

22 October 2019



INNOVATION FOR IMMUNIZATION

PATH Center for Vaccine Innovation and Access (CVIA)

David C. Kaslow, MD

PATH
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Mitundu Community Hospital Malawi



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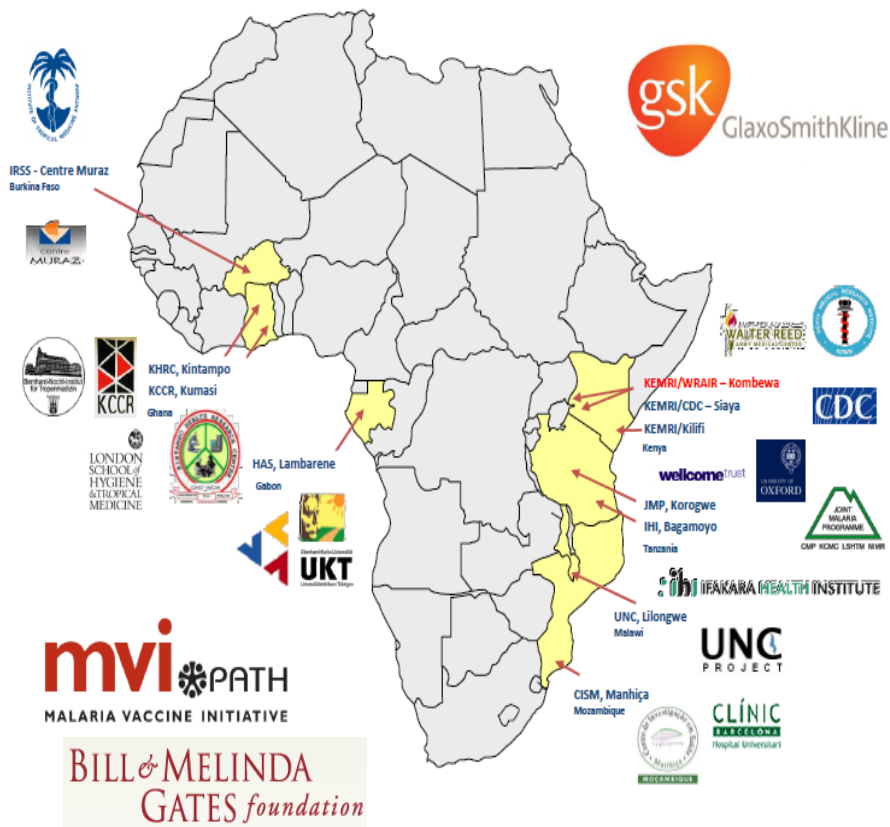
Lusitana Taziona
5-months old
23 April 2019

*1st child in the world
to receive
malaria vaccine
through
routine immunization*



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Phase 3 Study



Pilot Implementation



Phase 3 Study

Pilot Implementation

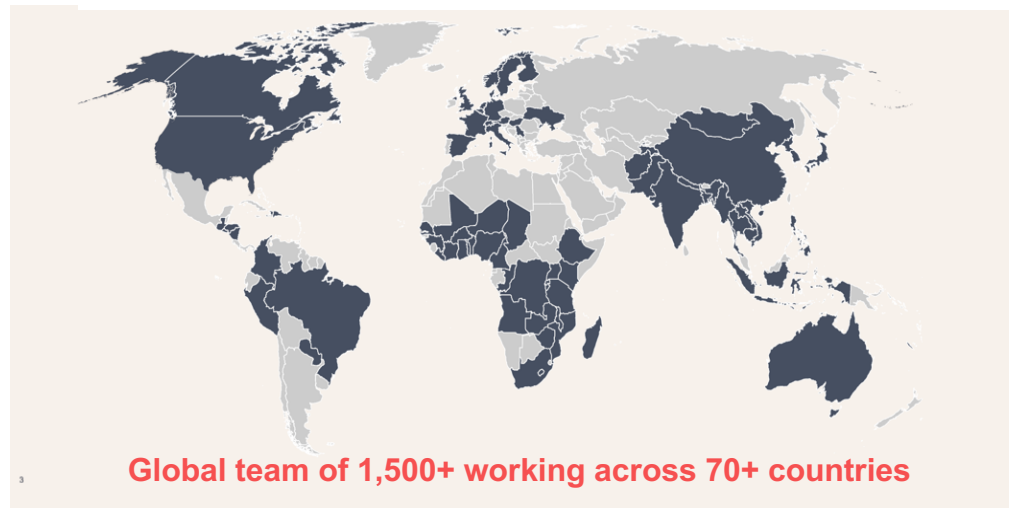




7+ billion vaccine vials
with **Vaccine Vial Monitors**
(VVMs) to ensuring vaccines
potency when given



6+ billion autodisable syringes
used to deliver single use
(**Soloshot**) vaccines



Malaria vaccine



Rotavirus vaccine



310+ million children
vaccinated in 6 countries with
Japanese Encephalitis Virus
Vaccine



300+ million people
immunized with **MenAfriVac®**
in the African meningitis belt



