in preventing precancerous cervical lesions caused by these virus types.
- The quadrivalent vaccine is also highly efficacious in preventing anogenital warts, a common genital disease which is virtually always caused by infection with HPV types 6 and 11.
- The nonavalent provides additional protection against HPV types 31, 33, 45, 52 and 58.
- Data from clinical trials and initial post-marketing surveillance conducted in several continents show HPV vaccines to be safe.
- The primary target group in most of the countries recommending HPV vaccination is young adolescent girls, aged 9-14. For all vaccines, the vaccination schedule depends on the age of the vaccine recipient.



HPV vaccines is one of the most cost-effective vaccines



Munkh-Erdene Luvsan, et al The potential cost-effectiveness of HPV vaccination among girls in Mongolia, *Vaccine: X*, Volume 11, 2022, 100161, ISSN 2590-1362, <https://doi.org/10.1016/j.jvacx.2022.100161>. (<https://www.sciencedirect.com/science/article/pii/S2590136222000213>)



Rosettie KL, et al. Cost-effectiveness of HPV vaccination in 195 countries: A meta-regression analysis. *PLoS One*. 2021 Dec 20;16(12):e0260808. doi: 10.1371/journal.pone.0260808. PMID: 34928971; PMCID: PMC8687557.

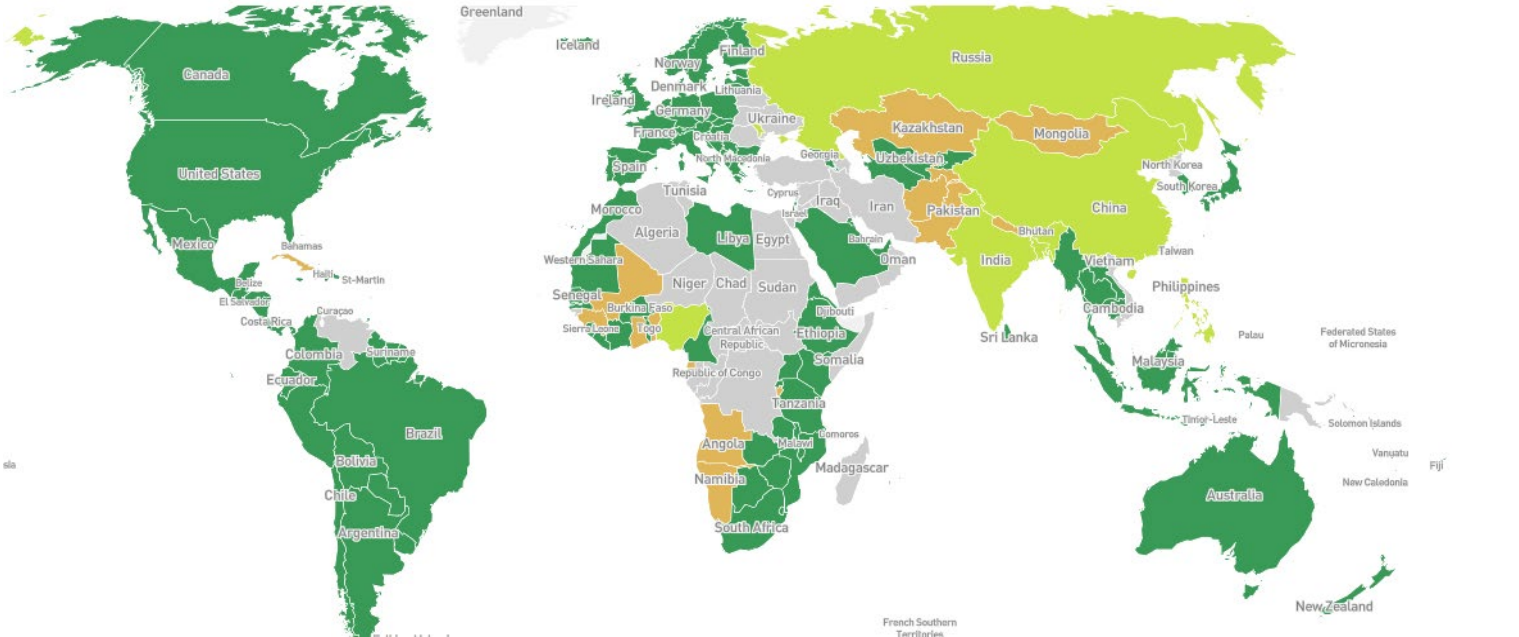
Global introduction map

HPV ▶ Vaccine Introduction ▶

Current Vaccine Intro Status i

Toggle Gavi

Filter or Select Region



Overview

	Global	Gavi
■ Introduced	137	26
■ Planning	18	10
■ Not Introduced	32	16
■ Introduced Subnationally	7	2

WHO recommended schedule

Girls 9-14 years

- One or two dose schedule

Girls 15-20 years

- One or two dose schedule

Women older than 21 years

- Two doses with a 6-month interval

A minimum of 2 doses and when feasible 3-doses remain necessary for those known to be immunocompromised and/or HIV-infected.

