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Beyond resistance: alternative innovation models for global access and stewardship of new antibiotics

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Accelerating the development, equitable access to, and stewardship of new antibiotics is critical to protect public health and address antimicrobial resistance (AMR). To understand and assess how the current antibiotics innovation sub-system – or 'niche' – addresses this task, we reviewed the literature, compiled and analyzed a database of 211 antibiotic developers, and conducted 10 stakeholder interviews. We found that the mainstream market-driven innovation model is still adopted by a substantial minority of antibiotic developers, but the majority of developers adopt one of two alternative models: The Publicly-Supported Private Initiative (PSPI) model is the most common, and is characterized by public and/or philanthropic financial and other support to small and medium enterprises. This model secures essential resources for R&D, but the current focus on innovation fails to ensure access and stewardship on a national or global scale. The Collaborative Network (CN) alternative innovation model includes a wider range of actors sharing resources and collaborating towards achieving innovation, access and stewardship goals. It consists of public and private actors supported by philanthropic and/or not-for-profit organizations such as Wellcome, CARB-X, or GARDP. We conclude that this model represents the most promising development to ensure innovation with access and stewardship. However, the model is relatively recent and must still demonstrate its capacity to deliver these outcomes. The rules and norms that govern the antibiotic niche are evolving, and policy decisions such as the adoption of pull incentives may profoundly influence which models may succeed in the future. Decision-makers should construct rules and incentives that create conducive conditions for models that jointly deliver innovation, access and stewardship of antibiotics, to help them improve, survive, and thrive.

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Introduction

The development of innovative antibacterial agents is critical to counteract the declining efficacy of existing antibiotics, and combat the escalating threat of antimicrobial resistance (AMR). Responsible for 1.27 million deaths in 2019 (Murray et al. 2022), drug-resistant infections are projected to claim up to 10 million human lives per year by 2050 (UNEP 2023), and cost the global economy up to USD$ 3.4 trillion yearly in gross domestic product (GDP) loss by 2030 (Jonas et al. 2017).

However, both the innovation of, and global access to antibiotics are critically deficient. Only 19 new antibacterial drugs were approved between 2013 and 2022, none of which are 'first-in-class', in the context of a thinning pipeline of only 27 antimicrobials in clinical development in 2021 (WHO 2022). Access to novel and existing antibiotics is insufficient in Low- and Middle-Income Countries (LMICs) (Kållberg et al. 2018), but this is also an issue for High-Income Countries (HIC) (Outterson et al. 2022). This study examines how innovation models operating in the antibiotics research and development (R&D) *niche*, navigate and overcome major innovation and access barriers.

Many factors contribute to failures in antibiotics innovation. Scientific challenges of developing new antibiotics are high (Livermore et al. 2011), while antibiotic developers also face unattractive market returns (Moulac and Theuretzbacher 2023). Expected revenues for new antibiotics at best only reach around USD$ 240 million over the first 8 years of commercialization (Rahman et al. 2021), while one estimate found the costs of R&D to reach USD$ 1.5 billion (Towse et al. 2017) over a minimum of 10 years. Methods for estimating R&D costs vary widely (Vieira and Moon 2020), however, and this estimate does not take into account public funding; Schmidt et al. (2025) found public funding for antibiotic R&D can outweigh private investment, and should be taken into account when analyzing sustainable innovation models. Nevertheless, it is clear that antibiotics are less profitable than other therapeutic areas due at least in part to short treatment courses, historically low prices for competing products, and the requirements to limit the use of antibiotics to reduce the risk of resistance – often referred to as *stewardship* (Klug et al. 2021; Wells, Nguyen and Harbarth 2024). Consequently, large pharmaceutical companies have either left or reduced their presence in the niche (Plackett 2020), leaving approximately 80% of antibacterial innovation projects in the hands of small and medium enterprises (SMEs) (WHO 2022). Every year, almost one in three preclinical developers either declares bankruptcy, or is assimilated through merger or acquisition by another company (Gigante et al. 2022). The rest of the pipeline is covered by academic institutions, large pharmaceutical companies, and a few not-for-profit organizations (WHO 2022). The vast majority of R&D projects are conducted in HICs (WHO 2022).

In the last decade, AMR has received increasing national and global attention from policymakers, as reflected in the EU, G7 or G20 agendas, the 2015 WHO Global Action Plan on AMR (WHO 2015), and in 2024 during the second United Nations General Assembly (UNGA) High-Level Meeting on AMR. In addition to promoting public health measures such as antibiotic stewardship and infection prevention (Årdal, Lacotte, Edwards, et al. 2021), policymakers are also prioritizing finding ways to re-invigorate antibiotic R&D (Årdal et al. 2018; Årdal, Lacotte and Ploy 2021). Building on consensus that the mainstream, market-driven model of pharmaceutical innovation is insufficient for antibiotics (Klug et al. 2021), a landscape of push and pull incentives is being developed to sustain the antibiotic pipeline and market. As a result, several partnerships and not-for-profit organizations were created to channel public, philanthropic, and private investment to *push* antibiotics development. Most of these organizations focus on financing certain stages of development (e.g., the EU's Innovative Medicines Initiative (IMI), Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), AMR Action Fund) (Wasan et al. 2023), while the Global Antibiotic Research and Development Partnership (GARDP) has a more comprehensive role, funding and conducting R&D, and expanding access to older and newer antibiotics (GARDP n.d.).

To complement these efforts, various new incentives have been proposed (to supplement prices alone) to *pull* developers afloat post-development, through the provision of certain forms of regulatory and/or financial assistance (Cama et al. 2021; Renwick et al. 2016)[1]. For example, subscription models offer innovators guaranteed revenues in exchange for national supplies of antibiotics, partially or fully delinked from volumes of sales (Barlow et al. 2022). This model is an alternative to using higher unit prices as a pull mechanism (Årdal, Lacotte and Ploy 2021). Subscription models are piloted at the time of writing in the United Kingdom (UK) and Sweden, and prompting efforts to replicate and adapt this incentive in Japan, Canada, and the United States (US) (Outterson and Rex 2023). Overall, such alternative pull incentives are relatively new, and most countries still struggle to decide on which strategies to apply, at what geographical level, and how to practically implement these measures (Årdal, Lacotte, Edwards et al. 2021).

Analysts have called for developing complementary push and pull incentives to correct the broken market for antibiotics (Årdal, Lacotte, Edwards, et al. 2021; Cama et al. 2021; Global AMR R&D Hub & WHO 2023). In addition, a growing body of literature is trying to identify and support new and sustainable innovation models for antibiotic R&D that can survive in this challenging niche (Klug et al. 2021; Outterson 2014; Outterson and Rex 2020). Meanwhile, little progress is made to address global access and stewardship shortcomings, despite several reports calling for embedding these deliverables in AMR drug development policies (Access to Medicine Foundation 2022; Årdal et al. 2018; Årdal, Lacotte and Ploy 2021; Carlet and Pittet 2013; EU-JAMRAI & Global AMR R&D Hub 2021; Global AMR R&D Hub & WHO 2023; Global Leaders Group on Antimicrobial Resistance 2024; ReACT 2021).

Despite widespread recognition that the mainstream market-driven innovation model will not work for antibiotics, it is not clear which alternatives are most promising to meet the specific demands in the antibiotic R&D niche: innovation, access, and stewardship – widely argued to be the three pillars for R&D to contribute effectively to tackling AMR (European Commission 2017; O'Neill 2016). Furthermore, there is a scarcity of literature assessing the ability of antibiotic innovators to adopt practices that further these goals. This study seeks to address these gaps, through an empirical description of the antibiotic R&D niche and the existent mainstream (i.e., market-driven) and alternative innovation models that operate within it; we then analyze how well they can advance the triple-objectives of innovation, access, and stewardship.