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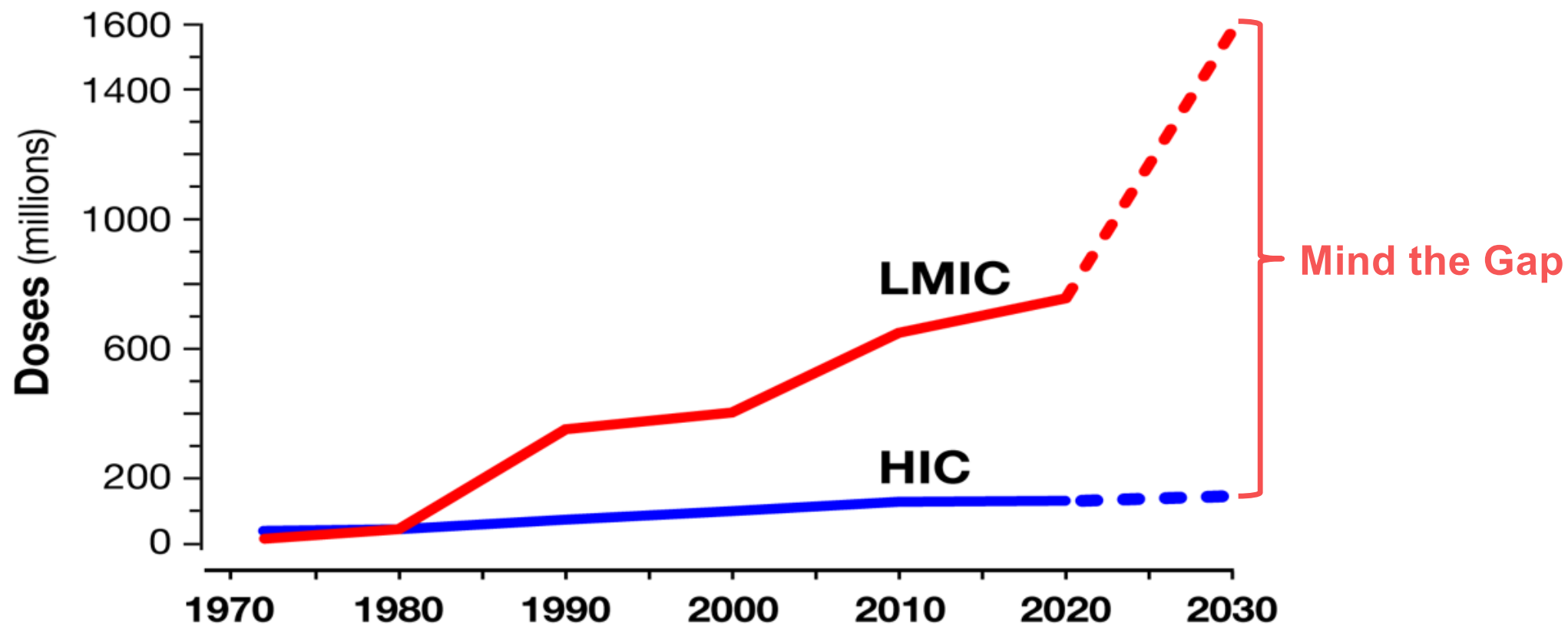


310+ million children
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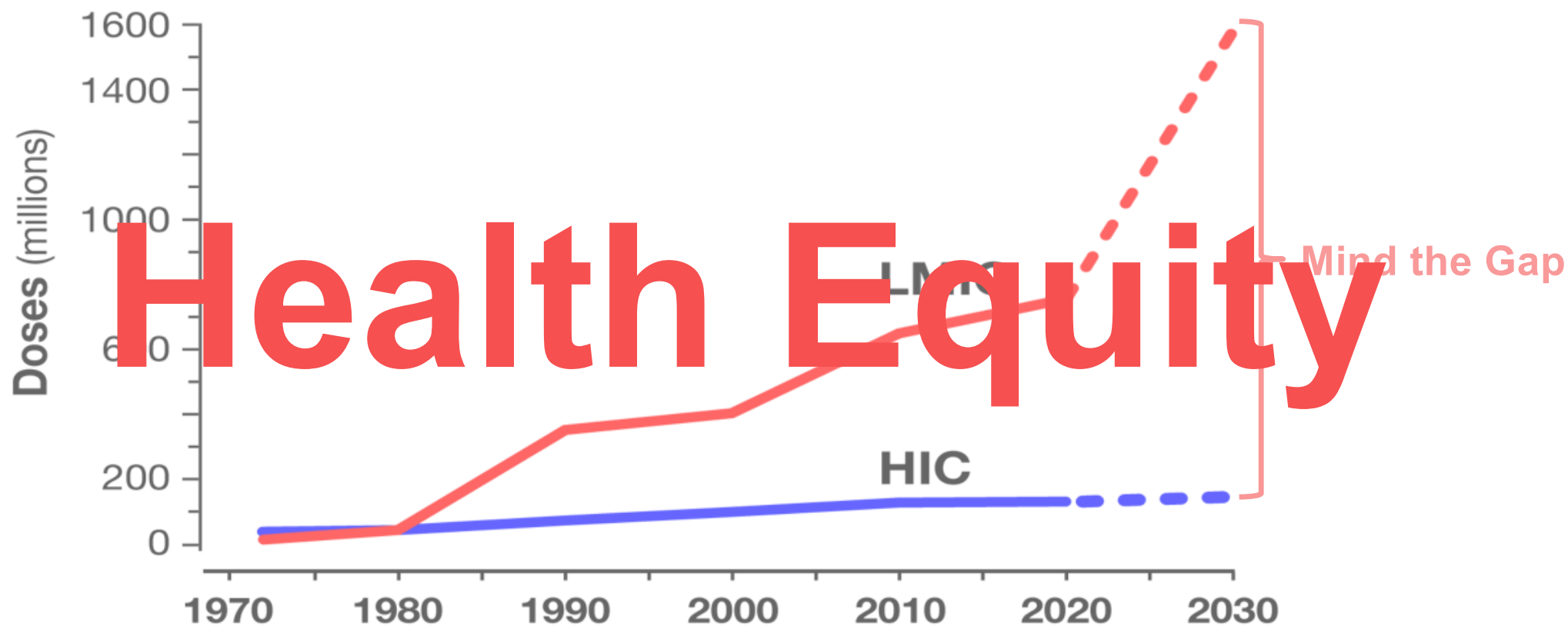
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Next decade of vaccine



Rappuoli et al., *Sci. Transl. Med.* 11, eaaw2888 (2019)
<https://stm.sciencemag.org/content/11/497/eaaw2888.full>

Next decade of vaccine



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<https://stm.sciencemag.org/content/11/497/eaaw2888.full>



