CARB-X
Combating Antibiotic-Resistant Bacteria

BOSTON UNIVERSITY

The economics of the antibacterial pipeline and access crisis

Kevin Outterson
Executive Director of CARB-X and Austin B. Fletcher Professor at Boston University

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The innovation problem: shortfall of public funding and private investments to support high-impact preclinical R&D projects

The CLINICAL pipeline is insufficient and not focused VS the PRECLINICAL pipeline is innovative but lacks funding

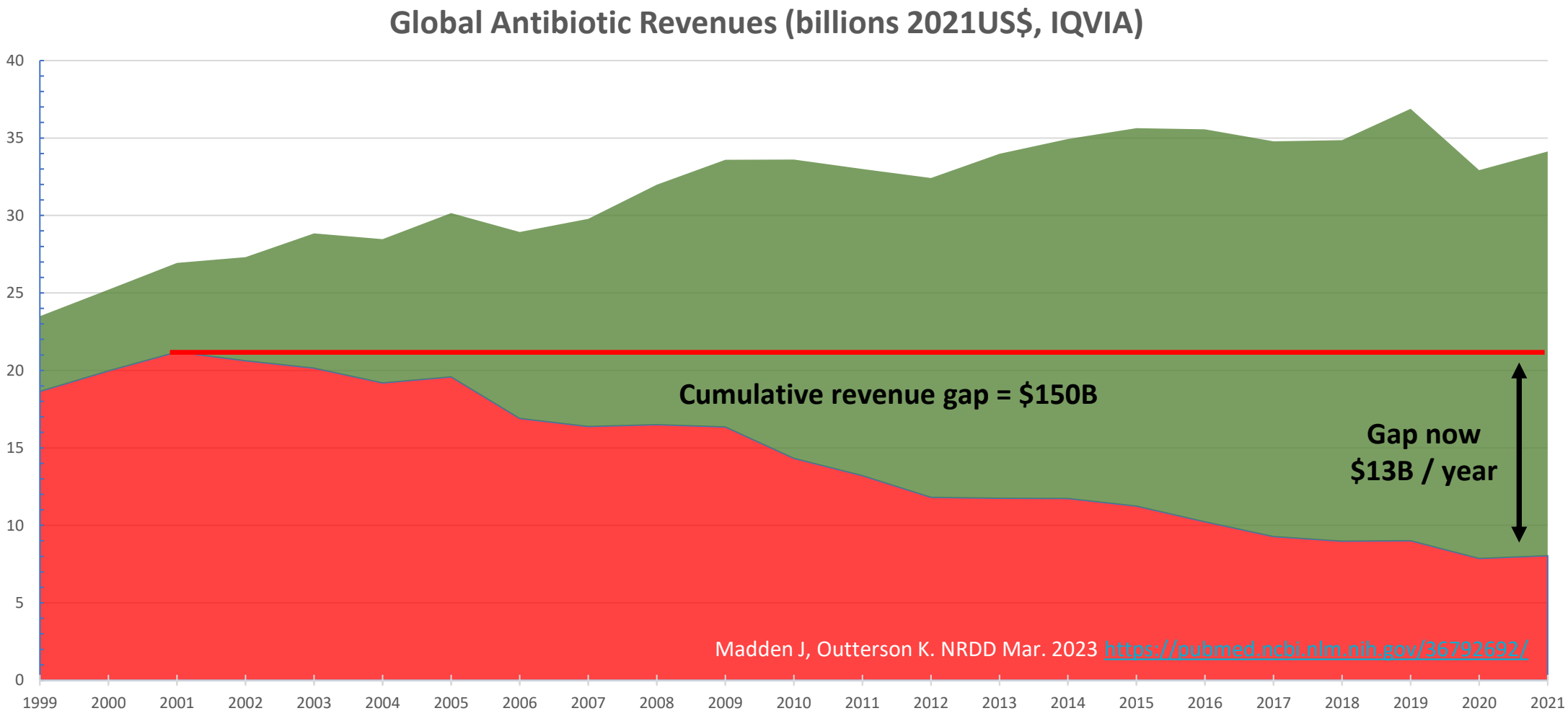
- The AMR Action Fund has struggled to find investment opportunities, with Henry Skinner saying the ***clinical*** pipeline is "much thinner" than he had originally realized.
- WHO agrees that "the ***clinical*** pipeline and recently approved antibiotics are insufficient." In contrast, "[t]he ***preclinical*** pipeline is innovative and includes a large number of non-traditional approaches." Yet, "[t]he ***preclinical*** antibacterial pipeline continues to rely on micro and small companies and academic institutions," and the analysis "clearly indicates significant volatility and turnover."
- It is clear that the problem is limited public and private investments in projects in ***preclinical*** development, failing to replenish an insufficient ***clinical*** pipeline.

