# New technologies for neglected diseases

## What is likely to come out of the pipeline, what is missing and what will it cost?

Webinar, Global Health Centre, Graduate Institute of Geneva
November 20, 2018

**Gavin Yamey** | Director, Center for Policy Impact in Global Health, Duke University
**Robert Terry** | Research Policy Manager, TDR
**Aex Gunn** | Policy Analyst, Center for Policy Impact in Global Health, Duke University

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

THE CENTER FOR POLICY IMPACT IN GLOBAL HEALTH

# How much does R&D cost?

## The $2.6 Billion Pill

► Average out-of-pocket company costs of $1.4B + time costs of $1.2B (expected returns that investors forego while drug is in development)

► Data from 10 unnamed companies, 106 unnamed investigational compounds

Di Masi J, et al. Innovation in the pharmaceutical industry: new estimates of R&D costs. *J Health Econ* 2016;47:20-33

## $35-195 Million Pill

► DNDi estimates it has spent $39-52 million developing a NCE

► Figure adjusts upwards to $130-195 million when risk of failure is taken into account

An Innovative Approach to R&D for Neglected Patients: Ten Years of Experience and Lessons Learned by *DNDi*.

## $1.5 Billion, 10 y

► Antibodies, probiotics, and vaccines in phase 2/3 trials

► First wave "will probably best serve as adjunctive or preventive therapies"

Czaplewski L, et al. Alternatives to antibiotics—a pipeline portfolio review. *Lancet Infect Dis* 2016;16:239-51.

# How much does R&D cost ?

# TDR REPORT: HEALTH PRODUCT R&D FINANCING (2016)

Less: how much does a drug cost?

More: how much do we need ?

"A financial and health impact model, named the Portfolio-To-Impact Model (P2I model) was developed specifically for this study to analyze and visualize **how different funding options** would assist in reducing R&D gaps and to bring new products to market for diseases of poverty."


http://www.who.int/tdr/capacity/gap_analysis/en/

# TDR REPORT: HEALTH PRODUCT R&D FINANCING (2016)

Less: how much does a drug cost?

More: how much do we need ?

Describes how a potential **pooled fund** could operate under WHO Member States.

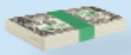
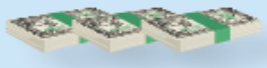
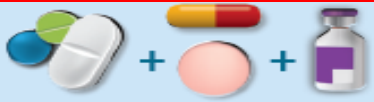
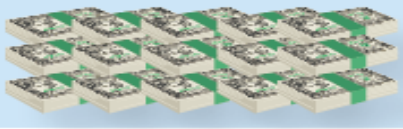
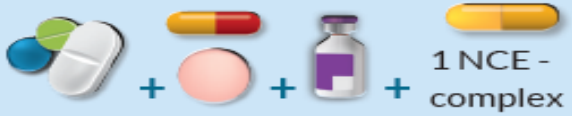
Three areas of work:

- Modeling a global financial mechanism
- Governance for an R&D portfolio
- Developing toolkit for portfolio management including Target Product Profiles

Discussion at WHA May 2017 (no go…)