Methodology

This article is part of a broader research project investigating strategies towards equitable pharmaceutical innovation, employing a Complex Adaptive Systems (CAS) framework (Hill 2011) to scrutinize the dynamics of the pharmaceutical innovation ecosystem (Moon et al. 2025). The CAS-based framework conceptualizes pharmaceutical innovation as an interconnected system of diverse actors - policymakers, academic institutions, industry, funders, non-profit organizations and other stakeholders - whose interactions are characterized by feedback loops and strategic adaptation in response to regulatory, economic, and scientific shifts, producing outcomes as emergent properties (Moon et al. 2025). The framework conceives of antibiotic R&D as a specialized niche within the broader pharmaceutical innovation ecosystem, characterized by different rules, norms, actors and resource flows from the mainstream system. The structure of this article aligns with these elements, by describing actor (antibiotic developers) characteristics, followed by an analysis of resource flows, and the interaction of actors and resources with the broader rules and norms of the antibiotic niche. The niche can be more or less successful at delivering desired outcomes, depending on the interaction of its constituent parts.

This study employs a mixed methods research design, triangulating a literature review with a quantitative descriptive analysis of the antibiotics pipeline, and qualitative findings from interviews with relevant stakeholders. First, a scoping review of the relevant literature in English was conducted to describe the current state of the active antibiotic R&D niche, and surrounding policy debates on how to incentivize further innovation. The review followed Arksey and O'Malley's (2005) scoping review framework. Searches were conducted between January and June 2023 in PubMed, Web of Science, and Scopus, complemented by targeted searches of grey literature in Google Scholar, institutional repositories (e.g. WHO, Global AMR R&D Hub, Access to Medicine Foundation), and reports from major funders and initiatives (e.g. CARB-X, GARDP, Wellcome). Search terms combined concepts relating to antibiotic research and development ("antibiotic R&D", "antimicrobial innovation", "pipeline"), financing and incentives ("push funding", "pull incentives"), and access/stewardship ("global access", "equitable access", "stewardship"). All retrieved records were imported in Zotero and screened for inclusion, with the broad aim of capturing the current landscape of antibiotic innovation models and their ability to meet access and stewardship goals. Then, a database was compiled collecting relevant up to date data on drug developers active in the preclinical and clinical antibacterials pipelines, from multiple sources, primarily the WHO (2024) and the Global AMR R&D Hub (2020). The information from the available databases was cleaned to remove drug developers that have become inactive and to reflect mergers and acquisitions (M&A), and to add new actors through desk research from publicly available information, such as funders' reports, which had not been included in the WHO (2024) or Global AMR R&D Hub (2020) databases. The resulting database records 211 unique organizations including 134 drug developers with active projects in the preclinical pipeline, 95 operating in the clinical pipeline, and 18 active in both clinical and preclinical, excluding those exclusively focusing on vaccines or M. tuberculosis projects. It provides information on the type of drug developers in the antibiotic niche (i.e., academic, SME, large pharmaceutical company, not-for-profit), their geographical location, and whether they received any public, philanthropic, or non-profit funding for the development of their antibiotics pipeline. Descriptive statistical techniques using Excel were used to analyze and visualize this data.

In addition, we sought to better understand how alternative innovation models were functioning by collecting primary qualitative data through semi-structured interviews with 10 directly involved key informants (Table 1). These participant organizations (POs) were selected from a database of alternative pharmaceutical R&D initiatives that appeared to fund, implement or facilitate pharmaceutical R&D in a manner that differs from the mainstream innovation model (Global Health Centre 2023). This database categorizes actors as implementers (i.e., those that conduct R&D), funders (i.e., those that finance R&D), or facilitators (i.e., those that facilitate R&D through a wide range of activities, such as technical assistance, advocacy, or match-making). Of the 17 organizations active in antibiotic R&D, all of whom were approached by email to be interviewed, the 10 that agreed constitute the sample of POs found in Table 1; an actor could play more than one role, e.g., funder and facilitator, as reflected in the Table. The interviews were conducted using a semi-structured guide designed to draw out perspectives from implementers on how their innovation model works and is able to jointly meet access and stewardship goals, and from funders and facilitators on how they advance these objectives in the antibiotic R&D niche. The interview data was transcribed, anonymized, coded, and analyzed thematically. We applied a thematic framework derived from the literature on pharmaceutical innovation and iteratively developed based on the broader research project's set of 53 interviews (Moon et al. 2025), and then adapted it to antibiotics by including stewardship. The coding framework (Supplementary File 2) categorizes data according to implementers' characteristics (e.g., purpose, organizational form), the resources they mobilize (i.e. financing, knowledge, manufacturing, and relationships), and their organizational practices (e.g., intellectual property, pricing, and access policies). Once coded, we iteratively analyzed the material by identifying patterns and divergences across actors and roles, and by examining how practices and resource flows interacted with the broader rules and norms of the niche. The interview data was complemented with publicly available information (e.g., statements, reports) found on the organizations' websites. This process allowed us to generate a typology of innovation models and to assess their strengths and limitations in achieving the goals of innovation, access, and stewardship.

The following interviewed POs consented to identity disclosure: VenatoRx Pharmaceuticals, GARDP, research group within the Institute for Molecular Bioscience at The University of Queensland, Bugworks, ReAct, AMR Action Fund, Helmholtz-Institute for Pharmaceutical Research Saarland (HIPS), and Wellcome.

Results

Characteristics of drug developers operating in the antibiotic R&D niche. To describe antibiotic developers adopting alternative innovation models, we identify their core characteristics, categorized under: purpose, organizational form, and geographical distribution. Table 2 provides an overview of implementers by income group and location (Table 2).

Purpose. All six interviewed implementers publicly state their primary purpose: to develop new antibacterial products that can counteract the rising threat of AMR. However, the interviews revealed variation in implementers' motivations to pursue innovation in this niche. For instance, many follow promising science, determined to overcome the economic challenges of the antibiotic niche to see their projects succeed (e.g., PO_1, 4, 5). Interviewees (implementers, funders, and facilitators alike) consider it a standard practice for scientists to create SMEs (PO_1) or join academic institutions (PO_6) to continue previous projects started in large pharmaceutical companies.

Other implementers frame their mission as solving the global problem of unmet societal need for new, effective antibiotics (e.g., PO_2, 3). This severe global health risk motivates PO_2 to focus on neglected populations, and to support other implementers in this niche.

> *'Antibiotics are fundamental to medical care. […] You can't set up an outpatient clinic anywhere in the world if antibiotics are not available. You can't set up surgery. You can't set up oncology, and so on.' (PO_2)*

Table 1 Overview of interviewed participant organizations in the antibiotic R&D niche.

Org.	Type	Organizational Form	Purpose	R&D Stages	Country Classification	Portfolio
PO_1	Implementer	Private company; SME	Innovation	End-to-end	HIC	1 registered product 2 products in development
PO_2	Implementer / Facilitator / Funder	Not-for-profit; PDP	Innovation Global access	Clinical stages; Supports end-to-end	Global	3 products in development
PO_3	Implementer	Private company; SME	Innovation Global access Affordability	End-to-end	LMIC	2 products in development
PO_4	Implementer	Private company; MNC	Innovation	End-to-end	HIC	3 registered products 9 products in development
PO_5	Implementer	Academic	Innovation	Discovery → Preclinical	HIC	3 products in development
PO_6	Implementer	Academic	Innovation	Discovery	HIC	1 product in development
PO_7	Funder / Facilitator	Not-for-profit; Academic	Innovation Access and stewardship	Invests Discovery → Phase I	Global	
PO_8	Funder	Not-for-profit	Innovation Access and stewardship	Invests Discovery → Clinical stages	Global	
PO_9	Funder	For-profit; Private investment fund	Innovation	Invests Clinical stages	Global	
PO_10	Facilitator	Not-for-profit	Address AMR Access and stewardship		Global	

Organizations driven by a social mission often stress the difficult necessity of simultaneously aiming for innovation with stewardship and global access (Laxminarayan et al. 2020; O'Neill 2016) (PO_7, 2, 3, 4). As long as AMR continues to rise in LMICs, where the burden of disease is higher, PO_3 underscores their commitment to make their products accessible and affordable:

> *'We said: "Let's do a company, let's invent a novel antibiotic that can save millions of lives over the decades". We thought it's a perfect storm, no new innovation, heavy abuse of antibiotics, millions impacted, hundreds of thousands dying. Big Pharma will not solve it. Nobody's going to come to our aid.' (PO_3)*

Organizational form. Consistent with previous studies (Theuretzbacher et al. 2020; WHO 2022), we find SMEs representing 79/95 (or 83%) of active drug developers in the clinical pipeline, and 101/134 (or 75%) of developers in the preclinical pipeline (Fig. 1).

