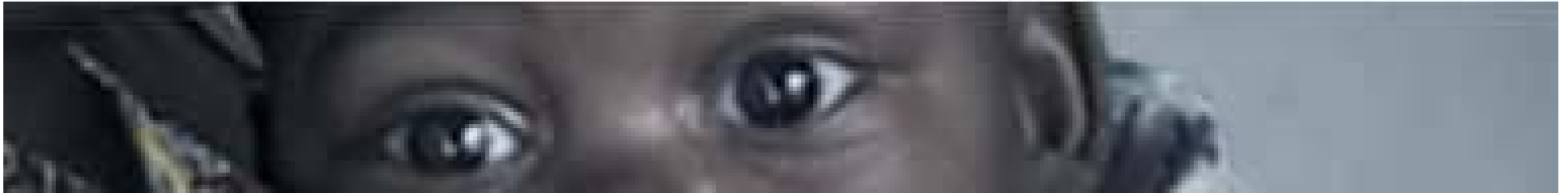


Network for Education and Support in Immunisation



Introduction of new vaccines: public health - policy decisions and programmatic implications

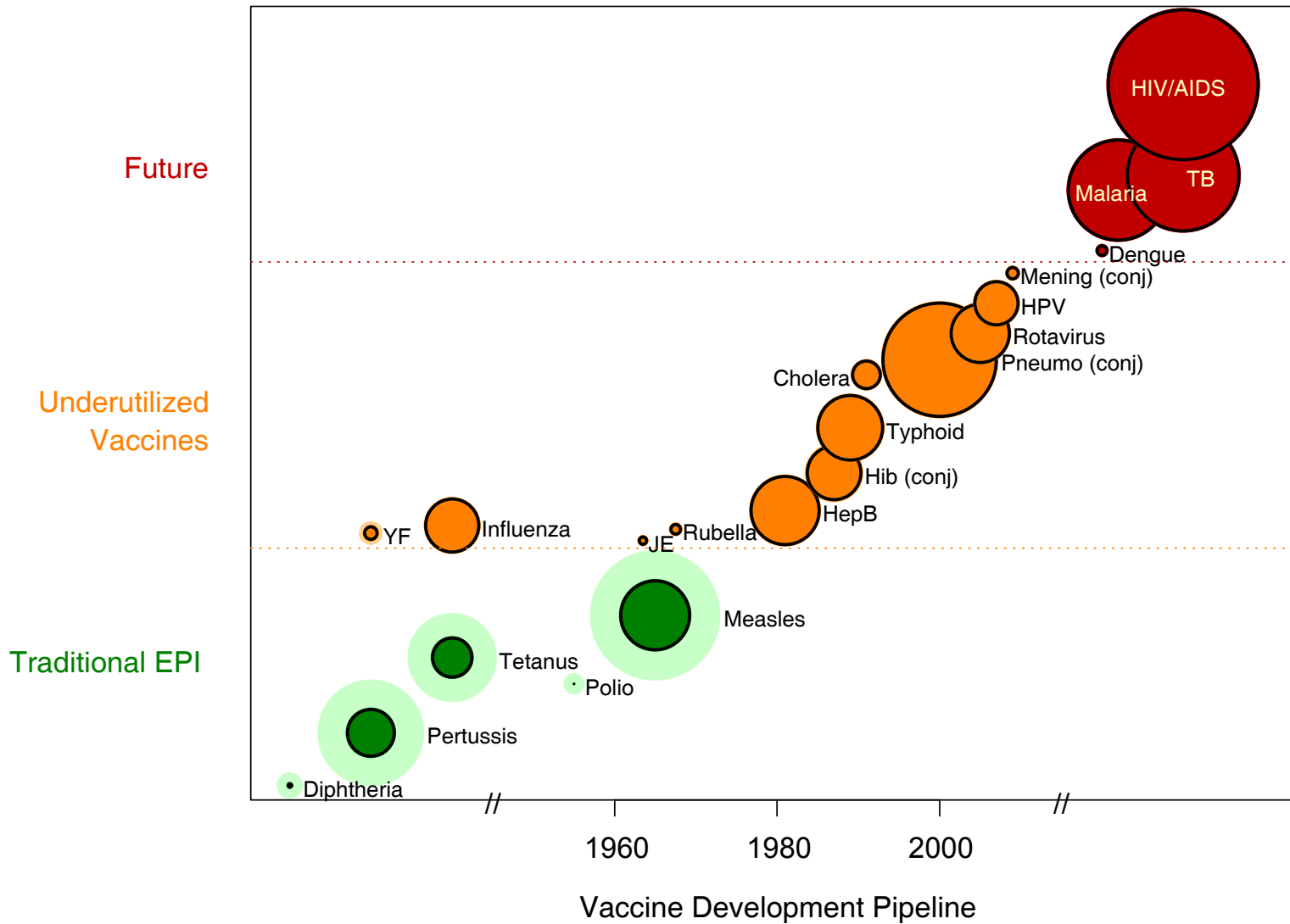
André Meheus & Fred van der Veen

SAVIC-Gauteng 2009 EPI symposium -
Introduction of new vaccines into national
immunisation programmes.
Johannesburg, South Africa, 2-3 February 2009