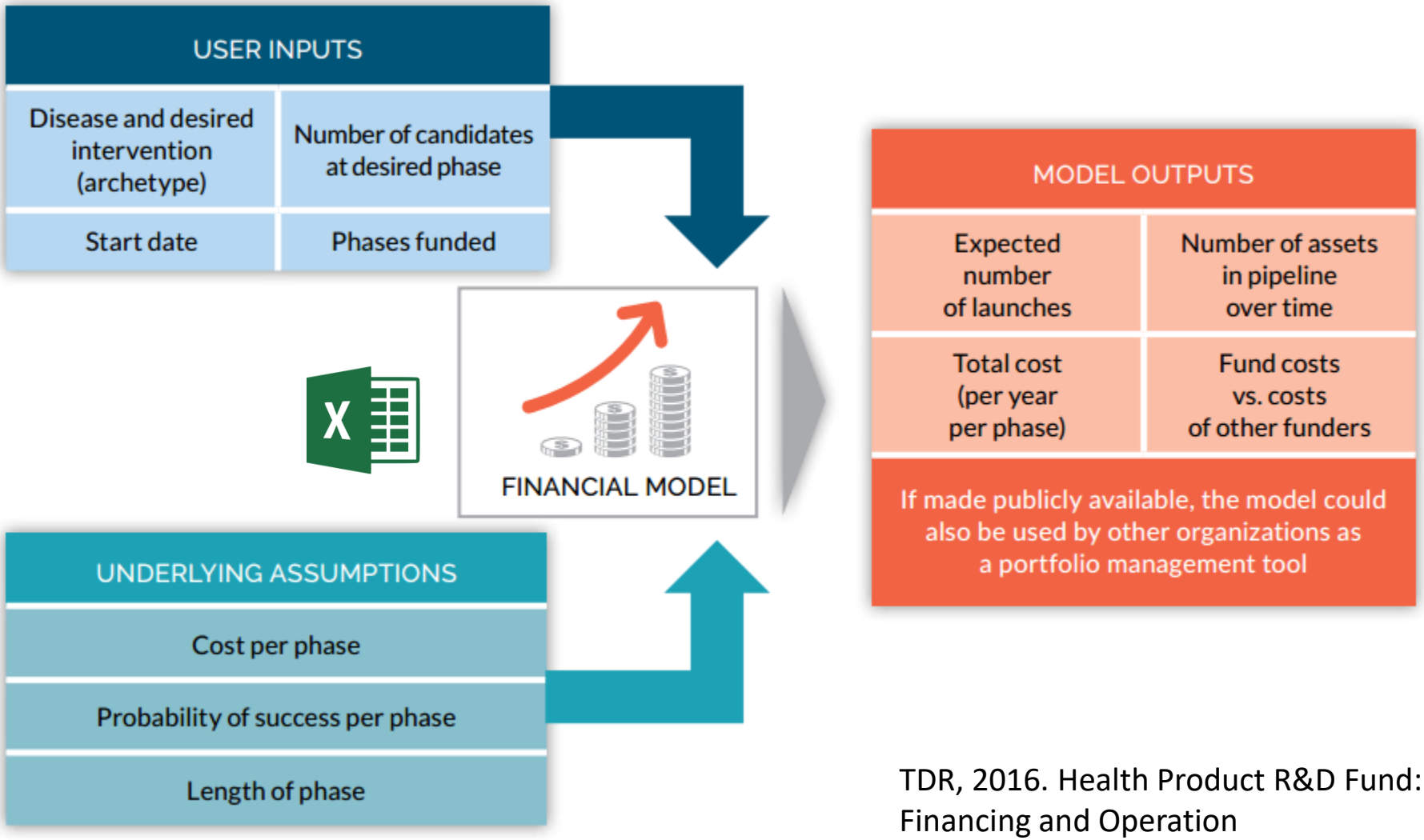

http://www.who.int/tdr/capacity/gap_analysis/en/

# OVERVIEW OF FUND OPTIONS AND MECHANISMS

| | ANNUAL FUND SIZE US$ millions (m) [a] | STEADY STATE PROJECTS/YEAR | ESTIMATED STAFFING NEEDS (FULL-TIME EQUIVALENT) | IF DEVELOPMENT STARTS IN 2017, WHAT IS EXPECTED BY 2030? |
|---|---|---|---|---|
| 1 | Passive coordination Up to US$ 1 m | Define and communicate global priorities across diseases | 1 | |
| 2 | Prioritization Forum Up to US$ 5 m | Review funding directions with donors and evaluate if funding is aligned with global priorities | 3 | |
| 3 | ~US$ 15 m (small)  | Fund 3-4 projects (no innovation-focused projects) | 3  | 3 repurposed drugs - simple |
| 4 | ~US$ 50 m (PDP size)  | Fund 15-20 projects (few innovation-focused projects) | 9  | 1 new chemical entity (NCE) - simple |
| 5 | ~US$ 100 m (medium)  | Fund 25-40 projects (including ~5 innovation-focused projects) | 14  | 1 repurposed drug - complex  |
| 6 | ~US$ 300 m (large)  | Fund 80-100 projects (a novel intervention to approval) | 26  | 1 simple biologic |
| 7 | >US$ 500 m (global)  | Fund 140-160 projects (can fund many projects in priority areas) | 40  | 1 NCE - complex |

[a] Costs shown represent annual amount of funds for disbursement to support R&D from preclinical to phase III. Costs related to management, infrastructure and fund hosting are not shown.

# New R&D model: Portfolio to Impact (P2I)




TDR, 2016. Health Product R&D Fund: A Proposal for Financing and Operation

# P2I model is based on averages for “archetypes”

| Archetype | | Description | Examples |
|---|---|---|---|
| **Repurposed Drug** | Simple | Drug has sufficient safety data to start development in phase II | azithromycin , doxycycline |
| | Complex | Drug requires some phase I clinical trials to verify safety in humans | Moxidectin |
| **New Chemical Entity (NCE)** | Simple | Validated target/mechanism of action | Primaquine |
| | Complex | Novel target/MOA without understanding of disease pathogenesis | Imatinib |
| **Biologics** | Simple | Validated target/MoA or developed from a combination of two approved biologics. | human monoclonal antibody m102.4 |
| | Complex | Novel target/mechanism of action | polyclonal IgG antibodies |
| **Vaccines** | Simple | Platform has been used to develop other vaccines. Likely to elicit robust protective response. | Hep A, Hep B, polio<br>Killed or live attenuated |
| | Complex | Requires completely novel approach/no platform/no existing research. | Pneumococcal conjugate vaccine (PCV, meningitis B, HIV DNA vaccines |

# Three steps in developing assumptions in the P2I model

Initial assumptions derived from bottom-up analysis based on **25,000 development candidates**

Refinement & validation based on **academic literature** & **industry publications**

Further validation with **PDPs, pharmaceutical companies, R&D funders***

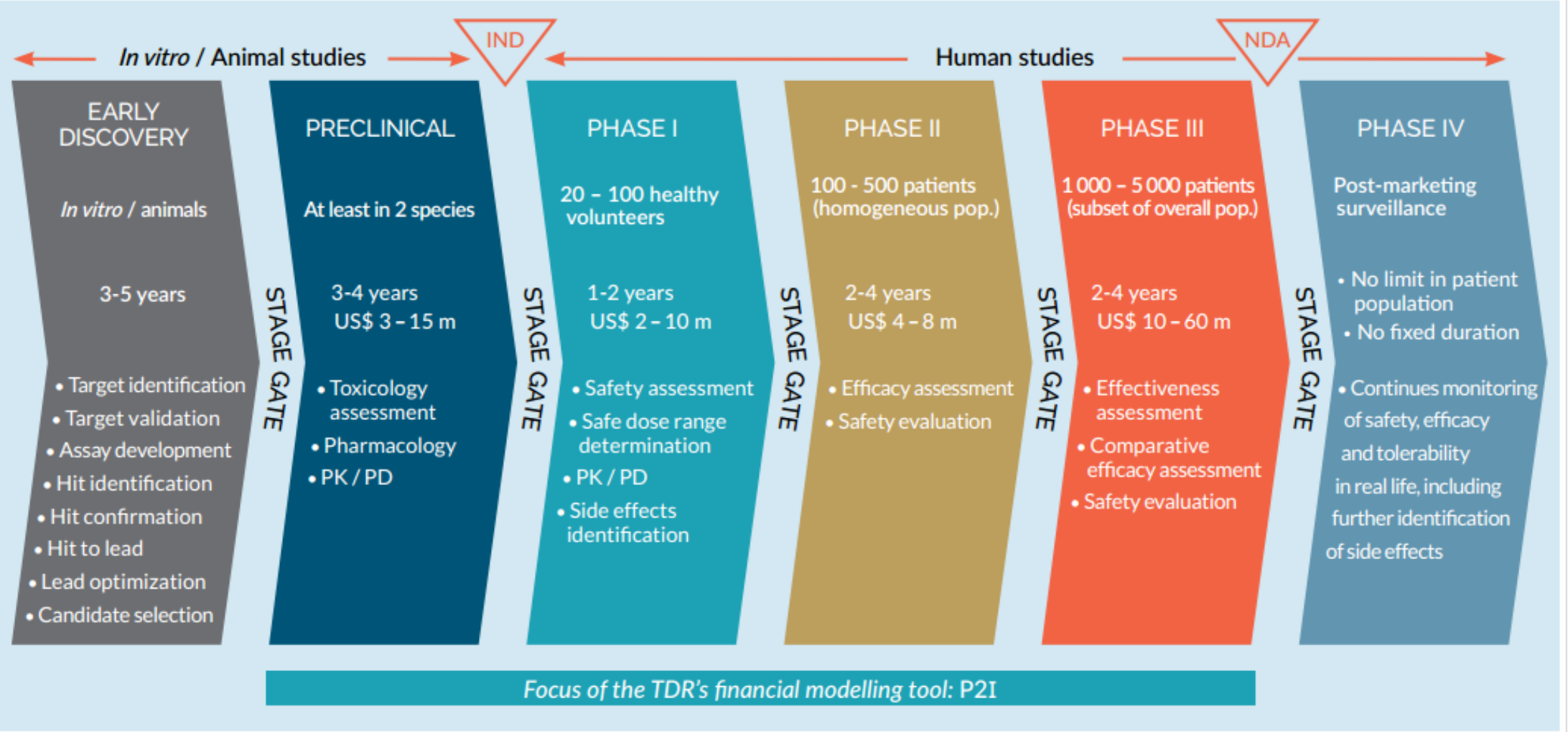
Assumptions on **cost**, **attrition rate**, & **cycle time** per phase *for each archetype*