**PATH's mission
is to advance
health equity
through
innovation and
partnerships**

- 1 Why and what is CVIA?
- 2 Innovations needed to overcome barriers
- 3 An assumption-based framework

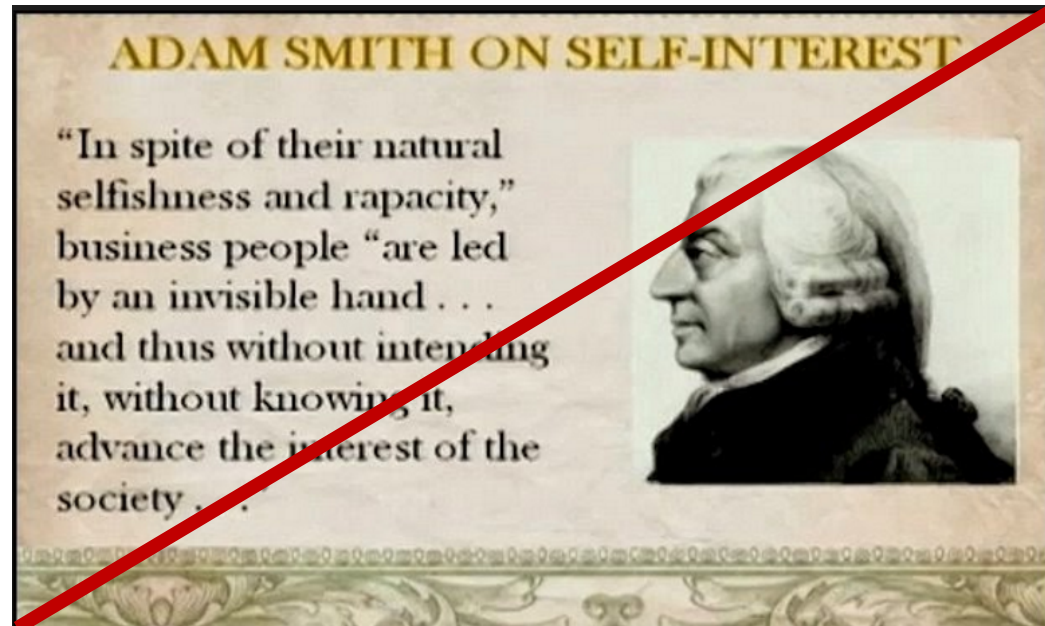


Why a Center for Vaccine Innovation and Access (CVIA)?

To fix John Snow's pump without the "invisible hand" of Adam Smith



Cholera outbreak
Soho, London (1854)



The Theory Of Moral Sentiments
(Part IV, Chapter I)



Product Development Partnerships: *Non-profit business model bringing together public, private, academic and philanthropic sectors to develop vaccines for public markets in low resource settings*

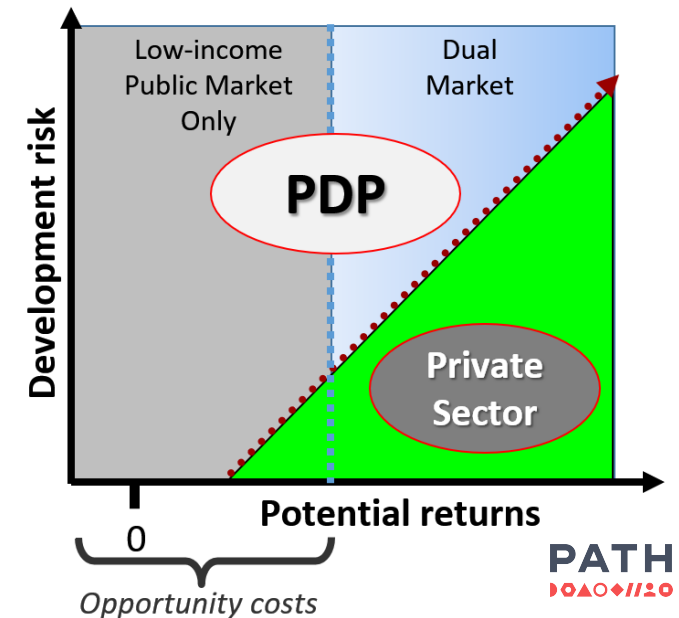
Circa 2008



Translation R&D gap
(aka First Valley of Death)

