Evolution of Medical Innovation to Improve Access to Vaccines in Developing Countries

Dr. Seth Berkley, CEO GAVI Alliance

WHO-WIPO-WTO Symposium

Geneva, 5 July 2013

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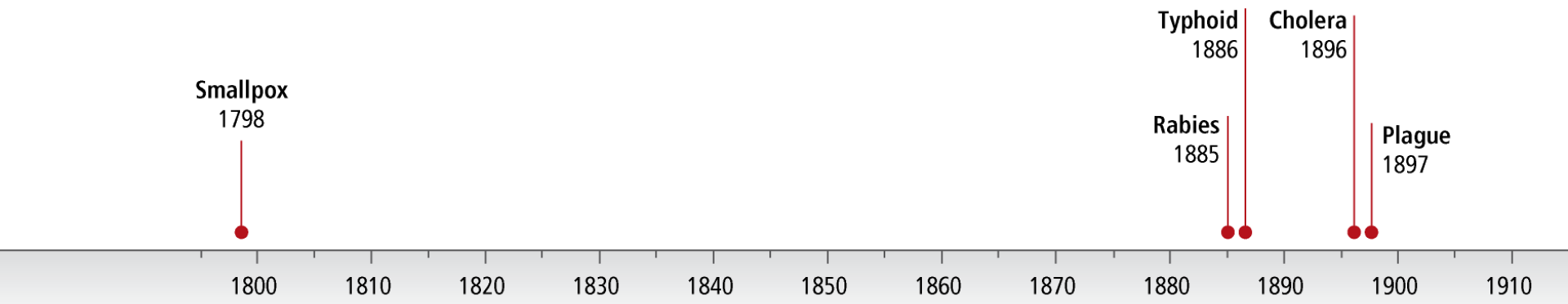
PATENT
ON
AIDS
DRUGS
BEFORE PROFIT
Against
Indian Gov
order by: DN
DNP
urge NOVA
to drop the
THE CASE
Reuters

Key differences between vaccines and drugs

Preventive		Therapeutic
Biologics		Small molecules
Biosimilars		Generics
Process patents		Product patents
High capital costs	vs.	Lower capital costs
Long and complex manufacturing		Manufacturing relatively simple
Very large clinical trials		Smaller clinical trials
Limited secondary market		Often significant secondary market

Vaccine development timeline: 1798-1910



With Thanks to Stan Plotkin

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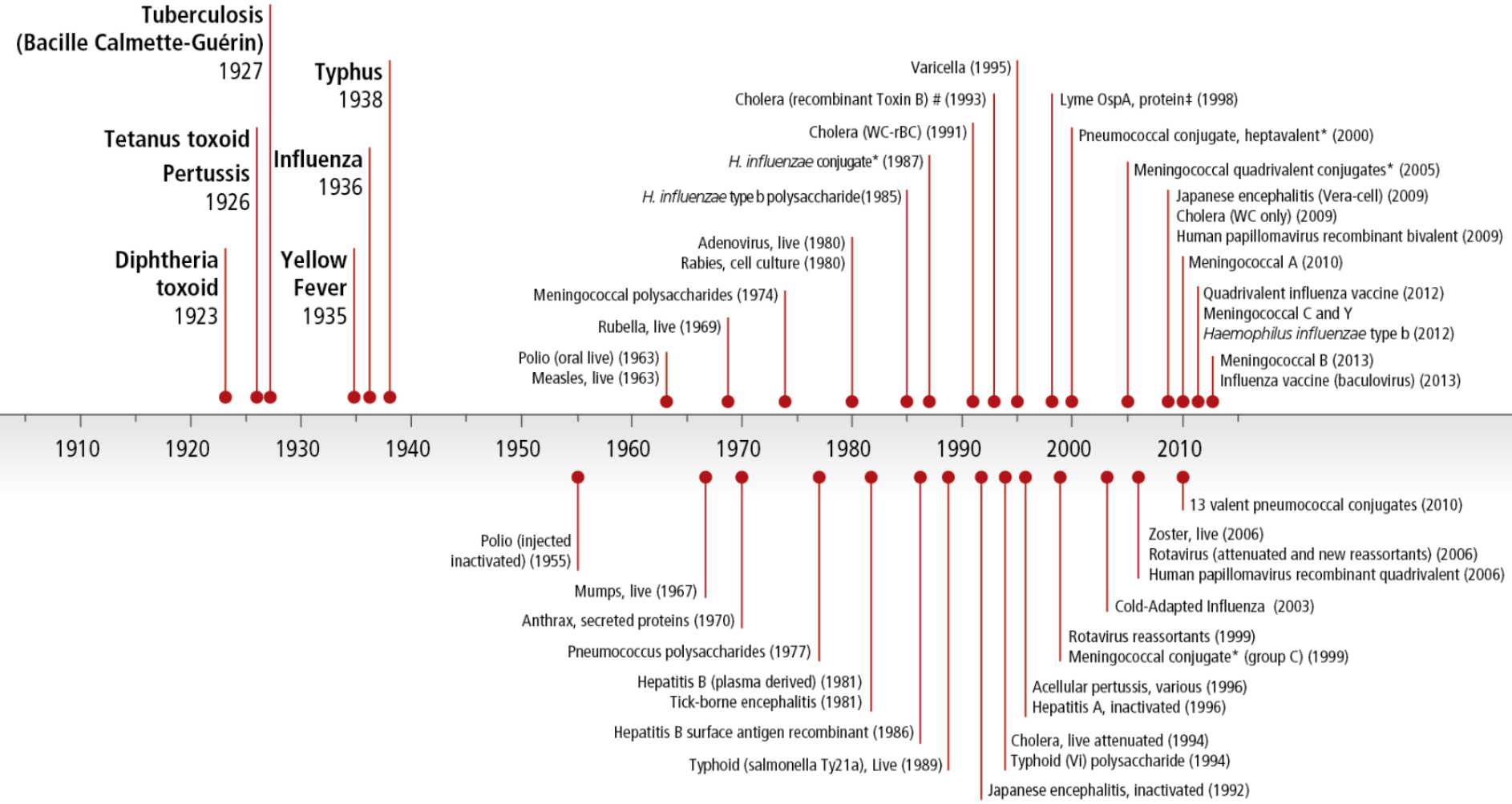
Vaccine development timeline: 1910-



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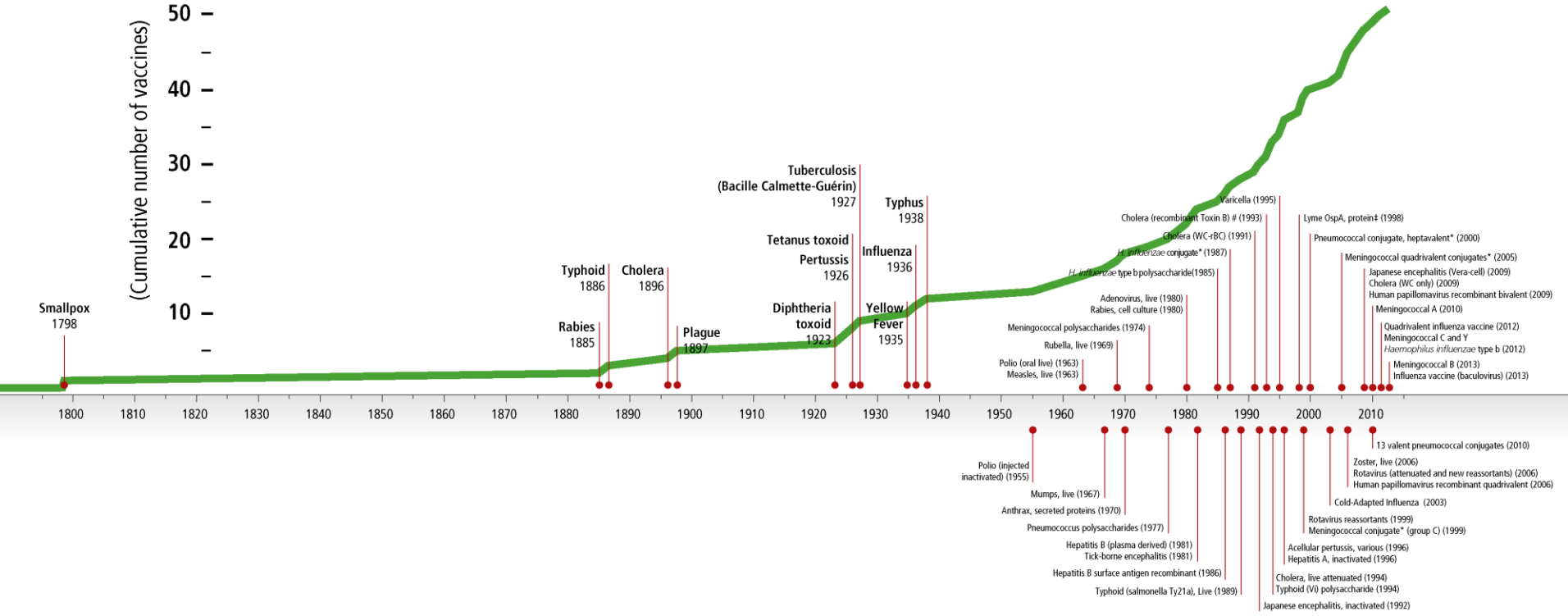
Cumulative number of vaccines developed



With Thanks to Stan Plotkin

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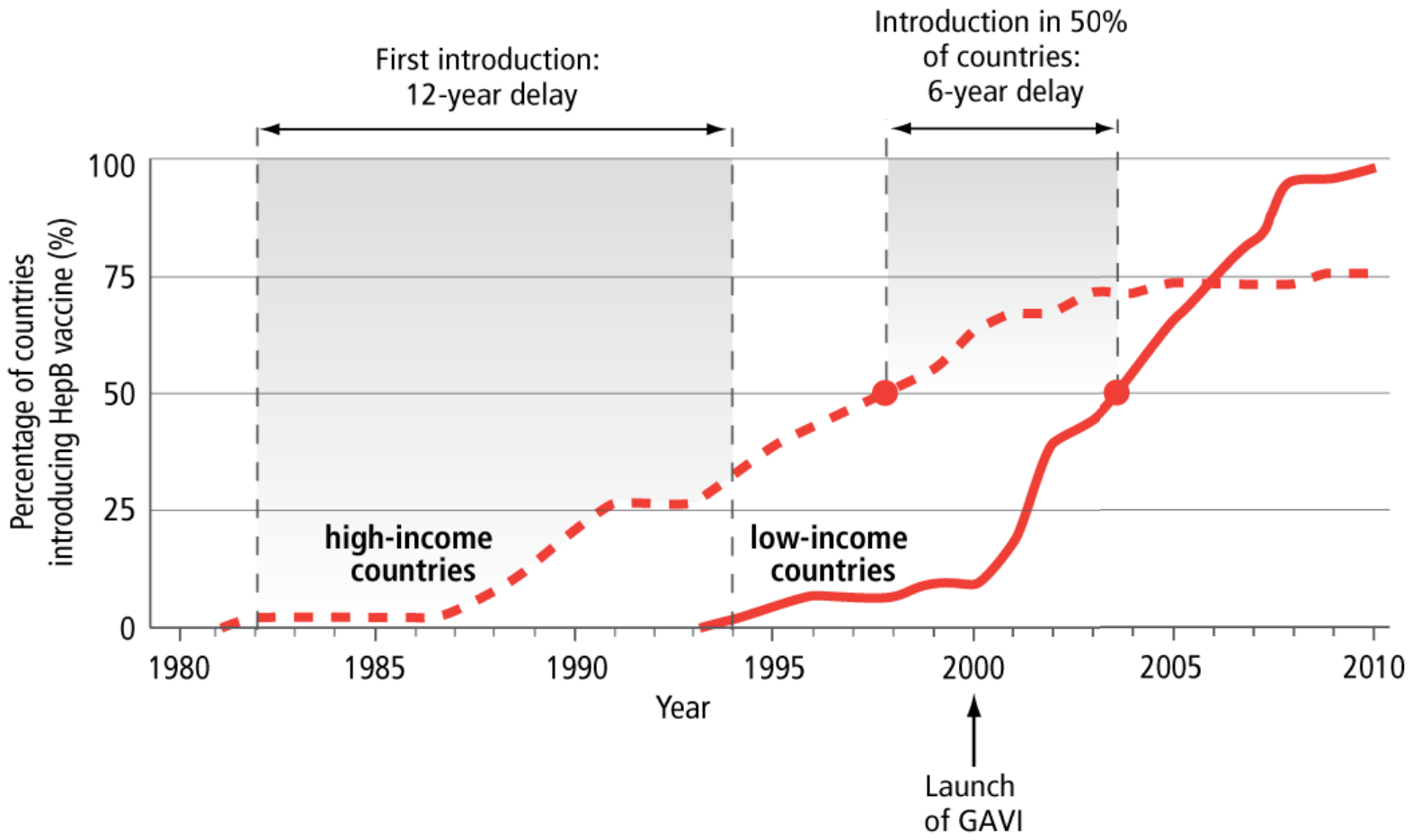
Closing the gap between countries