*130+ interviews, 80+ organizations

# Process: consulted 130+ stakeholders from 80+ organizations

## Data collection and analysis undertaken with McKinsey & Company

# Scope of P2I v.1




TDR, 2016. Health Product R&D Fund: A Proposal for Financing and Operation. PK – pharmacokinetics PD – pharmacodynamics IND – investigational new drug NDA – new drug application

# New analysis led by Duke used adapted version of P2I

## Objectives

- **What is in the pipeline?** Pipeline portfolio review for poverty-related and neglected diseases (PRNDs)
- **Estimated costs?** Cost modeling: *current pipeline to production* and *cost of missing products*
- **Launches?** Applying attrition rates to identify what launches are likely given the current pipeline of candidates

## Scope

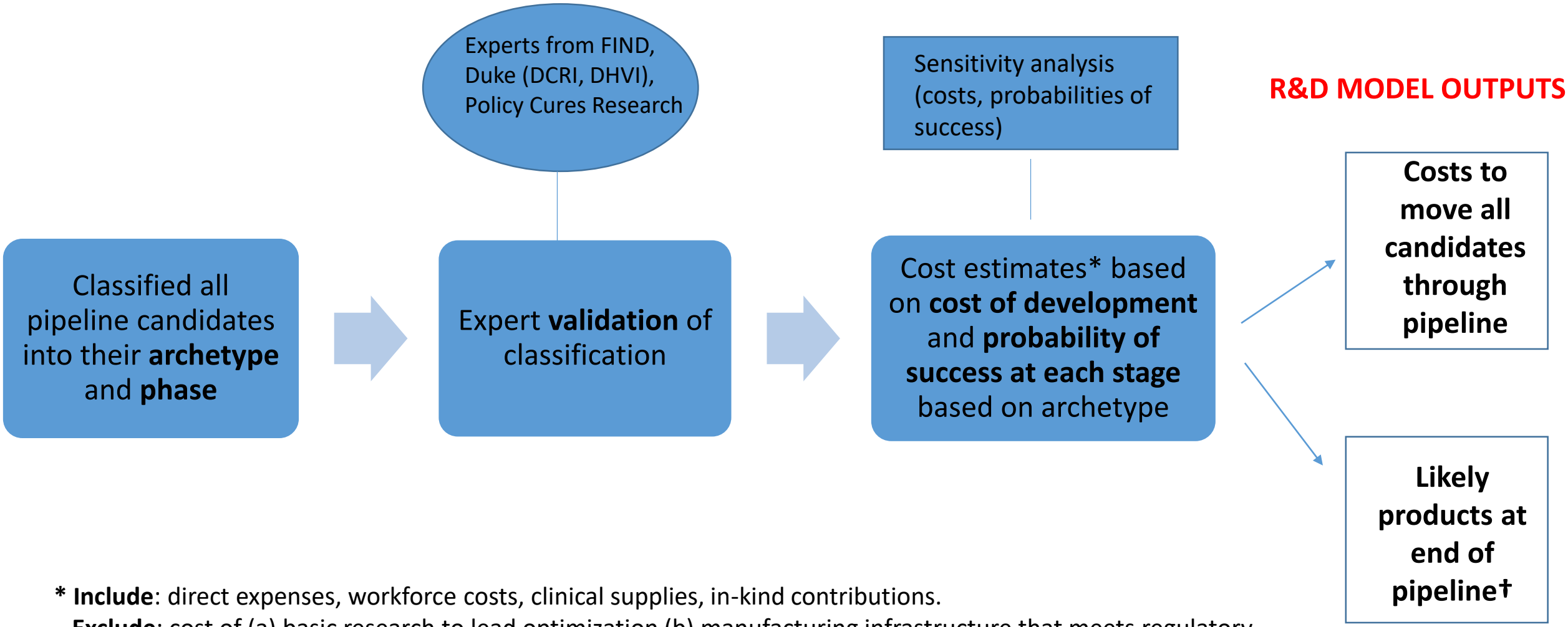
- 35 PRNDs as defined by Policy Cures Research, including HIV, TB, malaria, diarrheal diseases, NTDs, reproductive health conditions of LICs/MICs
- Key product areas: drugs, vaccines, diagnostics, vector control products (VCPs), contraceptives, multi-purpose prevention technologies (MPTs)