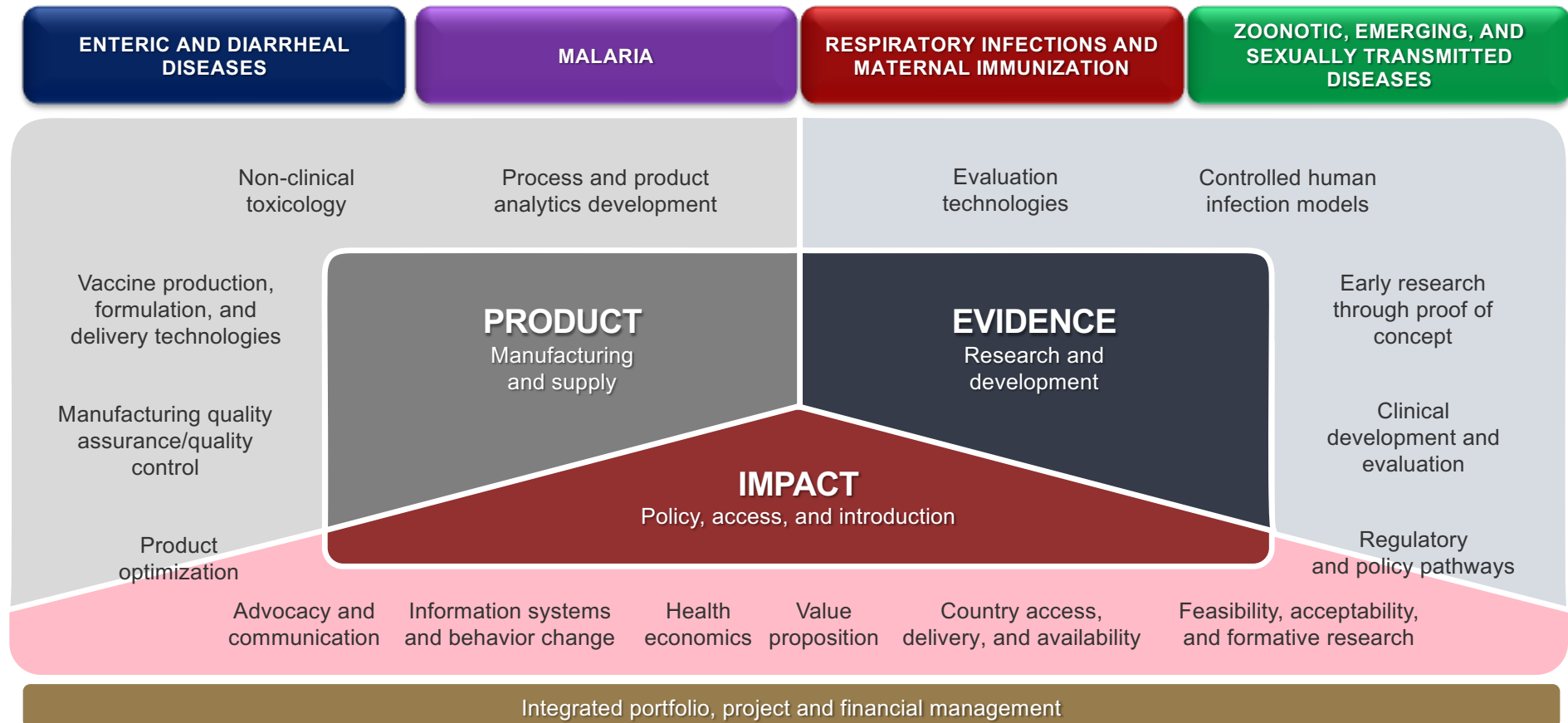


- Sharing the risk
- Sharing the cost





Industry standard cross-disciplinary product teams: Project teams cluster into four Diseases Areas supported by six Functional Areas in a typical balanced matrix with ≈ 175 staff





PATH's Vaccine & Immunization scope: Vaccine innovation and partnership from development, introduction, and improvement to impact



Cutting-edge research to tackle the toughest global health problems



Better data to reach more kids

Progression of vaccine development and introduction to impact for low- and lower middle-income countries



Solving with a country-centered approach



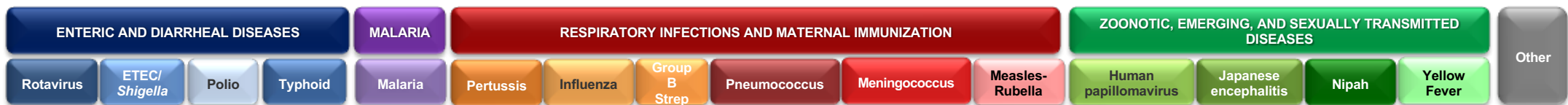
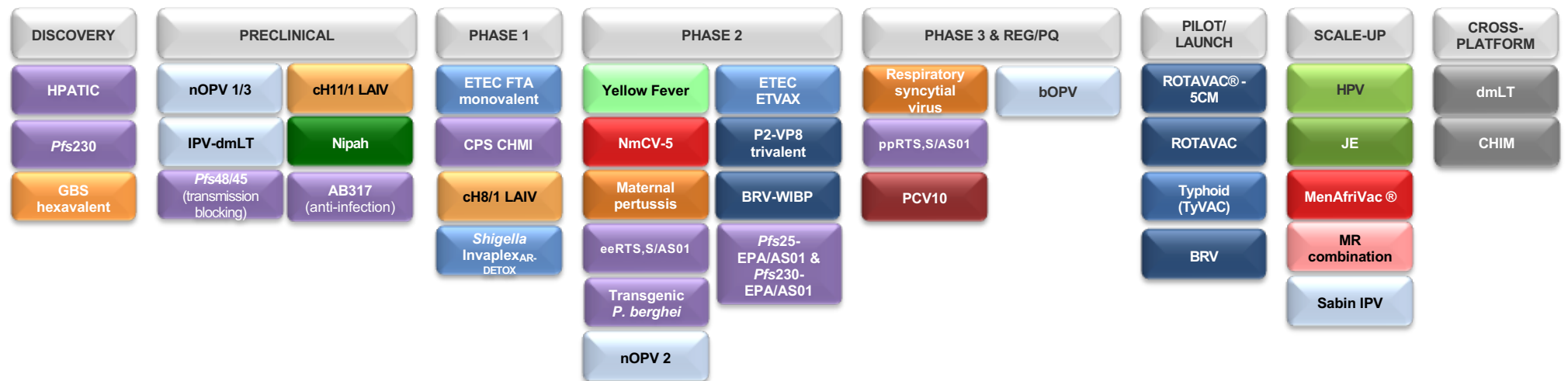
Strengthening immunization in primary health care

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PATH CVIA Portfolio: Over two dozen vaccines in development and use across 17 disease targets

2019



* Portfolio snapshot current as of **June 2019**; does not include new/ongoing proposal development work in dengue, Zika, or Ebola, nor ongoing support to the Expanded Programme on Immunization in multiple countries.