Innovation needed to address challenges across the value chain

- Basic research
- Translational research
- Clinical development

- Manufacturing
- Pricing
- Product quality

- Supply chain
- Data
- Health systems

IAVI's Early positioning in AIDS vaccine R&D

A well-established continuum of players moves new drugs to market

Basic research → Applied research → Preclinical development → Clinical development → Advanced development → Large-scale Efficacy trials

Public sector, academia — Biotech companies — Pharmaceutical companies

IAVI initially worked to ensure a vaccine for the developing world by focusing on product development

Basic research → Applied research → Preclinical development → Clinical development → Advanced development → Large-scale Efficacy trials

Public sector, academia — Biotech companies, pharmaceutical companies

iavi

Advocacy
Clinical trial network in developing world
Gap-filling science

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IAVI created to address gaps in vaccine R&D

As product failures forced big players out or moved them downstream, a development gap grew …

Basic research → Applied research → Preclinical development → Clinical development → Advanced development → Large-scale Efficacy trials

Public sector, academia

Pharmaceutical companies, product-development partnerships

… and IAVI moved to fill the void, creating new programs as needs arose

- Human Immunology Lab (2001)
- Neutralizing Antibody Consortium (2002)
- Live Attenuated Consortium (2006)
- Vectors Consortium (2007)
- AIDS Vaccine Design and Development Lab (2008)
- IAVI Neutralizing Antibody Center at The Scripps Research Institute (2009)

Product development partnership (PDP) model critical to fill gaps

IAVI is an integrated organization that links its …

Industry-style labs and diverse research portfolio

Academic, government and private-sector partnerships

Network of clinical trial centers in Africa and India

Advocacy and outreach from community to international level

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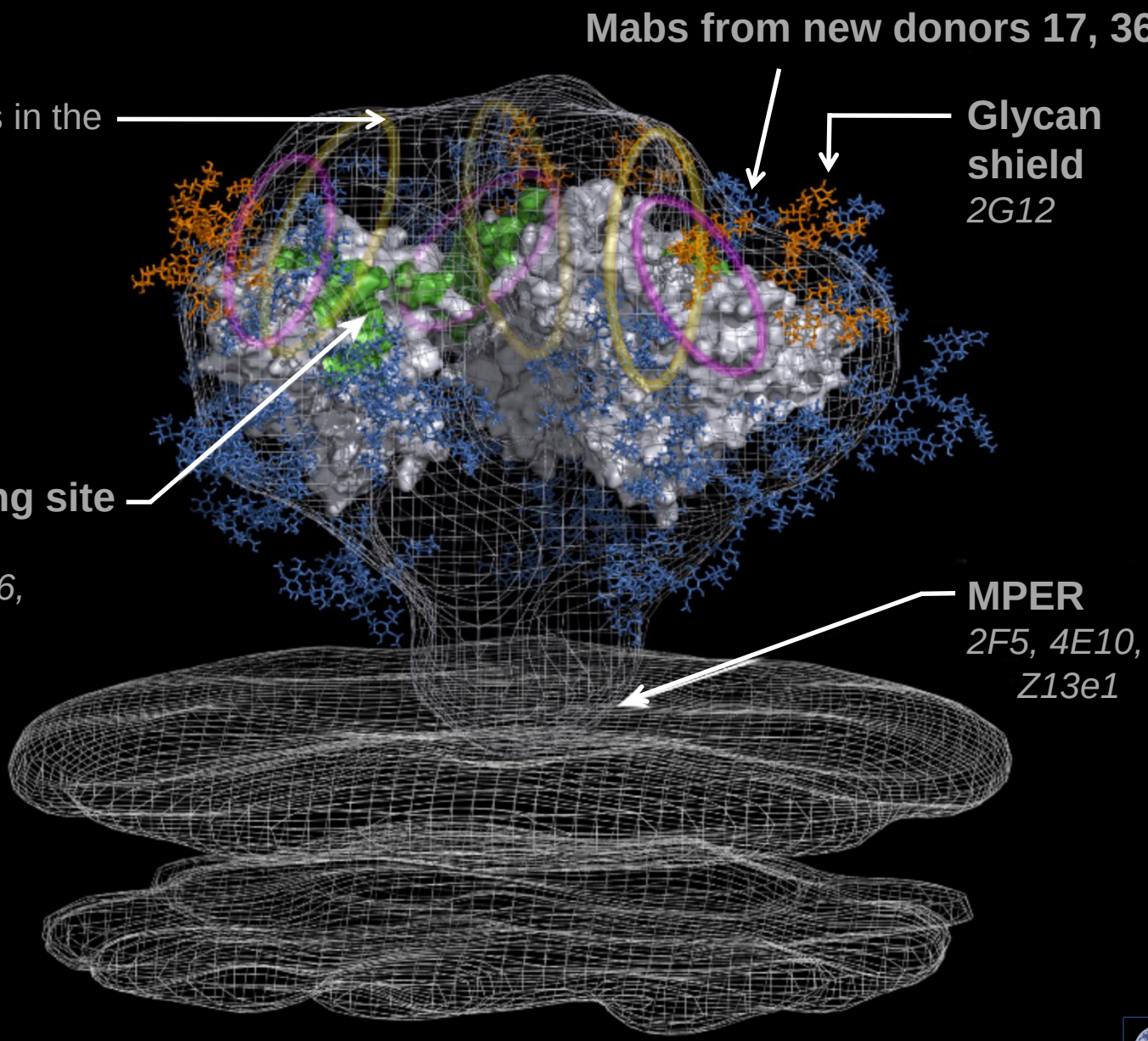
Need cohorts with **sufficient incidence**

RESEARCH CENTER	STUDY POPULATION	PERSON YEARS OF OBSERVATION	CASES PER 100 PERSON YEARS
Lusaka *Zambia*	Discordant couples	3,468	**6.3** *(5.5, 7.2)*
Copperbelt *Zambia*	Discordant couples	1,448	**7.1** *(5.7, 8.5)*
Kigali *Rwanda*	Discordant couples	1,682	**2.8** *(2.3, 3.3)*
Entebbe & Masaka *Uganda*	Discordant couples	1,897	**3.4** *(2.7, 4.4)*
Entebbe & Masaka *Uganda*	Fishing community	738	**5.6** *(3.9, 7.3)*
Kilifi & Mtwapa *Kenya*	Female sex workers	357	**2.8** *(1.8, 5.3)*
Kilifi & Mtwapa *Kenya*	Men who have sex with men	573	**8.9** *(6.8, 11.7)*
Rustenburg *South Africa*	Other risk	169	**5.3** *(1.9, 8.8)*

Source: IAVI

With new antibodies, **new targets**



Source: Schief, W.R. et al.. Curr Opin HIV AIDS. 2009 Sep; 4(5):431-40.

Better tools to meet key challenges

e.g. Neutralizing Antibody Consortium

Accelerating the search …

Broadly neutralizing antibodies	Determining structure of novel antigens	High-throughput immunogen design	Assays to rapidly screen immunogens
Characterize sera and identify broadly neutralizing monoclonal antibodies	Structural biology	Immunogen design	Immunogen screening	Clinical development
Protocol G	High-throughput robot	Indian Medicinal Chemistry Program; Innovation Fund	VAXDESIGN

… with new high-throughput approaches

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Acceleration in number of PDPs