Interviewed SMEs report choosing for-profit organizational forms to remain sustainable (PO_1, 3). According to some, this strategy need not impede global access:

> *'"Affordable and accessible" does not mean running an NGO. You can still run a private enterprise and make reasonable margins if you have innovative products. Most of the West can pay affordable rates. LMICs [...] If you take 8 billion people, 6 billion of them are not in the rich countries. We need to make these medicines available and affordable to those local contexts.' (PO_3)*

Other implementers are academic institutions (e.g., PO_5, 6), large pharmaceutical companies (e.g., PO_4), and one not-for-profit organization. Large pharmaceutical companies such as PO_4 (counting over 500 employees) are a minority in the niche, representing 15% of clinical, and 6% of preclinical developers:

> *'[PO_4] is one of the few [large] companies that has maintained an active research organization in the AMR space when most major pharma companies have really given up on antibacterial research.' (PO_4)*

Academic institutions represent only 24/134 (or 18%) of organizations operating in the preclinical pipeline, and 2/95 (or 2%) in the clinical. The academic institutions interviewed admit their limited scope, planning either to transfer their technology (PO_5), or to spin off an SME (PO_6).

Finally, PO_2 operates as a not-for-profit Product Development Partnership (PDP) to fill the gaps of R&D that do not attract commercial interest, such as pediatric indications for antibacterials. The flexibility of the PDP format allows the organization to act as an implementer, but also R&D funder, and facilitator of global access.

Table 2 Distribution of antibiotic R&D implementers by income group and geographical location.

Org. Form Income group	Academic	SME	Large Pharmaceutical Companies	Not-for-profit	Total
Preclinical pipeline					
HIC	16	98	7	1	**122**
UMIC	7	1	0	0	**8**
Lo-MIC	1	2	1	0	**4**
Total	**24**	**101**	**8**	**1**	**134**
Clinical pipeline					
HIC	0	76	9	0	**85**
UMIC	1	2	3	0	**6**
Lo-MIC	1	1	2	0	**4**
Total	**2**	**79**	**14**	**0**	**95**

The bold numbers represent cummulated totals of the numbers right above them.

Geographical distribution. The vast majority of antibiotic R&D is based in HICs, which host 91% of organizations in the preclinical pipeline, and 89% in the clinical pipeline (Fig. 2).

The US hosts the largest number of SMEs, active in 37% of the clinical, and 31% of the preclinical pipelines. However, there is more geographical diversity amongst the other types of developers. For instance, Russian research institutes are active in both pipelines, representing 6/26 (or 23%) of all academic actors active in the antibiotic niche. Other relevant hubs for academic actors are Germany (5/26) and Australia (4/26). At the same time, 5/20 (or 25%) of large pharmaceutical companies active in both pipelines are Japanese, 3/20 (or 15%) are Indian, and 3/20 (or 15%) are Chinese. Two large pharmaceutical companies are present in both clinical and preclinical pipelines, both from Japan.

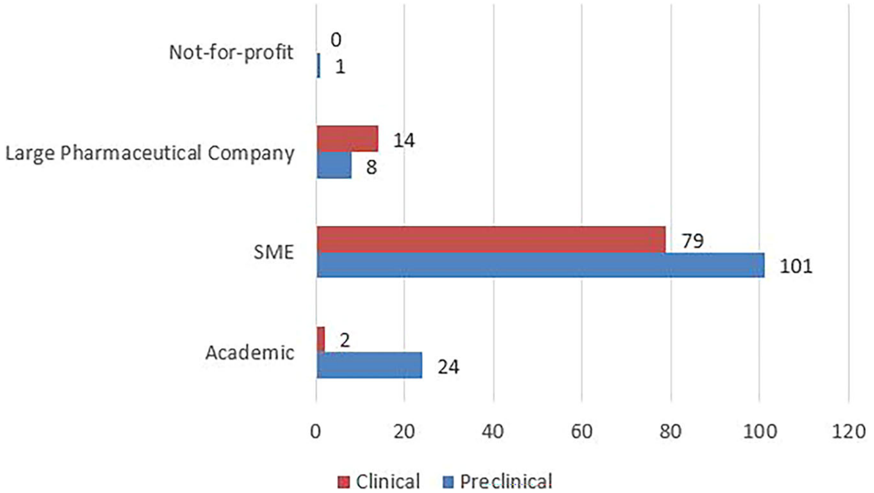

Fig. 1 Distribution of antibiotic R&D implementers across organizational forms.

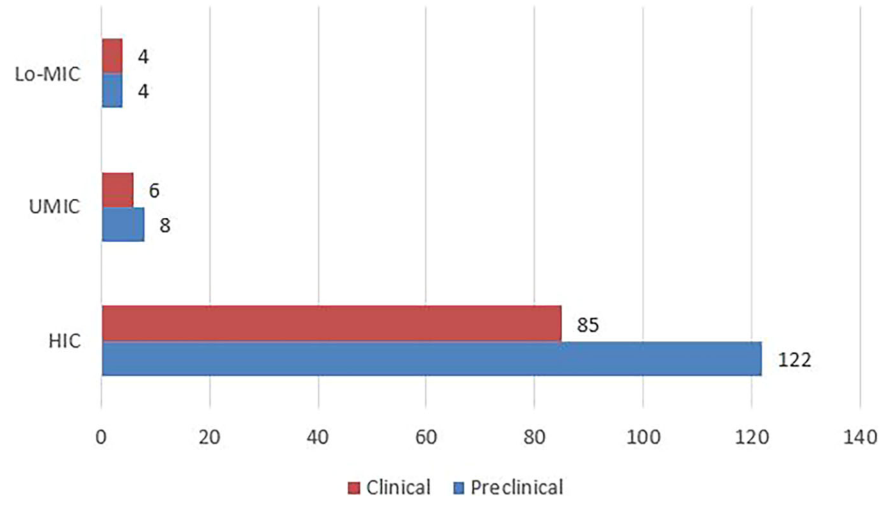

Fig. 2 Distribution of antibiotic R&D implementers, across income-level groups.

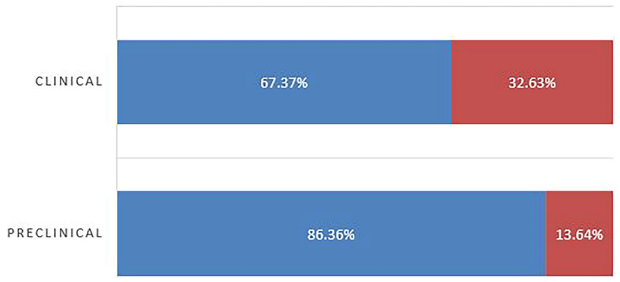

Fig. 3 Proportions of drug developers receiving different types of funding.

Resources. To achieve their objectives, implementers have to mobilize essential resources (e.g., financing, knowledge sources, manufacturing), and optimize their organizational practices (i.e. knowledge management including intellectual property, transparency, and approaches to global access).

Financing. The antibiotic R&D niche is depicted as a '*tough area*' with a high scientific failure rate estimated at 95%, and '*broken economics*' (PO_3) (Årdal et al. 2020; Bhavnani et al. 2020; Klug et al. 2021; Outterson et al. 2015; Payne et al. 2007). In a therapeutic space relying heavily on SMEs to drive innovation, the scarcity of funding is particularly problematic:

> *'I was at a conference last week. And the moderator of the panel asked people to raise their hands if they were currently a small company involved in antibiotic R&D. And dozens of hands went up. And then he said: "Keep your hands up if you have more than 18 months of cash on hand to pay your bills, to cover all of your operations". Every hand in the room went down. This is an area where companies are just struggling to stay afloat.' (PO_9)*

Most organizations accept funding from public, philanthropic, and not-for-profit sources, while a substantial minority is still entirely reliant on private investment (Fig. 3).