- 1 Why and what is CVIA?
- 2 **Innovations needed to overcome barriers**
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graph LR
    A[Discovery] --> B[Preclinical]
    B --> C[Proof-of-Concept]
    C --> D[Proof-of-Efficacy]
    D --> E[Registration]
    E --> F["WHO policy & PreQual.  
Proof-of-Effectiveness/  
Implementation"]
    F --> G[Financing & Procurement]
    G --> H[Uptake]
  
```

Discovery Preclinical Proof-of-Concept Proof-of-Efficacy Registration WHO policy & PreQual. Proof-of-Effectiveness/Implementation Financing & Procurement Uptake

Third-dose pentavalent vaccine coverage

First-dose measles vaccine coverage

Year	Third-dose pentavalent vaccine coverage (%)	First-dose measles vaccine coverage (%)
2015	80%	78%
2016	81%	80%
2017	82%	81%
2018	81%	81%
2020 (Target)	85%	83%



Innovation for Immunization in the late stage and introduction gap?

Progression of vaccine development and introduction for public markets in LMICs



Translation R&D gap
(aka First Valley of Death)



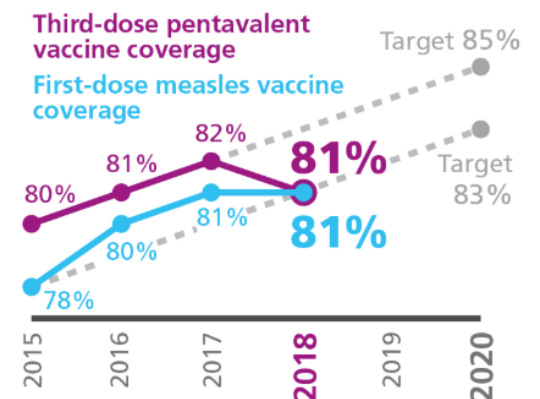
<http://www.nature.com/news/2008/080611/full/453840a.html>

Late Stage & Introduction gap
(aka Second Valley of Death)



www.lancet.com Vol 387 May 7, 2016
<https://www.nature.com/articles/d41586-018-07758-3>
<https://stm.sciencemag.org/content/11/497/eaaw2888.full>

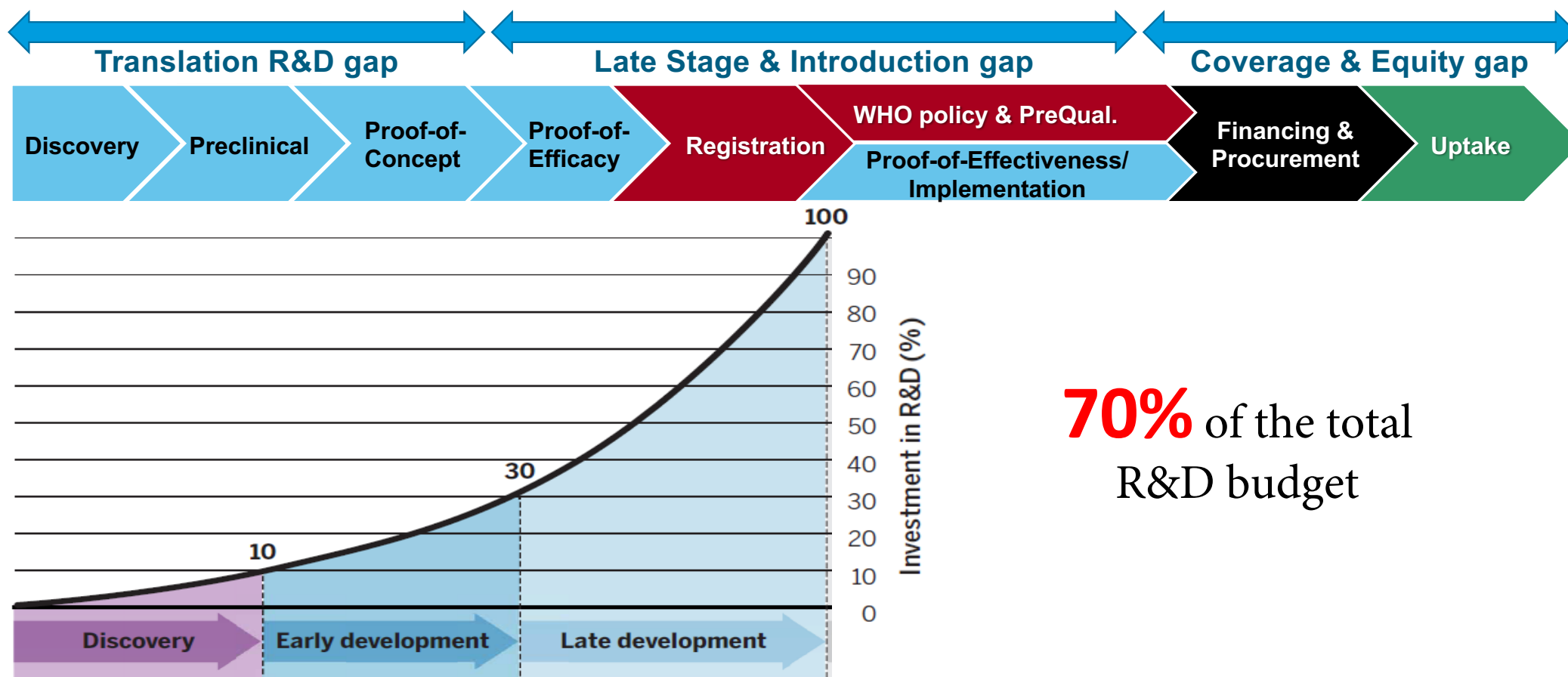
Coverage & Equity gap



Source: WHO/UNICEF Estimates of National Immunization Coverage, 2019

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Late stage development is the most labor- and cost-intensive phase of vaccine development



70% of the total R&D budget