BY YEAR STARTED

Selected other
public-private partnerships
Working on health issues

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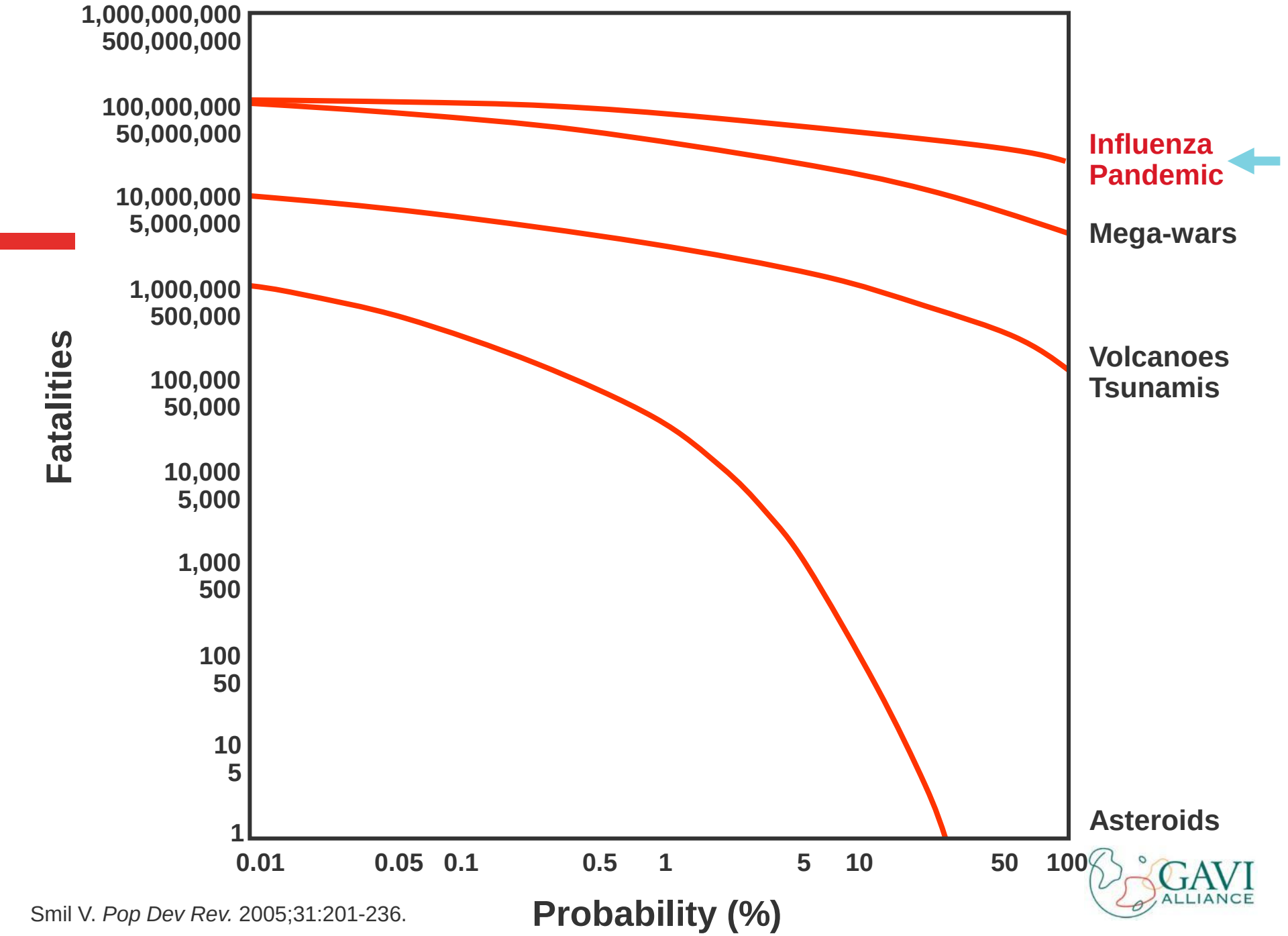
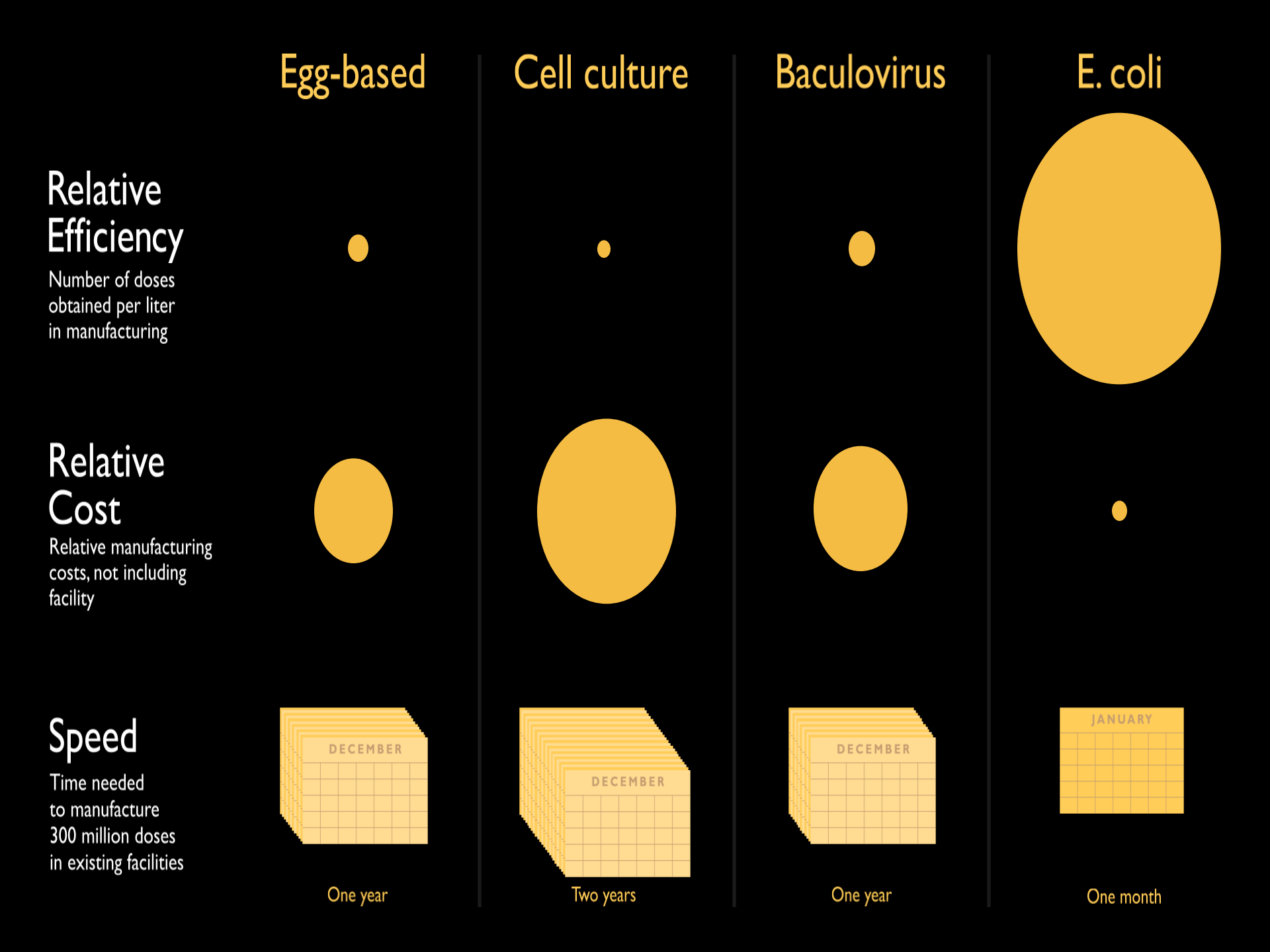
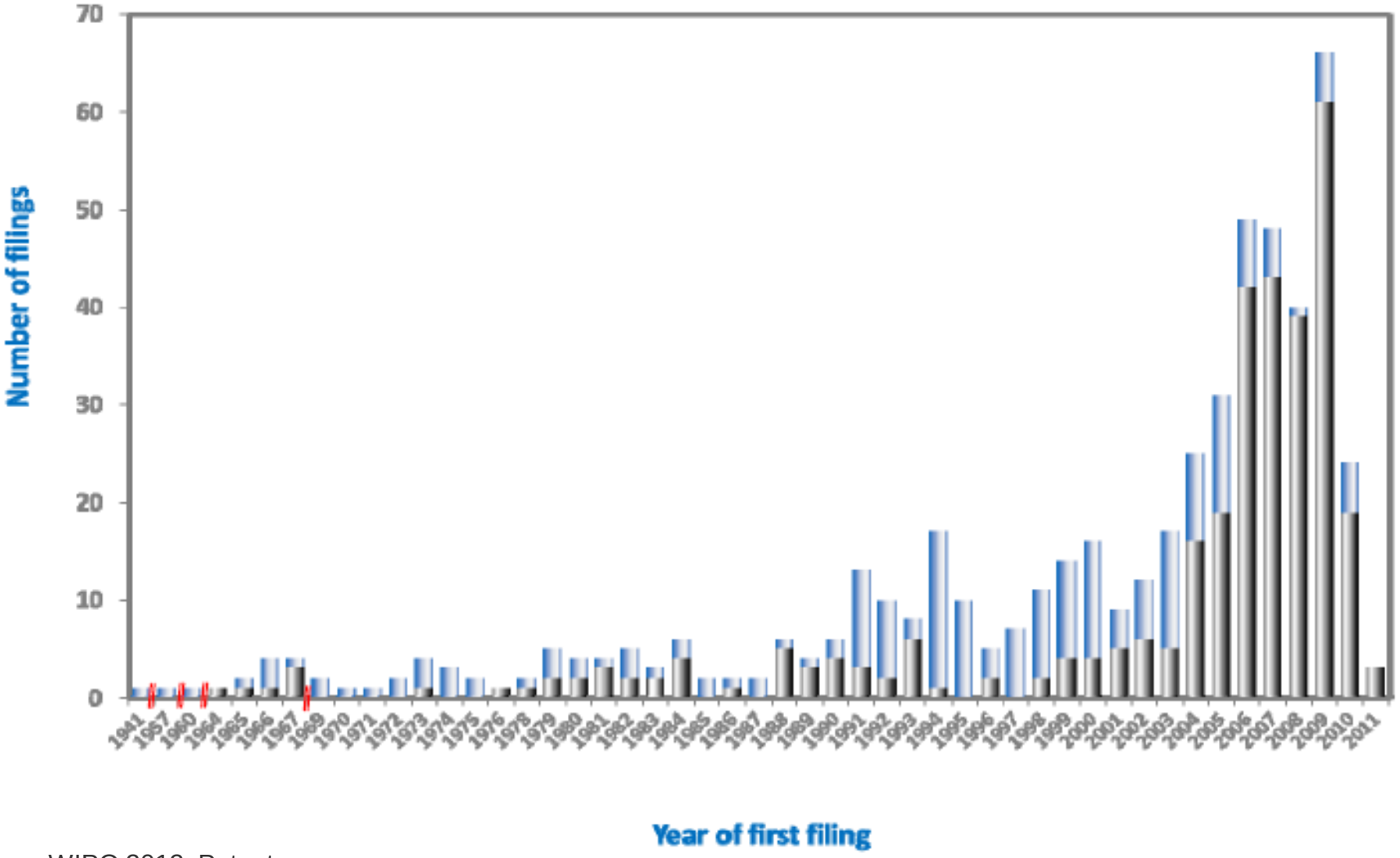


Smil V. *Pop Dev Rev.* 2005;31:201-236.


Egg-based
Cell culture
Baculovirus
E. coli
Relative Efficiency
Number of doses obtained per liter in manufacturing
Relative Cost
Relative manufacturing costs, not including facility
Speed
Time needed to manufacture 300 million doses in existing facilities
DECEMBER
DECEMBER
DECEMBER
JANUARY
One year
Two years
One year
One month

Evolution of number of annual patent filings for human vaccines against influenza virus,1941-2011



From: WIPO 2012. Patent Landscape Report on Vaccines for Selected Infectious Diseases

Patents – barriers to access?

In some cases…

CHIRON | VACCINES

- First to identify Hepatitis C (HCV)
- Over 100 patents in more than 20 countries
- High upfront royalty fees impeded R&D

…but not always

CSL™ MERCK

THE UNIVERSITY OF QUEENSLAND AUSTRALIA

- Gardasil (first HPV vaccine) based on research at University of Queensland (UQ)
- CSL and UQ waived royalty fees for sales in GAVI countries

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Patents thickets a growing challenge for many new vaccines

Originators

GlaxoSmithKline

MERCK

Pfizer

sanofi pasteur

Pneumococcal

Rotavirus

HPV

Developing country manufacturers

SERUM INSTITUTE OF INDIA LTD.

Panacea Biotec

Bharat Biotech

bioFarma

Biological E. Limited

Celebrating Life Everyday

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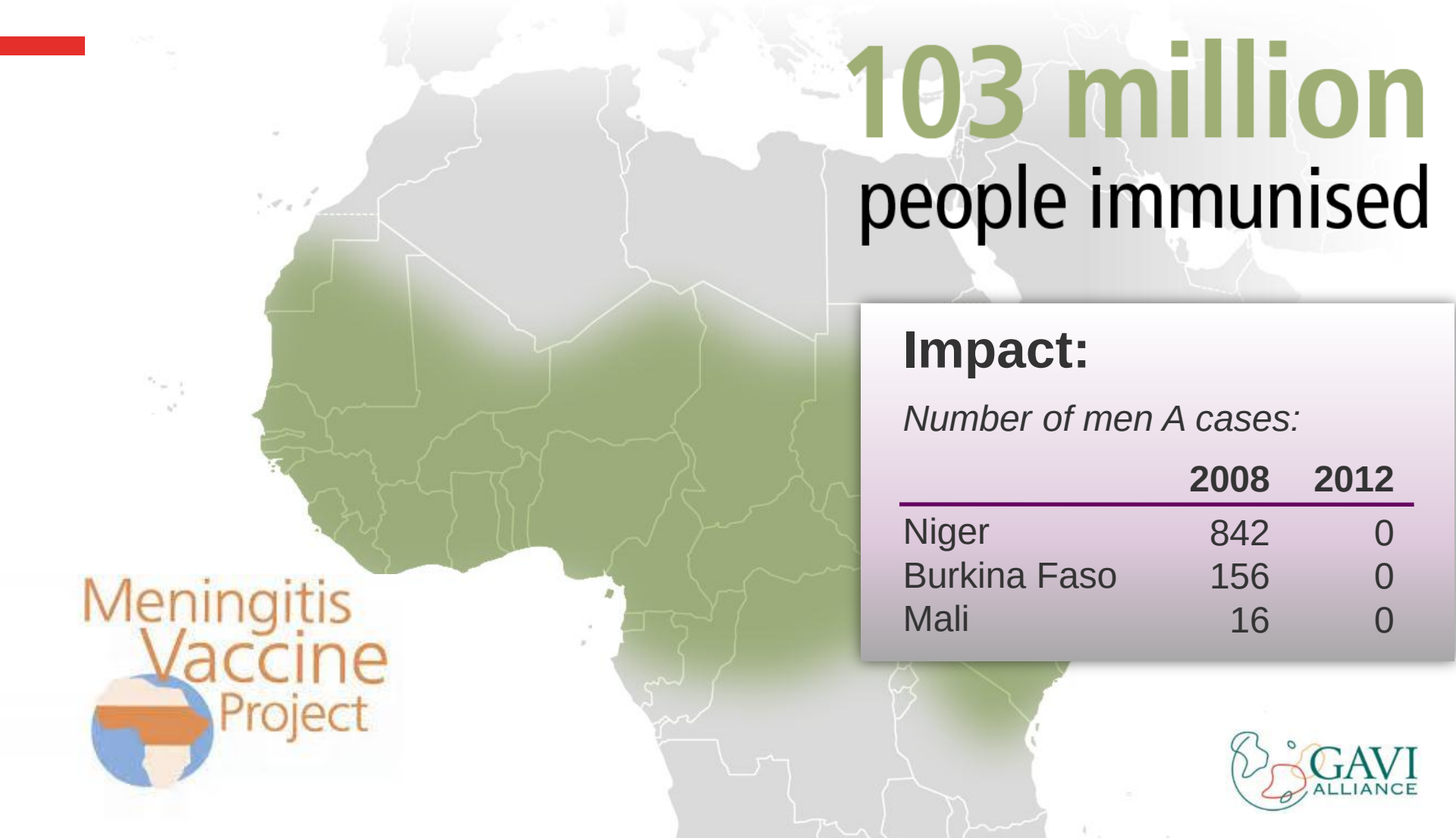
Different R&D models – “Push”



103 million
people immunised

Impact:

Number of men A cases:

	2008	2012
Niger	842	0
Burkina Faso	156	0
Mali	16	0

Meningitis Vaccine Project

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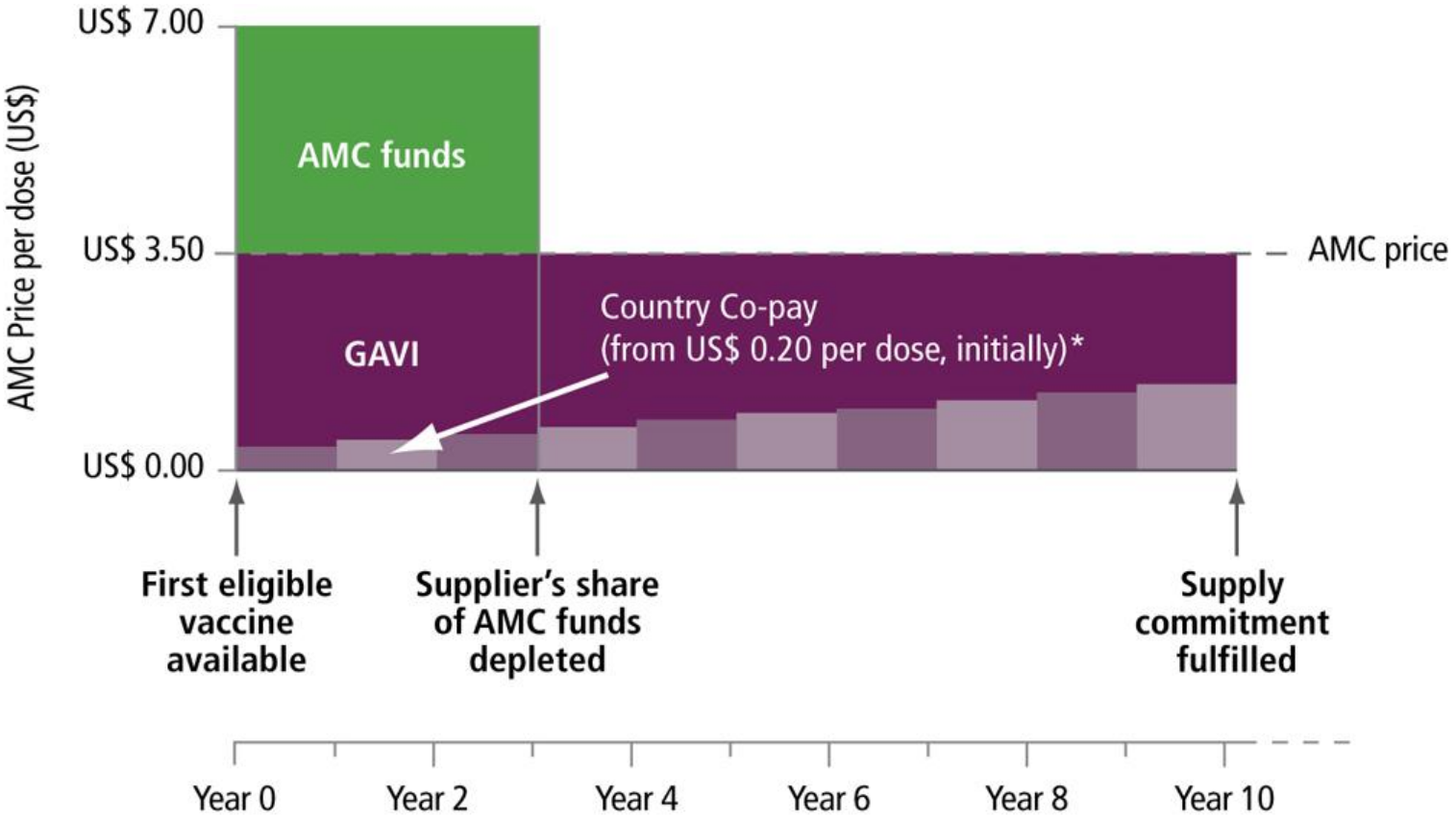
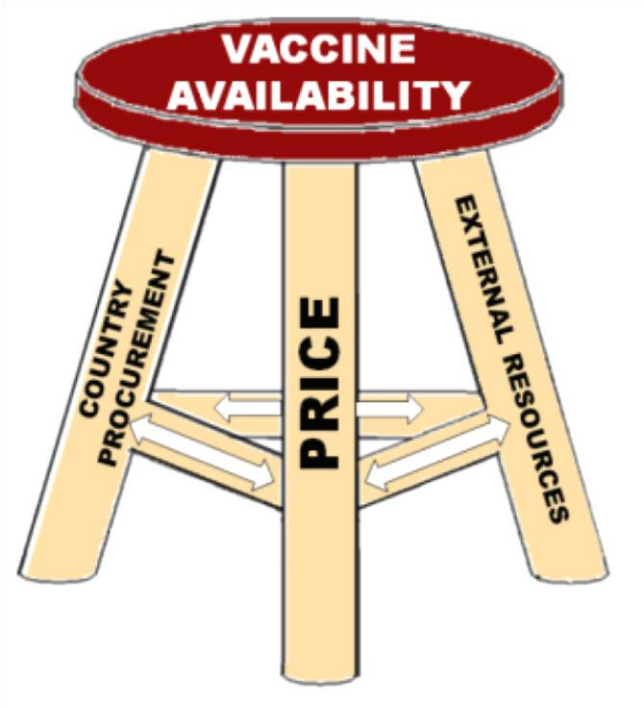
AMC funding sources

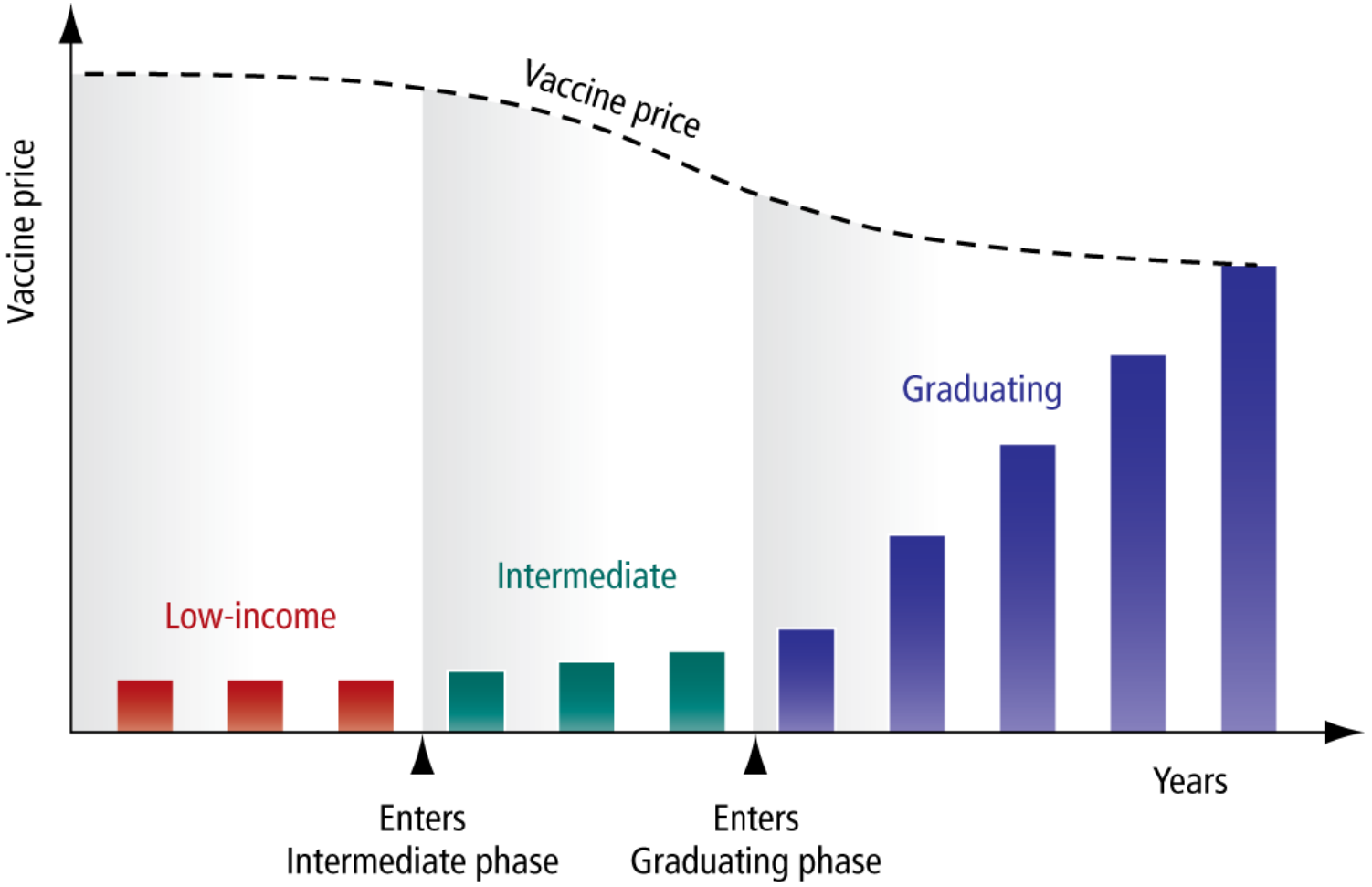


* Co-financing levels will be in line with the applicable GAVI co-financing policy

Factors Affecting Vaccine Availability

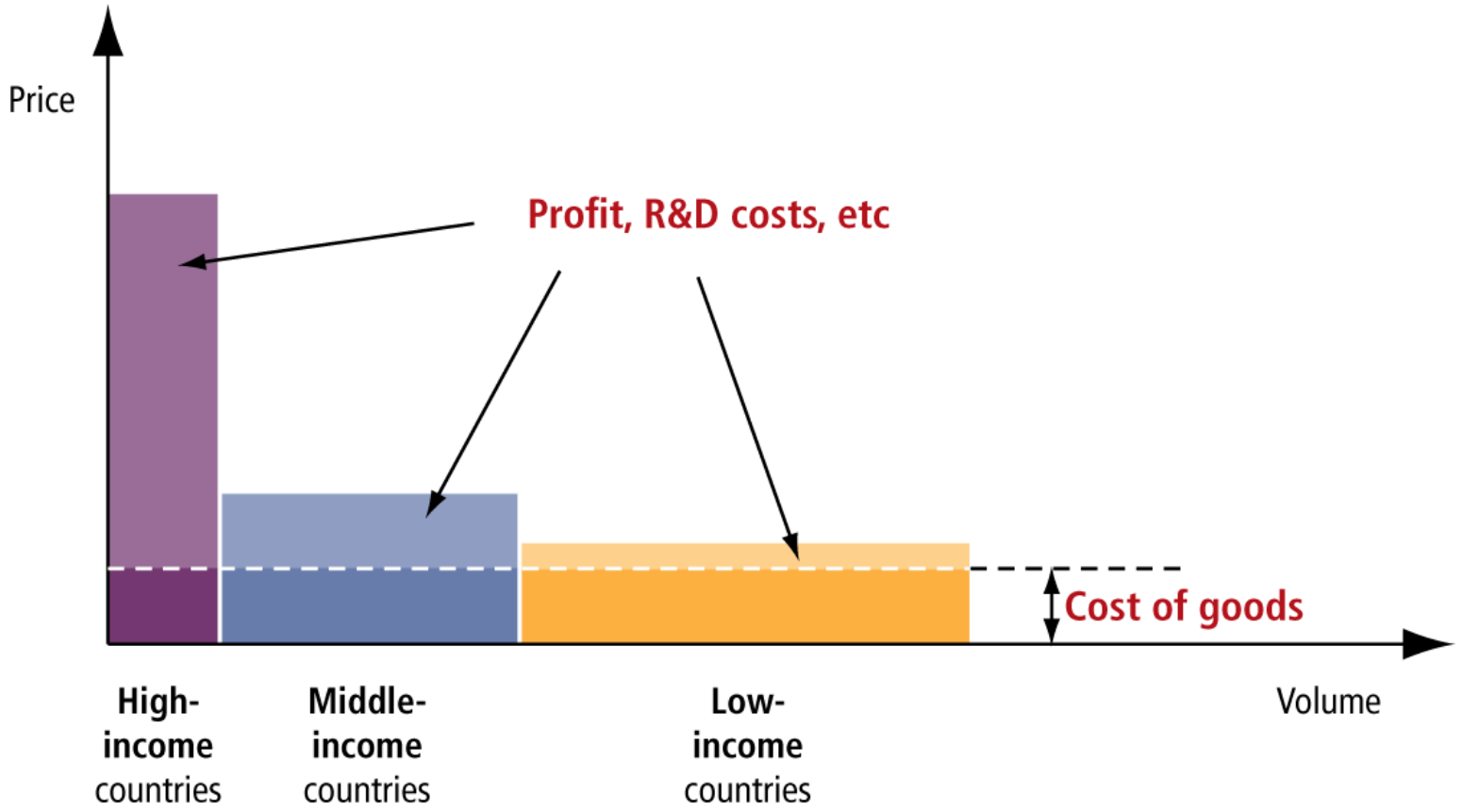


How the co-financing policy works



Source: GAVI Alliance 2012

Ramsey pricing



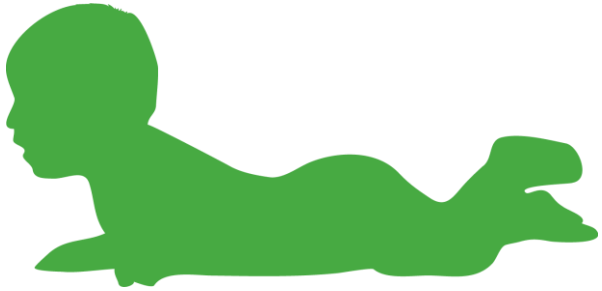
Source: GAVI Alliance, 2012

GAVI countries
birth cohort

Non-GAVI countries
birth cohort

2012
global birth cohort:

135 million



GAVI countries birth cohort:

80 million

Source: GAVI Alliance, 2012

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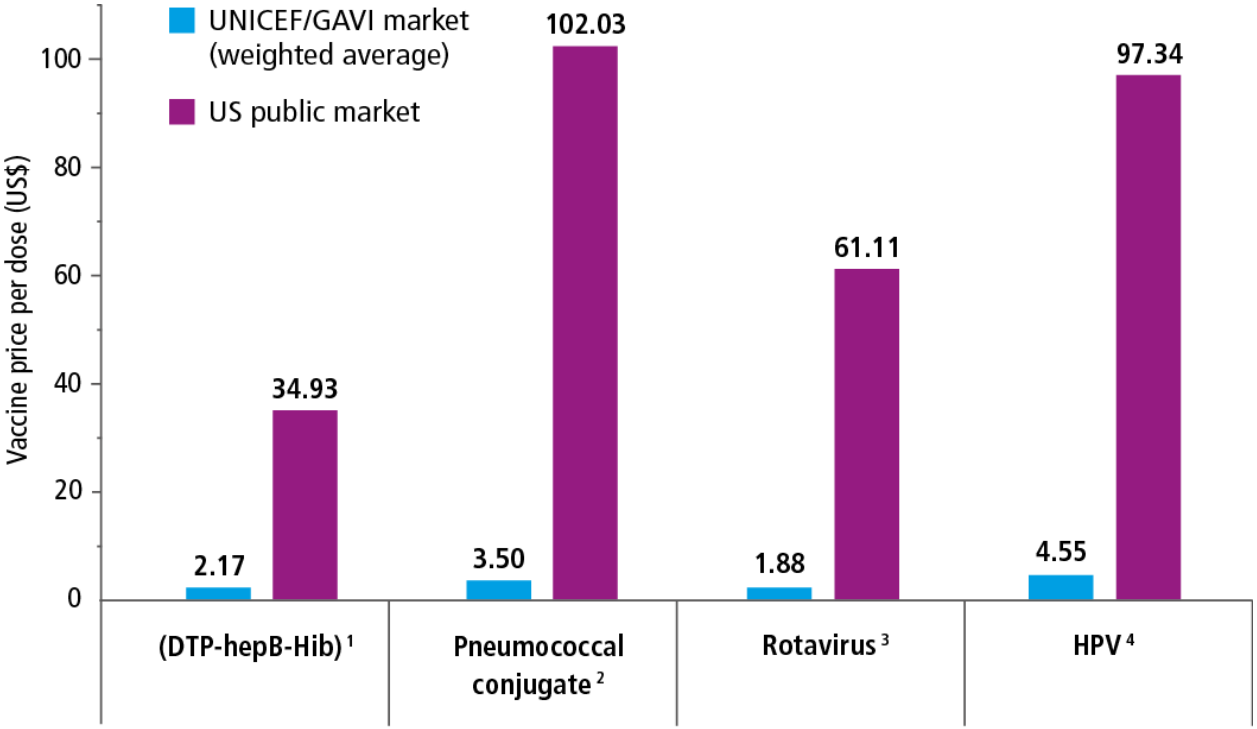
Changing the mindset of the vaccine manufacturing industry

Changing the mindset of the vaccine manufacturing industry

Achievements: Encouraging tiered pricing



1 The UNICEF/GAVI price is the 2012 weighted average across multiple suppliers and presentations of pentavalent vaccine; the US public market price is lowest total 2012 price per dose for DTP, hep B and Hib vaccinations (via separate DTP, hep B and Hib vaccines). The UNICEF/GAVI pentavalent vaccine includes whole-cell pertussis vaccine, while the US public market DTP includes acellular pertussis vaccine.

2 The US public market price is the 2012 price for 13-valent vaccine; the UNICEF/GAVI price is the tail price under the AMC.

3 The UNICEF/GAVI price is 2012 weighted average assuming 3-dose equivalence; the US public market price is the average 2012 price assuming 3-dose equivalence.

4 The UNICEF/GAVI price is the average price of bivalent and quadrivalent vaccines negotiated in 2013; the US public market price is the 2012 average.

Source: UNICEF Supply Division; CDC

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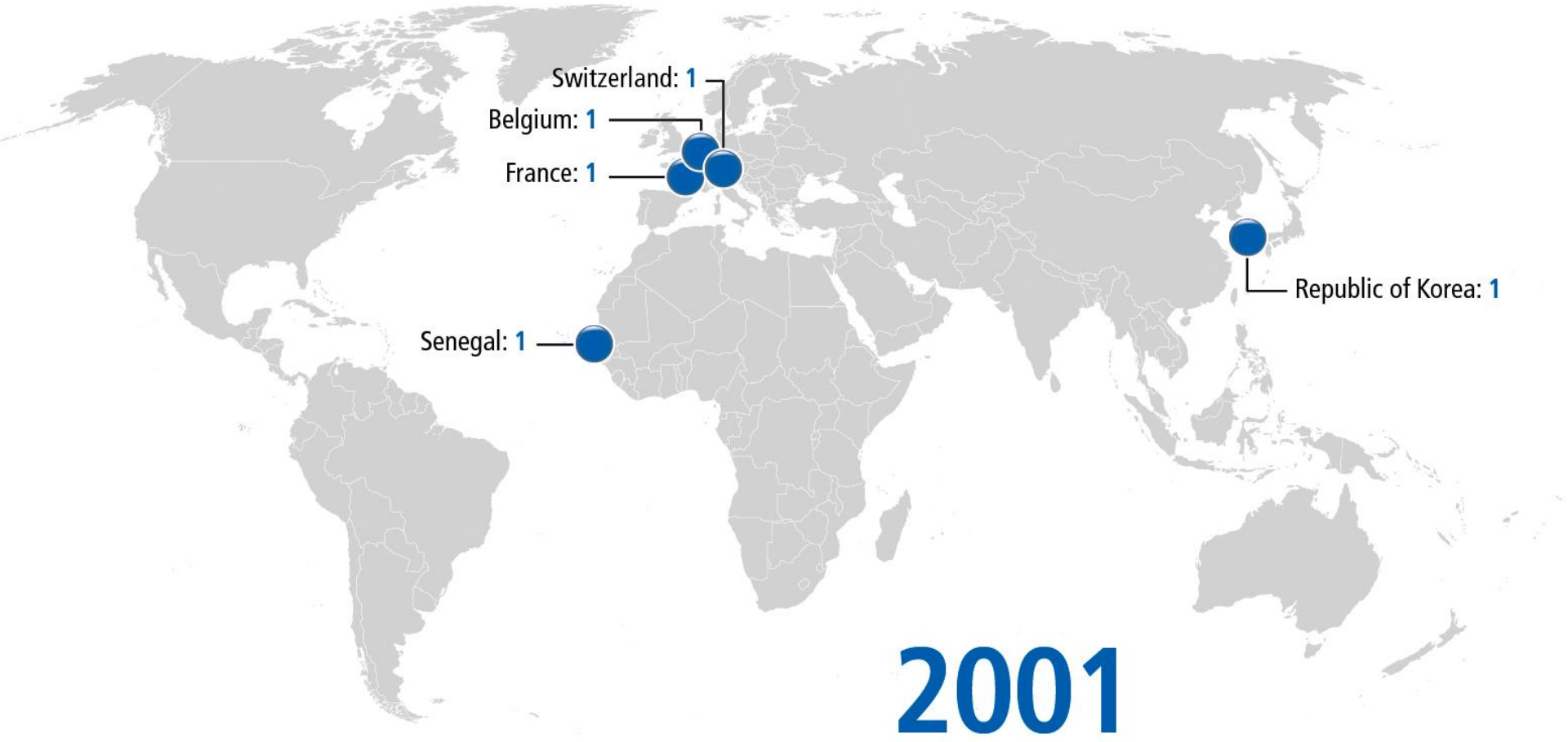
Evolving the manufacturing base

2001 – Vaccine supply:
5 suppliers from 5 countries



Source: UNICEF Supply Division, 2013

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Evolving the manufacturing base

2012 – Vaccine supply:
10 suppliers from 8 countries

Source: UNICEF Supply Division, 2013

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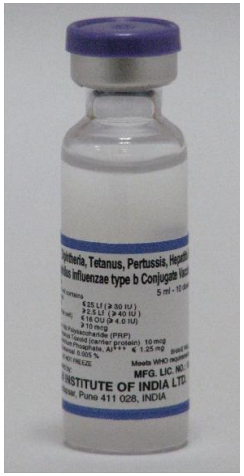
GAVI's vaccine portfolio

Manufacturers with pre-qualified vaccines in 2013	Total
Pentavalent (DTP-HepB-Hib)	5
Rotavirus	2
Pneumococcal conjugate	2
Yellow fever	4
Meningococcal A	1
Measles-Rubella	1
HPV	2

Achievements: Optimizing products



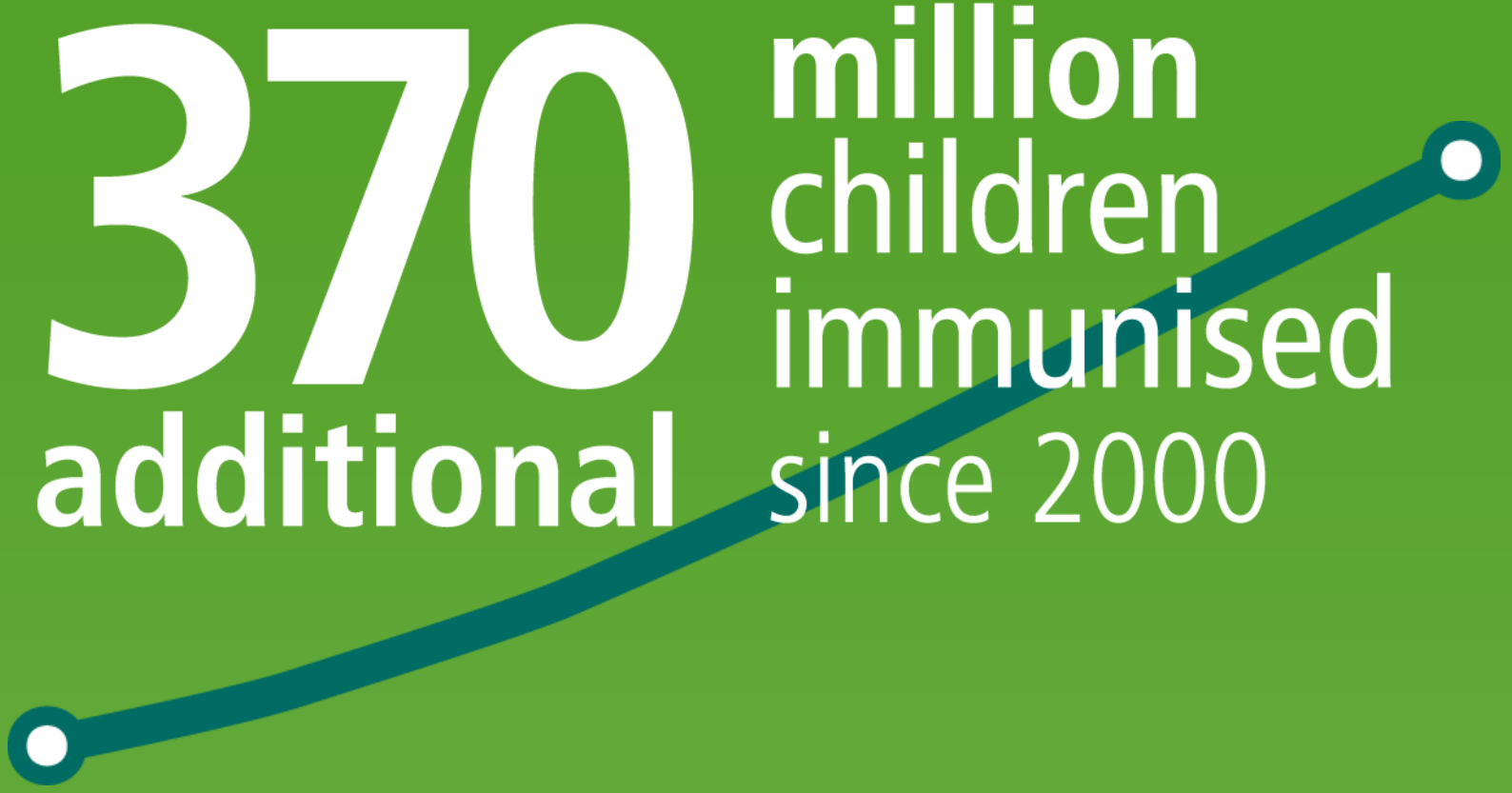
Rota: 1 dose tube
Cold Chain volume per dose (cm³): 46
Vaccine Vial Monitor: NONE

