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ARTICLE

Historicising the "Empty Pipeline": How Antibiotic Innovation Became a Market Failure (1980–2024)

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Abstract

Antibiotic innovation has slowed. Despite substantial public investment, research and development (R&D) remains insufficient to address rising antimicrobial resistance (AMR). In this historical review, we draw on quantitative and qualitative historiographic methodologies, as well as on testimony from key stakeholders, to reconstruct antibiotic innovation challenges and public interventions since 1980. Emerging in the 1990s and gaining traction around 2010, the "empty antibiotic pipeline" metaphor, as well as its market failure diagnosis, has played a key role in structuring the global R&D response. This reframing described AMR as an incentives-based innovation challenge, which suited industrial and high-income country interests. However, the introduction of so-called push and pull incentives has so far failed to halt the exit of large developers, sustain diversified R&D ecosystems, or address global access challenges. This article explores challenges and conflicts involved in the implementation of the incentives-based innovation approach alongside the ever-greater subsidies required to stabilise small and medium-sized enterprises (SMEs) and attract larger pharmaceutical companies and investment from financial markets. Several SME bankruptcies since 2019 and the mothballing of novel compounds suggest that this is an unsustainable innovation model. This article also explores whether public interventions have been insufficient or whether there is a deeper problem with the central metaphor structuring global action.

Keywords: antibiotic access; antibiotic innovation; antimicrobial resistance; market incentives; pharmaceutical research and development; public private partnerships

1. Introduction - A Deficit Imaginary

Narratives have power. Social scientists have long highlighted how language structures humans' capacity to perceive the world, reflects power imbalances, and impacts policy-making.[1] This historical review examines the rise, circulation, and impact of one of the most

[1] Fairclough 2013; Hoare and Smith [1971] 2010; Leach, Scoones, and Stirling 2010.

influential narratives in antibiotic governance—the metaphor of the "empty antibiotic pipeline." Starting in the 1990s and gaining traction since 2010, the empty pipeline metaphor spurred calls to "fix" the "broken antibiotic market" and "restore" research and development (R&D). The resulting inflows of public and philanthropic funding have outpaced other forms of antimicrobial resistance (AMR) investment and intervention, including those in vaccines and diagnostics.[2] The underlying linear imagery has galvanised a directed innovation ecology consisting of publicly funded incentives to "push" or "pull" compounds through the empty pipeline alongside dedicated public–private partnerships (PPPs) and product development partnerships (PDPs).[3] Yet antibiotic innovation remains insufficient to address AMR, large developers have continued to exit, and economic volatility within the pipeline has not diminished.[4] Meanwhile, questions of affordability and access-oriented design of novel technologies have long been neglected.[5] Have public interventions been insufficient? Or is there a deeper problem with the central metaphor structuring global action?

Our historical review of antibiotic innovation since 1980 illuminates the sociopolitical roots of the "empty pipeline" metaphor. Each part addresses a distinct question: (1) How did the historical ecosystem for antimicrobial innovation function, and why did it rupture? (2) Who shaped the emergent "empty antibiotic pipeline" narrative? (3) How did remaining R&D companies adapt to antibiotics' declining commercial status? (4) What were the geopolitical dynamics impacting the uptake of the pipeline metaphor and the resulting ecosystem of incentives, PPPs, and PDPs? (5) Can assetised public–private R&D align with what anthropologist Clare Chandler describes as antimicrobials' infrastructural role within essential health and food production systems? (6) To what extent do current attempts to "fix" the innovation pipeline take into account questions of drug access and R&D ecosystems outside of high-income countries (HICs)?[6]

To answer these questions, we draw on the substantial body of social sciences research on discursive performativity in biomedical R&D, and combine a quantitative thematic-trends evaluation of antibiotic innovation-centred publications (Figure 1), with a qualitative analysis of relevant historiography, policy reports, and U.S. Securities and Exchange Commission (SEC) records.[7] We also draw on a 2024 historical witness seminar recording reflections of key decision-makers from clinical medicine, industry, and international organisations who shaped AMR policy and financial models for antibiotic development from the 1990s.[8]

Part One reconstructs antibiotic innovation prior to the 1980s. It highlights a diversity of public and private R&D approaches and factors contributing to the dissolution of the early innovation ecology.

Part Two examines the rise of the "empty antibiotic pipeline." Although the use of a pipeline metaphor to describe drug development dates to the mid-twentieth century, our analysis of

[2] Global AMR R&D Hub 2025; Laxminarayan et al. 2024.
[3] Abbott 2016, 33, 36; Gotham et al. 2021.
[4] WHO 2024a, xvii; 2024b.
[5] Adeoye et al. 2025.
[6] Chandler 2019.
[7] See, for example, Gaudilliere 2021; Hilgartner 2000; Jasanoff 2006; Latour 2007; Latour, Salk, and Woolgar 2013; Pfotenhauer, Juhl, and Aarden 2019.
[8] Alas Portillo et al. 2024b.

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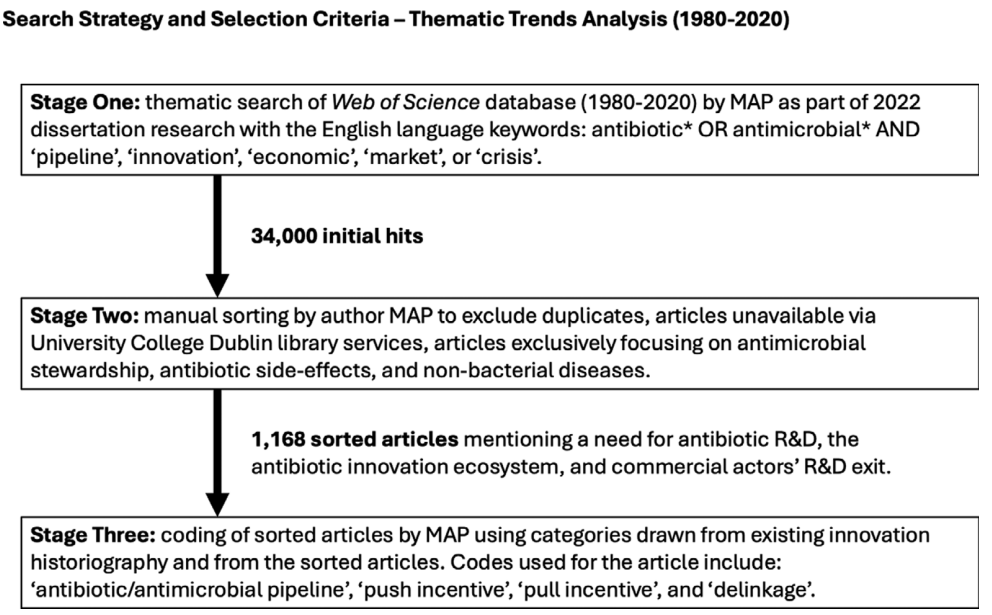

Figure 1. Thematic trends analysis search strategy.

scientific literature and policy reports indicates that the application of the "empty pipeline" metaphor to the antibiotic R&D space only began during the mid-1990s.[9] Implicit in the metaphor's use was an assumption that innovation was a unidirectional process primarily entailing proprietary development of novel molecular compounds.[10] Characterisation of the antibiotic pipeline as "empty," despite ongoing R&D, created what social scientists have termed a "deficit model of innovation" that justified selective market-focused public interventions.[11] Industry use of this deficit model to reframe AMR as an innovation challenge coincided with expiring blockbuster patents and controversies about intellectual property (IP) impacts on drug access. Company histories show that many large developers were uninterested in returning to or reprioritising antibiotic R&D.[12]

Part Three reconstructs how, from the 2000s, the remaining large companies began prioritising mergers and acquisitions over in-house R&D, leaving antibiotic innovation increasingly dominated by small- and medium-sized enterprises (SMEs).[13] While SMEs focused on adapting known compounds for emerging hospital "superbugs" like Methicillin Resistant *Staphylococcus aureus* (MRSA), their financially vulnerable business models—and dependence on speculative investment and value-based pricing—contributed to a more volatile R&D ecosystem.[14]

Part Four analyses how the failure of this volatile innovation ecosystem to keep up with AMR became evident around 2010, amidst surging Gram-negative infections. Funders' preference

[9] Gaudillière 2021, 422; Spilker 1989, 16–19.
[10] Gaudilliere 2021, 420.
[11] Pfotenhauer, Juhl, and Aarden 2019.
[12] Drews 1998; Overbye and Barrett 2005; Skender 2024.
[13] Roy 2020, 96–99; Wells, Nguyen, and Harbarth 2024a.
[14] Anderson, Panteli, and Mossialos 2023; Doganova and Rabeharisoa 2024; Roy 2020, 102–4.