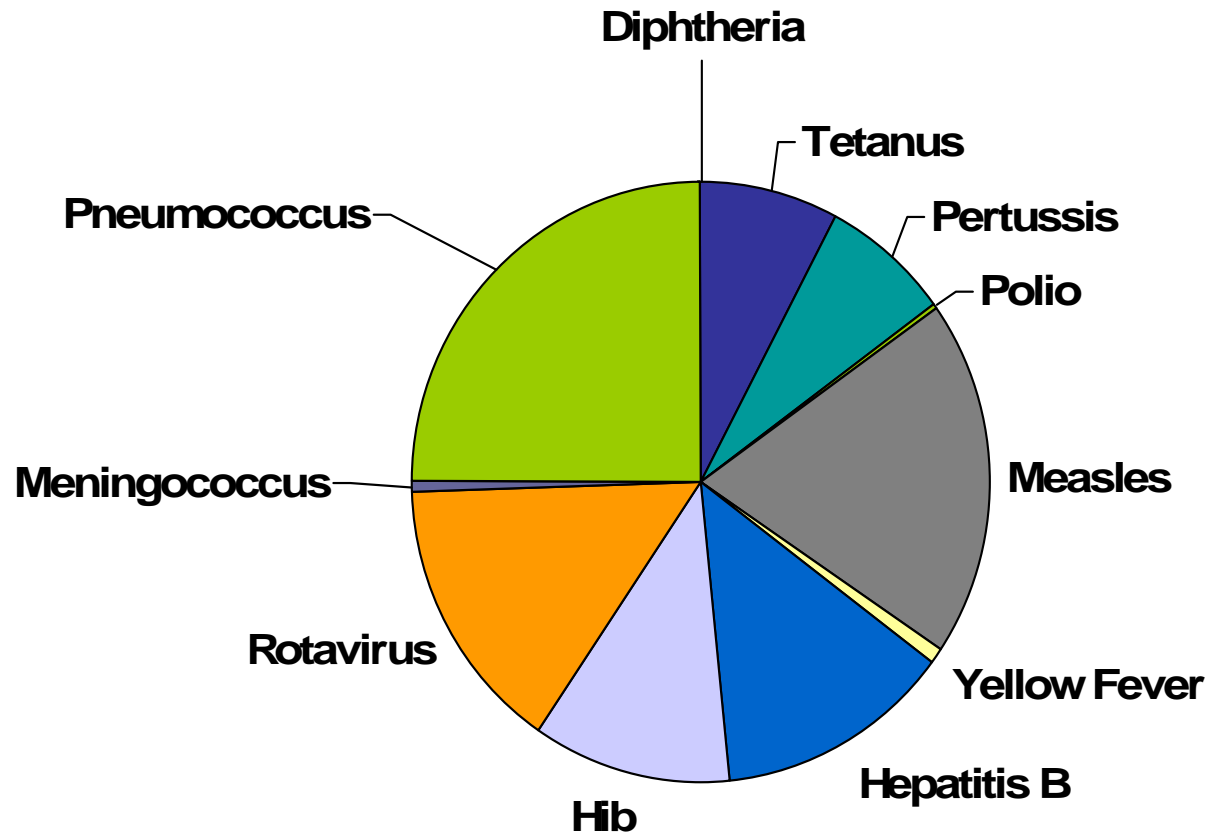
Four Strategic Areas

- Protecting **more** people in a changing world
- Introducing **new** vaccines and technologies
- Integrating **immunization, other linked interventions and surveillance in the health systems context**
- Immunizing in a context of **global interdependence**