Penta:10 dose vial
Cold Chain volume per dose (cm³): 2.6
Vaccine Vial Monitor: Type 14

Packaging Reductions for GAVI Countries

Rotarix 1 dose plastic tube: 85% reduction in packaging size

Rotateq 1 dose plastic tube: proposed 29% reduction in primary container


370
million
additional
children
immunised
since 2000

More than

5.5 million

future deaths averted

since 2000

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2013 Measles rubella

2013 HPV

2011 Meningitis A

2009 Pneumococcal

2008 Rotavirus

2007 Measles

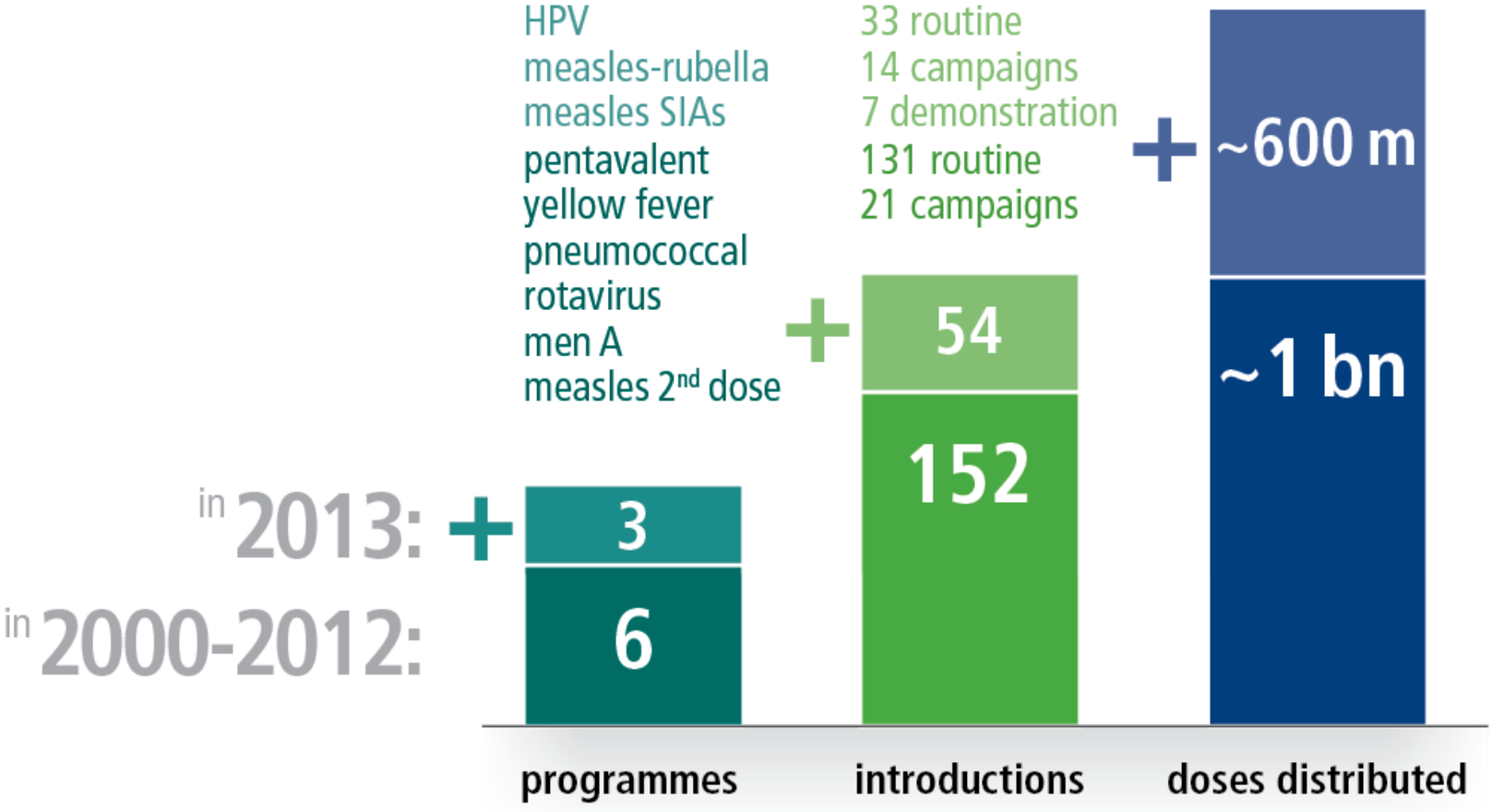
2006 Pentavalent

2002 Hib

2001 Yellow fever

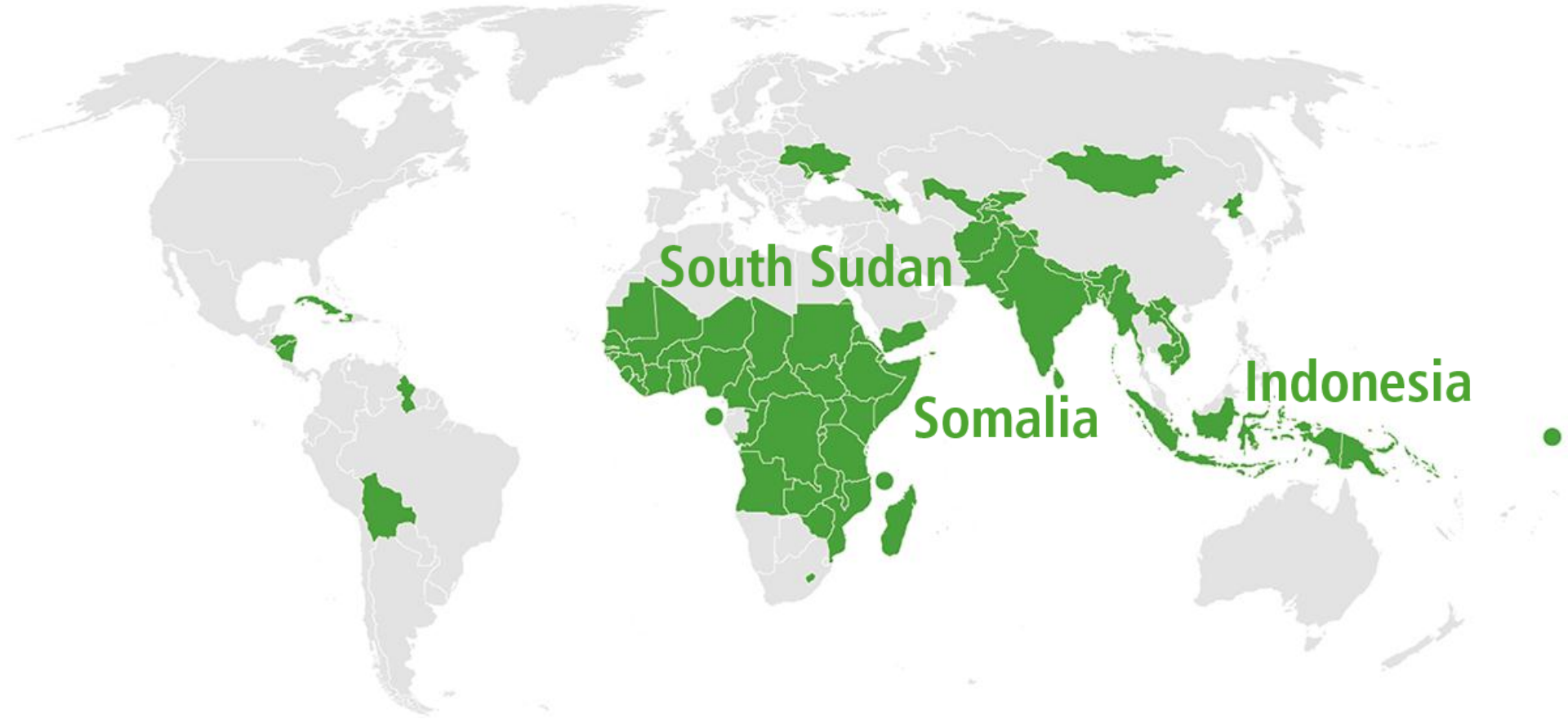
2001 Hepatitis B

Accelerating vaccine programmes



Source: GAVI Alliance

Pentavalent vaccine introduced in every GAVI country by 2014



Source: GAVI Alliance, 2013

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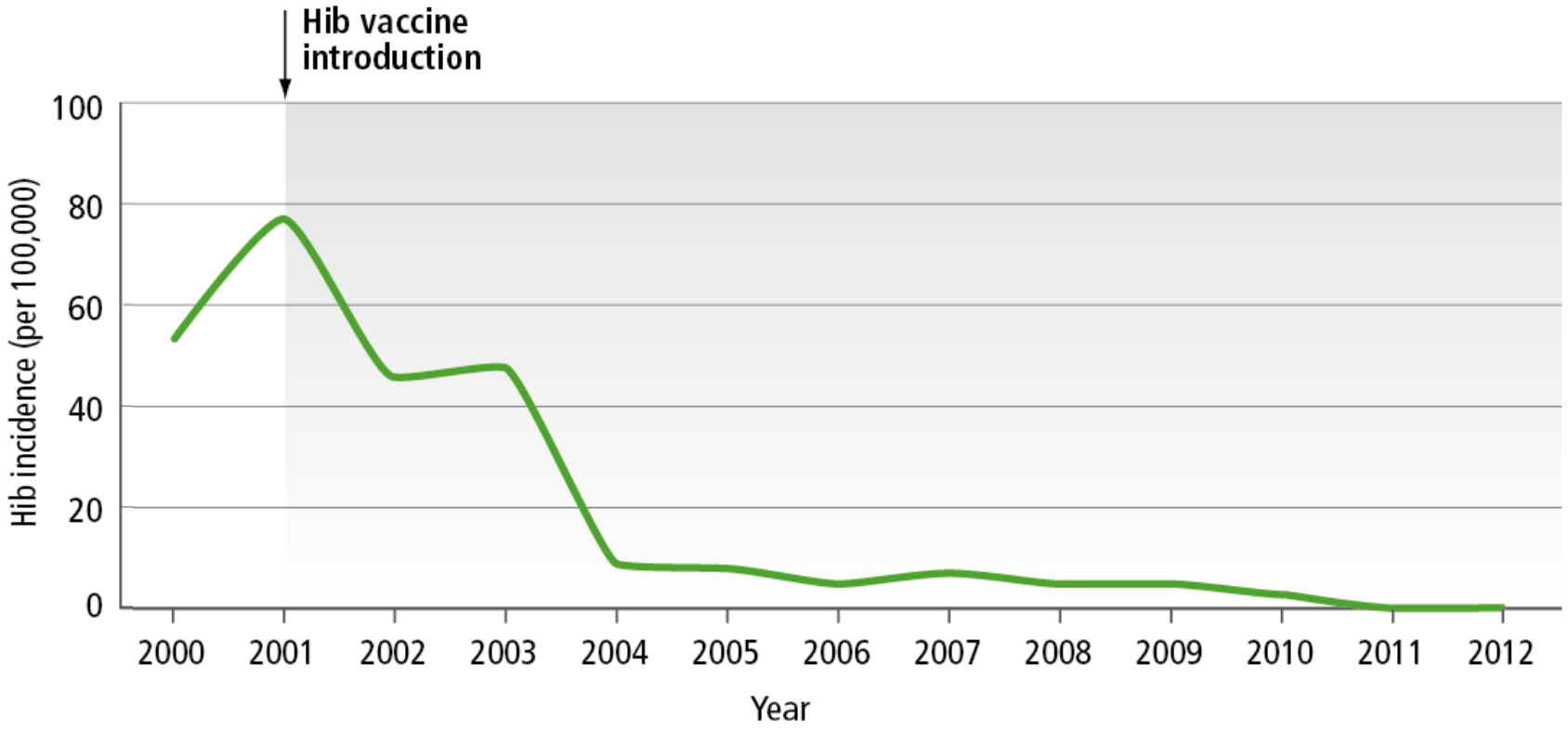
Impact of pentavalent vaccine on the ground