Adapted from: Rappuoli et al., *Sci. Transl. Med.* 11, eaaw2888 (2019)
<https://stm.sciencemag.org/content/11/497/eaaw2888.full>

Late stage development and introduction is also CAPEX-intensive

Ave. cost of Phase 1 for CMC **USD12M** Total costs can range from **USD200M - 500M**



Review

The complexity and cost of vaccine manufacturing – An overview

Stanley Plotkin^a, James M. Robinson^{b,*}, Gerard Cunningham^c, Robyn Iqbal^d, Shannon Larsen

Plotkin, S. *Vaccine* **35**:4064–71, 2017
doi:10.1016/j.vaccine.2017.06.003

Major cost drivers that impact on COGS*

- Development
- **Facilities & Equipment CAPEX**
- Consumables/raw materials
- Direct Labor
- Overhead
- Licensing/Regulatory and commercialization

See also:

https://docs.gatesfoundation.org/Documents/Production_Economics_Vaccines_2016.pdf

*Cost of Goods Sold



Innovation in the **Late Stage & Introduction Gap** to address three **barriers**:

- Biological

- Technical

Many **but certainly not all** of the biological and technical gaps and uncertainties should have been addressed before entering into late stage development

Current exception are **implementation evidence** gaps

- **Human-controlled**

- Funding
- Political Will
- Stakeholder Alignment
- Regulatory-Policy-Financing Pathway

- 1 Why and what is CVIA?
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Key assumption:
Its not just about the money

“Innovations” to overcome human-controlled barriers beyond just funding: ABCs