The Vaccine pipeline

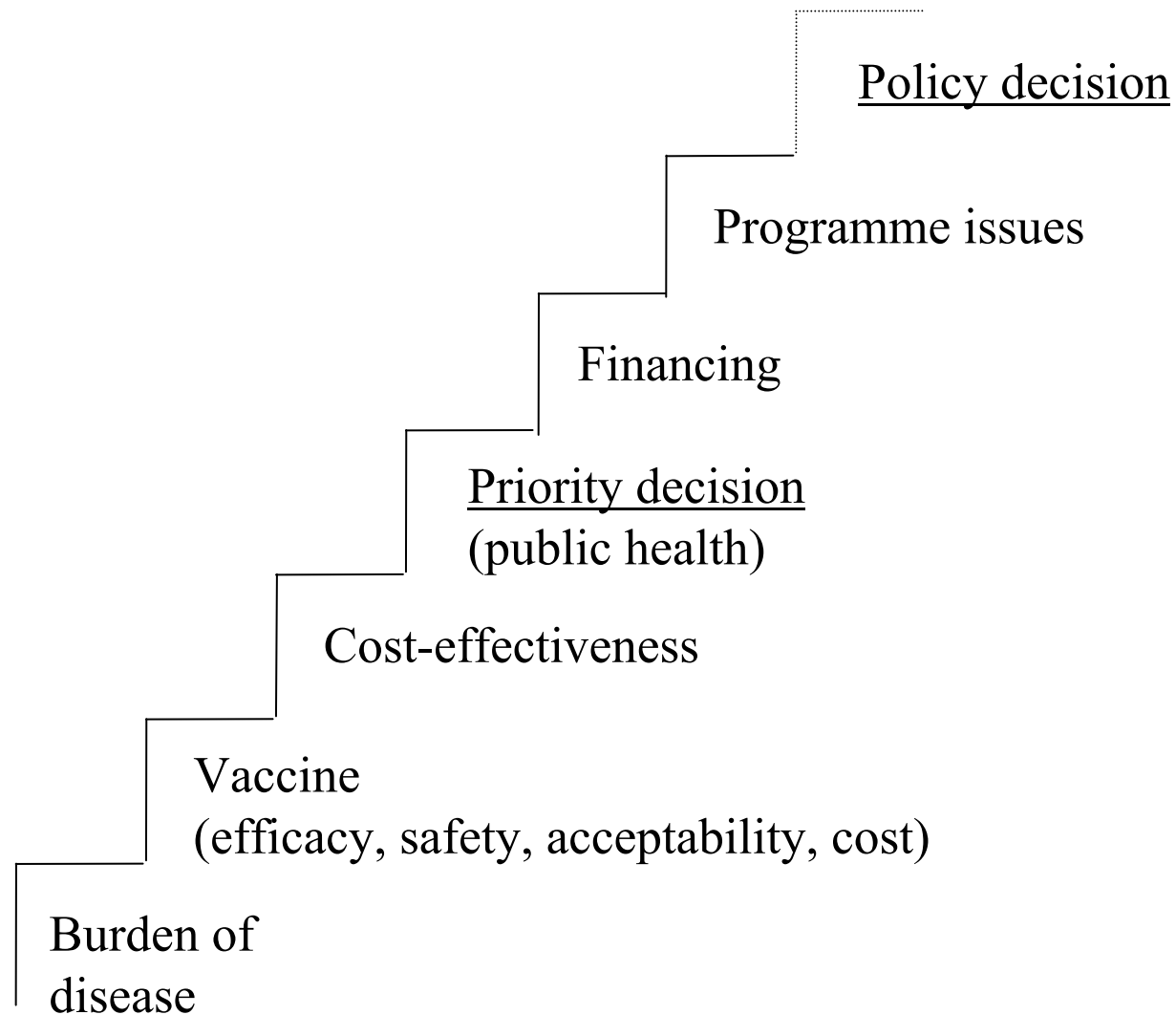


Deaths from Vaccine-Preventable Diseases - 2000

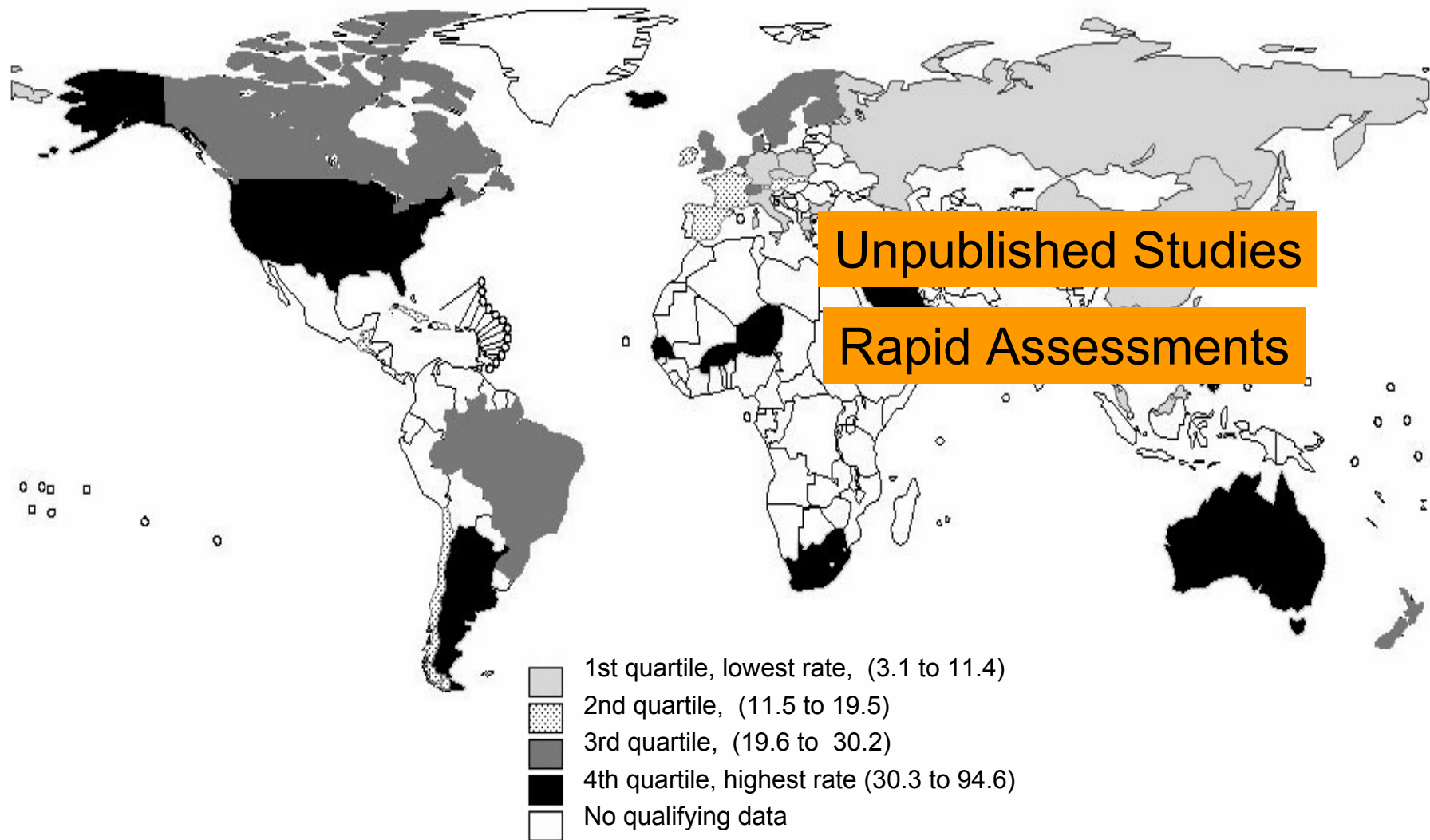


4 Million Deaths to Be Prevented

Steps for Decision Making Introduction of New Vaccine

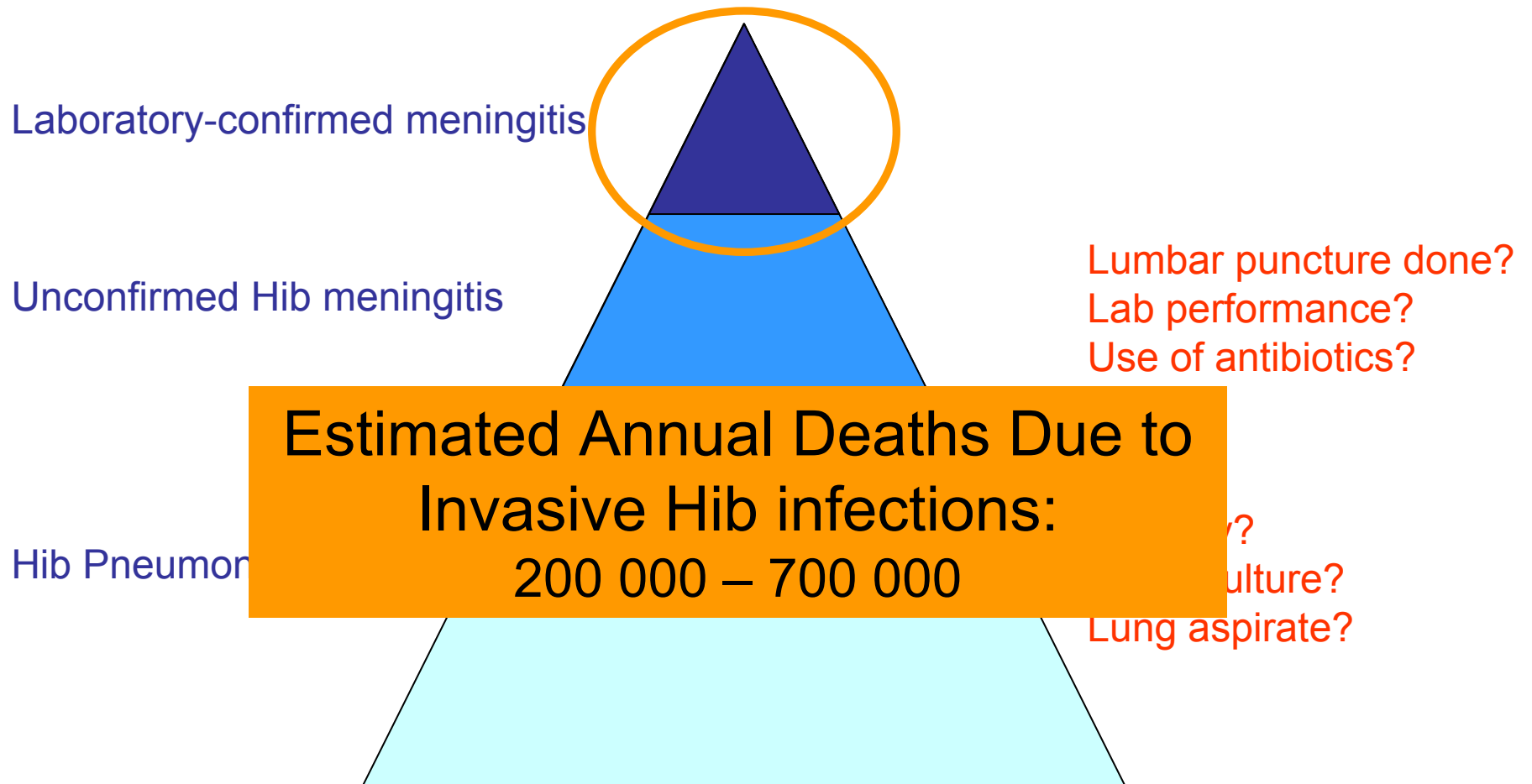


Country-specific incidence, by quartile, of Hib meningitis per 100 000 children < 5 years of age in the pre-vaccine era, 46 countries



Excluding studies of special-risk groups and those with <15 cases.

Burden of Hib Diseases



Quadrivalent HPV vaccine Efficacy in 16-26 year old women

	Quadrivalent vaccine		Placebo		Efficacy
	N	Cases	N	Cases	%
HPV16/18 related CIN2/3 or AIS	8487	0	8460	53	100
HPV16/18 related VaIN 2/3	7897	0	7899	7	100
HPV16/18 related VIN 2/3	7897	0	7899	8	100
HPV6/11/16/18 related genital warts	7897	1	7899	91	98.9

Quadrivalent HPV vaccine efficacy CIN & AIS

Per-protocol population (protocols 007, 013, 015)
End-of-study data, mean follow-up 44 months

Endpoint	Vaccine	Placebo	
	N=9075	N=9075	% Efficacy
HPV 6/11/16/18 related CIN or AIS	9	225	96
By Type			
HPV 6-related	0	47	100
HPV 11-related	0	12	100
HPV 16-related	8	137	94
HPV 18-related	1	61	98
By Disease			
CIN 1	7	170	96
CIN 2/3	2	110	98
AIS	0	7	100

“Models are simplifications of reality and the strengths of the conclusions drawn from modelling depend on the reasonableness of the assumptions and parameters that make up the model”

Mathematical modeller, 2008

When is a programme cost-effective?