# Development of the P2I v.2 model

Changes from P2I v.1 to v.2

- **Additional archetypes:** vector control products and unprecedented vaccines. Unprecedented vaccines are candidates for HIV, TB, and malaria
- **Refined TB candidate assumptions**
- **Modified a small number of archetype assumptions for biologics** based on data shared by BMGF (*Per Liljenberg*)

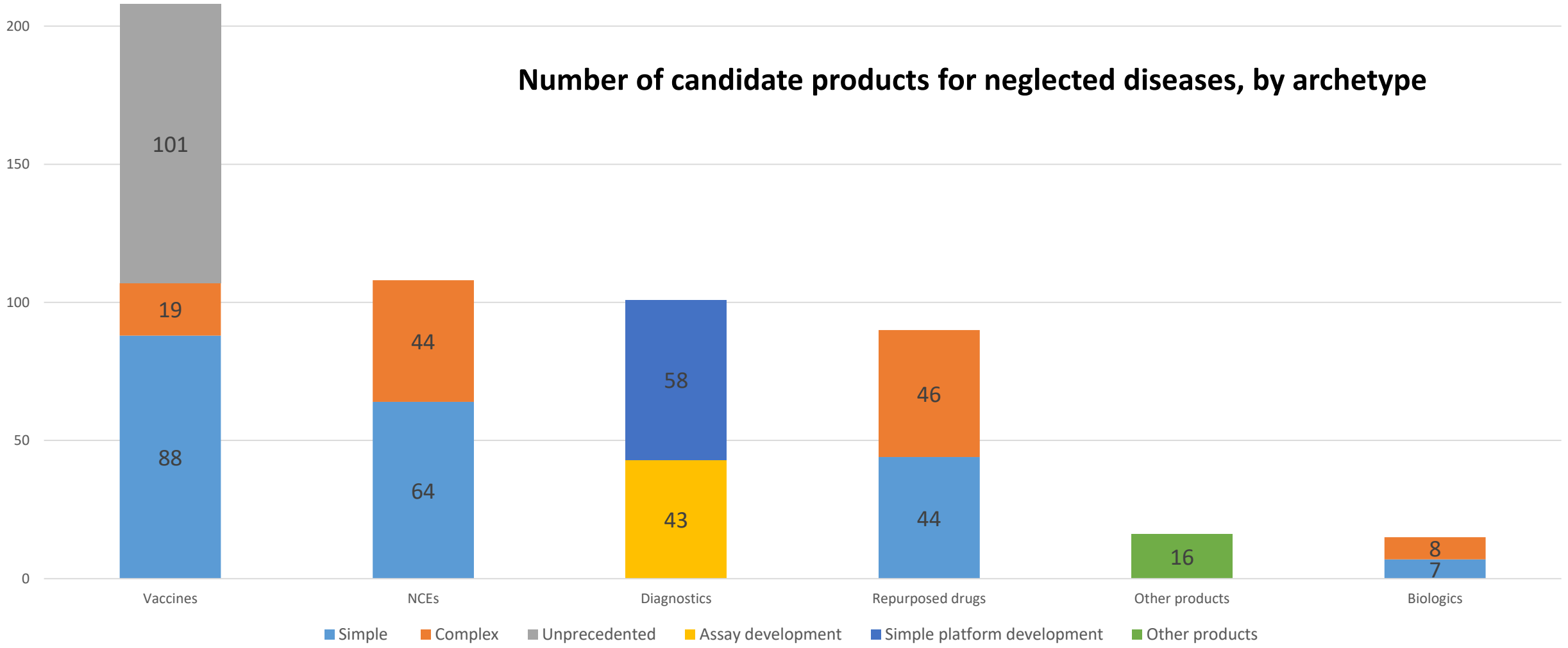
# Steps in the model



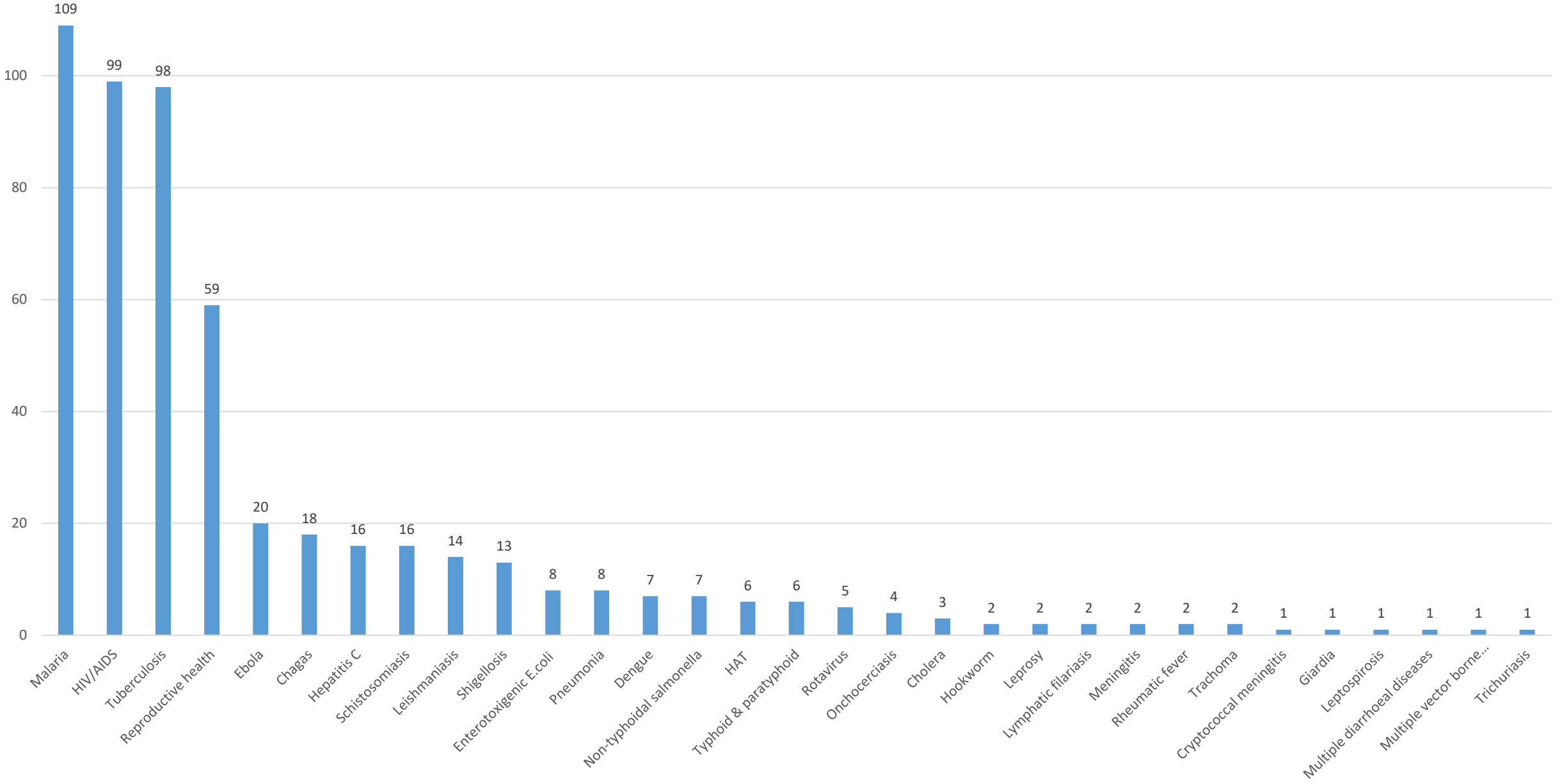