- **A** **Acceptable** innovative approaches and tools to reduce late stage development costs and accelerate the pathway to licensure, (i.e. CHIMs, adaptive trial designs, regulatory acceptable biomarkers, including those that bridge from first-in-class to next generation candidates)
- **B** **Binding alignment** across the regulatory-policy-financing pathway continuum—what evidence is needed when to make seamless transitions and accelerate the process?
 - Aligning profiles:
 - Target Product (licensure) Profiles
 - Target Policy Profiles (?)
 - Target Financing Profiles (?)
- **C** **Country-based** activities including understanding demand, creating the required infrastructure and workforce capacity, and building community acceptance



Key assumption:
“One size” won’t fix all cases

Four Vaccine Business Cases

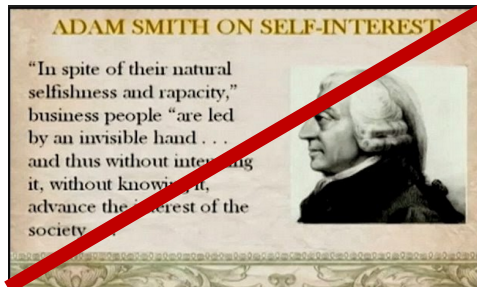
Compelling—Uncertain—Assistance—No

Assistance-dependent business case (LMIC only; Outbreak)

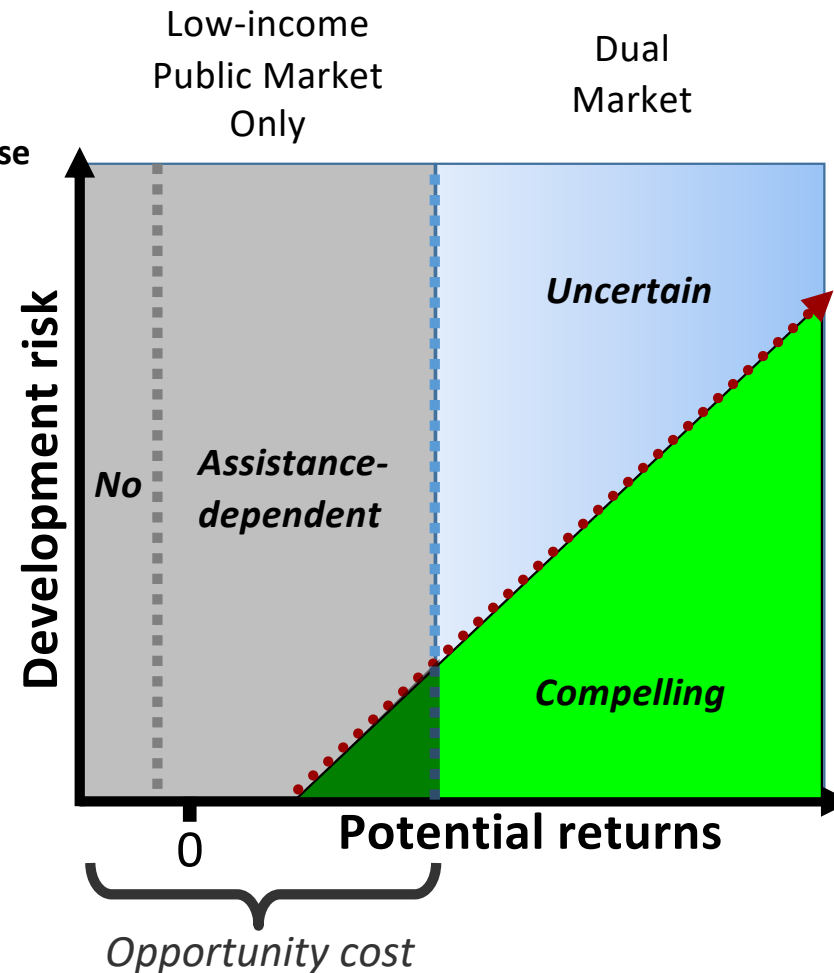
(e.g., LMIC: Cholera, Malaria, Men A, Shigella; Outbreak: Ebola, MERS, Nipah, Lassa Fever)

Solutions:

- Public funding
- Priority Review Vouchers
- LMIC Manufacturers
- Push & Pull mechanisms



The Theory Of Moral Sentiments
26 (Part IV, Chapter I)



Uncertain business case (LMIC ↔ HIC)

(e.g., Grp A Strep, Grp B Strep, TB)

Solutions:

- Reverse tiered pricing
- Push & Pull mechanisms

Compelling business case (HIC → LMIC)

(e.g., HBV, HiB, HPV, PCV, RSV, Rota)

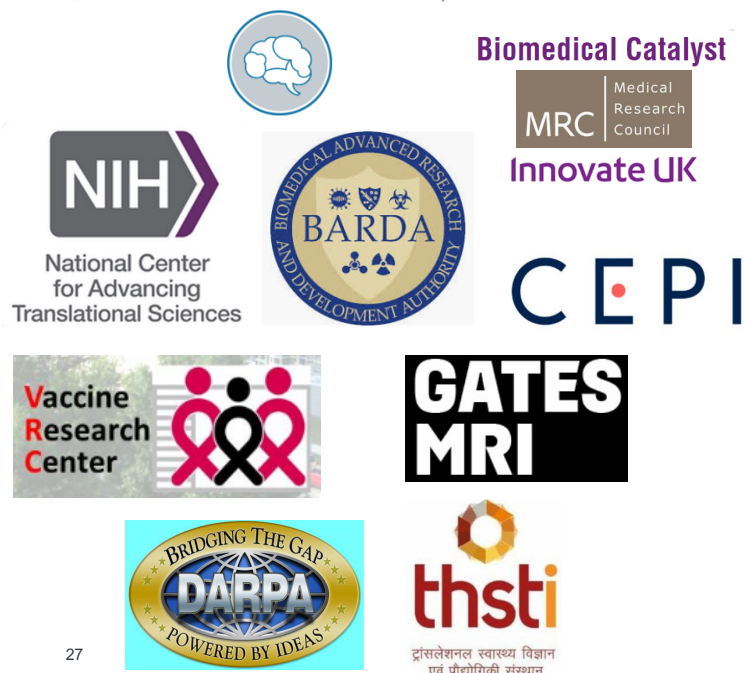
Solutions:

- Tiered pricing
- Push & Pull mechanisms

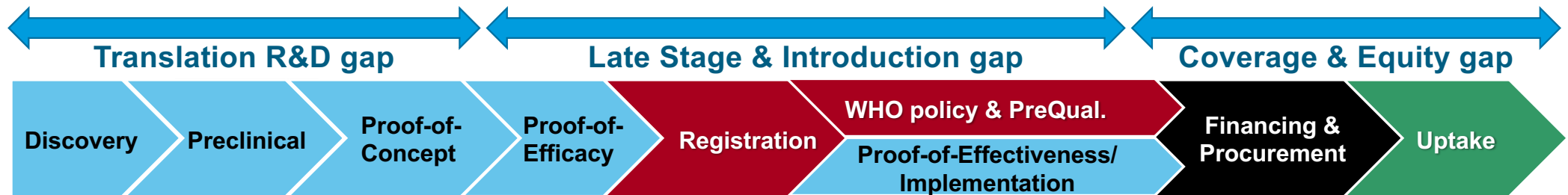
When no one owns it, everyone pays—who owns it?



Strategic Health Innovation Partnerships



Single v multiple entities?



Pathogen-specific?