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for incentives-based interventions led to a doubling-down on the "empty pipeline" metaphor's market failure diagnosis and attempts to reattract large companies via "push" subsidies for early-stage R&D, and market-shaping "pull" incentives for licensed compounds.[15] "Delinkage" emerged as a second key narrative to reconcile stewardship proponents (who initially resisted prioritising innovation) with industry strategists (who were sceptical about state intervention).[16] Proponents argued that value-based public subscriptions, or prizes for access to novel compounds, could rejuvenate commercial R&D and avoid overmarketing.[17]

Part Five studies how "fixing" the pipeline with incentives led to a growing divide between what novel antibiotics should cost as an essential infrastructure for health service delivery according to value-based pricing models, and what societies can afford to pay.[18] The article discusses the SME Achaogen, which "got everything right" in funding terms, raising almost $800 million of public and private investment to develop its antibiotic plazomicin, but suffered bankruptcy after generating only $0.8 million in revenues.[19]

Part Six ends by assessing how the rise of the pipeline metaphor and incentives-based innovation interventions have impacted antibiotic drug access. It argues that chronic shortages of generic antibiotics are indicative of a wider crisis of antibiotic supply chains and markets. These issues are not adequately being addressed by current innovation initiatives and may require novel forms of decentralised R&D.[20]

The conclusion argues that attempting to satiate open-ended investor expectations using public incentives is not sustainable. Diversifying R&D ecosystems is key to securing sustainable antibiotic innovation and equitable access.

2. Part One: the "Golden Era" of antimicrobial innovation

Between 1900 and the 1970s, antimicrobial innovation surged. Over the past decades, historians of science and medicine have published both witness seminars and detailed historical overviews of the rise of arsenic-based antimicrobials around 1900, synthetic sulphonamides in the mid-1930s, and biological and semi-synthetic antibiotics from the 1940s and 1950s.[21] According to scholars such as Vivianne Quirke, Robert Bud, Jean-Paul Gaudillière, and John Lesch, early innovation ecosystems were "big," integrated, and spanned public and private sectors.[22] R&D was often undertaken in proximity to sites of testing and production. In an age of process rather than product patents, this combination of scale and proximity enabled compounds and know-how to circulate amongst institutions and across borders. In the case of fermentation-based production, close interaction between scientists and engineers also enabled a rapid upscaling of production.[23] Infrastructural integration of innovation ecosystems also facilitated retention of expertise and repurposing of compounds for novel targets.[24] The described combination of comparatively open

[15] Alas Portillo et al. 2024b, 42–47; Glover et al. 2021.
[16] Alas Portillo et al. 2024b, 43–49.
[17] McEnany and Outterson 2024; Outterson et al. 2016.
[18] Chandler 2019.
[19] Anon. 2020; Wells, Nguyen, and Harbarth 2024a.
[20] Fox, Sweet, and Jensen 2014; Quadri et al. 2015.
[21] Bud 2007; Greenwood 2007; Hüntelmann 2010; Jolliffe 1993; Lachenal 2017, 20–41; Lesch 2007; Santesmases 2018; Tansey and Reynolds 2000; 2008.
[22] Bud 2007, 23–53; Lesch 2007, 40–67; Quirke 2012, 5–7, 10–11, 111–23, 134; Quirke and Gaudillière 2008.
[23] Bud 2007, 23–53; Daemmrich 2009.
[24] Daemmrich 2009; Quirke 2012; Swann 1988.

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knowledge flows, long-term expertise, and integrated infrastructures also meant that innovation often occurred in unforeseen non-linear ways, as in the case of the 1939 decision to turn penicillin—an unpatented compound discovered eleven years earlier—into a therapy.[25]

Molecular and use-based innovation involving the discovery of new compounds and the repurposing of existing compounds for novel targets continued after 1945.[26] Far from engendering gloom about the future of antibiotics, Christoph Gradmann has shown how rising AMR was seen as an "exciting" development in an anti-infective market that was already considered saturated during the 1950s.[27] From the 1960s, many R&D departments thus focused on modifying particularly effective compounds to target evolving resistance mechanisms.[28] It would, however, be wrong to believe that the post-war surge of antibiotic compounds and applications implied a standardised innovation model or concepts of a wider "pipeline" of antimicrobial R&D. Instead, histories of companies such as Glaxo and Eli Lilly (first-generation cephalosporins), LEO Pharma (fusidic acid), or Bayer (ciprofloxacin) reveal often haphazard and disconnected approaches to innovation.[29]

Addressing the needs of low- and middle-income countries (LMICs) was not a major priority for most R&D centres. In contrast to the rapid saturation of HIC markets, most LMICs' experience of the "Golden Era" of antibiotic innovation was characterised by trickle-down access to new compounds.[30] With few exceptions, such as post-war UN attempts to spread penicillin production, access depended not only on one's ability to pay for novel compounds, but also on Cold War geopolitical alignment.[31] Historical research on West and East-African health systems shows that early twentieth-century arsenic-based treatments remained common well into the late 1960s.[32] Sustained supplies of newer and safer biological antibiotics were often limited to disease-specific international health campaigns.[33] Starting in the 1970s, HIC companies increasingly tried to develop LMICs into markets for now off-patent—occasionally more toxic—human and veterinary compounds, as well as combination therapies that had been abandoned in the West.[34] In LMICs themselves, shortages drove scarcity-based innovation, such as alternative fermentation media in China, East-Germany's development of nourseothricin to replace tetracyclines, Spain's development and distribution of fosfomycin to South America, and the Yugoslavian pharmaceutical company Pliva's discovery and out-licensing of azithromycin to Pfizer.[35]

The integrated innovation ecosystems underlying the "Golden Era" started dissolving around 1980. Declining attention to microbial infections led to funding shortfalls and the

[25] Bud 2007, 23–53; Gradmann 2016; Leisner 2020.
[26] Bud 2007, 116–39; Gradmann 2016; Podolsky 2015, 19–30.
[27] Gradmann 2016, 157.
[28] Gradmann 2016; Greenwood 2007, 248–49.
[29] Gradmann 2016; Leisner 2020; Tansey and Reynolds 2000, 39–43; 2008, 46-9, 53.
[30] Podolsky 2015, 19–30.
[31] Capocci 2014; Kirchhelle 2018; Li 2024; Tobbell 2009.
[32] Lopez et al. 2022.
[33] McMillen 2015, 125–67; see ongoing research by Adedamola Adetiba at the University of Manchester: https://wellcome.org/research-funding/funding-portfolio/funded-grants/nigeria-antimicrobial-and-post-antimicrobial-eras.
[34] Kirchhelle 2018, 4, 7–8; Kunin et al. 1987, S276; Silverman, Lee, and Lydecker 1982.
[35] Alas Portillo 2025; Banić Tomišić 2011; Brazelton 2019; Chu 1974; Greenwood 2007, 239; Santesmases 2018, 133–55; Schramm 2008, 184–89; Zhou 2023, 4.

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closure of public anti-infective innovation centres.[36] Companies also began divesting from antibiotic innovation due to perceived market saturation and new managerial doctrines focusing on maximising shareholder value, streamlining product portfolios, and concentrating on cancer and chronic diseases.[37] Having mostly abandoned large-scale screening, remaining companies saw little return from genetic and high-throughput analyses of pathogens and compound libraries.[38] Meanwhile, increased emphasis on protecting proprietary knowledge in industry and academia slowed circulation and adaptation of compounds and expertise.[39] Knowledge cycling was also constrained due to growing distances between R&D and production sites, which reduced interactions between researchers and engineers.[40] Although structural adjustment programmes disrupted many LMIC pharmaceutical industries, Good Manufacturing Practice (GMP) certification intensified outsourcing of manufacturing to regions with cheaper labour costs and weaker environmental regulations.[41]

By the 1990s, the diverse post-war innovation and manufacturing ecosystem had fragmented along geographic and proprietary silos. Whereas global manufacturing and packaging were rapidly shifting to China and India, R&D remained concentrated in HICs, but was also transforming due to intensifying mergers of traditional developers and the growing prominence of SMEs.[42] The 1995 Agreement on Trade-Related Aspects of Intellectual Property Rights further narrowed definitions of what counted as valuable innovation by universalising product patents associated with molecular novelty.[43]

3. Part Two: a pipeline born empty

Consequences for antibiotic innovation were profound, with R&D activity falling from the 1980s onwards.[44] However, widespread public and scientific alarm about declining antimicrobial innovation was relatively slow to emerge. Alarm about failing bug-drug combinations had been voiced since the 1940s, and both antibiotic activist Stuart Levy and the 1992 Institute of Medicine report on *Emerging Infections* reacted to slowing innovation by noting that AMR required "replacement drugs to be in the 'pipeline'."[45] However, few early commentators conceived of antibiotic innovation as an interconnected—let alone empty—pipeline. Indeed, our thematic trends analysis shows that the pipeline metaphor only gradually emerged as an overarching deficit imaginary for antibiotic R&D from the mid-1990s onwards (Figure 2).[46]