Private Investment. Despite implementers' efforts to access private investment (e.g., PO_1, 3, 4), only 13.64% of implementers in the preclinical pipeline, and 32.63% in the clinical rely exclusively on private investment, including PO_4 (Fig. 3).

Connections with angel investors (high-net-worth individuals) can be an important source of private funding during initial project stages for SMEs. They also mention receiving little private investment from venture capitalists, having to '*scrounge for every dime*' (PO_1):

> *'Today, it's almost impossible to raise venture capital money for an antibiotics company, because they didn't make money, they lost money, or it's locked and inaccessible.' (PO_1)*

While private investors '*always expect return*' on investment (ROI) (PO_4), interviewees argue that many accept a lower ROI in exchange for social impact (PO_3, 4). To attract investors, SMEs may expand their R&D portfolio with more profitable therapeutic areas, such as immune-oncology (e.g., PO_3). Others may tap into growing sources of private investment outside of HICs, such as Chinese investors (PO_1, 2).

To support the antibiotic pipeline, the AMR Action Fund was created in 2020 and receives funding from larger established pharmaceutical companies, the European Investment Bank and Wellcome. The Fund aims to invest USD$ 1 billion in SMEs' clinical stage projects, and support the development of 2-4 new antibiotics by 2030 (About Us - AMR Action Fund n.d.), with modest expectations of ROI. The Fund is conceived as a temporary solution to the dearth of private investment in the niche:

> *'If market dynamics change, maybe more Big Pharma companies will return to the space. The hope is to see a sustainable R&D ecosystem take shape and that the Fund will really have only been a temporary bridge to help companies return to this space.' (PO_9)*

Public, Philanthropic and Not-for-profit Funding. We found that 86.36% of drug developers active in the preclinical pipeline and 67.37% in the clinical, receive public, philanthropic, or non-profit support (Fig. 3). All academic and not-for-profit implementers receive public funds, including PO_2, 5, 6.

For many implementers in the niche, funding from governments and public agencies represents the core financing resource (including PO_1, 2, 3, 5, 6), usually in the form of grants. Important public funders identified in the pipeline are civilian agencies based in HICs such as the US (e.g., National Institutes of Health (NIH), Biomedical Advanced Research and Development Authority (BARDA)), UK, Germany, or regional actors (e.g., European Commission). National defense agencies (e.g., US's Department of Defense (DoD), UK's Defence Science and Technology Laboratory) also finance antibiotic R&D in clinical, advanced stages. Organizations with a global access objective are especially reliant on public funding:

> *'Most not-for-profit entities in the AMR space are almost entirely government funded at the moment. That may change but I don't think not-for-profits in this space will ever be minority government funded […] nevertheless, not-for-profit entities are not driven with an ODA agenda […] even though in many respects, not-for-profits may try to continue to receive ODA financing because AMR is largely playing out in LMICs.' (PO_2)*

Nonetheless, some organizations find the public funding available for antibiotic R&D to be insufficient, including in HICs that do not yet have a national AMR strategy to funnel financial support (PO_4, 6). All interviewees agree that public actors should contribute more financially, particularly through the adoption of pull incentives, a view that reflects the broader consensus in the literature that public intervention is essential to correct the market failure for antibiotics and to ensure long-term sustainability of the pipeline (Årdal et al. 2018; Outterson et al. 2015; Renwick et al. 2016).

In antibiotic R&D, philanthropic and not-for-profit funding is not only present, but perceived as essential (PO_1, 2, 3, 5). Wellcome is the '*largest donor outside of any government institutions towards antibiotic R&D*' (PO_8), holding a broad financing portfolio in the niche. They fund SMEs directly through grants or loans (e.g., convertible debt granted to PO_1); take diluted equity in companies by funding the AMR Action Fund; fund not-for-profit organizations such as CARB-X and GARDP; and support other initiatives working on AMR topics. Through their investment, philanthropic and not-for-profit funders attempt to fill a funding gap and jointly achieve innovation with improved global access (PO_7, 2, 8) (detailed in section 5.4.).

Philanthropic and not-for-profit sources of funding represent the core budget for some implementers: for example, PO_5 reported receiving 75% of their project funding from CARB-X, and 4/6 interviewed implementers received CARB-X funding (PO_1, 3, 5, 6):

> *'Without CARB-X we'd have been dead and gone. We can put on record that we're deeply thankful that without CARB-X and the support of that network […] we just couldn't survive.' (PO_3)*

Across the pipeline, we found that CARB-X supports 26.86% of preclinical pipeline implementers, their area of focus, as well as 25.26% of drug developers active in the clinical phase.

To support a promising R&D project throughout development, actors that finance early R&D stages such as CARB-X or ENABLE-2 rely on other groups (e.g., BARDA, GARDP, or the AMR Action Fund) to '*pick up clinical development*' and support later stages (PO_7). Clinical development funder PO_9 confirms this practice:

> *'We have very good dialogue with [CARB-X or GARDP], which helps us in evaluating potential investments and identifying companies that may be struggling to raise the capital needed to proceed to the next stage of clinical development.' (PO_9)*

Implementer PO_2 also acts as a funder in the antibiotic niche, albeit wielding relatively small amounts.

Other sources of funding: Interviewees report mobilizing other funding sources as well, such as royalties from licenses (PO_1, 2, 4, 5), and revenues from sales (PO_4).

Because stewardship objectives limit the market volume for new antibiotics (Anderson et al. 2023), revenues can be insufficient to keep companies sustainable post-approval. However, commercializing in emerging large markets such as China can act as a '*natural pull mechanism*' (PO_1, 2). According to PO_1, China '*has turned out to be one of the most dynamic and important markets for new antibiotics*'.

Knowledge sources. Besides funding, access to knowledge is identified as a key resource by interviewees. We found both internal capabilities and external sources to be significant sources of knowledge for antibiotic developers.

Internal: The success of implementers in the antibiotic niche is connected to their science: staff with antibiotic development experience in large pharmaceutical companies are often central to R&D projects (PO_1, 3, 4, 5, 6). Witnessing a '*brain drain from the antibiotic space*', large pharmaceutical company PO_4 stresses the need to have '*young scientists enthusiastic about getting into R&D for products in the antibiotic space*'. If this issue is not addressed, the niche risks losing skilled organizations and researchers essential for antibiotic innovation, endangering progress even if the financial landscape improves (PO_4) (AMR Industry Alliance 2024).

The other key scientific component to antibiotic R&D projects is data on candidate compounds. Some implementers continue projects started with other organizations, be it other SMEs (PO_3, 6), or large pharmaceutical companies that shut down their antibiotic programs (PO_1). Others have tested and developed their candidates in-house (PO_4, 5), or work on known molecules (PO_6).

In addition to scientific knowledge, some drug developers such as academic implementers or large pharmaceutical companies rely on internal institutional expertise for fundraising, management of intellectual property, or other legal issues (PO_4, 5, 6).

External. The emerging network of funders supporting the niche (e.g., CARB-X, Wellcome, GARDP, AMR Action Fund) provide expanded access to expertise, from scientific to administrative:

> *'We pay for access to global experts, in whatever it is that looks like the team could use some help. So, the [implementer] team has a lot of people in various areas, but they don't have a toxicology expert. We will say: "Here's five people that are global top experts, pick one. And we'll pay for them to work with you so that you get up to speed on what you need to know." We call that "accelerator support"; we have a global network of subject matter experts.' (PO_7)*

Such expertise is of great value for implementers, who mention that CARB-X can take a '*hands-on*' approach in their partnerships, using a set of Key Performance Indicators (KPIs) to monitor progress (CARB-X grantees PO_5, 6):

> *'In most externally funded projects, you receive the funding, carry out the project along its milestones and deliverables and finally write your interim and final reports. With CARB-X, there is a lot of support, we have monthly meetings. […] the project develops based on a mixture of our own thoughts and the input of external experts.' (PO_5)*

This network offers other types of support: for instance, PO_7 can provide advice on IP management, fundraising for following R&D stages, and regulatory support for registration dossiers. In their access-facilitating role, PO_2 supports partners with expertise on how to roll out a product globally.