Eliminating Hib meningitis in Kenya (Kilifi district)



Source: Anthony Scott, Wellcome Trust Senior Research Fellow in Clinical Science
KEMRI-Wellcome Trust Research Programme , Kilifi, Kenya

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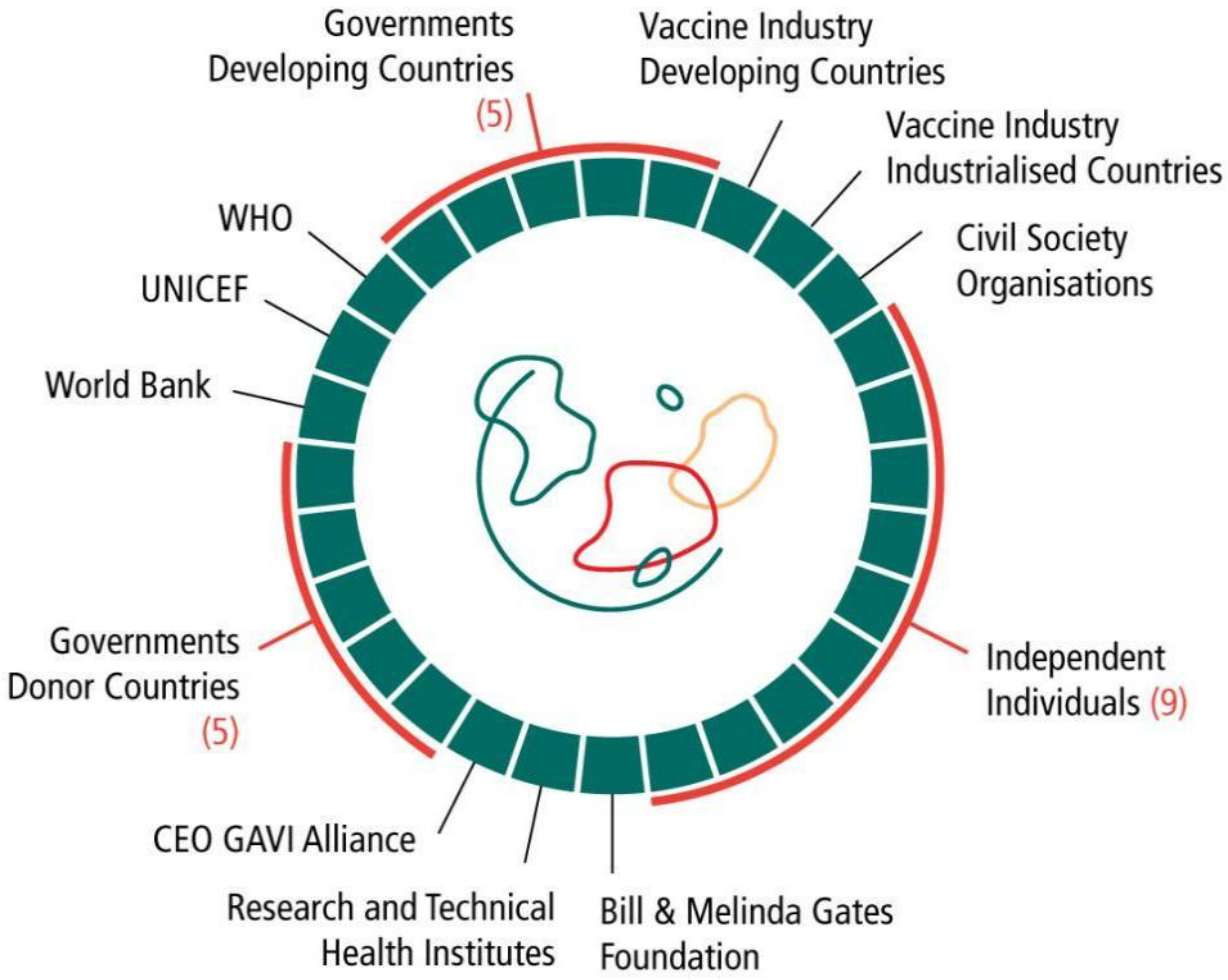
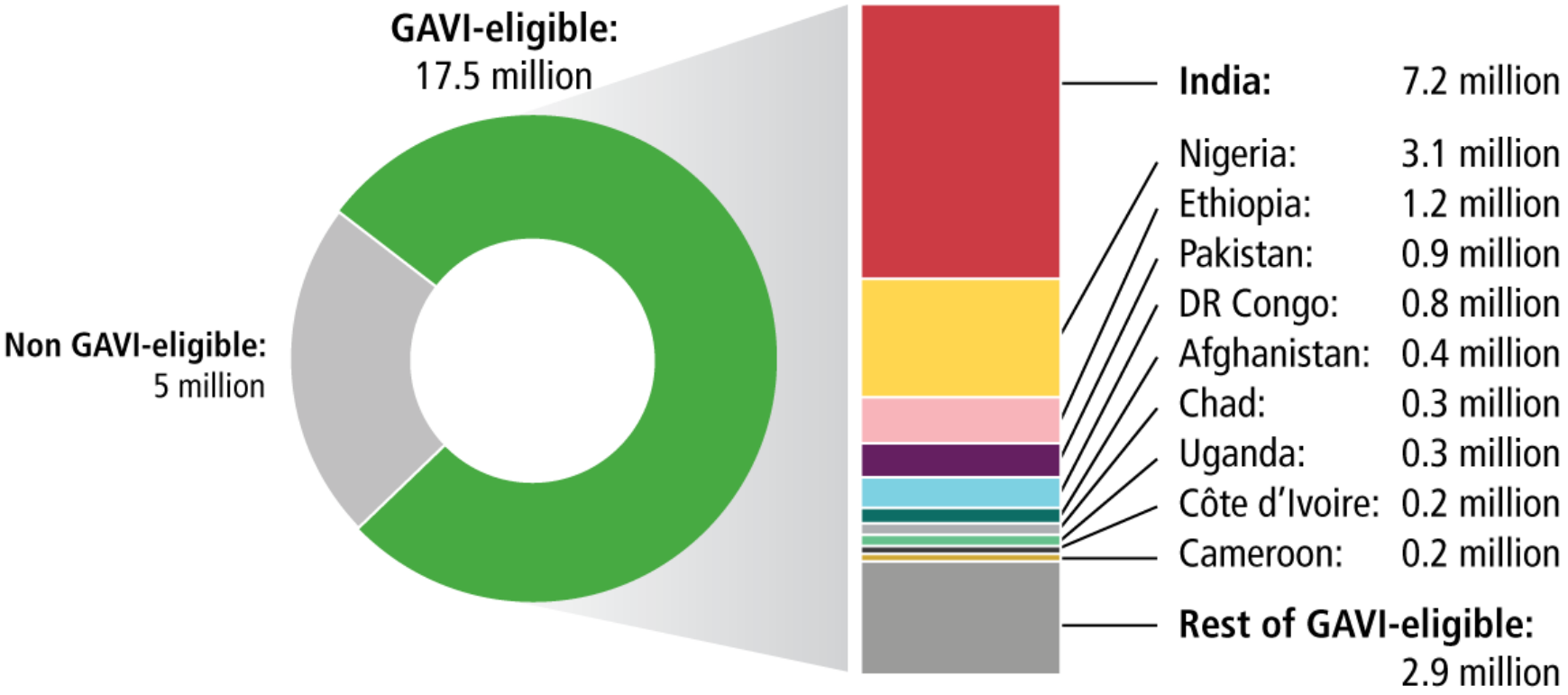
The GAVI Alliance: 21st century model of development



Over 22 million children not fully immunised despite progress on supply and pricing



Indicator: DTP3 2011
WHO/UNICEF estimates

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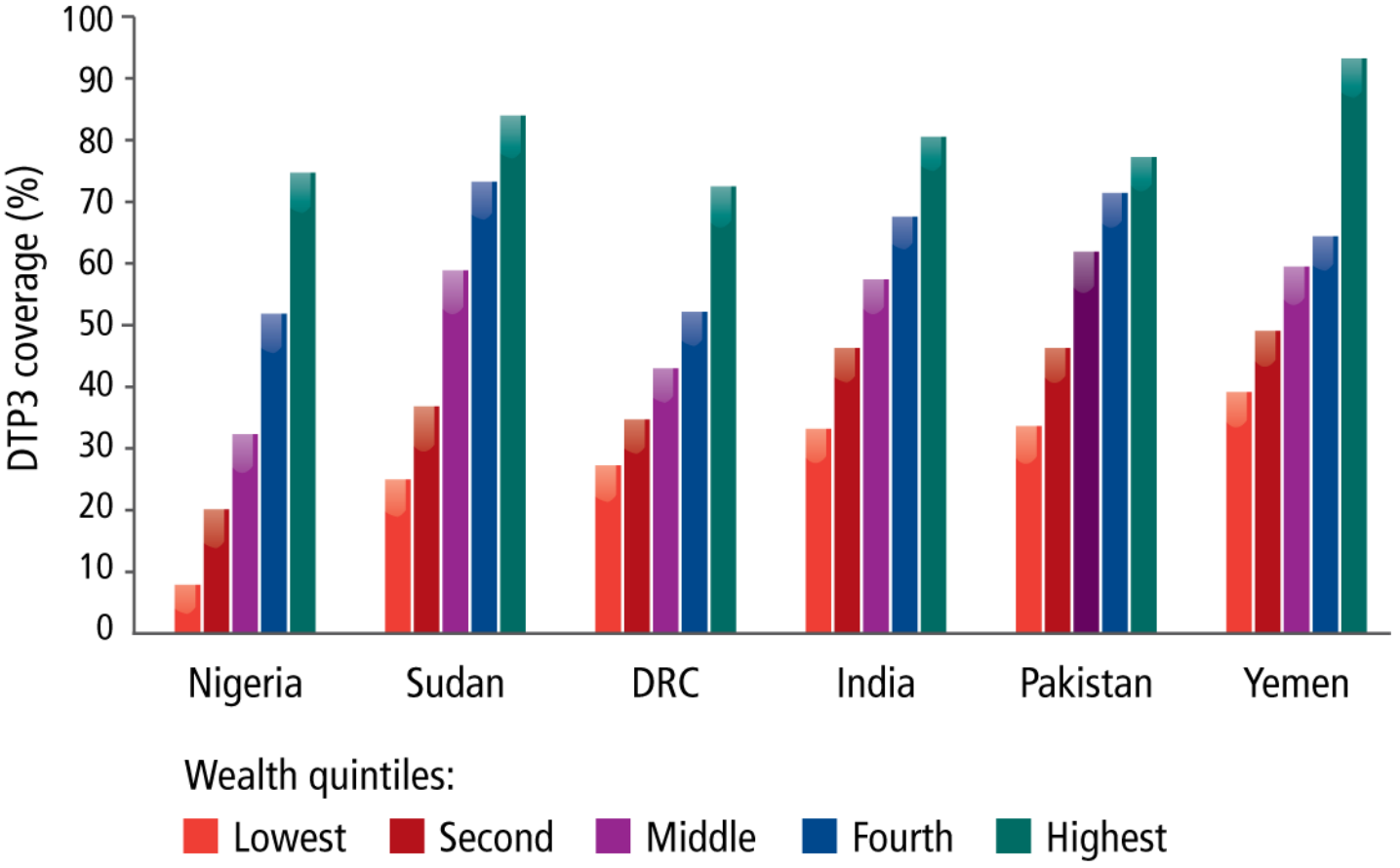
Children from poor families less likely to be fully immunised