*** Include**: direct expenses, workforce costs, clinical supplies, in-kind contributions.
**Exclude**: cost of (a) basic research to lead optimization (b) manufacturing infrastructure that meets regulatory requirements (c) scale up costs (d) manufacturing the product; regulatory or registration fees; post-marketing costs; capacity building costs associated with the product

†Rounded *down*

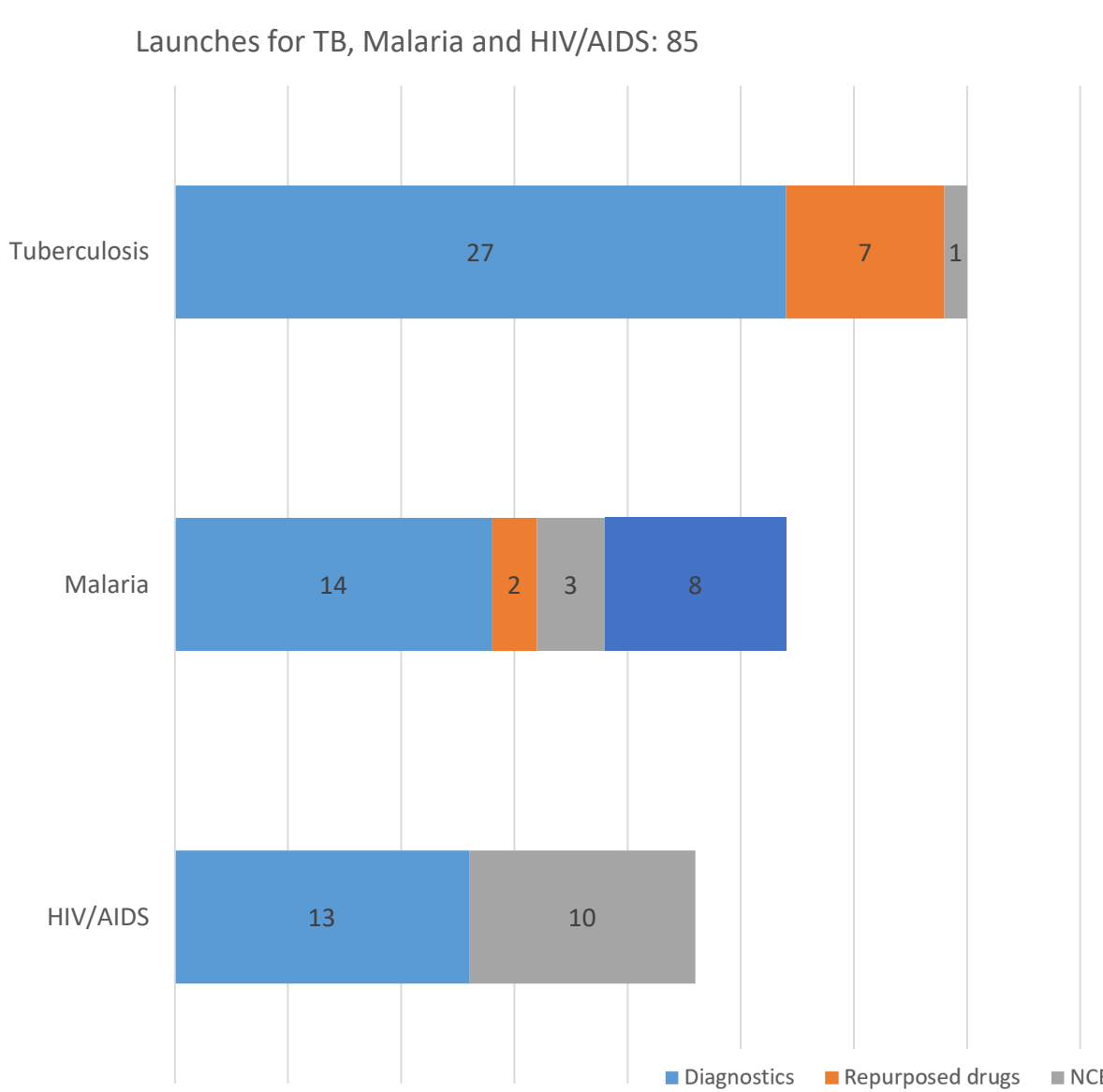
# Results: 2017 pipeline of 538 candidates included in model