The rise of the "empty pipeline" metaphor coincided with surging international attention for AMR as a problem exceeding individual "superbugs."[47] However, the implied deficit imaginary was slow to gather steam. In the infectious disease community, many contemporaries prioritised stewardship interventions over branding AMR as an innovation

[36] Blume and Baylac-Paouly 2021, 9–17; Lezaun 2018.
[37] Drews 1998, 278–80; Gradmann 2016; Monnet 2005; Timmermann 2025.
[38] Alas Portillo et al. 2024a; Overbye and Barrett 2005; Skender 2024.
[39] Rasmussen 2014, 72–100; Yi 2015, 138–212.
[40] Daemmrich 2009.
[41] Baxerres and Cassier 2021, 33–39; Mackintosh et al. 2016; Wells, Nguyen, and Harbarth 2024a; Zhang 2023.
[42] Drews 1998, 252–54; Thomas 2008, 15–19, 29–33; Williams and Bax 2009.
[43] Gaudilliere 2021, 420; Rajan 2017, 47–53, 112–13.
[44] Monnet 2005, 135.
[45] Shlaes, Levy, and Archer 1991; IoM 1992, 159; Gradmann 2017.
[46] Pfotenhauer, Juhl, and Aarden 2019.
[47] Overton et al. 2021.

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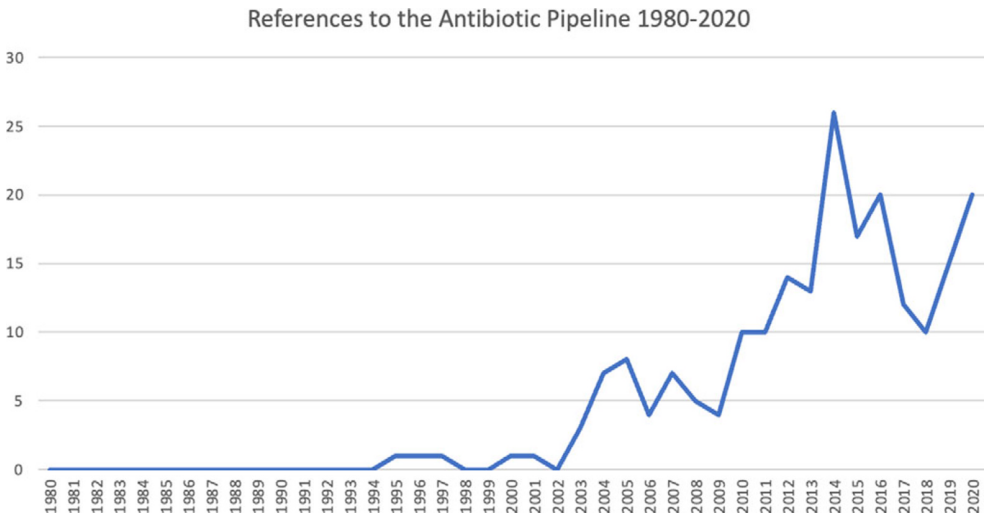

Figure 2. References to "antibiotic pipeline" in sorted articles (n = 210).

challenge.[48] In 1994, John La Montagne, director of microbiology and infectious diseases at the U.S. National Institute for Allergy and Infectious Diseases, noted that industry was still "producing drugs at a reasonable clip."[49] Four years later, at the annual Infectious Diseases Society of America (IDSA) meeting, physician Dennis Maki hyperbolically compared calls to prioritise innovation over stewardship to "providing finer brandy to your alcoholic patients."[50]

Who was behind the push to reframe AMR governance around the "empty pipeline" metaphor? Authorship analysis of 92 sorted *Web of Science* articles on antibiotic innovation between 1995 and 2005 shows that 77% were from HIC universities (Figure 3). LMIC voices (1%) were remarkably absent despite expanding antibiotic industries (e.g., China) and vocal contemporaneous participation in HIV debates.[51] The global divide in reporting indicates that, for most of the world, antibiotic access rather than molecular innovation remained the primary challenge. Meanwhile, industry authors (19%) played a notable role in warning that "the pipeline may be drying up" and calling for incentives-based market fixes for innovation, such as extended patents and reduced trials requirements, "to stem the tide of companies leaving the area."[52]

Industry advocacy for public interventions was not linked to an acute crisis of the antibiotic market. Between 1998 and 2009, global antibiotic revenues continued to grow from approximately $22 billion to over $25 billion.[53] However, antibiotic profitability compared increasingly unfavourably with other fields such as cancer therapy. Whereas antibiotics had long ranked amongst the most lucrative medicines, a 2002–04 list of U.S. pharmaceutical best-sellers featured none.[54] Seeking to maximise return on investment, many R&D companies

[48] Alas Portillo et al. 2024b, 31–33.
[49] Culotta 1994, 363.
[50] Quoted according to Harbarth 2007, 554.
[51] Mindry 2008.
[52] Culotta 1994, 363; Shlaes 2003, 472; see also Casadevall 1996.
[53] Williams and Bax 2009, 157; Tansey and Reynolds 2000, 45.
[54] Maggon 2005, 740; Podolsky 2015, 19–30.

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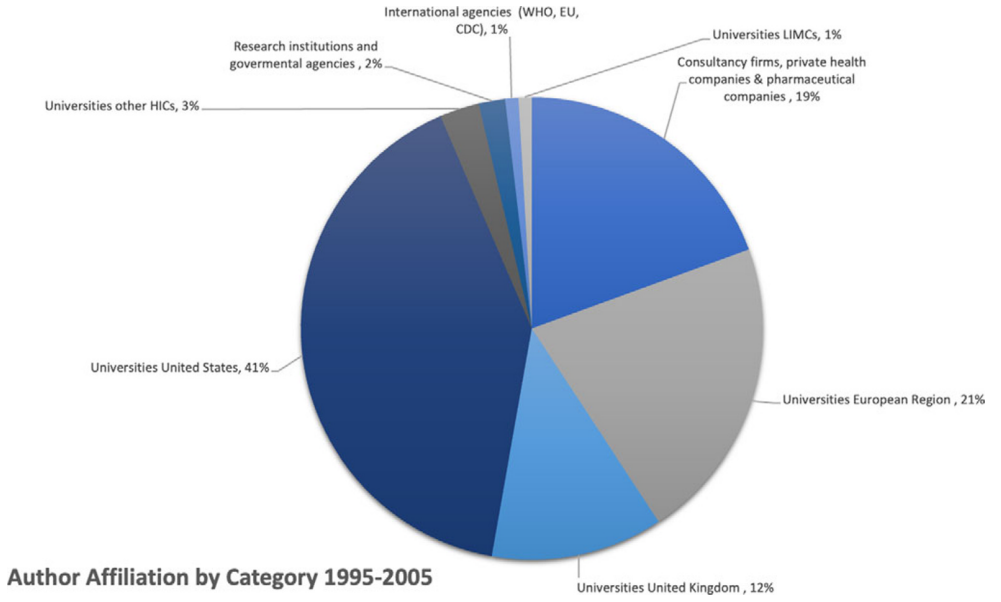

Figure 3. Author affiliations in sorted antibiotic innovation articles (1995–2005) (*n* = 92).

with lucrative existing antibiotic portfolios were completely abandoning the field. Historical analysis of Bayer, a long-standing antibiotic innovator, reveals that in-house R&D had been dismantled by 2002.[55] Similar divestments occurred at Eli Lilly, Aventis, Bristol Myers Squibb, Proctor & Gamble, and Lederle.[56] Roche provoked particular attention when it announced that it would not pursue R&D on a successor to Rocephin (ceftriaxone) despite the drug generating well over $1 billion per year.[57] Even within companies continuing antibacterial research, scientists were said to face "a daily battle for resources compared with colleagues working in other therapeutic areas."[58]

Why then call for public interventions in a market that was neither in crisis nor of particular strategic interest? One reason may be that mobilising the spectre of an "empty pipeline" enabled industry to push back against wider problems facing contemporary R&D. In the context of stricter clinical trial requirements, expiring blockbuster patents, and public backlash against high pricing for patent-protected antiretrovirals, the empty pipeline metaphor offered a way to reframe the emergent health threat of AMR as a market problem.[59] This pipeline could be "fixed" via deregulation, incentives, and exclusivity without a wider systems critique of proprietary HIC drug innovation.

The market and innovation reframing of AMR aligned with broader trends within the field of Global Health. During the 1990s, the World Bank and new non-governmental donors, such as

[55] Skender 2024, 7.
[56] McKenna 2010, 184.
[57] Tansey and Reynolds 2008, 58.
[58] Williams and Bax 2009, 161.
[59] Williams and Bax 2009, 160. Blockbuster antibiotics, including ciprofloxacin (Bayer), Rocephin (Roche), and Augmentin (GSK), went off-patent between 2002 and 2005; some commentators also highlighted that promising antibacterial molecules had already been patented for other purposes. Tansey and Reynolds 2008, 58–59; Hoen et al. 2011, 3–4.