- Do we need an explicit rule to decide if the additional benefit is considered worth the additional cost ?
- WHO recommendations following the Commission on Macroeconomics and Health studies
 - \$ per DALY averted $<$ GNI per capita = highly CE
 - \$ per DALY averted $1-3 * \text{GNI per capita}$ = CE
 - \$ per DALY averted $> 3 * \text{GNI per capita}$ = not CE

Cost per Disability Adjusted Life Years due to immunisation

- In general, available literature on DALYs suggests immunisation is a highly cost-effective intervention
- Most vaccination campaigns cost less than \$ 50 per year of healthy life gained (GAVI)
- EPI vaccine program costs \$ 14-20 per year of healthy life gained
- Similar cost for the Hib vaccine
- Hepatitis B immunisation costs \$ 8–11 per DALY averted

M Jit, YH Choi, WJ Edmunds: Economic evaluation of HPV vaccination in the UK

BMJ 2008; 337:a769

- Transmission dynamic model (includes herd immunity)
- Constructed 50.000 meta-scenarios based on combinations of epidemiological and economic assumptions
- Measured QALY's
- Discounted costs and benefits at 3.5% per year
- Health care provider perspective
- Willingness to pay threshold at 30.000 £ per QALY

M Jit, YH Choi, WJ Edmunds: Economic evaluation of HPV vaccination in the UK

BMJ 2008; 337:a769

- Base case scenario:
 - Vaccination of girls 12 year of age
 - 80% coverage school health programme
 - Quadrivalent vaccine (HPV types 6, 11, 16 & 18)
 - Vaccine protection: 20 years (>10 years)
- Result:
 - Median cost per QALY = 22.500 £
(95% range 13.800 - 32.900 £)

M Jit, YH Choi, WJ Edmunds: Economic evaluation of HPV vaccination in the UK

BMJ 2008; 337:a769

- Vaccination is considered cost-effective (unlikely it is cost saving)
- Vaccination also of boys 12 years old not cost-effective
- Catch-up of girls 13-18 years old is cost-effective; not of older age groups (e.g. up to 25y.)
- Better cost-effectiveness under optimistic scenario duration of vaccine protection, efficacy against non-cervical cancers, cross protective effects

M Jit, YH Choi, WJ Edmunds: Economic evaluation of HPV vaccination in the UK

BMJ 2008; 337:a769

- Sensitivity analysis: major determinants of cost-effectiveness are:
 - Duration of vaccine protection
 - Duration of HPV natural immunity
 - Cost of the vaccine
 - Discount rate
- At cost of 60-80,5 £ per dose of quadrivalent vaccine, the bivalent vaccine must be 13-21 £ ($\pm 25\%$) less expensive to have equal cost-effectiveness

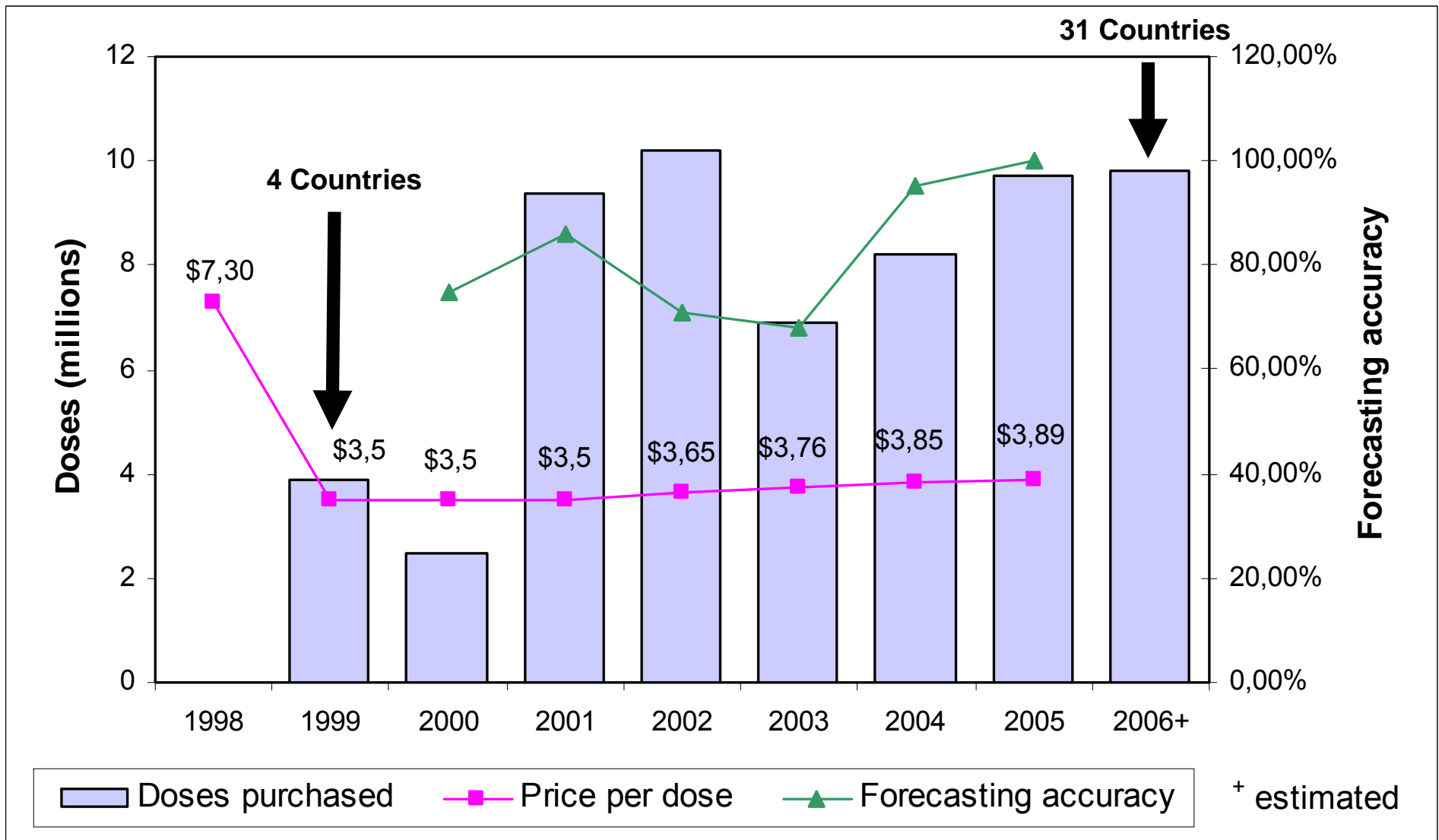
Rationale – new vaccines

- Cost to develop and produce new generation vaccines has increased
- Firms consider developing country market as small (in \$ terms) and often unpredictable
 - profitability of these markets is limited
- As a result poorest countries may not have access to newest vaccines for 10-20 years after initial licensure in industrial countries
 - was the case with introduction of Hep B and Hib
- Innovative financing mechanisms could address some of these challenges

Vaccine pricing

- Differential pricing = tiered pricing
 - Higher prices in middle income and industrialized countries
 - Lower prices in poorest developing countries
 - Force-down pressure on prices (margins) in industrialized countries?
- Pooled procurement
 - UNICEF procurement
 - PAHO-revolving fund
 - lower transaction cost → lower price

Pentavalent; Volume of doses purchased, forecasting accuracy, and price 1998- 2006