Patterns of DTP 3 vaccination coverage across wealth quintiles since 2005



Source: DHS and MICS data (since 2005)
Courtesy: Save the Children UK, 2012

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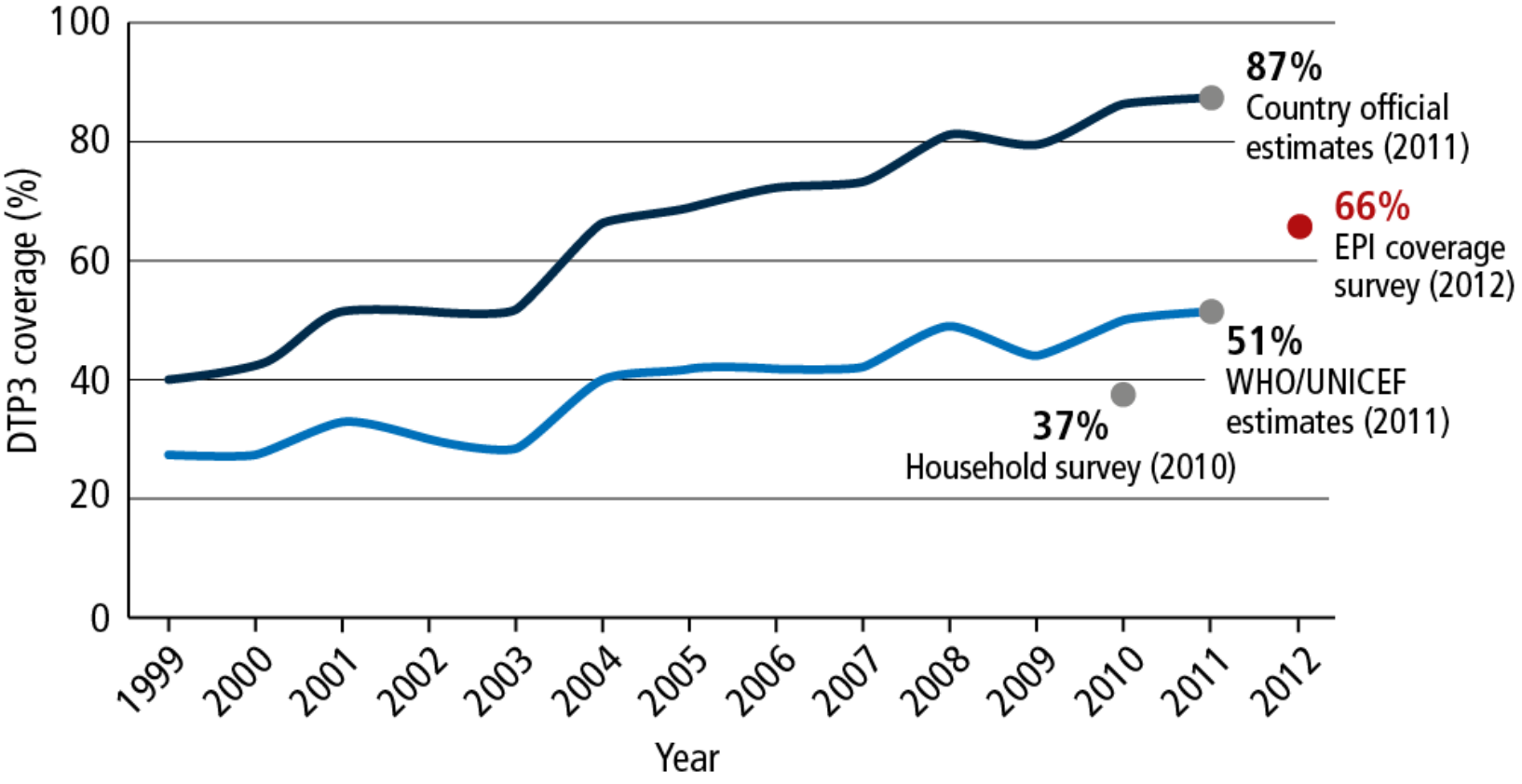
DARSHAN

Improving data



Alliance supply chain strategy: initial examples

Tracking and tracing vaccines through bar codes

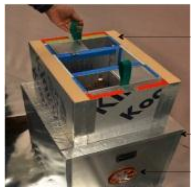
Streamline and improve transparency of short-term forecasting

Country

Global Sources

Short term forecast

New cold chain technology to market



Private sector expertise

aramex
delivery unlimited

TNT

hp

vodafone

ups

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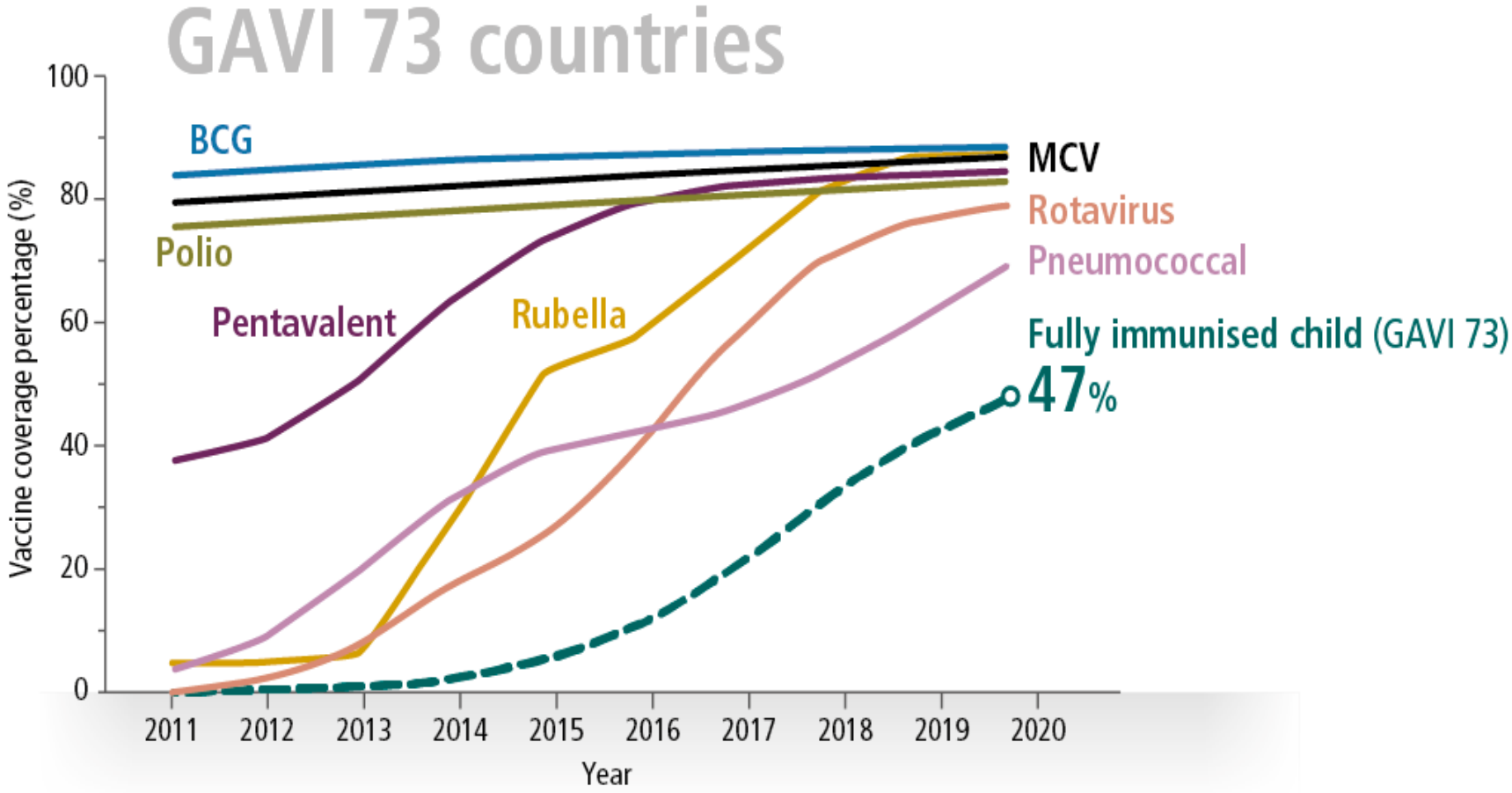
Rapid ramp-up in number of fully immunised children from low base



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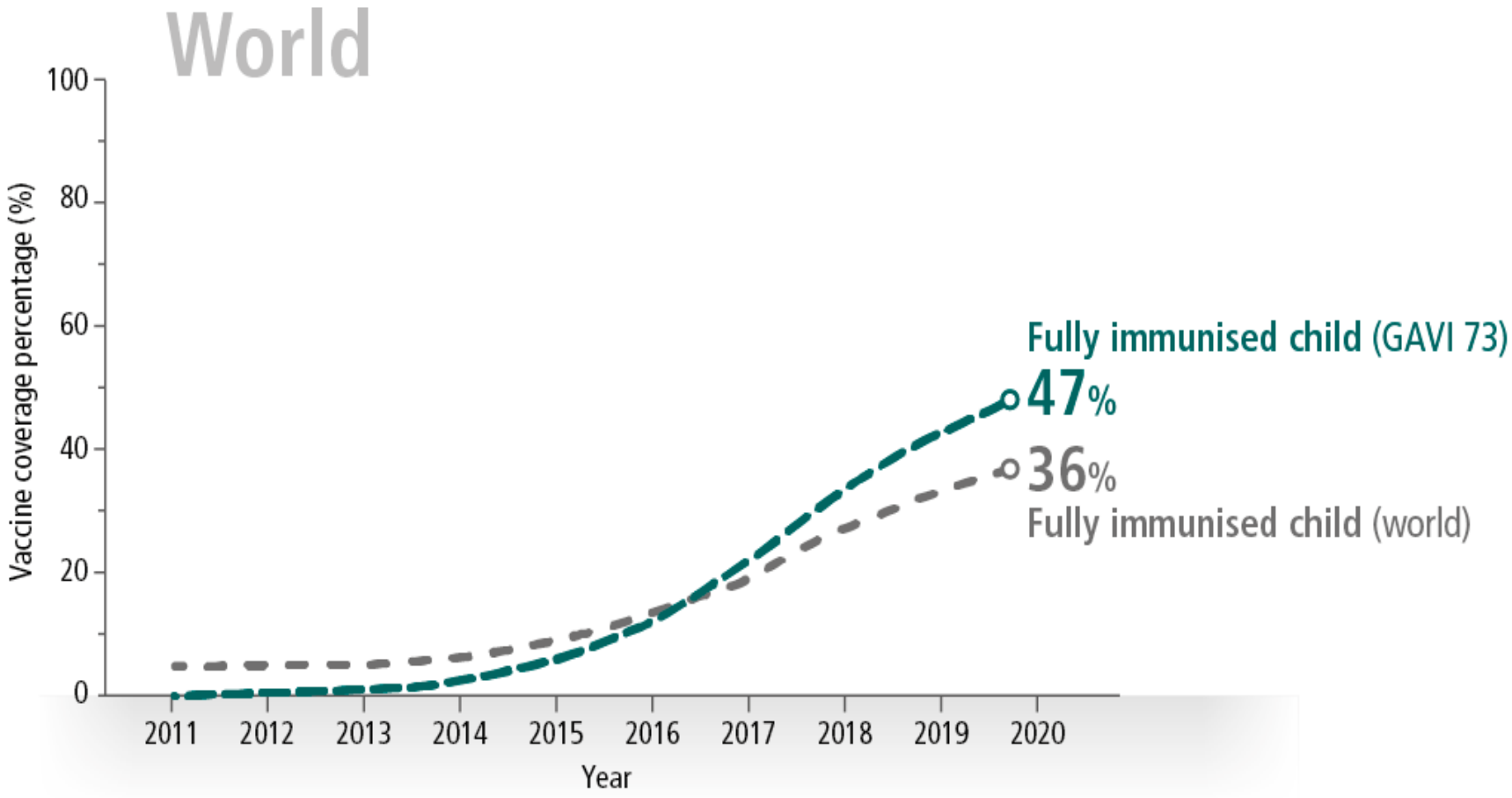

Thank you

GAVI/2011/Ed Harris

www.gavialliance.org