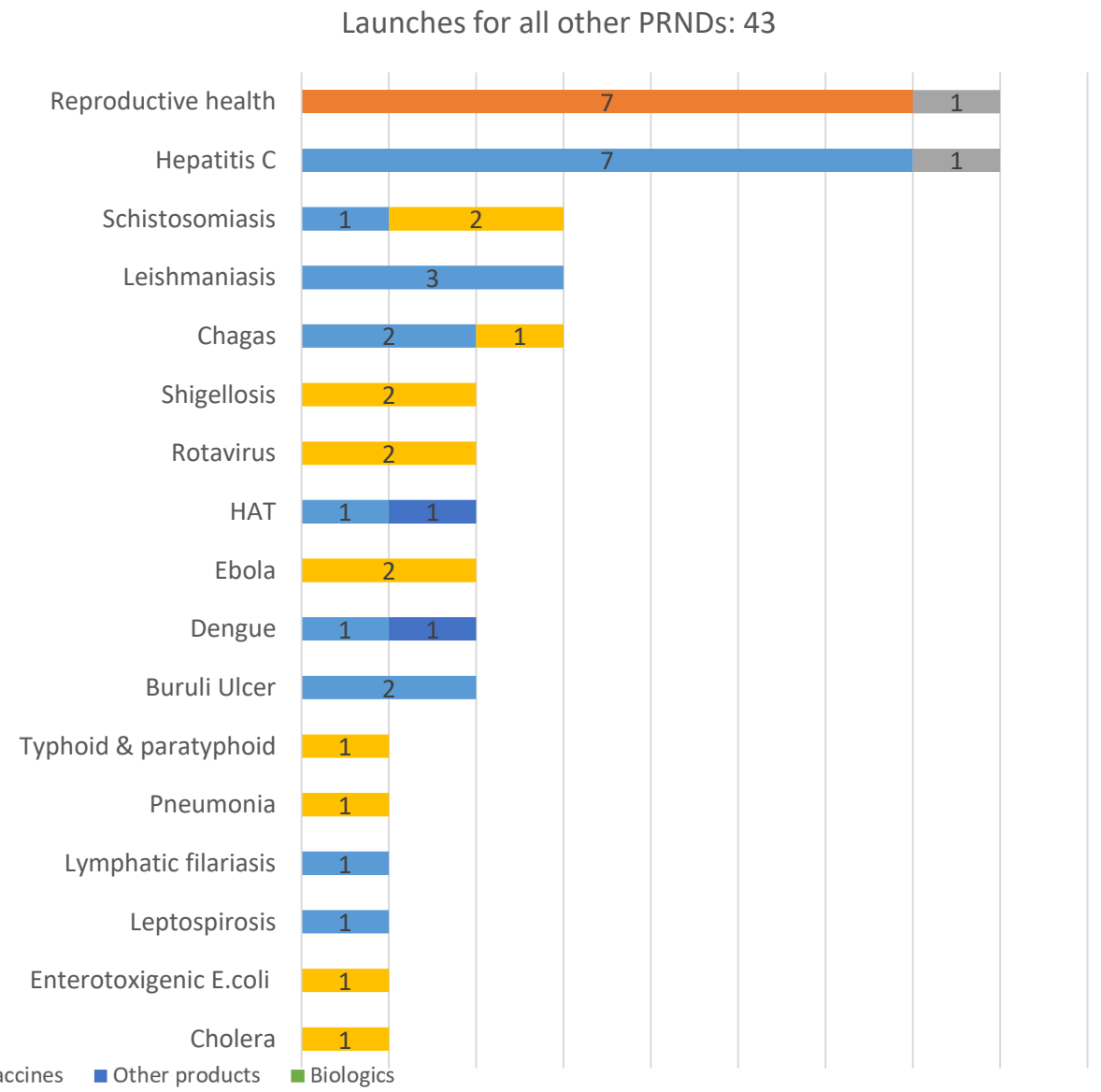


# Results: pipeline of candidates included in the model, by disease



# 128 “anticipated” launches at end of pipeline (range 89-160)



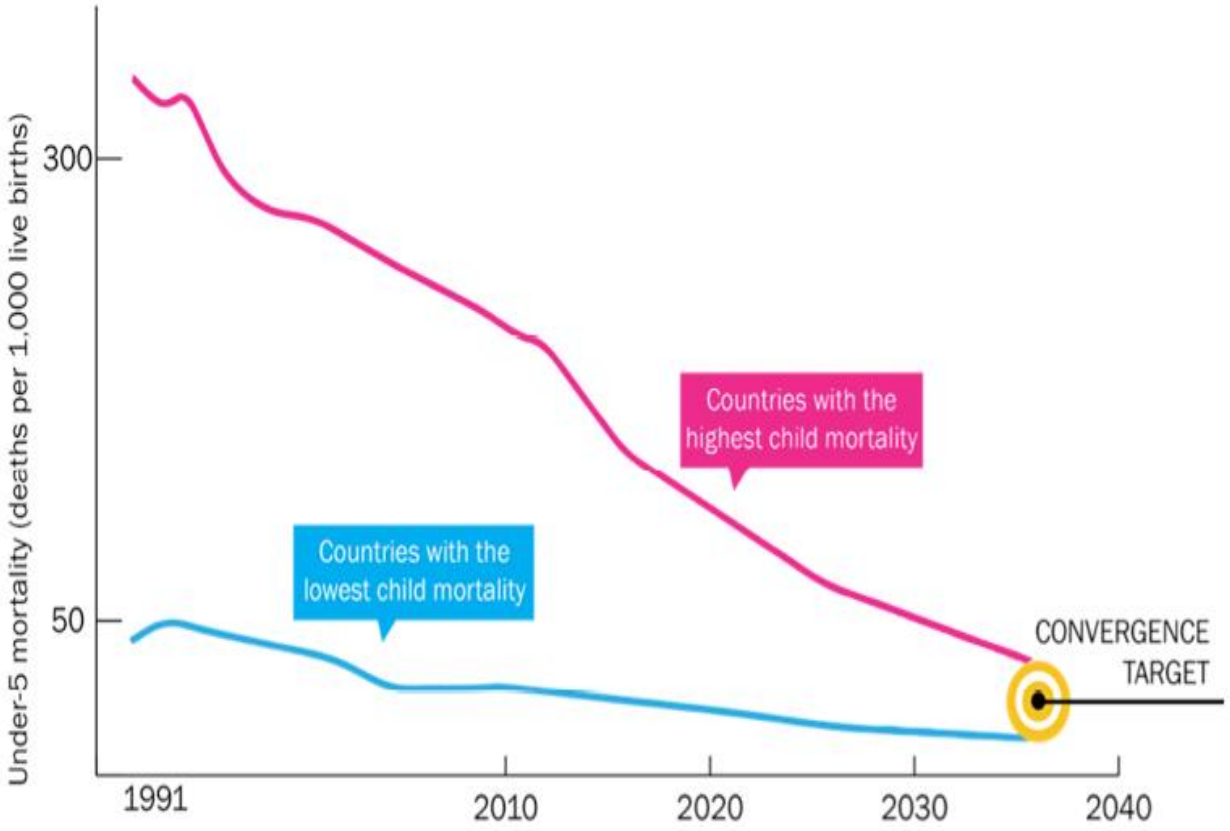



# 18 important or game changing products would be “missing”

**Game changing products that could help achieve convergence:**

| | |
|---|---|
| **Diagnostics** | HIV, TB, Malaria |
| **Drugs** | Malaria, **TB**, Hepatitis C, Influenza, Long-acting contraception, **neglected tropical diseases**, new classes of antimicrobials, new classes of antiviral drugs |
| **Vaccines** | **Malaria**, Typhoid, Pneumoccocal, Influenza, **Multiple diarrheal diseases**, **Hepatitis C, HIV/AIDS, TB** |

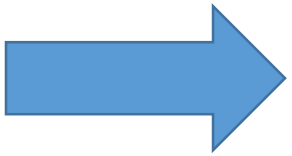
**Based on the current pipeline of candidates, there would be 18 "missing" products**




**Source:** Jamison DT, *et al.* Global health 2035: a world converging within a generation. *Lancet* 2013; 382: 1898–955.

# Future R&D: How much do we need?

Total cost of moving existing candidates to launch: **$16.3B** (range $13.4-19.8B)



- **18 "missing" products**
- Highly effective vaccines against HIV, TB, malaria, hepatitis C; combined vaccine for multiple diarrheal diseases; complex NCE for TB
- NCEs for 12 NTDs *

*NCEs for Buruli ulcer, Chagas disease, dengue, HAT, hookworm, leishmaniasis, leprosy, lymphatic filariasis, onchocerciasis, schistosomiasis, trachoma, and trichurias

Additional cost of R&D for missing candidates to launch: **$13.6 to $21.88 B**

**$4.5B - $5.8B annually over the next 5 years**

***Note current annual spend $3 B so annual shortfall $1.5 B – $2.88 B (a highly conservative estimate)***

# Policy implications

**Pipeline dominated by HIV, TB, malaria** (60% of candidates in model), reflecting funding (G-Finder 2017: 70% of