Interviewees underscore the absence of industry know-how in the antibiotic niche (PO_2, 9). Funder PO_9 is well positioned to collaborate with large pharmaceutical companies that have experience with clinical development and regulatory approval, and bring this knowledge to their grantees.

Manufacturing. To produce the final products, implementers have to mobilize the necessary manufacturing infrastructure.

From our sample, large pharmaceutical company PO_4 is one of the few antibacterial drug developers that reached the commercialization stage, reportedly manufacturing their product in-house.

Reflecting on manufacturing as a future goal, some interviewees expressed concern about the lack of capacity in the context of global supply chain fragility (PO_1, 2, 3), while others were less concerned about this stage (PO_9, 5, 6). For instance, the academic institutions interviewed aim to transfer their technology long before this stage (PO_5, 6). Funder PO_9 acknowledges the potential manufacturing complexities for novel antibacterials, but explained that the small volumes needed in this market should mean that manufacturing occurs at a limited number of facilities:

> *'With stewardship, you actually want to reserve the use of antibiotics, so as not to make the drug resistance problem worse. But of course, this limits the volume. […] So, we could anticipate slightly less complex manufacturing challenges when compared to something like HIV therapies or even COVID vaccines, where they were trying to get many vaccine manufacturing facilities popping up.' (PO_9)*

Especially for SMEs with limited capacity to invest in manufacturing, their expectation is to find partners that can help them '*deal with the supply chain*' (PO_1). It is a common practice for implementers to be expected to work virtually and '*outsource everything*', because owning the in-house capacity is often seen as a waste of resources (PO_2).

Organizational practices. The organizational practices that implementers adopt alongside the evolution of rules and norms in the niche are expected to shape downstream access to novel antibiotics. We identified three categories of practices relevant for outcomes: knowledge management including IP, global access: affordability and availability.

Knowledge management, including IP. Some stakeholders consider intellectual property (IP) as a core business asset to incentivize private investment in the niche, One not-for-profit funder remarks:

> *'We're in a competitive environment. All of the companies have intellectual property. We actually want them [the implementers] to have it, so that they have a nucleus around which to organize a company, and to receive financing from private sources. They need the IP.' (PO_7)*

Even implementers that pursue global access strategies see patents primarily as assets, and not as barriers to access (PO_1, 2, 4). Organizations that plan to retain rights, or partner with large pharmaceutical companies for HIC markets, sometimes out-license (or plan to) the rights for LMICs to expand global access (PO_1, 3, 4). To this end, they rely on partners such as GARDP, with the expertise and economic resources to facilitate access:

> *'If you're asking: "what is [PO_1] going to do to enable access in Sub-Saharan Africa, if you didn't have the GARDP deal? How would you enable access?" I'll be frank, I have no idea. We would not have the economic resources to be able to do it.' (PO_1)*

Currently, GARDP's assumed role as access facilitator is unique in the antibiotic niche:

> *'GARDP has signed two very important and wonderful licenses […] in which GARDP takes the poor countries of the world, […] they accept the licensee will have responsibility for manufacturing, distribution, and marketing and stewardship of those drugs, access and stewardship in those countries. I think that's a beautiful model.' (PO_7)*

In this approach, GARDP receives the rights for the LMICs of interest, which they sub-license to local manufacturers in a better position to commercialize in LMICs (PO_2, 3). However, a number of challenges are anticipated:

> *'You inevitably lose some degree of control when you sublicense - even if this can be mitigated to a degree by monitoring you do. […] There's other issues around how a company will market the drug, which will impact stewardship.' (PO_2)*

> *'I think [GARDP] haven't necessarily solved exactly how they're going to do the actual drug introduction yet, how they're going to ensure the uniform registration of drugs in all the countries covered by the license, in a speedy manner. But they have the intention to do so, and are actively working on solving it. Which I think sets them apart from all the other actors in the field.' (PO_10)*

Besides collaborating with GARDP, implementers can transfer technology directly to local actors, if they have the networks and there is local know-how (e.g. PO_1, 3).

Another knowledge management practice found in the antibiotic niche is the open sharing of scientific knowledge and data amongst academic networks, to stimulate early-stage discovery. Examples include the Pew Trust's SPARK platform and the Community of Open Antimicrobial Drug Discovery (CO-ADD) (Klug et al. 2021). Our pipeline analysis also found data sharing collaborations between university networks and academic spin-off SMEs in the form of collaborative initiatives such as Ultupharma AB, Sano Chemicals, or Immunethep.

Finally, PO_7 points to the lack of transparency on research in the antibiotic niche, which particularly impedes access to company knowledge and data in the case of bankruptcy. They believe that a platform acting as a repository for this type of data is necessary.

Global access: affordability and pricing policies. Implementers' pricing policies can make drugs more affordable and accessible. However, in a market with low volumes such as for novel antibiotics, drug developers can perceive that '*antibiotics are priced too low*' in HICs, relative to the high cost of development (PO_1).

POs acknowledge that LMICs cannot sustain high prices (PO_2, 8, 3, 4). When out-licensing rights in LMICs to organizations such as GARDP, interviewed implementers do not participate in pricing discussions (PO_1, 2, 4). Interviewees expressed support for tiered pricing policies, wherein HICs pay a higher price than LMICs for new antibiotics (PO_2, 2, 3, 9). For instance, SME PO_3 is considering a cost-plus pricing strategy for LMICs, while planning to collaborate with large pharmaceutical companies for HICs, who can negotiate higher prices with payers (i.e., insurance systems).

Finally, PO_2 underscores that some countries can only access antibacterials in a non-profit model:

> *'We think that there may be a non-profit model for certain countries, which is subsidized. A non-profit model in other countries, which is not subsidized, which is working as "no profit, no loss". And there may be a for-profit model for other countries.' (PO_2)*

Global access: availability and stewardship. To combat AMR, a stable pipeline of innovative antibacterials should be globally accessible to those in need, while avoiding antibiotics' overconsumption to slow resistance (O'Neill 2016) (PO_1, 2, 3, 7, 4, 10). This need to both expand and limit the consumption of both new and older essential antibiotics is perceived as an '*inherent contradiction*':

> *'In LMICs, people simply don't have antibiotics, and they die because of the lack of access. So, we need a careful balance and not overdo the stewardship so tight that it never reaches the people it is intended to reach, which is why stewardship is a dual edged sword.' (PO_3)*

Interviewees underscore the risk of expanding access without stewardship provisions in place, a prevailing challenge in both HICs and LMICs (PO_1, 2, 3, 9, 4). As a solution, PO_3 endorses regulation that limits the use of their product to clinical, in-patient settings.

Although witnessing a rising stewardship and 'access norm' (Hein and Moon 2013), the path to meeting both goals and delivering '*sustainable access*' is still being built:

> *'Sustainable access to effective antibiotics is essentially another way of saying "access without excess". So, you want everyone to be able to have access to the drugs that they need without misusing or overusing them.' (PO_10)*

> *'We frequently have presentations addressing AMR with 3 key legs to a stool - innovation, access and stewardship. [...] What does it mean? That we have to think of all three? Yes, sure. But what does it really mean? How are you actually going to do that, whether it's from a policy perspective, or even from a technical, or scientific perspective? Maybe there should be just some recognition to say: "These are issues that are not easily reconcilable at the moment. There are clear conflicts and conflicts of interest when you start talking about those three aspects at the same time." That would actually be a more honest way to start the discussion.' (PO_2)*

There seems to be widespread agreement on the importance of stewardship, but concrete measures to achieve it are still to be defined.

Norms and rules in the antibiotic niche. The antibiotic niche is in flux, with the norms and rules governing innovation and access activities within it evolving. This section discusses three such rules: the tying of access conditions to push funding, the creation of new rules for pull-incentives, and regulatory requirements.