Sources of financing for immunization services

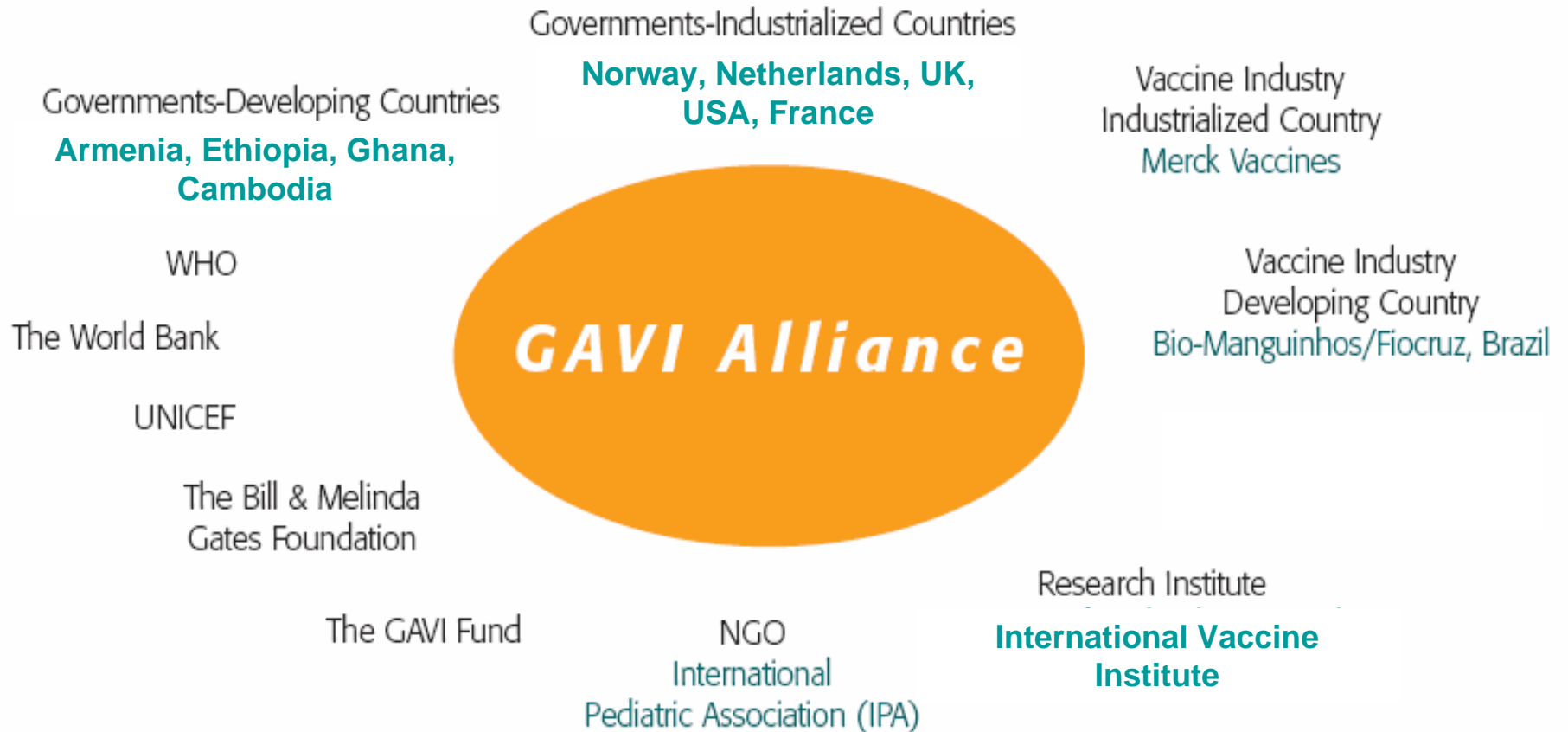
	Domestic
Public	<ul style="list-style-type: none">– National or sub national tax revenues– Social health insurance (compulsory)
Private	<ul style="list-style-type: none">– User fees– Cross-subsidies– Health insurance

Sources of financing for immunization services

	External
Public	<ul style="list-style-type: none">– Project grants from bilateral or multilateral agencies– Grant portion of development loans– Debt relief proceeds (HIPC II, bilateral debt)– Sector-wide approach (SWAPs)– Budget support– GAVI and the GAVI Fund– IFFIm
Private	<ul style="list-style-type: none">– International NGO's– Project grants from philanthropic institutions– Contributions from vaccine manufacturers (often in-kind)

The GAVI Alliance

GAVI Alliance: An Innovative Public-Private Partnership



International Finance Facility for Immunization = IFFIm

1. New multilateral development institution (UK Charity);
proposed in Jan 2003 by UK Treasurer (Gordon Brown) and
DFID
2. Anticipated funds: 4 billion US\$ (over 20 years)
3. Donors: France, Italy, Norway, Spain, Sweden and UK;
Brazil, South Africa (would pay 1 million US\$ a year for 20
years)
4. Makes funds available through the GAVI Alliance (target =
GAVI countries, 70 poorest countries with per capita GNP of
< 1000 US\$); the World Bank as Treasury Manager

International Finance Facility for Immunization = IFFIm

5. 'Frontloading' resources for new and underused vaccines; strengthening vaccination services (basic EPI) = reliable, predictable, faster funding, extended period.

('Frontloading' = investing resources 'up front' in the expectation that it is more efficient than spreading small increases in funding over time).

6. IFFIm to raise funds through emission of bonds on international capital markets; triple A credit ratings; Goldman-Sachs Int. is financial advisor.

Bondholders are repaid by IFFIm using the guaranteed grants of its donors.

International Finance Facility for Immunization = IFFIm

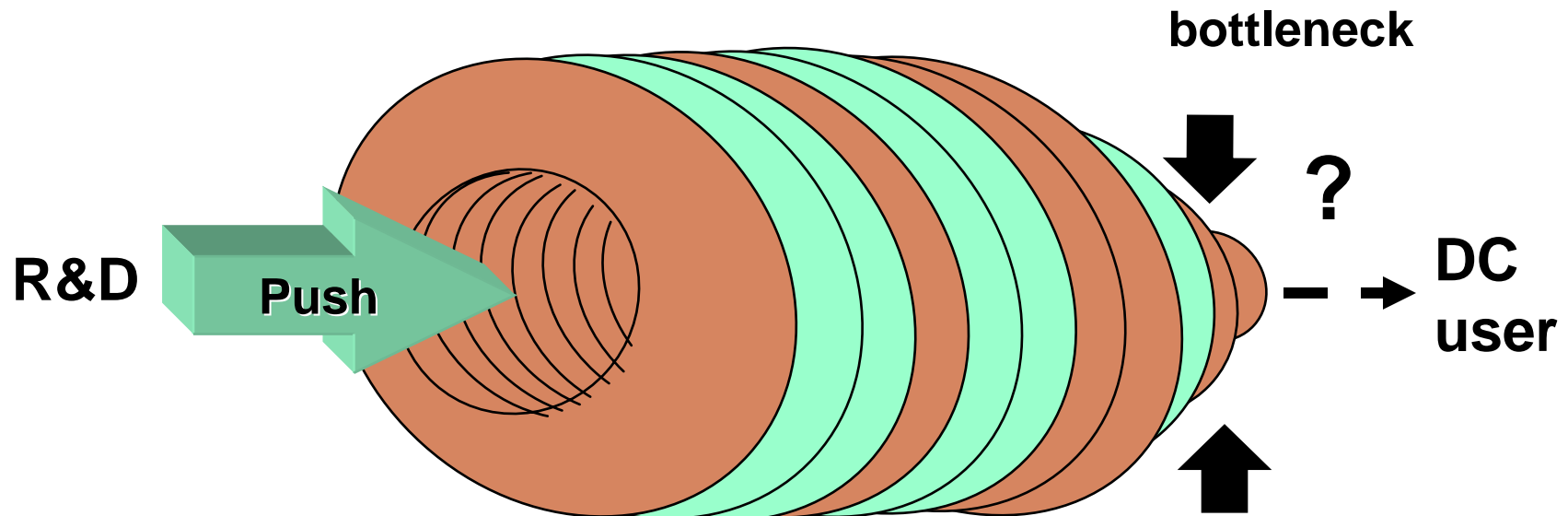
7. Support achievement of MDGs, e.g. MDG 4: save more children's lives and do so faster (30 US\$ needed to fully immunize a child)
8. Prevention of 5 million child deaths (2006 – 2015) and 5 million future adult deaths, above the estimated 1.5 million lives saved through GAVI