The causes of the problem: lack of incentives for private investments in antibacterial R&D

Why don’t innovative antibiotics enjoy blockbuster sales?

- Initial sales are low because innovative antibiotics are held in reserve to prevent the development of resistance (and diagnostic devices are slow to update to include new antibiotics in susceptibility panels)
  - WHO AWaRe: new innovative antibiotics = RESERVE category
- Prices are low because of multiple reasons:
  - Health technology assessments (HTAs) focus on benefits for individual patients and do not recognize the societal value of antibiotics (see STEDI values, e.g., avoiding transmission and enabling other medical procedures)
  - Comparators in HTAs are low-cost generic antibiotics, and it is difficult/unethical to run superiority trials when existing treatments still save lives
  - Very expensive new antibiotics would block access in poorer countries and would incentivize potential marketing

Global antibiotic markets: decades of generic growth, but $150B decline in the engine behind R&D



Recent private R&D investors lost >$3.7b in AMR

	OOP cash to first antibiotic approval	Current market cap or $ realized for R&D investors
AKAO	$637m	$0
CDTX	$395m (P3)	$118m
ETTX	$247m (P3)	$113m*
MLNT	$593m	$0
NBRV	$507m	$5m
POLN:SW	$397m (P3)	$18m (SPEX:SW)
PRTK	$624m	$105m
MCRB	$671m	$650m (microbiome)
TTPH	$657m	$16m
	$4.728B	**$1.025B**

OOP from Outterson K, Health Affairs 2021 (Supp. Fig. S6) + public filings 2Q22 for Achaogen, Cidara, Entasis, Melinta, Nabriva, Polyphor, Paratek, Seres, & Tetraphase.
* Acquisition price May 2022
Market caps as of 16 May 2023

The magnitude of the problem: the funding gap for push and pull incentives

6+ innovative high-impact treatments are needed per decade

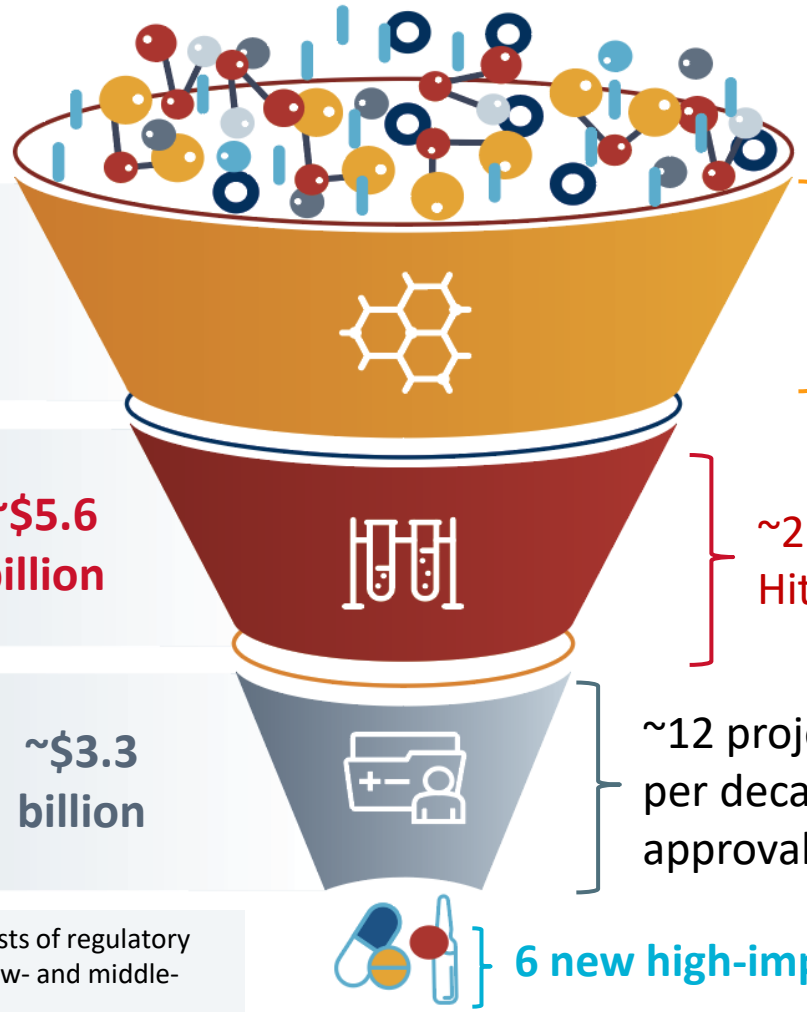
Report/strategy	Target (therapeutics)	Extrapolation for 10 years
IDSA 10x20	10 “new systemic” over 10 years	10
AMR Review	15 “new”, of which at least 4 “breakthrough”, over a decade	15 (of which 4 breakthrough)
GUARD	One additional “high-need” per year	10
DRIVE-AB	16-20 “truly innovative” over 30 years	5-7
U.S. NAP 2020-2025	Three “new” by 2025	6
BARDA Strategic Plan 2022-2026	Three “novel” by 2026	6