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the Bill and Melinda Gates Foundation, challenged the traditional leadership of the World Health Organization (WHO) within international health.[60] WHO Director-General Gro Harlem Brundtland (1998–2003) tried to regain influence by co-designing policies with donors and intensifying industry engagement.[61] In the case of AMR, HIC stewardship and biosecurity concerns engendered WHO emphasis on "vertical" technology-based solutions, including innovation.[62] With strong U.S., U.K., and Japanese input, the WHO published the first *Global Strategy for Containment of Antimicrobial Resistance* in September 2001, which called for R&D incentives, fast-track authorisation, orphan drug schemes, time-limited exclusivity, aligned IP rights, and industry partnerships.[63] Although the strategy's launch was overshadowed by the attacks of 9/11, WHO endorsement of an IP- and incentives-based response to AMR two months before the Doha Declaration on compulsory medicines licensing and weeks before Bayer's high-profile Amerithrax defence of ciprofloxacin patents was a consequential political decision.[64] It also helped embed the empty pipeline narrative of market failure within the wider AMR community.

4. Part Three: volatile values

Although funders such as the US National Institutes of Health (NIH) increased grants for early-stage research and influential IDSA reports called for market interventions, actual public investment in antibiotic innovation was slow to take off.[65] Remaining companies profited from mounting concerns about "superbugs" and an abundance of older compounds, and knowledgeable researchers created by exiting developers. Meanwhile, innovation finance and underlying business models became dominated by financial markets and speculation on compounds' downstream earning potential.

In a market where off-patent generic antibiotics often constrained pricing, MRSA presented an attractive target for commercial innovation. Emerging in the 1960s, MRSA gained notoriety as a hospital "superbug" in HICs during the 1990s.[66] As a Gram-positive single-walled bacterium, MRSA was easier to target than double-walled Gram-negative "superbugs," such as *Pseudomonas* or *Acinetobacter* spp.[67] Meanwhile, MRSA's healthcare-associated infection (HAI) status, complicating treatment of vulnerable patients, made it an ideal target for value-based pricing. Value-based pricing was rooted in the post-1970s rise of health technology assessment (HTA) and aligned shifts of pharmaceutical marketing, which priced drugs according to their projected value to patients or healthcare systems with no necessary relation to R&D or manufacturing costs.[68] Subject to shifting norms, HTA and value-based pricing drove a surge of industry interest in high-value targets such as cancer, but also transformed anti-infective pricing.[69]

Cubist and Pfizer were two companies that successfully adapted abandoned compounds for emerging high-value bacterial targets. Pfizer's Zyvox (linezolid) is an oxazolidinone

[60] Chabrol and Gaudillière 2023, 42–56; Birn 2014; Reubi 2018.
[61] Cueto, Brown, and Fee 2019, 280–300.
[62] Overton et al. 2021.
[63] WHO 2001, 6.
[64] Gringarten 2019, 69–79.
[65] Alas Portillo 2025; Alas Portillo et al. 2024b, 50–54; IDSA 2004; Paterson 2025.
[66] Condrau and Kirk 2011; McKenna 2010, 50–63; Tansey and Reynolds 2008, 53–57; Washer and Joffe 2006.
[67] Williams and Bax 2009, 158.
[68] Atkinson and Sheard 2025, 7–25; Sorenson and Chalkidou 2012, 25–26; Timmermann 2019, 104–5.
[69] Doganova and Rabeharisoa 2024; Roy 2023, 5–6; Sorenson and Chalkidou 2012, 25–26, 40–41; Wells, Nguyen, and Harbarth 2024a.

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analogue. Dupont synthesised oxazolidinones while working on agrochemicals in 1978 and accidentally discovered their antibacterial effects before abandoning R&D due to toxicity concerns in the late 1980s.[70] 1990s MRSA epidemiology prompted Upjohn Laboratories (latterly Pharmacia) to resurrect development and synthesise linezolid before Pfizer acquired the company.[71] Cubicin (daptomycin) is a cyclic lipopeptide discovered by Eli Lilly in 1984, which was also abandoned due to toxicity concerns, until Cubist adapted the dosage regimen, aided by former Lilly scientists.[72] Turning both compounds into lucrative medicines depended on robust patent protection and demonstrating value via cost savings relative to older drugs such as vancomycin, which had emerged as an important MRSA treatment in the 1980s and was now off-patent.[73] Cubist's adapted daptomycin regimen was approved in 2002. Following the 2003 FDA licensing, Cubicin pricing for a 10-day treatment regime of 6 mg/kg per dose was approximately $1,500.[74] The price reflected projected savings from shorter MRSA hospitalisations versus generic vancomycin-based treatment, and was calibrated to compete with Pfizer's Linezolid (licensed 2000).[75] Noting the high number of patients with staph-based endocarditis (infection of the lining of heart valves and chambers) and bloodstream infections, Cubist expected to "very easily get to a billion-dollar opportunity in the United States."[76] Pfizer similarly justified Zyvox's price by referencing its superior performance and savings versus vancomycin.[77]

Blockbuster profits (at the time defined as approximately >$1 billion) rewarded acquisitions-based development. Annual worldwide revenue from Zyvox totalled $1.1 billion in 2008 (with $4.4 billion total sales 2000–08).[78] In the case of Cubist, Cubicin revenues soared from approximately $40–50 million projected in 2004 to $966.7 million in 2013 before the company was acquired by Merck for $9.5 billion in 2014.[79] Legal challenges, however, revealed the fragility of the value and IP claims underlying these profits. In 2009, Pfizer paid a record-breaking $2.3 billion settlement after a whistle-blower lawsuit alleged fraudulent U.S. marketing of multiple drugs, including off-label marketing of Zyvox with claims that it was superior to vancomycin.[80] Merck's hopes for sustained blockbuster income were similarly dented when a U.S. court voided four of five Cubicin patents in 2015, resulting in a major fall in daptomycin revenue.[81] On the supply side, companies' shift to acquisitions-based development also failed to reinvigorate large-scale multi-pronged antibiotic R&D. Following Merck's takeover, all of Cubist's 120 scientists were let go, prompting *Science* to criticise large companies for "treating the scientists as annoying husks keeping you from sinking your corporate teeth into the delicious acquisition of corn."[82] Critics also highlighted that remaining commercial R&D nearly exclusively targeted high-value targets in HICs, that value-based pricing could make novel antibiotics unaffordable, and that less profitable targets in LMICs and double-walled Gram-negative targets were still being neglected.[83]

[70] Leach et al. 2011, 55–56, 60; Bozdogan and Appelbaum 2004, 113–14.
[71] Leach et al. 2011.
[72] Alas Portillo 2025; Eisenstein, Oleson Jr., and Baltz 2010; Oleson Jr. et al. 2000.
[73] Tansey and Reynolds 2008, 54–55.
[74] Cubist Pharmaceuticals, Inc. 2005, 10.
[75] Alas Portillo 2025; Hunt and Kirsch 2020.
[76] Cubist Pharmaceuticals, Inc. 2005, 10.
[77] Anon. 2004b; Sheller, P.C. 2009.
[78] Sheller, P.C. 2009.
[79] Anon. 2004a; CUBIST Pharmaceuticals, Inc.—Form 10-K 2014; Sagonowsky 2019.
[80] Sheller, P.C. 2009; Edwards 2009; U.S. Justice Department 2009
[81] Staton 2014.
[82] Lowe 2015.
[83] Amabile-Cuevas 2010, 3, 10; Cars et al. 2008; Harbarth 2007, 555; McKenna 2010, 200.

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The ability of the for-profit ecosystem to provide several first-in-class Gram-positive treatments nonetheless strengthened academic and political assessments that science was not the main barrier to antibiotic innovation and that the market could fix itself, given suitable rewards.[84] Meanwhile, the departure of additional large companies like Bristol Myers Squibb meant that the antibiotic innovation ecosystem gradually became dominated by SMEs. Speaking in 2008, former Glaxo Head of Research Sir Mark Richmond noted that SMEs offered traditional antimicrobial developers the opportunity to outsource high-risk innovation by "using the originality and excitement of the people that run those companies to find new molecules, at which point [large companies] will buy them."[85] For Richmond, SMEs signalled an "evolution of 'big Pharma,' which is the setting up of their out-of-house research activities, but under control, ..."[86] One year later, AstraZeneca's former Global Project Director Keith J. Williams similarly observed that SMEs were filling niches left by larger companies, but that loss of expertise in end-to-end development and "raising capital and finding major companies prepared to invest in clinical development will be a challenge."[87]

Williams' and Richmond's comments point to the high-risk, high-return business model at the heart of SME-based innovation.[88] As described by social scientists Kaushik Sunder Rajan and Victor Roy, SME-led biotech R&D often involves passing ownership over a small number of knowledge assets from one investor to another. Some companies retain control of IP and raise capital via successive investment rounds in the hope of out-licensing or selling assets to a big pharmaceutical company. To successfully raise capital and reach an eventual buyout, SMEs need to continuously project assets' increasing earning potential for investors. Patents and market exclusivity do not merely function to recoup R&D outlays via eventual product sales, but as tradable monetised assets whose downstream rent and value evolution is speculated upon. In other words, speculation on a treatment's future worth is what defines its value in the present.[89] SME attrition in this speculative—or assetised—innovation ecology is high.[90] Promising compounds can be lost behind IP walls if companies fail, and there is a temptation to (over)emphasise compounds' projected earnings in line with investor expectations for continuous value evolution (see Part Five).