How can the public sector motivate the pharmaceutical industry to invest in the development and production of new vaccines for diseases prevalent in the developing world ?



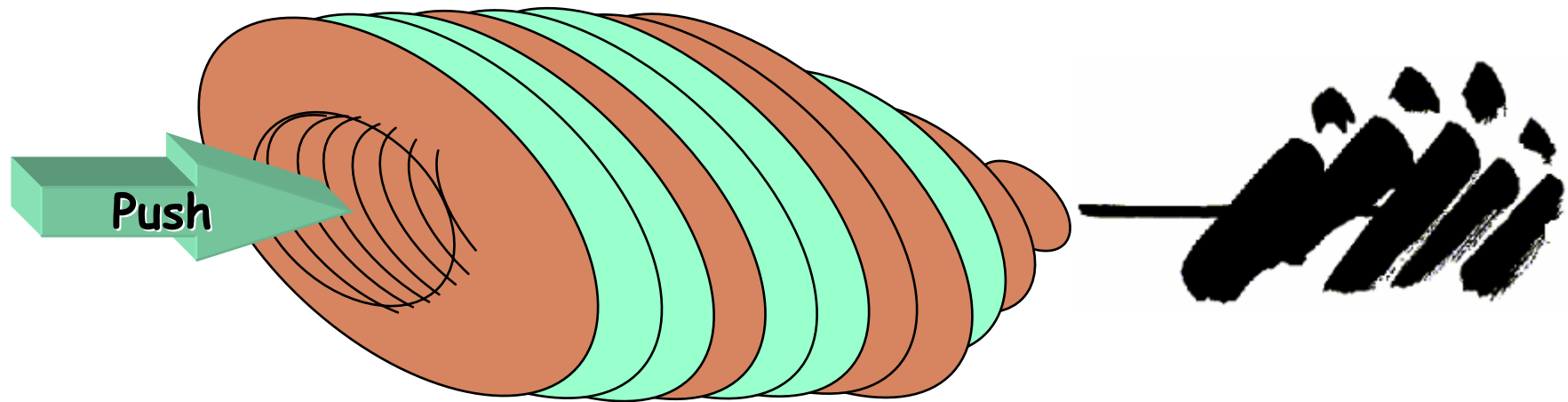
World Health
Organization

New vaccines- pipeline



Licensed or late-development candidates accumulating

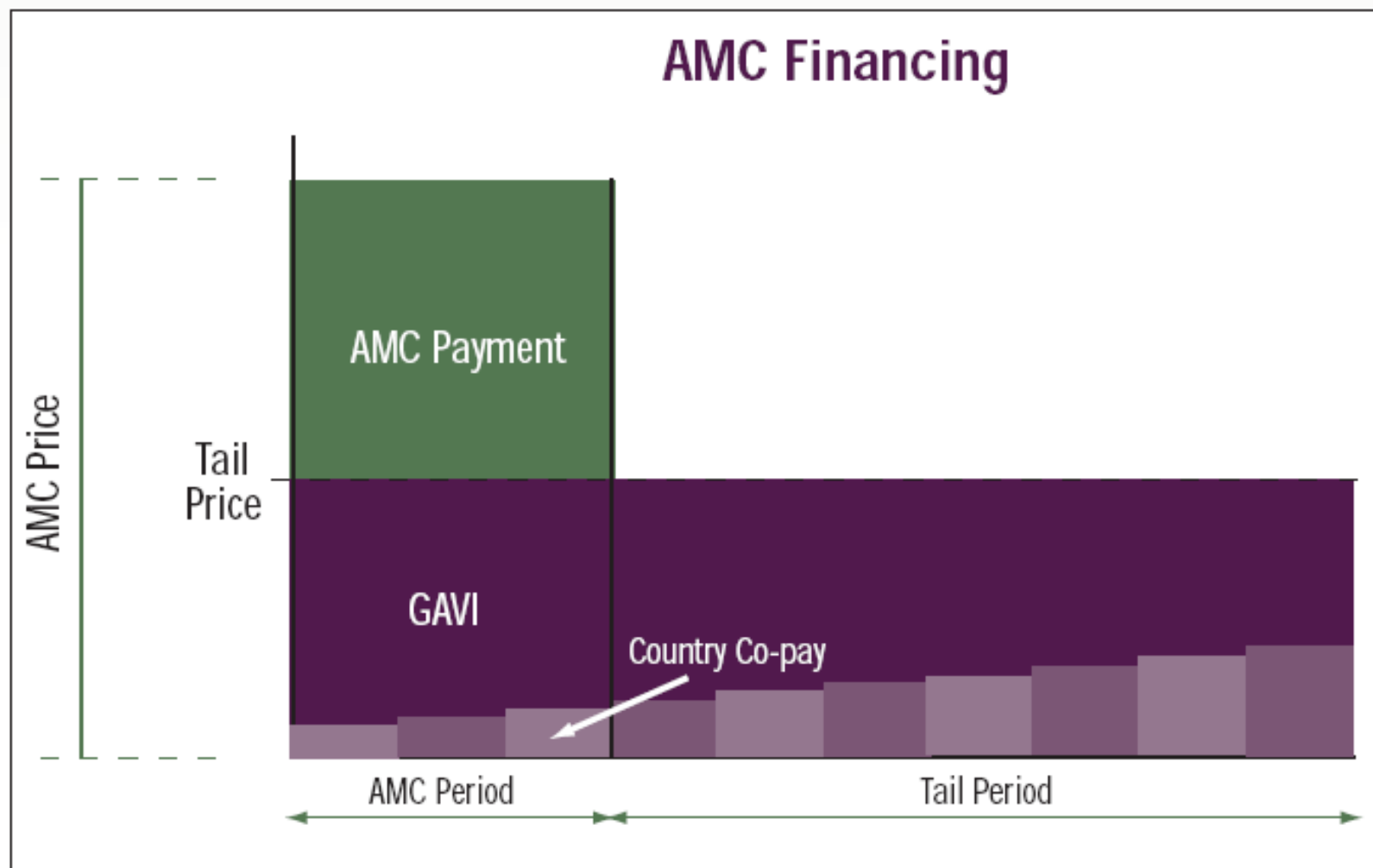
'Pull' incentives provide market incentive for product development