6+ innovative high-impact treatments require a pipeline

Basic Research ~$3 billion

Early-stage product development ~$5.6 billion

Advanced development and post-approval ~$3.3 billion



>6000 basic research projects per decade

~215 projects per decade, from Hit-to-Lead to First-in-Human studies

~12 projects beginning clinical efficacy studies per decade, including regulatory and post-approval costs in HICs only

6 new high-impact treatments per decade

3+ years

6 years

6.5 years

Approved

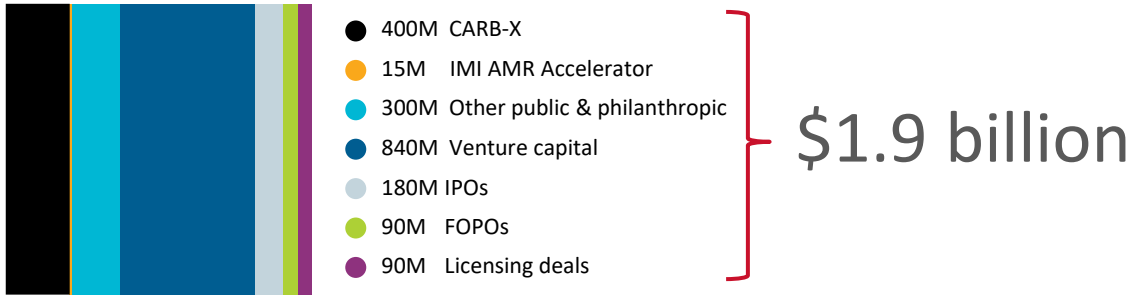
IMPORTANT: These estimates do not account for the costs of regulatory submissions, post approval and access in high-burden low- and middle-income countries. Also, TB is not included.

Preliminary results based on probabilities of success and phase costs from best available data. Validation is underway with upstream and downstream partners, including AMRAF and GARDP.

Magnitude of the funding gap in the PRECLINICAL stages of antibacterial R&D for therapeutics over the next 10 years

Total investment needs

Expected investments at current levels

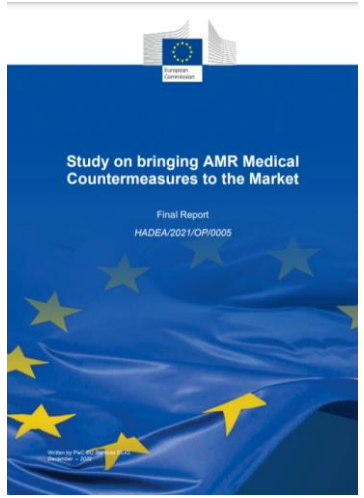


Funding gap

Preliminary results based on data from the Global R&D Hub and BIO, plus expert views.

PwC study for DG HERA (2023)

- "There is a broad agreement that **push funding** should complement the pull models above, acting where the pull models are least efficient: **in the early phases of development**."
- "There is relative consensus on the need to provide additional push funding, **in a range between USD 250 and USD 400 million on an annual basis, and at a global level** … This range corresponds to what is necessary for reinvigorating the pipeline in conjunction with the pull incentives."



https://op.europa.eu/en/publication-detail/-/publication/51b2c82c-c21b-11ed-8912-01aa75ed71a1/

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By Kevin Outterson

Estimating The Appropriate Size Of Global Pull Incentives For Antibacterial Medicines

- Best estimate for a global antibacterial subscription = **$310M** (**range: $220M-$480M**) per drug annually over 10 years
  - The PASTEUR Act is within this range, as is the global pull incentive implied by the UK pilot
- Both push and pull incentives are necessary for sustainable and robust antibacterial drug development