5. Part Four: a directed ecosystem

Stabilising and reinvigorating the increasingly volatile antibiotic innovation ecosystem became subject to a profound governance shift towards public interventionism from 2010. This shift coincided with surging Gram-negative resistance and a globalisation of AMR discourse, which no longer saw AMR as a problem that could be mitigated via HIC stewardship alone.[91] In line with the 2015 WHO Global Action Plan's renewed call for "incentives for innovation," the empty pipeline metaphor functioned as the structuring principle for an increasingly directed "public–private" innovation ecology, whose various initiatives were subject to geopolitical contestation.[92]

[84] Alas Portillo 2025.
[85] Tansey and Reynolds 2008, 58.
[86] Tansey and Reynolds 2008, 58.
[87] Williams and Bax 2009, 159; see also Williams and Hurst 2013.
[88] Gleadle et al. 2014.
[89] Rajan 2017, 38–44; Roy 2020, 3; 2023, 40-50; see also Lazonick and Tulum 2011.
[90] Birch and Muniesa 2020, 1–2; Roy 2020, 90.
[91] Alas Portillo et al. 2024b, 50–56, 58; Gradmann and Kirchhelle 2023; Overton et al. 2021.
[92] WHO 2015, 4.

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Nearly all early innovation initiatives were based on PPPs and targeted pre-registration R&D stages (Figure 8 in Supplementary Appendix Page 2). Although public–private sector collaboration had long been common, the 1990s saw PPPs emerge as a formal policy tool for private sector delivery of public infrastructure and services.[93] In Global Health, PPPs gained traction due to inefficiency allegations against international organisations, successes in vaccine, tuberculosis, and malaria R&D, and PPPs' popularity amongst HIC decision-makers and funding bodies, which were often headed by former industry executives or originated in pharmaceutical companies.[94]

Antibiotic PPPs emerged on both sides of the Atlantic (Timeline Figure 7 in Supplementary Appendix Page 1). While the TB Alliance (est. 2000) was the first antibiotic PPP, the European Union's (EU) Innovative Medicines Initiative injected significant capital into broader antibiotic research programmes and PPPs between 2008 and 2021.[95] In the United States, the Obama administration also favoured PPPs. From 2010, the Biomedical Advanced Research Defence Authority (BARDA), which had initially focused on stockpiling critical antibiotics, also started subsidising research on new antibiotics relevant to national security.[96] Funded by BARDA, with contributions from the Wellcome Trust, the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) was established to bridge gaps between basic research and clinical development in 2016. CARB-X provides developers with non-dilutive investment and advice from former industry experts to "push" compounds through early development stages.[97] Emulating regulations for neglected diseases, U.S. officials also introduced the Limited Population Pathway for Antibacterial and Antifungal Drugs to reduce regulatory burdens and speed licensing in 2016.[98]

Having previously resisted state intervention, pharmaceutical companies formed consortia to steer PPP debates and lobby for further public investment. Distinct platforms emerged for SMEs and for larger companies (Figure 8 in Supplementary Appendix Page 1), with the BEAM alliance representing EU SME interests and the AMR Industry Alliance representing a coalition of larger and smaller commercial enterprises.[99] New joint funding initiatives resulted from these efforts. In 2020, the industry- and EU-funded AMR Action Fund set out to bring two to four antibiotics to market by 2030 and "facilitate needed long-term policy solutions."[100]

Surging public investment occurred amidst political tensions about financing models. As highlighted by participants of our 2024 witness seminar, senior WHO officials had seen AMR as an opportunity to breathe new life into plans for a proposed global R&D fund and generate support for a PDP for antibiotics.[101] Although frequently used interchangeably with PPPs, PDPs emerged around 2000 as a new form of non-governmental R&D. PDPs function as non-profit intermediary hubs to develop and widen access to health products via targeted service partnerships with industry.[102] Despite finding a receptive audience amongst officials

[93] Custos and Reitz 2010, 562–64.
[94] Abbott 2016; Chabrol and Gaudillière 2023, 40–50; Cueto, Brown, and Fee 2019, 285–89; de Bengy Puyvallée 2024, 26–27.
[95] Paterson 2025
[96] Alas Portillo et al. 2024b, 29–31, 55, 74–75.
[97] CARBX 2022.
[98] FDA 2020.
[99] Alas Portillo et al. 2024b, 52–53; Beam Alliance 2025; AMR Alliance 2020; Repair Impact Fund 2025.
[100] European Investment Bank 2020.
[101] Alas Portillo et al. 2024b, 53–57.
[102] Abbott 2016, 30–31, 37.

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planning Germany's 2014–2015 G7 Presidency, the WHO plan failed to make it onto the official policy agenda due to competing national innovation concepts.[103]

Britain, in particular, advocated a more incentives-focused approach. Under Prime Minister David Cameron, AMR had emerged as a foreign policy priority in which the United Kingdom could assert leadership. In addition to financing stewardship and surveillance via the Fleming Fund (2015-2025), British efforts focused on "fixing" the antibiotic pipeline. This emphasis was supported by influential AMR "policy entrepreneurs," Chief Medical Officer (2010–19) Sally Davies, and Wellcome Trust Director (2013–23) Jeremy Farrar.[104] In her 2011 annual report, Davies' described the dearth of novel antibiotics as a "market failure" to be overcome by public investment commensurate to societal value: "If we are to secure a 'pipeline' of new antimicrobial drugs for the future, then we must align the private and societal risks, and the costs and benefits of research and development of these agents."[105] In 2014, Davies prompted Cameron to commission Goldman Sachs economist Jim O'Neill to calculate AMR's economic burdens, propose solutions, and galvanise action. Based in Wellcome Trust headquarters, the final O'Neill Review was submitted in 2016 prior to the first UN high-level meeting on AMR.[106]

At our 2024 witness seminar, key stakeholders, including senior former WHO officials, noted that the British desire to maximise attention for the O'Neill Review was one reason why no AMR R&D fund made it onto Germany's G7 policy agenda.[107] A second reason highlighted by several witnesses was a preference from U.K.—and U.S.—actors for fiscal investment incentives, like those proposed by the O'Neill Review, over more direct market interventions.[108] This was also true for influential funders, such as the U.K.-based Wellcome Trust, described by witnesses as "industry-friendly," who had opposed WHO R&D Treaty plans and instead favoured fiscal incentives for industry to take action.[109] Witnesses' memories align with political economists' contrast of an Anglo-American shareholder value-based liberal market economy versus a more interventionist German coordinated market economy model based on investment in corporatist partnerships.[110] Reflecting on differences around 2015, witnesses emphasised that "political ownership matters": despite there being "two super-committed governments… the two most committed European governments could not agree on what they would actually do."[111]

In 2016, Anglo-American funders and governments thus invested in CARB-X's PPP model with BARDA cumulatively providing $200 million, the Wellcome Trust $155 million, and U.K. agencies £21.1 million by 2023. In contrast, Germany became the primary early sponsor of the WHO-founded PDP, the Global Antibiotic Resistance Development Partnership (GARDP), providing €116.8 million (60% of cumulative funding by 2023) (Figure 4, and Figure 9 in Supplementary Appendix Page 2). While official Anglo-German push-funding differences gradually subsided, Germany remains GARDP's largest sponsor. Meanwhile, the

[103] Alas Portillo et al. 2024b, 53–54.
[104] Rubin and Baekkeskov 2023, 194.
[105] Davies 2011, 20.
[106] AMR Review 2016; Rubin and Baekkeskov 2023, 196.
[107] Alas Portillo et al. 2024b, 53–54.
[108] AMR Review 2015; 2016, 52–59.
[109] Alas Portillo et al. 2024b, 69; KEI-Online 2012b; some commentators have drawn attention to potential conflicts of interest resulting from philanthropic funders' advocacy for incentives in markets in which they hold stakes. Schwab 2021.
[110] Deeg 2012.
[111] Alas Portillo et al. 2024b, 54.