Access conditions on push-funding. In exchange for their support, philanthropic and not-for-profit funders such as CARB-X, GARDP, and Wellcome require grantees to develop global access and stewardship plans. These conditions are an effort to ensure access downstream if a product is successfully developed:

> *'[Companies financed by CARB-X] they're a decade away from their first approval by any regulatory authority, but all 92 [at the time of the interview] have signed extensive contractual language that binds them to the identical stewardship and access commitments that follow the intellectual property for the molecule, all the way to patent expiration. So, it's a powerful contractual provision.' (PO_7)*

In their capacity as a not-for-profit funder, PO_2 is fighting the '*very strong mantra in the AMR space*' that public funding should remain non-dilutive and unconditional:

> *'If you are the government, and you want to invest some money into AMR, [...] what are the outputs you desire? [...] It can be that you are aiming to have two or three new antibiotics developed and introduced. You want it introduced in a certain way; you want to look at some rules of stewardship. But more importantly, you want it to be available for your marketplace. [...] This is why the term non-dilutive is difficult to understand, because [...] it's diluted by nature.' (PO_2)*

This strategy has drawbacks as well: if conditions are too demanding, drug developers might have difficulties implementing them, or reject the funding altogether:

> *'There is a risk that we shoot ourselves in the foot if funders try to attach conditions that are seen as unreasonable, or an undue burden, or impossible to work with. Then you just create even more of an incentive for companies to turn to private finance, and not be bound by those conditions.' (PO_8)*

Nonetheless, the previously '*trailblazing*' practice (PO_10) of tying conditions for access and stewardship to push funding is perceived as less controversial today, especially since HICs such as the EU also face access challenges (PO_2). Funders that do not attach conditions themselves (e.g. PO_9), claim to support drug developers to fulfil their commitments downstream. For their part, implementers work together with this push funding network to '*learn [the process] together*' (PO_1), and translate conditionalities into practice. However, several observers note that many small biotech firms lack sufficient expertise, infrastructure, or capacity in stewardship or access planning (Renwick et al. 2016; Doernberg et al. 2018). At this stage, it remains too early to assess how well these conditions work to safeguard access or stewardship, since products funded under these conditions have not yet completed development.

Pull incentives. A highly anticipated reform is the adoption of pull incentives that would delink revenue streams from the units of antibiotics sold, and address the market failure for antibiotics. These policies would primarily address the issue of financial sustainability for implementers post-development, but their impact on R&D, access, or stewardship can differ. For instance, PO_2 characterizes the Swedish subscription model as a national access model for Sweden, and '*not a model for incentivizing R&D*'. Supplementary File 1 delineates broad possible implications of the pull incentives under discussion on antibiotics innovation, access, and stewardship.

In particular, six POs anticipate the adoption of the PASTEUR Act in the US. Pledging up to USD$ 6 billion to secure national access for each new antibiotic, this subscription model is described as a financial '*game changer*' by interviewees (PO_1, 7, 2, 3, 94). In contrast, civil society organization Médecins Sans Frontières has raised concerns that the PASTEUR Act risks driving up prices for novel antibiotics outside U.S. federal procurement, limiting global access, and will not ensure adequate stewardship (Médecins Sans Frontières 2024). Moreover, some interviewees (PO_2, 10) also flagged its potential weaknesses:

> *'It is a lot of money. But I don't think it will lead to the broader transformational systems change that is needed in antibiotic R&D. [...] You can have stewardship requirements put on payments in the public sector, but how will the drug be used in the private sector? There is no mechanism to enforce your requirements for stewardship there. And beyond the US, how will access and stewardship be ensured there? There is a built-in limitation to these national-level proposals.' (PO_10)*

Regulatory requirements. Finally, an important identified barrier to access are regulatory requirements of national and regional

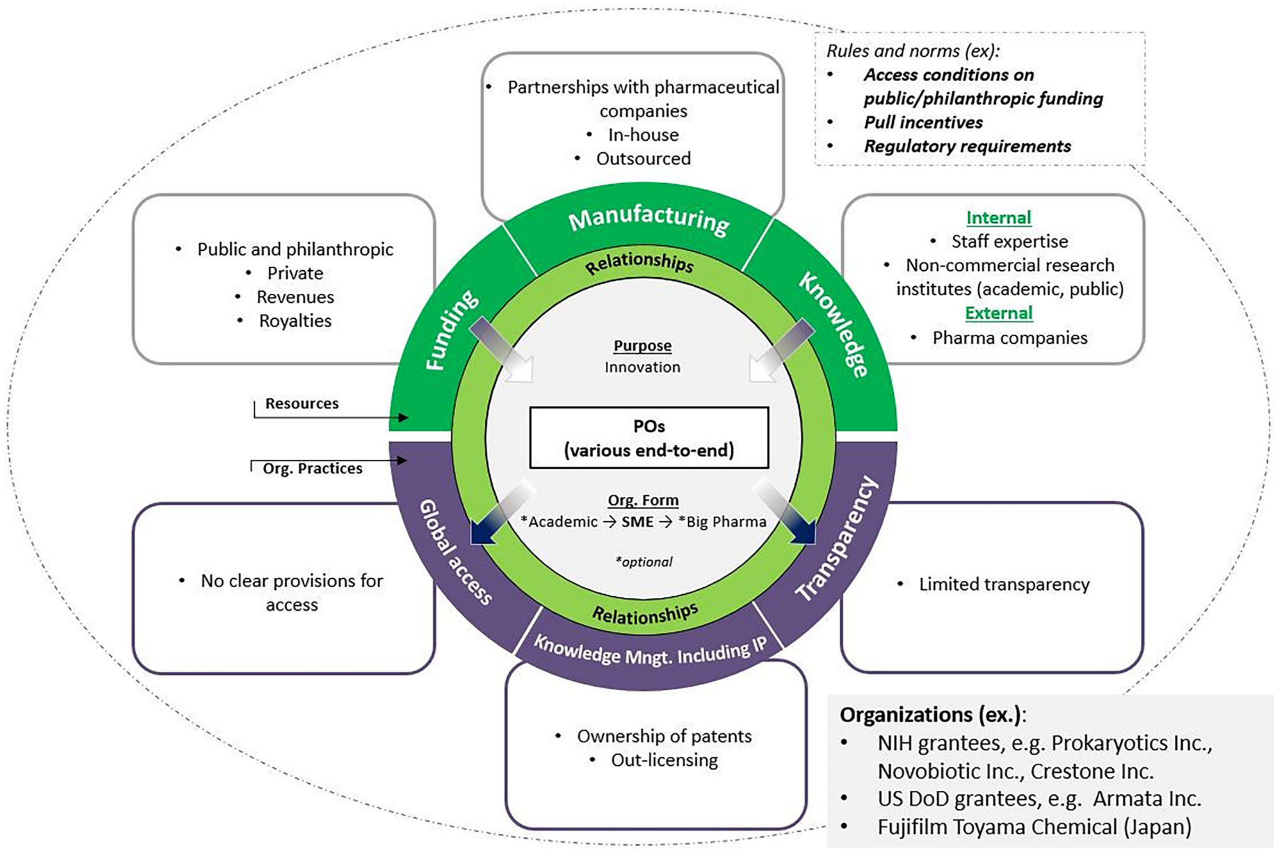

Fig. 4 Characteristics of the Publicly-Supported Private Initiative (PSPI) Alternative Innovation Model for antibiotics.

medicines agencies, including demands to conduct supplementary clinical trials and pay high fees to submit applications for registration (PO_1, 3).