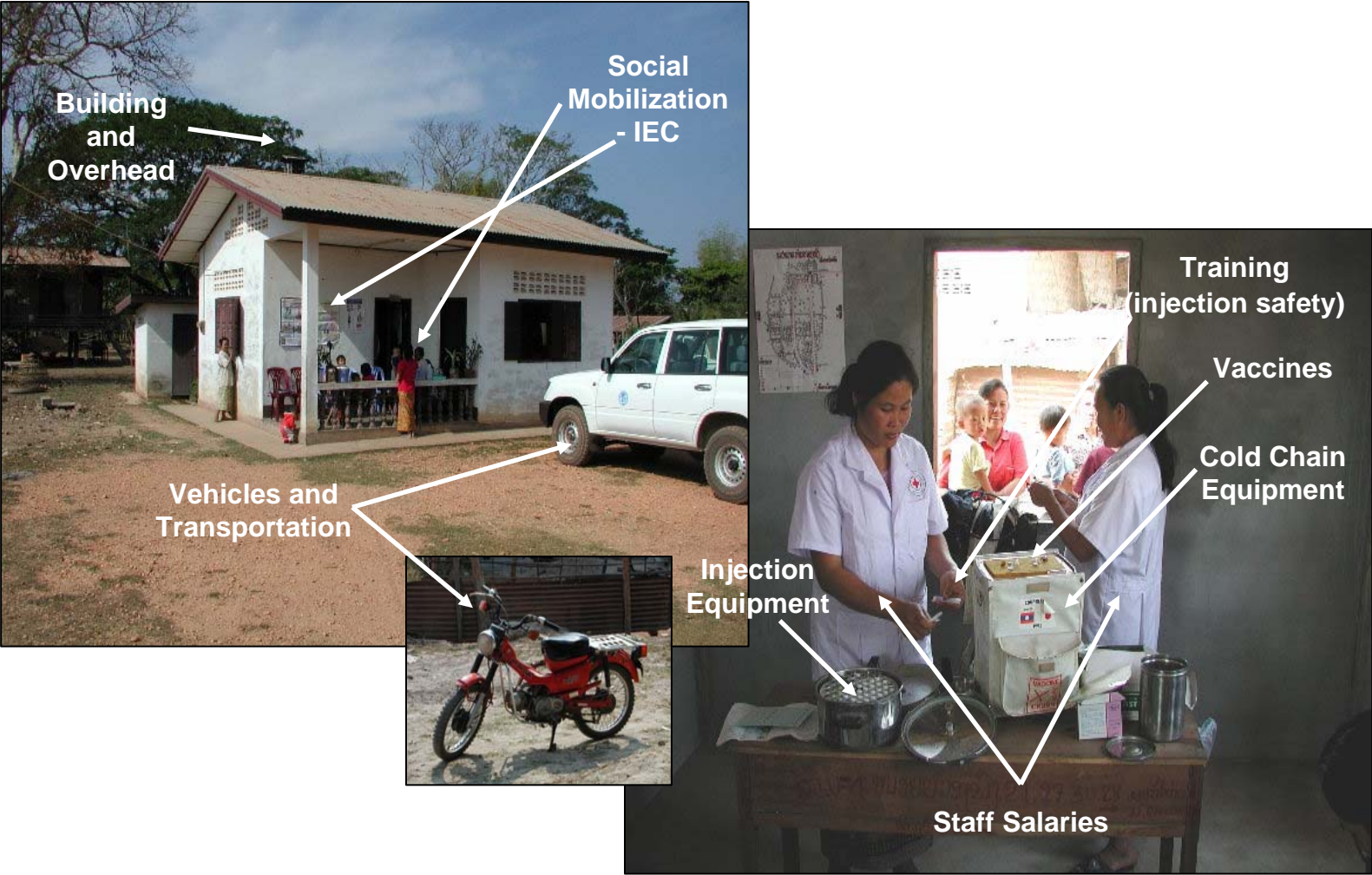
AMC initiative

Pneumo, HPV, rotavirus, HIV, TB, malaria

The Advanced Market Commitment (AMC) mechanism



What to Cost for Immunization



GAVI's Definition of Sustainability

“Although self-sufficiency is the ultimate goal, in the near term sustainable financing is the ability of a country to mobilize and efficiently use domestic and supplementary external resources on a reliable basis to achieve current and future target levels of immunization performance in terms of access, utilization, quality, safety and equity”.

16.04.07 Business Day
S.Afr.

Expansion of vaccine regime 'a problem'

Tamar Kahn

Science and Health Editor

CAPE TOWN — SA's crippling shortage of doctors and nurses would make the addition of Wyeth Pharmaceuticals' new vaccine against pneumonia and meningitis to the routine jabs given to children extremely difficult, a senior health department official said recently.

SA's National Advisory Group on Vaccines and the World Health Organisation have recommended that the vaccine, which protects children against seven dangerous strains of pneumococcal bacteria, be added to the national immunisation programme.

Pneumococcal diseases are a major killer of small children, particularly those infected with the virus.

However, the health department's immunisation programme manager, Johann van den Heever, expressed caution about the feasibility of adding another vaccine to the seven jabs the government already provides to young children. These protect against diphtheria, tetanus, pertussis, polio, hepatitis B, haemophilus influenzae type B (Hib) and tuberculosis.

"Currently, there is no capacity at national level to implement a new vaccine," he said.

"Implementing a new vaccine is a complex process," he said.

Staff needed to be trained to use the new vaccine, infrastructure such as cold-chain management systems had to be put in place, and data on adverse reactions would need to be collected, he said.

The high price tag of Wyeth's new pneumococcal vaccine, branded Prevenar, was also a major obstacle for a middle-income country such as SA, he said.

The jab itself costs about R1 800 for the three shots needed to provide protection against the pneumococcal bacteria.

Prevenar was approved by the Medicines Control Council in late 2005, which means it is already available to private sector patients who can afford it.

Wyeth sells the drug to wholesalers and pharmacists at R450 a shot, but they add further mark-ups, generating a retail price of about R600 a jab.

Van den Heever said the health department had asked the National Advisory Group on Vaccines to evaluate the cost-effectiveness of introducing Prevenar into the national immunisation programme.

The health department was also weighing up the merits of introducing two other new vaccines, the rotavirus jab, which protected children against diarrhoea, and a vaccine against HPV, the primary cause of cervical cancer, he said.