all funding is for 3 diseases)

**"Tier three diseases" (<0.5% of funding) have few candidates** e.g. just 1 for cryptococcal meningitis, 1 for leptospirosis, 2 for leprosy

**Around 6 in 10 launches are likely to be diagnostics**

**Current pipeline unlikely to lead to critically needed products e.g. highly efficacious vaccines for HIV, TB, malaria, hep C**

**Mobilizing additional finance will be crucial (yet funding has stabilized or even declined since 2009)**

# Strengths of the study

**1. Novelty**

- First estimate of development costs from pre-clinical to phase III across 35 PRNDs
- Costing the portfolio (not a single product) aligns with the way in which funders pursue a diversified portfolio of product development projects
- First study to use P2I tool in this way

**2. Broad picture of the pipeline**

- Shows where pipeline is most robust, where it is lacking, which product launches are most likely, & which products will probably still be missing based on existing candidates
- For global health R&D advocates, this broad picture could potentially help to highlight critical funding and product development gaps

# Strengths of the P2I tool

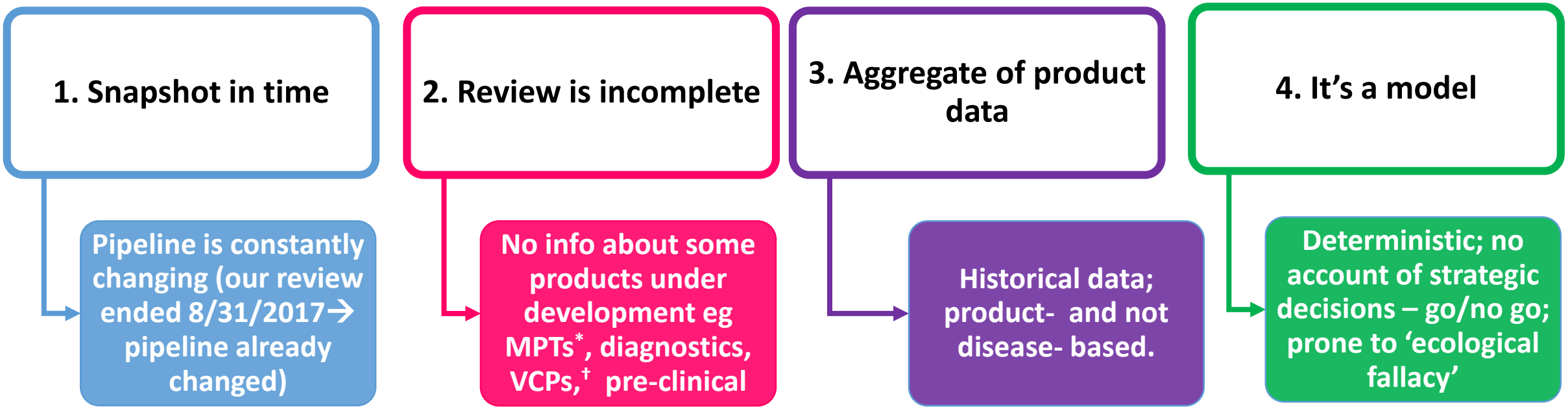
**1. Tool is a public resource**

- Model assumptions, model inputs/outputs, detailed information on portfolio review are all available online
- Readers can replicate, improve on, further adapt our work
- We hope others will share data on costs, attrition rates, cycle times to continually improve model

**2. Evidence-based assumptions**

- Model assumptions were based on large no. of data points (e.g., assumptions on success rates/cycle times: data from of 25,000 development candidates)
- Validated through examining peer-reviewed literature, industry reports/databases, and expert interviews
- “Good enough”?