> *'Regulators are not necessarily harmonized between FDA, EMA, Japan, India, etc. So, you spend a lot of time and money doing clinical trials in one country after the other. And the economics of this space does not allow you to do so many clinical trials. […] You can do one large phase III with multiple countries. Then you get regulatory approval in one shot in multiple countries. That's the thinking. […] One large pivotal study that has five countries and those five countries' approval. Can we dream of a world like that?' (PO_3)*

In response to these types of concerns, networks such as the European Clinical Research Alliance on Infectious Diseases (ECRAID) in Europe, or The ADVANcing Clinical Evidence in Infectious Diseases (ADVANCE-ID) in Asia have been recently established to coordinate clinical trial networks. In addition, some national medicines regulatory agencies have also changed their approach, according to interviewees (PO_1, 8). For example, in 2018 the Chinese FDA adopted a new regulatory stance as a member of the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), whereby they accept data from Phase III clinical trials conducted in other parts of the world. Discussing the regulatory environment more generally, funder PO_8 notes that it '*is much better than it was 10 or 15 years ago*'.

Discussion

The antibiotic innovation niche operates differently from the mainstream innovation model, defined "as a market-driven one in which a commercial profit-maximizing firm conducts at least the later stages of R&D (e.g., preclinical to clinical trials) and brings a product to market" (Moon et al. 2025). In this niche, the market-driven, mainstream commercial model of pharmaceutical innovation is represented by only 13.64% of drug developers in the preclinical pipeline, and 32.63% of the clinical. Aside from this significant minority, we found most antibiotic developers adopting one of two *alternative innovation models*, which we inductively derived from the data: Publicly-Supported Private Initiatives (PSPIs) and Collaborative Networks (CNs) (Moon et al. 2025, manuscript under review). We articulate these models as archetypes to facilitate analysis, recognizing that specific initiatives may differ from a model's exact contours. The organizations adopting these alternative models have to choose between a wide range of traditional (e.g., retaining patents as assets) and alternative practices (e.g., transferring technology and sharing data more openly), and are often opting for a mix of traditional and alternative elements in the building of their model. These models offer different strengths and weaknesses for the joint pursuit of innovation, global access, and stewardship.

Alternative innovation model: Publicly-Supported Private Initiative (PSPI). The currently predominant model in the antibiotic niche is the Publicly-Supported Private Initiative (PSPI) model. Typically, these are SMEs, particularly from HICs, who struggle to remain financially sustainable during R&D and post-development stages and mobilize resources from different sources. They are likely to be supported by multiple private, public, and philanthropic actors, who might also provide expertise to help implementers overcome innovation, regulatory, and commercialization barriers. They hold patents, which they might license to larger pharmaceutical companies for product

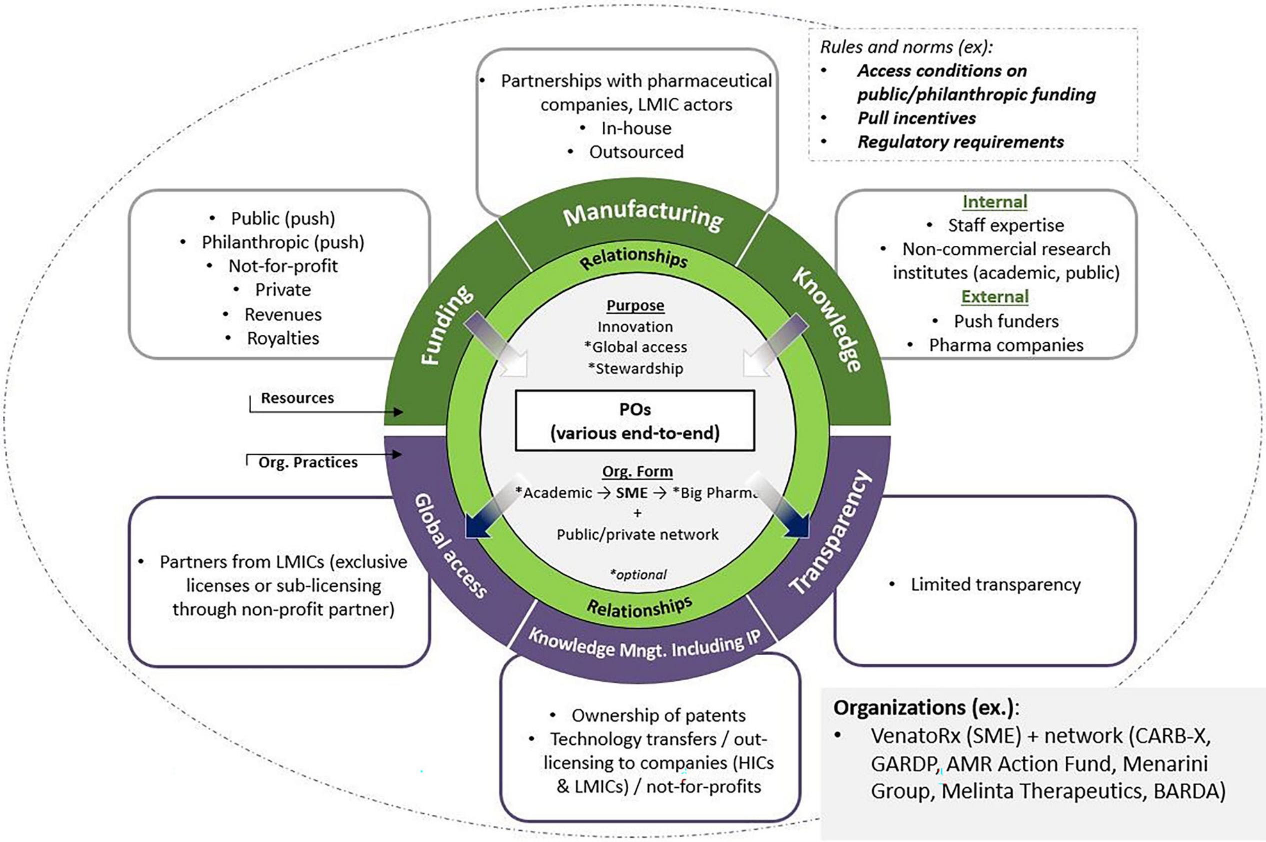

Fig. 5 Characteristics of the Collaborative Network Alternative Innovation Model for antibiotics.

development, manufacturing, or distribution. Figure 4 provides an overview of this model's characteristics, resources mobilized, and practices adopted (Fig. 4).

This innovation model is alternative to the mainstream model, in that it relies substantially on funding and facilitation from public and philanthropic sources, and expects lower returns on investment compared to the mainstream model. However, it fails to guarantee the joint achievement of innovation, access, and stewardship objectives. The distinct strength of this model is its ability to continue innovating in a broken market, by mobilizing resources creatively - from public, philanthropic, and private sources alike. The predominant weaknesses of the model are: the de-prioritization of global access and stewardship, and the inability to safeguard financial sustainability post-development in the absence of pull incentives.

Alternative innovation model: Collaborative Network (CN). We also found evidence of an emerging alternative innovation model in the form of a Collaborative Network (CN). Similar in many respects to the PSPI model, the CN is potentially better suited to achieve the three-pillar balance of the antibiotic niche. This model expands the number and scope of partnerships found in the PSPI model to include a multitude of private, public, philanthropic, and not-for-profit actors that work together to achieve innovation, access, and stewardship objectives. Organizations adopting this model benefit from an '*accelerator support*' network constituted by organizations such as CARB-X, GARDP, Wellcome, or AMR Action Fund, that supplies antibiotic developers with funding, knowledge, and other key resources. In exchange, implementers accept contractual obligations to develop access and stewardship plans, typically attached by funders such as CARB-X or Wellcome in the early stages of R&D. The objective of expanding global access to their products drives them to expand the network further: implementers are relatively small organizations unable to commercialize products worldwide, and they typically search for external support from larger companies for HICs, or not-for-profit partners such as GARDP, who can intermediate licenses and/or technology transfers between antibiotics developers and local manufacturers in LMICs. Organizations following this model seem more likely to share knowledge and contractually externalize decisions that can affect affordability and accessibility, such as pricing policies. In practice, we see CNs taking shape through SMEs such as VenatoRx, which was supported by actors such as BARDA, CARB-X, GARDP, and AMR Action Fund to develop cefepime-taniboractam. Post-development, they out-licensed rights to Melinta Therapeutics for registration and commercialization in the US, to Everest Medicines for select countries in Southeast Asia, to Menarini Group for 96 HICs and LMICs of commercial interest, and to GARDP for 64 LMICs, as well as public markets in India and South Africa (Fig. 5).