Outterson K. Estimating the appropriate size for global antibacterial pull incentives. Health Affairs 2021 https://pubmed.ncbi.nlm.nih.gov/34724432/

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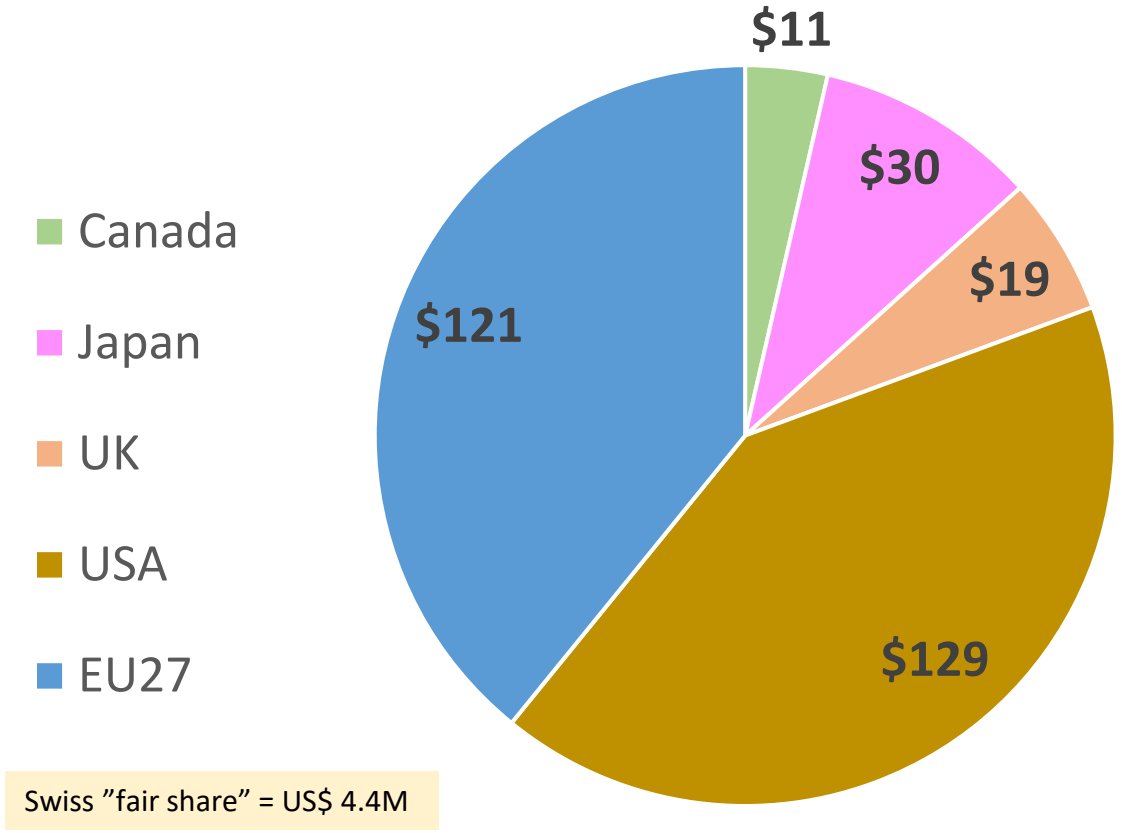
“Fair share” pull incentive targets within G7+EU27



Swiss ”fair share” = US$ 4.4M

Fair share of a $3.1B global subscription pull incentive, allocated by relative GDP

Figures are average per drug, per year, paid over 10 years

Payments might be lower at registration, but could increase as stronger evidence is presented

All figures 2022 US$, millions

Outterson 2023, https://open.bu.edu/handle/2144/42568

How should ideal pull incentives look like?

- Delink revenues from sales
- Be of sufficient magnitude and predictable (see prior slides about global amount and fair share)
- Be rapidly implementable
- Coordinate across countries/regions to select a similar set of products based on a similar balance of novelty and patient utility
- Include sound but realistic guardrails regarding both access and stewardship

Three innovation and financial targets for UNGA 2024

Innovation:

- At least 6 new high-impact antibacterial treatments by 2034

Financial (in order to achieve the innovation target):

- Double existing push incentives focusing on preclinical development, with a minimum of USD 200 million per year globally from governments and philanthropic organizations
- Implement a coordinated set of pull incentives totaling $310M (range: $220M-$480M) per drug per year over 10 years globally, fully delinked

Q&A

Website: carb-x.org | Email: mko@bu.edu | Twitter: @koutterson