National Immunisation Programme (NIP) – criteria of readiness for new vaccine introduction - 1

- Obtaining full benefit from existing vaccines
 - cMYP; high coverage; limited drop-out; specific objectives met (e.g. hep B birth dose; two-dose measles)
- Financially sustainable programme
 - NIP able to secure current and future financing
- Functional cold chain
 - National cold chain policy and vaccine management system performing well

National Immunisation Programme (NIP) – criteria of readiness for new vaccine introduction - 2

- Well managed vaccine stock
 - Two-year to five-year forecast; vaccine wastage monitoring in place
- Safe immunisations and monitoring of adverse events
 - Auto-disable (AD) syringes; AEFI's adequately investigated and responded
- High quality disease surveillance
 - For major VPD's; data allow monitoring of impact

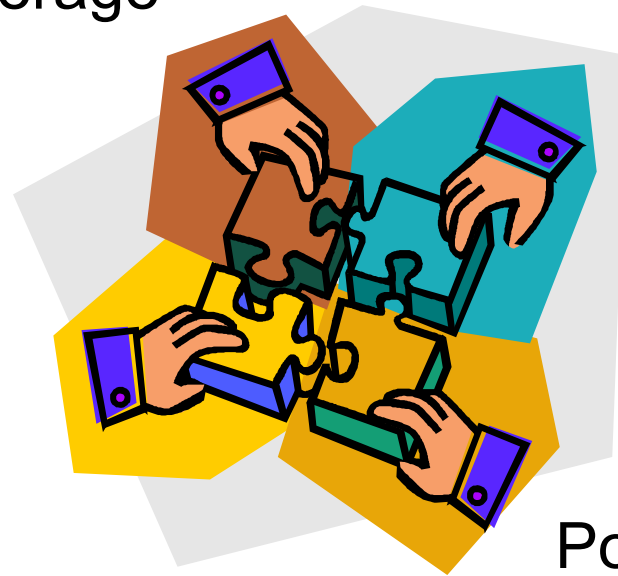
Implementation aspects of new vaccine introduction

- Product selection
- Vaccination schedule
- Introduction strategy
- Supply needs
- Cold-chain readiness
- Vaccine wastage
- Injection safety
- AEFI monitoring
- Revision of records and reporting tools
- Staff training and supervision
- Information, education and communication
- Financial sustainability
- Vaccine impact evaluation

Monitoring impact

Vaccination coverage

Disease and AEFI
surveillance



Special studies

Post-introduction
programme evaluation

CALL TO ACTION

Agreed by

the Ministers of Finance
and the Ministers of Health
from 35 countries

Presented by

Mr Trevor Manuel,
Minister of Finance,
Government of South Africa,

Dr Manto Tshabalala-Msimang,
Minister of Health,
Government of South Africa,

at the

International Vaccination Conference
Cape Town, South Africa
12 April 2002



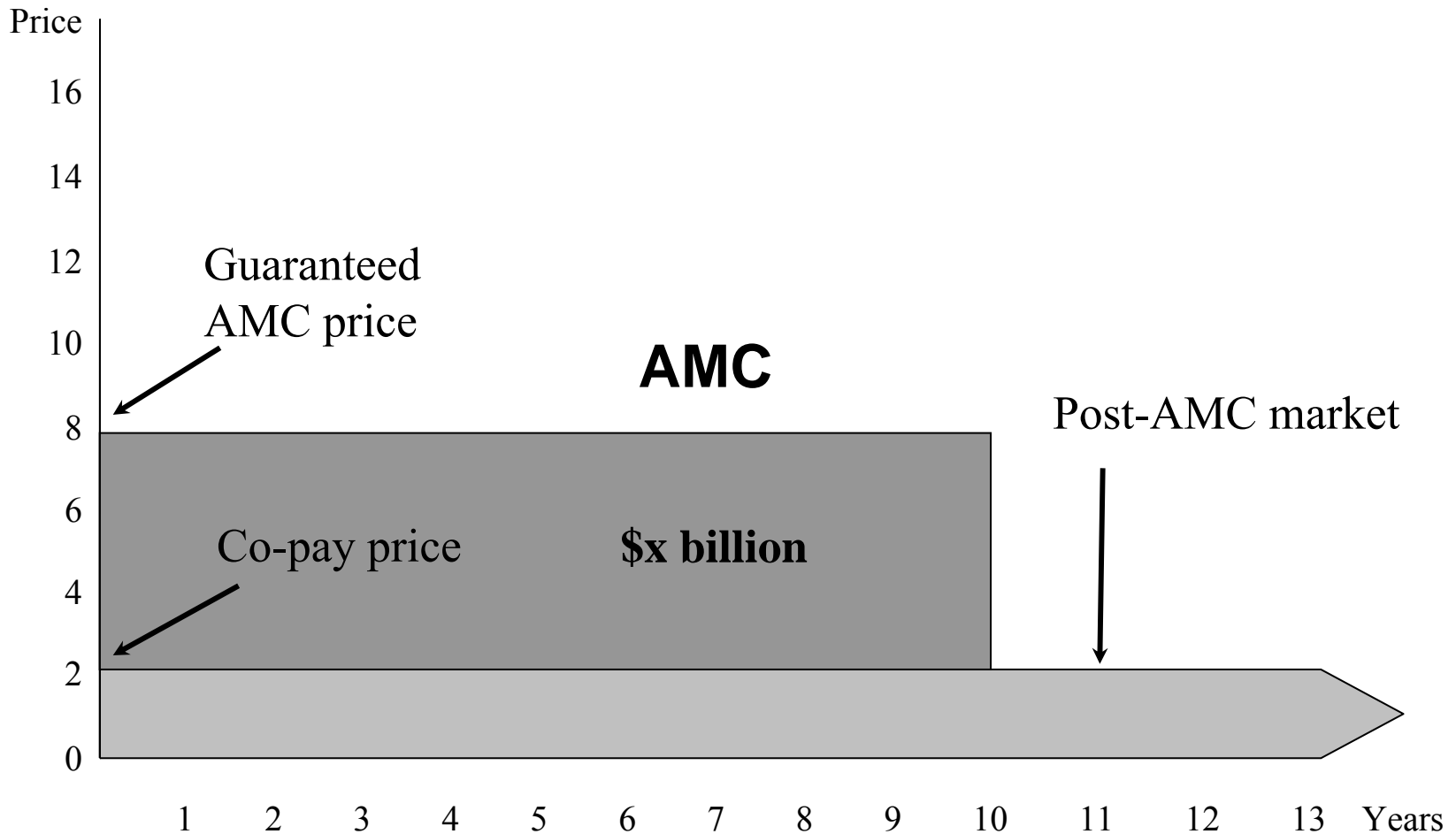
Cost Effectiveness of Hib Vaccination

- Cost per life year saved: \$17 - \$54 000
(Brinsmead et al. *Pediatr Inf Dis J* 2004)
- Variable methodologies
 - Most studies only include meningitis
 - Costing not standardized
- Only 3 published studies from developing countries (South Africa, Chile, Philippines)

Investment decisions by industry

- Factor's influencing their view of developing country (DC) market:
 - Potential vaccine revenue from DC is limited
 - strong price to volume bias:
 - EPI vaccines 80% of doses, 15% of revenue; varicella vaccine: 1% of doses, 32% of revenue
 - expectation of extremely low prices
 - Historically, demand forecasts for uptake of new vaccines in DC have been inaccurate
 - actual uptake much slower than predicted
 - need \neq actual demand
- These factors influence production decisions by firms

The Advanced Market Commitment (AMC) mechanism



Increasing challenges of new vaccines

- Immunization services
 - Establish and maintain immunization at the top of the public health agenda
 - Reinforce countries capacity in reaching high vaccine coverage to optimize impact
 - Continue advocacy for equitable access to vaccine by the children who need them the most
- Challenges specific to new vaccines
 - Develop partnerships with manufacturers in order to reduce barriers to production of affordable vaccines
 - Reinforce vaccine production capacity especially in emerging economies
 - Establish sustainable vaccine financing systems