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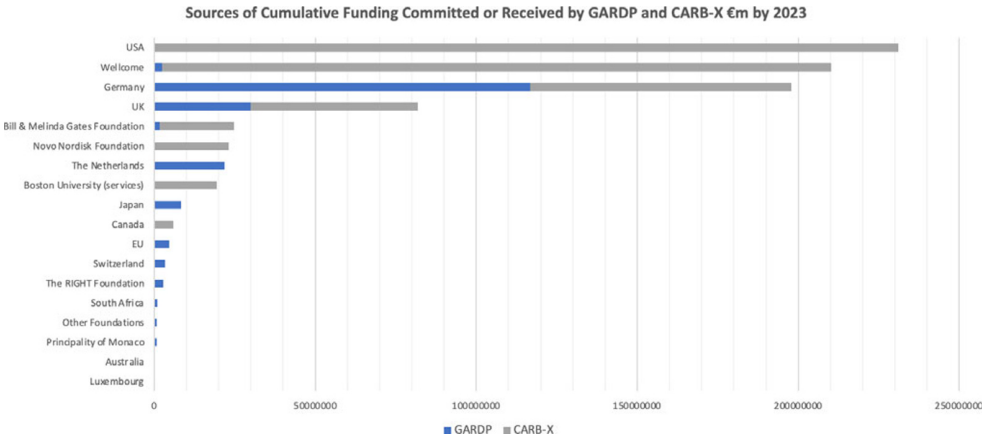

Figure 4. GARDP and CARB-X cumulative funding sources (2016–23, € million).
Source: GARDP and CARB-X 2023 reports. CARB-X funding reported in USD/GBP converted to Euros using the 2023 average exchange rate from http://www.ofx.com.
Note: Chart displays funds received since inception and commitments announced by 2023, including those made for future periods up to 2027. Not shown is a potential additional commitment to CARB-X from BARDA of $300 million 2022–32. More information is available at https://gardp.org/publications/annual-report-2023/; https://carb-x.org/wp-content/uploads/2024/07/CarbX_AnnualReport_FINAL-compressed.pdf; https://carb-x.org/partners/funding-partners/; and https://carb-x.org/wp-content/uploads/2023/05/2023-0502-CARBX-annual-report-combined-sm.pdf (accessed April 25, 2025).

U.S. and philanthropic (Wellcome Trust, Gates Foundation, and Novo Nordisk Foundation) foundations have continued to nearly exclusively support CARBX (Figure 4).

Disagreement over funding models also arose regarding accelerating calls for market-shaping post-registration "pull"-incentives (Figure 5).[112] In 2012, the United States introduced the Generating Antibiotic Incentives Now (GAIN) Act, which extended nonpatent market exclusivity for Qualified Infectious Disease Products by five years. Although the GAIN Act prompted some SMEs to reinvestigate off-patent drugs, its perceived failure to regalvanise R&D by larger companies prompted calls for more ambitious market entry rewards (MERs).[113] MERs advocacy was often linked to the concept of "delinkage" (Figure 5). Delinkage had initially evolved around 2000 as a way to improve LMIC drug access by delinking drug prices in poorer countries from companies' R&D outlays and pricing in HICs.[114] In the AMR space, delinkage became a way to reconcile formerly distinct stewardship and industry profitability concerns (Part Two) by delinking profits from volume of sales and extending the concept of value-based pricing (Part Three).[115] Health systems would try to simultaneously stimulate innovation and avoid overmarketing by using MERs or subscriptions to reimburse patent holders for novel antimicrobials' projected societal worth rather than via traditional product sales.[116]

The concept of "pulling" compounds through the "empty pipeline" via incentives such as MERs again proved most popular in the United Kingdom. Between 2014 and 2015, London's

[112] Årdal et al. 2018.
[113] Alas Portillo 2025; Darrow and Kesselheim 2020, 1.
[114] Alas Portillo et al. 2024b, 28, 37–38, 44, 54; KEI-Online 2012a.
[115] Darrow and Kesselheim 2020; Abbott 2016, 40.
[116] Duke-Margolis Center 2016, 4–5.

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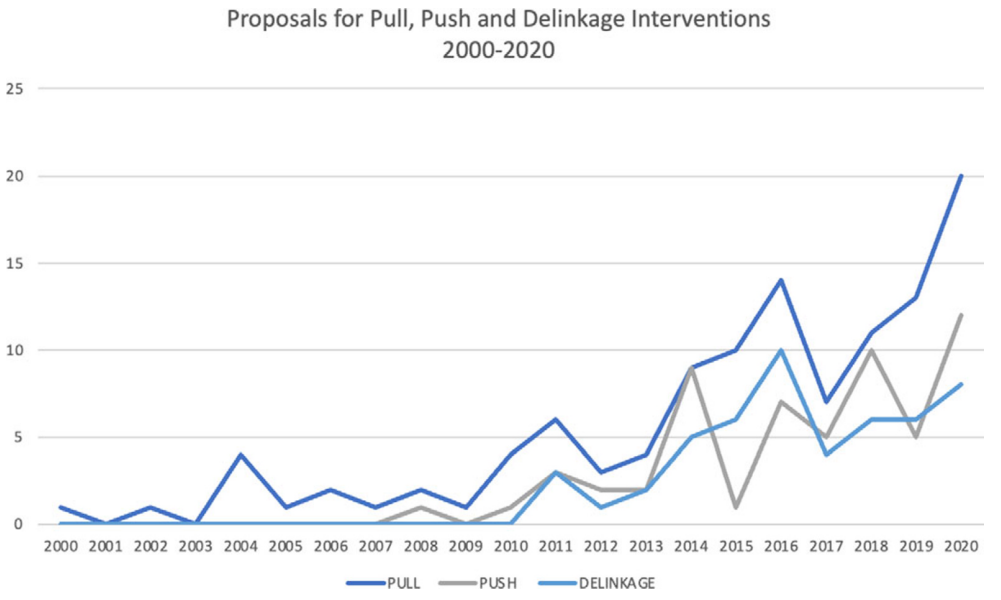

Figure 5. Mentions of pull (n=114), push (n=58), and delinkage (n=51) in the coded innovation literature (2000–20). Some articles mention multiple intervention categories.

Royal Institute of International Affairs (Chatham House) proposed a delinked business model for antibiotics.[117] Following similar MERs proposals in the 2016 O'Neill Review, then Wellcome Trust Director Jeremy Farrar highlighted the need for "finding creative new models to stabilise the antibiotics market and stimulate private-sector innovation without exposing public funders to all the risk."[118] In the same year, the United Kingdom embarked on a policy experiment, which paid industry for access to, rather than use of, compounds for very drug-resistant infections.[119] U.K. officials expanded their subscription scheme in 2024 by committing to pay fees of up to £1.9 billion over sixteen years for new antibiotic drugs.[120] Since then, significant advocacy has focused on convincing other countries to develop additional pull incentives with frameworks estimating a "fair share" contribution from HICs.[121] In contrast to the fully delinked U.K. model, pull proposals in the EU and United States are based on blended public–private contributions and conventional market-based structures.[122] In the EU, the introduction of Transferable Exclusivity Vouchers would see companies rewarded for the development of novel antimicrobials by market exclusivity extensions transferable to lucrative drugs (Transferable Exclusivity Extensions).[123] These could either be applied to an in-house drug or sold to another company. In the United States, the PASTEUR Act would lead to subscription contracts with individual companies.[124] However, at the time of writing, both initiatives remain stalled in the legislature.

Varying innovation cultures may again be at play. According to a witness at the 2024 seminar, U.K. funders were convinced "that if they only lobby enough for pull incentives the

[117] Chatham House Working Group on New Antibiotic Business Models 2015; Holmes 2014.
[118] Farrar 2019; AMR Review 2016, 6, 54–58.
[119] Sweden launched a subscription scheme to secure access to existing drugs on a small market in 2020.
[120] Duddy 2024; Glover et al. 2023.
[121] Outterson 2022; Goh et al 2025.
[122] Årdal et al. 2021.
[123] EFPIA 2022.
[124] H.R. 8920—116th Congress 2020; IDSA 2020.