HPV Revitalization Programs- Global focus

- Gavi alongside other stakeholders are working to
 - *accelerate quality HPV vaccine introductions; (2)
 - *rapidly improve global and national coverage; and
 - *generate long-term programmatic sustainability through integration and optimizing whole-of-family services.



IVAC is supporting the HPV vaccine roll out in Nigeria

The Johns Hopkins International Vaccine Access Centre (IVAC) with funding from Gavi, is working with Direct Consulting and Logistics (DCL) to support the Nigeria with the HPV vaccine roll out in Nigeria

IVAC has trained and equipped > 200 CSOs and young people across 37 states to support demand generation for the HPV vaccine introduction.

The CSOs and youths have in turn activated more than 2,000 community-based vaccine champions

IVAC is a member of the national HPV technical working group and provides technical assistance

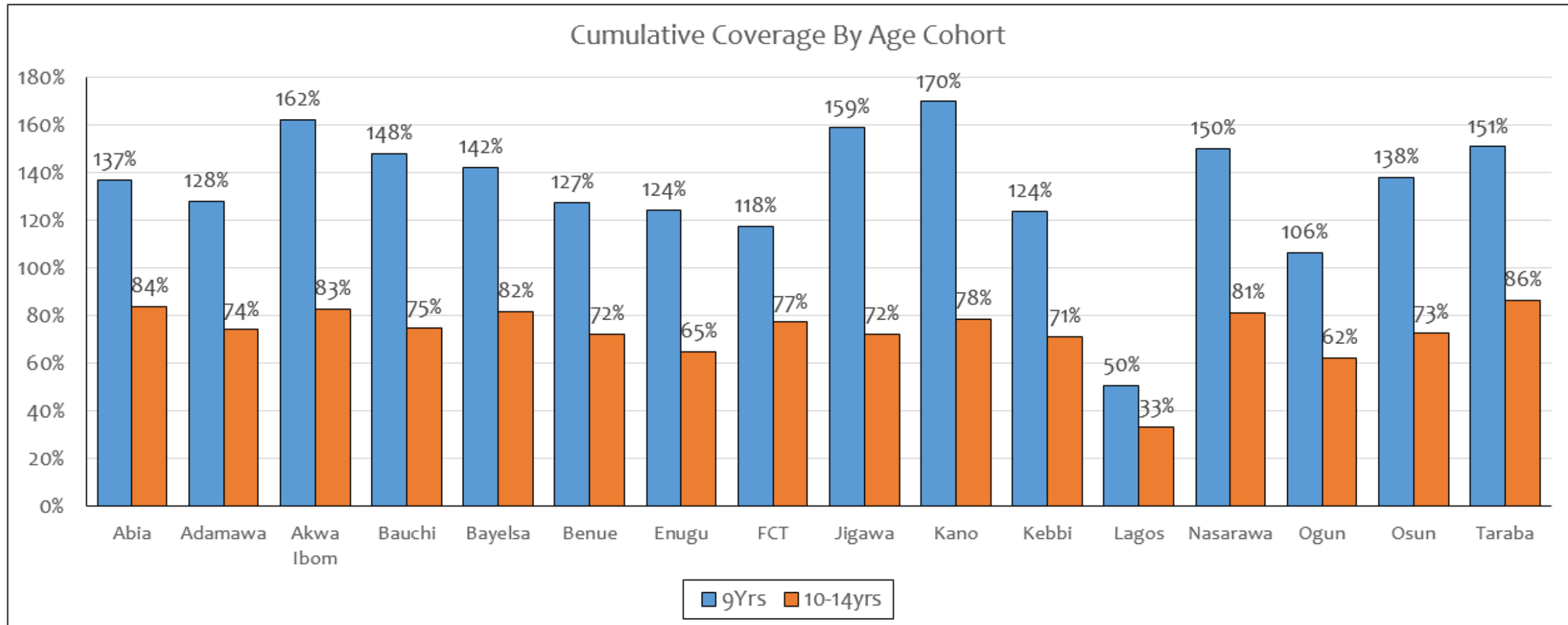


CSOs and the WAVA/DCL team at the training



Dr. Zainab Bagudu and Dr. Chizoba Wonodi

HPV Vaccination Rate Using MAC Campaign Targets (80% of TP). Data as at Feb 6th



In summary

- HPV is a major cause of cervical and other anogenital cancers globally, with 90% of deaths occurring in low- and middle-income countries.
- Despite the vaccine's introduction in over 137 countries, global coverage stands at 21%. Efforts to optimize coverage include school-based campaigns and catch-up initiatives.
- Challenges include access, affordability, and misinformation.
- IVAC supports countries with technical assistance, advocacy, and capacity building to improve coverage and address challenges.

Thank you