(Pneumo ADIP, Rota ADIP, Hib Initiative)

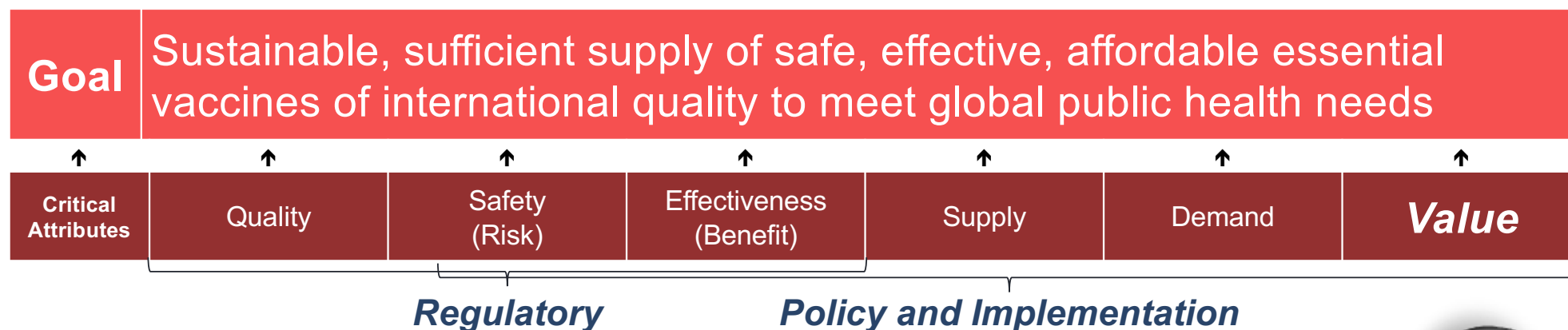


A single entity?

Key assumption:

A favorable and sustainable value proposition for all key stakeholders

Value as a critical vaccine attribute to optimally achieve strategic goal



Value as Driver of Vaccine Product Development



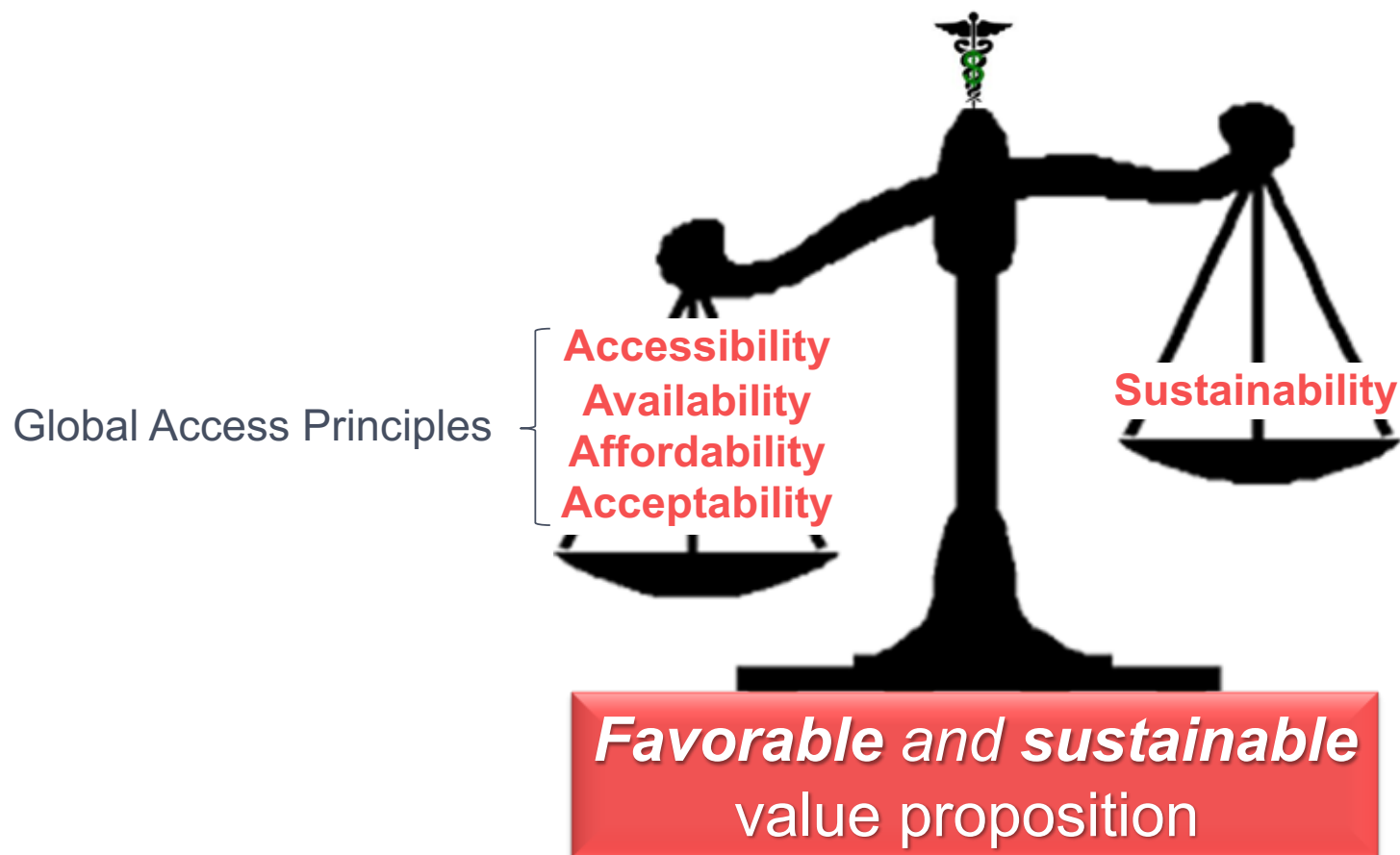
Typical stakeholders include:

- Public and private funders and donors;
- Developers (large pharma, biotech and academic) and manufacturers;
- Global and national policymakers including WHO;
- National/global advocacy groups including in countries with high disease burden.

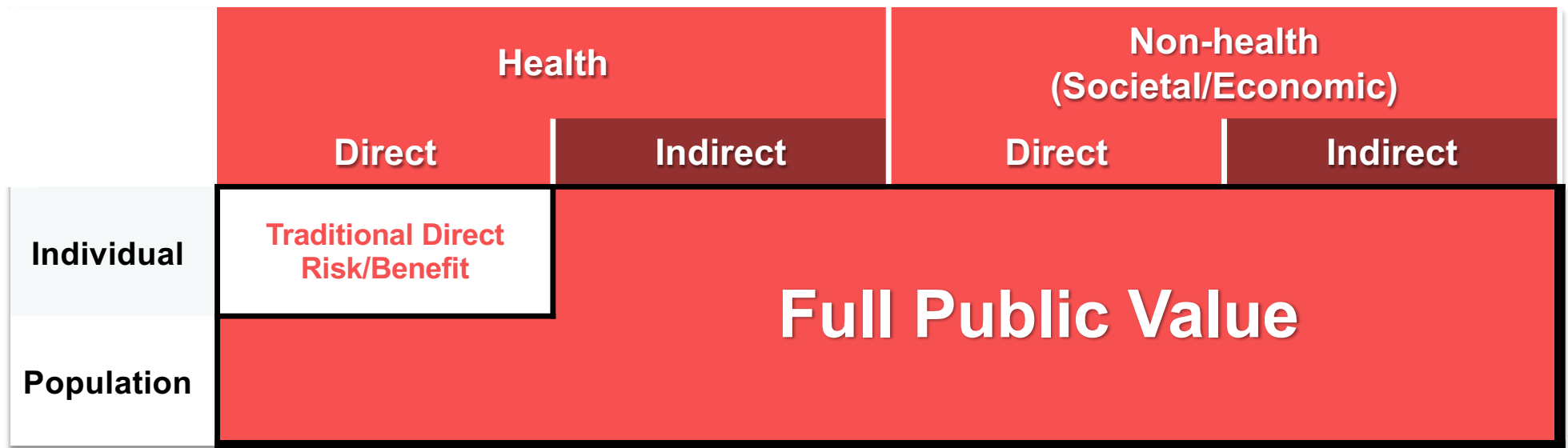
Other stakeholders:

- Households;
- Third-party payers;
- Government (e.g. MoH, MoF, MoD);
- Donors;
- Innovators;
- Society as a whole.

Finding the optimal balance of value for all key stakeholders



Traditional Direct Risk/Benefit v Full Public Value



Key assumption:
*Public sector championship
required (political will)*

Creates alignment across a range of stakeholders, with respect to global health priorities

Provides a resource to effectively advocate for development and introduction of vaccines

Informs rapid, disciplined investment decisions at all stages of development and implementation

Increases the likelihood of suitability for and access and sustainability of vaccines to LLMICs

Full Public Value
of Vaccines
as driver of
sustainable
vaccine development
and
access

— INNOVATION — PARTNERSHIP — HEALTH EQUITY —



Lusitana Tazona
23 April 2019



Susana Heavenly Joy
30 April 2019



Elian Koech
13 September 2019