A key strength of this model is its inclusion of access and stewardship objectives alongside innovation, and the diversity and growing reach of collaborations. For instance, when CARB-X finances and supports an R&D project in early stages, and includes conditions to develop access and stewardship plans, funders such as AMR Action Fund can provide the financial means downstream to allow them to follow-through on these obligations. At the same time, GARDP can continue R&D for certain neglected indications such as pediatric use, and/or facilitate the global rollout of the new antibacterial by brokering technology transfer to LMIC-based manufacturers.

The primary weaknesses of this model are its relative novelty and decentralized nature. Since most of the drug developers joining CNs are still in drug development stages, the ability of the model to expand access and deliver on stewardship remains to be demonstrated. In addition, the multiplicity and diversity of a growing, diffuse network can raise challenges for coordination, monitoring, and accountability, especially in the absence of a legitimate 'orchestra conductor' to ensure the network as a whole achieves innovation, access, and stewardship goals.

A pharmaceutical niche in transition. Overall, in the antibiotic R&D niche we found: a substantial minority of actors continuing to adopt the market-driven, mainstream model; a majority of organizations adopting a PSPI model that prioritizes innovation over access and stewardship; and an emerging collaborative network (CN) model that brings together a diverse set of stakeholders in the joint pursuit of innovation, access, and stewardship. Key differences are that the CN model tends to involve a broader range of organizations, to share knowledge more openly (e.g., data, technology transfer, patent licensing) and to put greater priority on global access and stewardship objectives than the PSPI model, which focuses on innovation and financial sustainability. However, this analysis provides a snapshot of the antibiotic niche at the time of writing. The evolution and distribution of these models will be influenced to a considerable extent by the potential adoption of new rules such as pull incentives (see more detailed analysis in Supplementary File 1).

Many interviewees seemed comfortable with adopting a set of sizable pull incentives that could "fix" the antibiotic market by creating incentives for private investors and large pharmaceutical companies to return to the niche. In this scenario, a significant risk is the development of publicly-supported markets that foster profit-maximizing, mainstream innovation models, with highly inequitable societal outcomes - similar to the evolution of the rare diseases niche after the adoption of the Orphan Drug Act (Alonso Ruiz et al. 2023). While this path can be attractive for HIC policymakers as a solution to secure national access to new antibiotics, global access and stewardship (including in HICs) risk being left unaddressed, thus undermining longer-term efforts to combat AMR.

Nevertheless, the effect of pull incentives remains to be seen. At this point, public actors remain well-positioned to embed global access and stewardship obligations into funding agreements. It is not too late for policymakers to carefully select and draft pull incentives in collaboration with stakeholders, including civil society organizations (CSOs) and public-interest organizations, to secure and bolster the three pillars of AMR. It is important to note that if new incentives lead to the return of large pharmaceutical companies to the antibiotic R&D niche, this could significantly influence the development and function of PSPIs and CNs. The entry of (high) profit-oriented actors may increase the availability of private capital, reducing the dependence of PSPIs and CNs on public and philanthropic funding. However, this shift could also reshape the niche by reinforcing traditional market-driven strategies, such as patent monopolies and high prices. For PSPIs, partnerships with large pharmaceutical companies could bring financial stability but also introduce stronger commercial priorities that deprioritize equitable access and stewardship measures. Similarly, CNs may face pressures to accommodate industry-driven pricing and distribution strategies, potentially limiting their ability to pursue access and/or stewardship commitments. While these models currently offer a more socially oriented alternative to mainstream pharmaceutical R&D, their long-term viability and impact will depend on how pull incentives are designed and whether safeguards are in place to protect their ability to deliver on innovation, access, and stewardship commitments in an evolving ecosystem.

This study has several limitations. First, while the interviews with POs provided valuable insights into how alternative innovation models function, they are not exhaustive; additional interviews or in-depth case studies would provide further nuance and detail. Second, although the pipeline database we constructed is, to our knowledge, the most extensive publicly available source, its completeness cannot be guaranteed, as we did not have access to information from privately held (paid) databases. Finally, a comprehensive mapping of all organizations active in the antibiotic R&D niche was beyond the scope of this paper, and some relevant actors may therefore have been missed. These limitations suggest caution in generalizing the findings, while also highlighting areas for future research.

Conclusion

To counteract the rising threat of AMR, it is imperative to develop innovative antibiotics that are at the same time accessible and used responsibly. This paper describes the characteristics and features of existing innovation models in the niche, weighing their ability to meet innovation, access, and stewardship goals – an emergent property of this CAS. We highlight the co-existence of two alternative innovation models operating in the antibiotic R&D niche, in addition to a minority that adhere to the mainstream, market-driven innovation model that characterizes more lucrative pharmaceutical sectors, such as non-communicable diseases (NCDs).

The predominant alternative model adopted by antibiotic developers is the PSPI, which barely sustains innovation in a broken market through the contributions of public funders, but ultimately does little to expand access at the national or global level, or to meet stewardship requirements. To improve, this model requires public actors to commit to and reflect these goals through their extensive support and influence over drug developers in the niche. In addition, we found a second alternative innovation model in the form of CNs, representing extended networks that collaborate to support innovation, expanded access and (in principle also) stewardship of new antibacterials. This model is promising and offers important advantages over the other two, but is relatively recent, small-scale relative to the mainstream model, with results to be demonstrated in practice.

This article offers a snapshot of the antibiotic R&D niche in a moment of possible transition, when policymakers are assessing new pull incentives in high-income countries (e.g., the PASTEUR Act in the US) that may transform this CAS. Safeguarding financial sustainability for antibiotic R&D is necessary to deliver innovative drugs that can offset the diminishing effectiveness of old antibiotics. However, equally important is ensuring globally-equitable access and stewardship to address public health needs and mitigate rising antibiotic resistance. The survival, form, and considerable potential of the PSPI and CN alternative innovation models to address these triple objectives depends to a large extent on the rules that will be adopted to govern the niche. Decision-makers should construct rules and incentives that jointly deliver innovation, access, and stewardship of antibiotics, to help them improve, survive, and thrive.

Data availability

The dataset generated and analyzed during the current study, containing information about the drug developers active in the preclinical and clinical antibiotics pipelines, is included in this published article as a supplementary file. This dataset, along with the interview transcripts generated and analyzed during the current study are made publicly available, where confidentiality preferences expressed in signed consent forms allows, on a public repository accessible at https://doi.org/10.5281/zenodo.15064024.

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Note

1 A list of the current pull incentives implemented and discussed are available in Supplementary File 1.

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Author contributions

Iulia Slovenski [IS]: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Validation, Visualization, Writing–original draft, Writing–review & editing. Adrián Alonso Ruiz [AR]: Conceptualization, Project administration, Validation, Writing–original draft; Writing–review & editing. Marcela Vieira [MV]: Conceptualization, Validation, Writing–review & editing. Kaitlin Elizabeth Large [KL]: Conceptualization, Validation, Writing–review & editing. Adam Strobeyko [AS]: Conceptualization, Validation, Writing–review & editing. Yiqi Liu [YL]: Conceptualization, Validation. Suerie Moon [SM]: Conceptualization, Funding acquisition, Supervision, Validation, Writing–review & editing.

Competing interests

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Ethical approval

This study involved human participants who took part in interviews. All participants underwent a process of written informed consent prior to participation. The study was approved by the Ethics Review Committee, Graduate Institute of International and Development Studies on 16 March 2021, in adherence to the Declaration of Helsinki.

Informed consent

In the case of representatives of studied participant organizations, written informed consent has been obtained via email prior to the interviews (conducted between 2022–2023), to include the collected data and selected quotes for this publication. By completing the informed consent form, participants accepted to be part of the study and expressed their preference with regards to reviewing the final transcript, publishing the transcript on an open platform, and disclosing the identity of their organization.

Additional information

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