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industry is going to fix the problem," whereas "the Germans wanted to put public money into something which is real, and they can touch."[125] Critics have also highlighted that pull incentives by themselves are no magic bullet. Focusing on the PASTEUR Act, the Médecins Sans Frontières Access initiative warned that poorly designed HIC pull-incentives can detrimentally impact drug access in LMICs by redirecting constrained global drug supplies and raising prices in other markets.[126] In the context of HICs, proposed transferable exclusivity extensions may lead to European health systems overpaying for antibiotic innovation via higher reimbursement for other important drugs.[127] In the US, the PASTEUR Act's intended cap on antibiotic sales may impede domestic access by raising prices for patients not covered by Federal procurement mechanisms.[128] Scholars have also warned that paying private companies for access rather than use of drugs is vulnerable to political challenges.[129] Others have highlighted that investing in open innovation and public antibiotic development may be cheaper than financing market-shaping incentives for proprietary innovation.[130] Indeed, a recent study on the German pull mechanism found that Germany would either need to increase volumes of antibiotics covered or increase prices by as much as 3.3 times to provide a de-linked revenue model for proprietary developers.[131]

Despite the outlined criticism, the past fifteen years have nonetheless seen remarkable HIC consensus on the need to "fix" the "broken antibiotic market." While some advocates claim that existing incentives only provide a fraction of funding needed, over $2 billion of public and philanthropic investment already targeted antibiotic innovation between 2017 and 2023.[132] In parallel, a heterogeneous public funding system has evolved to cover nearly all aspects of the "empty pipeline" from pre-clinical development to post-registration income. The pipeline metaphor has also enabled funders and developers to stake out remits. An informal division of labour has emerged with CARB-X funding earlier stages of development, GARDP de-risking more advanced development and access projects, and WHO trying to direct R&D with its priority pathogens list (est. 2017) and pipeline reviews (est. 2018).[133] So far, however, pipeline fixes have not restored self-sustained commercial innovation but have dramatically expanded public intervention and created a "transnational bureaucracy" of non-governmental entities disbursing significant public and philanthropic funds.[134] Meanwhile, core drivers of R&D fragility and precarious antibiotic access remain unresolved.[135]

6. Part Five: divergent values

The most recent 2024 WHO review concludes that antibiotic innovation remains insufficient to meet public health needs.[136] Meanwhile, the R&D exodus of large companies, such as Novartis, AstraZeneca, Sanofi, and Johnson & Johnson, has continued.[137] The remaining

[125] Alas Portillo et al. 2024b, 54.
[126] MSF Access Campaign 2024.
[127] Årdal et al. 2024.
[128] MSF Access Campaign 2024.
[129] Dutescu and Hillier 2021.
[130] Glover et al. 2021; Todd 2019.
[131] McEnany and Outterson 2024, 1, 9.
[132] Global AMR R&D Hub 2025.
[133] Piddock et al. 2024; WHO 2017; 2018.
[134] de Bengy Puyvallée 2024, 26; Abbott 2016, 36–42.
[135] Wells, Nguyen, and Harbarth 2024a; Zhang 2023.
[136] WHO 2024a, xvii.
[137] Shlaes 2019.

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large companies have licensed a limited number of compounds, such as Avycaz (ceftazidime/avibactam, Pfizer, 2015), Fetroja (cefdicerol, Shionogi, 2019), Recarbrio (imipenem/cilastatin/relebactam, Merck, 2019), and Gepotidacin (GSK, 2025).[138] However, molecular innovation remains limited, with 10 of 13 U.S.-licensed traditional antibiotics between 2017 and 2023 belonging to classes for which AMR is known. Rather than fixing the "broken" pipeline, fifteen years of end-to-end incentives and subsidies have mostly stabilised an innovation ecosystem dominated by volatile "micro" or "small" companies with limited molecular portfolios.[139] Worryingly, every SME with approval for its compounds has suffered bankruptcy or unfavourable market exit since 2010.[140]

The high-profile 2019 bankruptcy of SME Achaogen illustrates that proposals to incentivise innovation, for example, by providing one-off payments at registration, may be inadequate to support sustainable patient access or survival of SMEs critical to novel antibiotic development. Achaogen adapted an aminoglycoside compound, sisomicin, discovered in 1970 by Bayer. In 2009, the company began trials of its sisomicin analogue, Zemdri (plazomicin), against complicated urinary tract infections (cUTIs) before achieving fast-track licensing in 2018 as a "breakthrough therapy" under the GAIN Act. Achaogen mobilised push investment, largely from BARDA and U.S. biosecurity agencies. Private investor interest was garnered with a 2014 forecast that plazomicin would generate $63 million per annum in the United States and additional EU royalties of $3 million.[141] Estimating approximately $15,000 incremental cost per U.S. hospital patient of antibiotic-resistant HAIs, the market entry price was $4,955 per treatment course.[142] This proved overambitious in a market where existing alternative treatments cost between $21 (polymyxin B) and $56 (colistin) per day.[143] Failure to gain FDA approval for Carbapenem-resistant Enterobacterales further constrained earning potential. Generating only $0.8 million of sales in 2018, Achaogen filed for bankruptcy in 2019, wiping out almost $800 million of investment.[144]

Plazomicin was subsequently criticised for providing limited clinical benefits over existing cUTI treatments and, to date, has only been reintroduced to India.[145] However, during a time of strong support for push/pull incentives, this did not prevent Achaogen from attracting significant public and private investment at every R&D stage. In a 2020 interview, Achaogen's Ryan Cirz noted: "We got everything right, and it still don't work."[146] This was correct —at least regarding SMEs' assetised business model.

As the case of Achaogen and other SME failures shows, the income new antibiotics can realistically generate had become incommensurable with the speculative dynamics shaping a compound's supposed commercial worth and earning potential.[147] According to social scientists, antibiotics constitute an essential infrastructure propping up the basic functioning of global health and food production systems.[148] Although improved countermeasures, such as infection control and stewardship, will hopefully reduce antibiotic

[138] Outterson et al. 2022.
[139] WHO 2024a, xvii, 2024b, 2024c.
[140] McEnany and Outterson 2024.
[141] Wells, Nguyen, and Harbarth 2024a, 4.
[142] Althobaiti et al. 2023, 12.
[143] Clancy et al. 2019, 6.
[144] Wells, Nguyen, and Harbarth 2024a, 6.
[145] CIPLA 2024; ReACT 2021.
[146] Anon. 2020.
[147] Wells, Nguyen, and Harbarth 2024a.
[148] Chandler 2019; Kirchhelle et al. 2020.

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dependency, continuous access to affordable and effective antibiotics will remain a prerequisite for human and animal health.[149] Similar to other essential services, such as water or electricity, where value-based pricing is capped to ensure access, there is also a cap on what societies can afford to pay for the perpetual and equitable renewal of antibiotic infrastructures in the face of AMR.[150] This cap poses an ultimately unsolvable problem for an assetised mode of R&D dependent on investors and companies seeking open-ended earning potential from anti-infective innovation. It also lends credence to calls by social scientists and development economists to treat essential medicines such as antibiotics as a commons requiring access and reimbursement mechanisms beyond the "classic commodity framework" underpinning HIC drug development.[151]

MERs and delinked value-based reimbursement seemingly provide a solution to the increasing divide between public health and market values. If, as in the case of daptomycin, health systems are willing to pay high prices, then the innovation system works (see Part Three). However, profit expectations change over time. In 2000, a drug expected to generate approximately $500 million per annum would have been considered a worthwhile investment.[152] This estimate has long changed: in 2016, revenues of the top cancer drug totalled more than all antimicrobials combined, while two semaglutides, Ozempic and Rybelsius, generated $17.8 billion for Novo Nordisk in 2023.[153] Although prices for novel antimicrobials have increased significantly since 2010, they remain an order of magnitude below other drugs: Teflaro (licensed 2010) and Nuzyra (licensed 2018) only generated between $66.4 and $58 million in the first nine quarters after registration (Figure 6).[154]

To remain attractive to executives considering the opportunity cost of allocating capital, MERs need to evolve accordingly. In 2016, the O'Neill Review calculated an $800 million to $1.3 billion partially delinked MER for a new antimicrobial meeting unmet need.[155] One year later, another group calculated $1–2.5 billion per drug in a fully delinked scheme spread over multiple years.[156] By 2022, another estimate for a fully delinked subscription amounted to $2.2–4.8 billion for ten years per drug.[157] Although some of the described rise can be explained by changing push-incentive estimates, mobilising even a fraction of these ever-increasing pull-incentives is challenging amidst failing multilateralism and health systems stress. By failing to address underlying business models, it will also do little to overcome the assetised market dynamics contributing to the fragmentation of the historic R&D ecosystem (Part One).

7. Part Six: access as innovation

Almost twenty-five years after the WHO's 2001 Strategy on AMR, it moreover remains unclear how much incentives-based attempts to fix the empty antibiotic pipeline will benefit LMICs.[158] Similar to other areas of AMR governance, LMIC voices have often been

[149] Varadan et al. 2024.
[150] Lafrance 2024.
[151] Baxerres and Cassier 2021, 285.
[152] Skender 2024, 6.
[153] Duke-Margolis Centre 2016, 3; Novo Nordisk 2023.
[154] Laxminarayan et al. 2024, 2541; Sertkaya and Franz 2022, sec. 6.2.1.
[155] AMR Review 2016, 54.
[156] Årdal et al. 2017, 1381.
[157] Outterson 2022, Slide 9.
[158] WHO 2001.