# Study limitations




* Multipurpose prevention technologies

† Vector control products

# Conclusions

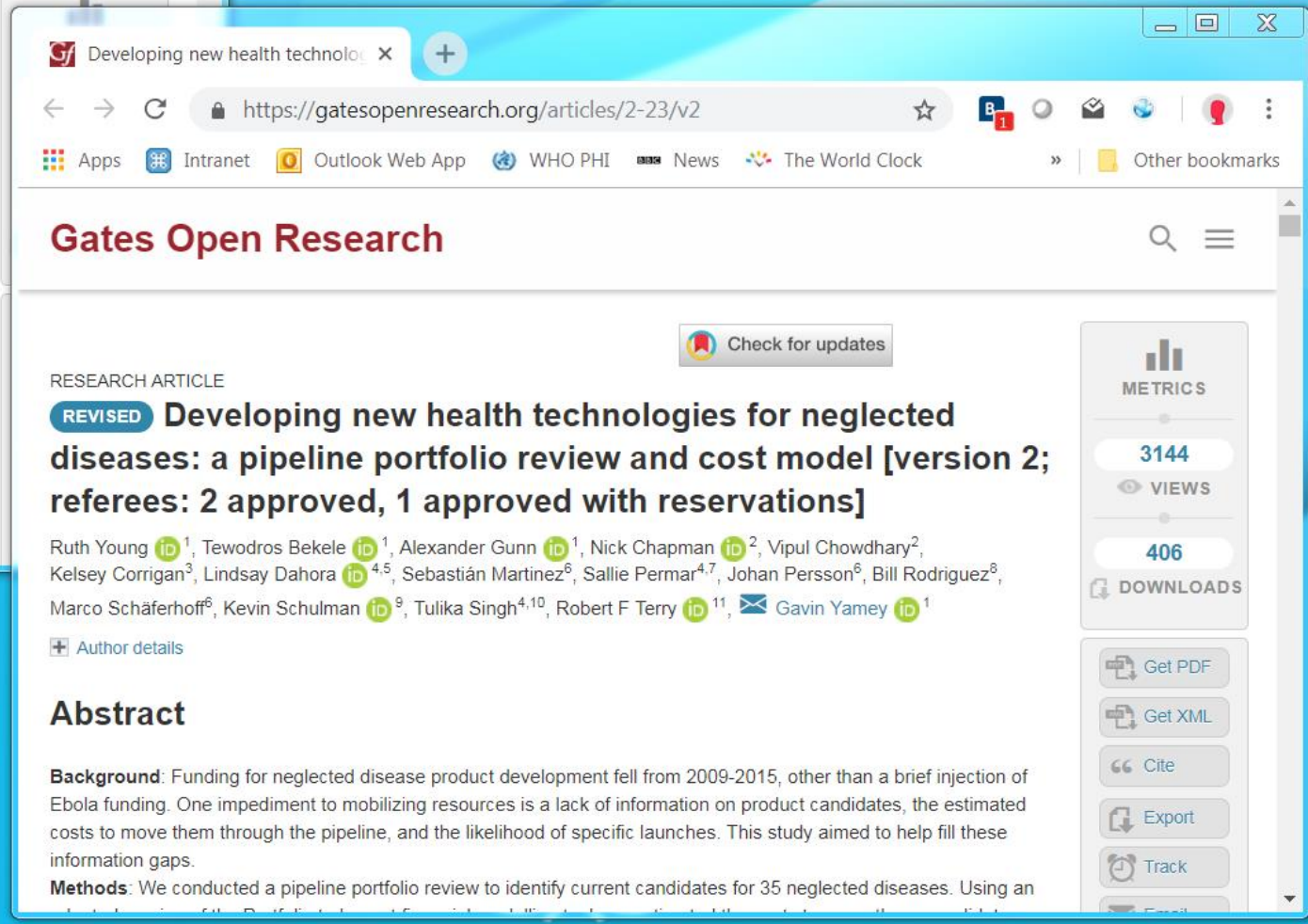
- ✓P2I tool is **flexible enough** to estimate costs and probable launches from a portfolio of current candidates
- ✓P2I points to **gaps in the pipeline** → valuable in directing and prioritizing future R&D financing
- ✓P2I gives an indication of the **size of the financing gap** → helpful for future resource mobilization
- ✓Coordination for global health R&D needed
- ✓What is the **role for WHO**? What **new funding** exists? Role for G20 ?
- ✓Can think of coordination as an **outcome**:

Agreed priorities (product profiles) + Funding = Coordination

# Next Steps

- What's missing?
  - Comprehensive cost estimates *across the whole portfolio* of PRNDs
  - Estimates that take into account all *missing products*
- TDR Research Call to support organizations to use and adapt the P2I tool to analyze their portfolios [http://www.who.int/tdr/grants/calls/portfolio-analysis-loi/en/)
  - MMV undertaking a portfolio analysis with P2I
- TDR developing a new online resource for product priorities (**product profile directory**)
- Update P2I in 2019: TDR, Duke University and Policy Cures Research

# Both papers open access – open peer review

# Acknowledgements


POLICY CURES RESEARCH.

SEEK DEVELOPMENT

STRATEGIC AND ORGANIZATIONAL CONSULTANTS

FIND

Because diagnosis matters

THE CENTER FOR POLICY IMPACT IN GLOBAL HEALTH

Duke University School of Medicine

Duke Clinical Research Institute

DHVI

DUKE HUMAN VACCINE INSTITUTE

# Thank you

Gavin Yamey | gavin.yamey@duke.edu
Robert Terry | terryr@who.int
Alex Gunn| alexander.gunn@duke.edu

TDR For research on diseases of poverty
UNICEF • UNDP • World Bank • WHO

THE CENTER FOR POLICY IMPACT IN GLOBAL HEALTH