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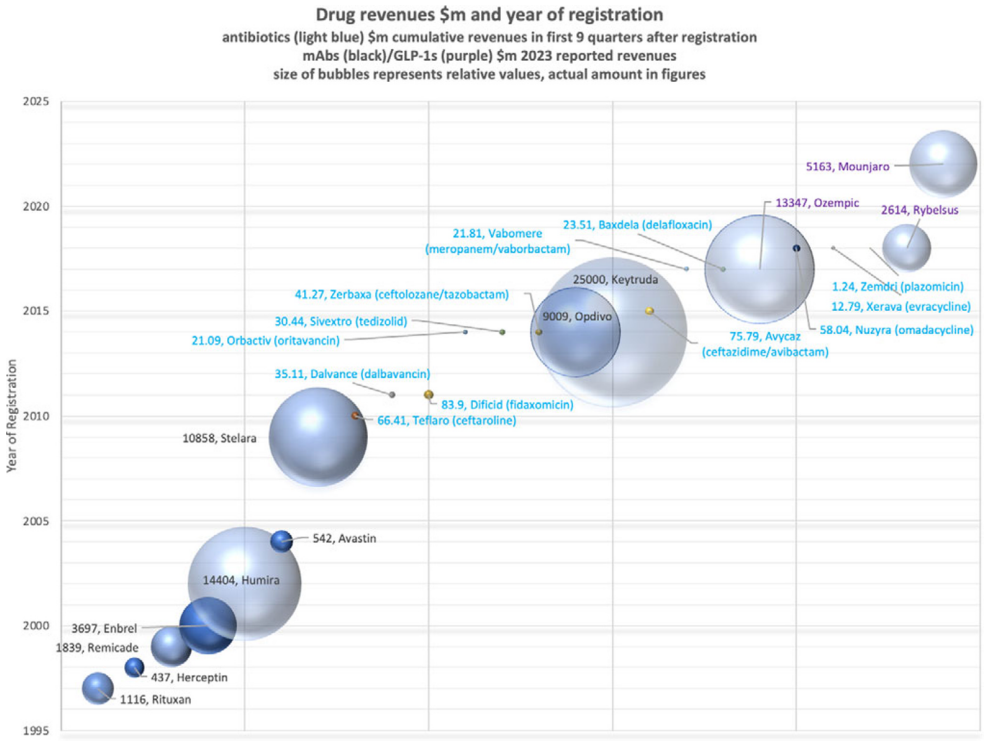

Figure 6. Comparison of antibiotic and non-antibiotic drug revenues by year of registration.
Source: Antibiotic revenues from "Antimicrobial Drugs Market Returns Analysis: Final Report, Office of the Assistant Secretary for Planning and Evaluation (ASPE), 2022," mAbs and GLP-1 revenues from company reports 2023. Novo Nordisk revenues in Danish Krone converted to USD using the 2023 average exchange rate from http://www.ofx.com.
Note: The bubble size reflects the relative revenues, and the number represents the drug revenues ($millions), followed by the name of the drug.

absent from relevant fora (Part Two).[159] Instead, global R&D frameworks and incentives-based interventions have been shaped by HIC priorities and values. In line with the pipeline metaphor's deficit imaginary, this means that innovation has often been framed as creating, rather than widening, access to novel molecular entities. It also means that international policy frameworks have often not adequately engaged with non-HIC R&D models.

The public health importance of improving global access to antimicrobials has regularly been referenced since the first WHO Global Strategy on AMR in 2001.[160] Access considerations have also been embedded in PPP and PDP frameworks. CARB-X mandates that each company receiving funding must plan how their product will be accessible.[161] Meanwhile, a major focus of GARDP's work lies in making older and new drugs available in LMICs. Announced in 2022, a DNDi-inspired landmark agreement between GARDP and Japanese company Shionogi is designed to make cefiderocol (brand name: Fetroja) available via sublicensed manufacturing in a large range of countries (n = 135) at risk of delayed or no

[159] Gradmann and Kirchhelle 2023; Overton et al. 2021.
[160] WHO 2001.
[161] CARBX 2021, 5.

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access.[162] However, putting manufacturing agreements in place can be challenging, and so far, no other large R&D companies have introduced similar schemes. Meanwhile, the dominance of assetized SME-based R&D (Part Five) means that lucrative HIC markets—particularly the United States—remain the main targets of innovation.[163] According to the most recent WHO Pipeline review, around 90% of preclinical development is occurring in WHO Europe and Americas regions.[164] This divide has increased over recent years, with the number of drugs targeting LMICs and low-income countries either decreasing or flatlining despite an overall increase in R&D.[165] The ongoing geographic R&D bias (see Part Two) not only drives up price points, but also means that many newer antibiotics are designed without considering LMIC constraints (e.g., requiring cold chains and parenteral administration), which further restricts access to treatment.[166] Prioritising molecular innovation over access and supply chain security can also have negative consequences for HIC patients. In 2023, a U.S. Senate hearing revealed that "between 2021 and 2022, drug shortages increased by approximately 30 percent" with stockouts also impacting European patients.[167] Supply chain resilience for both old and new antibiotics is likely to be further strained by contemporary trade wars.[168]

Other countries have prioritised direct state investment over incentives-based innovation. Having established dominance of global active pharmaceutical ingredient production since the 1990s, the Chinese State has used direct investment to implement a series of policy projects to enhance drug discovery.[169] In 2008, a National Mega-Project for Innovative Drugs was implemented, supporting over 3,000 development pathways by 2020, including for emerging antibiotic resistant infections and multidrug-resistant tuberculosis (MDR-TB).[170] By 2022, Chinese R&D represented 20% of the global innovation pipeline, ranked second only to the United States, with three Chinese companies in the top 25.[171] Although many compounds are derivatives of existing molecules, 17 new antibiotics are currently at different clinical development stages, primarily focused on WHO priority pathogens and/or MDR-TB.[172] In contrast to HICs' focus on "repairing markets" via fiscal incentives, joint focus on using state policy and investment to steer manufacturing and innovation is making China critical to global innovation and supply, although some scholars speculate that China may eventually need a subscription model to cover return on investment for both generic and R&D companies.[173]

The rise of MIC pharmaceutical manufacturing and biotechnology expertise points to the role direct investment, state-owned companies, and long-term national planning can play in creating innovation ecosystems that are less reliant on HIC R&D companies or financial markets. This does not mean that MIC innovation will necessarily translate into more equitable global drug access. Indeed, it is unlikely that any one-size-fits-all R&D model will work across different bio-geographies and socio-economic contexts. Similar to the

[162] GARDP 2023.
[163] Outterson et al. 2022.
[164] WHO 2024b.
[165] WHO 2024c.
[166] Adeoye et al. 2025.
[167] U.S. Senate Committee on Homeland Security and Governmental Affairs 2023, 5.
[168] Murphy 2025; Oehler and Gompf 2020; Wells et al. 2024b.
[169] Kong et al. 2023.
[170] PhIRDA 2021.
[171] Lloyd 2023.
[172] Zhang et al. 2024.
[173] Husain, Hu, and Huang 2024; Yang et al. 2024.

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diversified vaccine R&D and manufacturing called for in the International Pandemic Agreement, some scholars have therefore proposed using current HIC incentives to build antimicrobial innovation and manufacturing hubs in underserved parts of the world.[174] Others have suggested diversifying HIC R&D cultures via new trial regulations, open access innovation, and further valorising the repurposing of older off-patent compounds.[175] While analysing or adding to this list is beyond the scope of our historical review, enabling local populations to shape R&D priorities seems a logical way of ensuring that access is the actual target of innovation. It also entails abandoning unhelpful one-size-fits-all approaches to drug innovation.

8. Conclusion: beyond the pipeline

As our historical review shows, the accelerating divide between what a compound must be worth to be considered financially worthwhile and its actual public health value points to a flaw at the heart of the "empty pipeline" metaphor: postwar antibiotic innovation ecosystems did not dissolve because global antibiotic markets broke, but because assetized markets broke them.

Following the rupturing of integrated R&D systems during the 1980s, the rise of the pipeline metaphor during the mid-1990s strategically reframed an emergent public health challenge as an incentives problem. The metaphor's narrow focus on unidirectional molecular innovation and focus on technical solutions suited contemporary Global Health philosophies and industry interests. However, it failed to capture the diverse world of mid-century R&D, which included non-linear R&D flows within and between public and private development sites, as well as distinct innovation cultures beyond HICs. Emphasis on "broken" antibiotic markets also reduced proposed solutions to a question of fiscal stimuli. Doing so glossed over the eroding speculative dynamics of financial markets themselves—with larger firms' exit increasing reliance on SMEs for innovation and SME dependence on speculative investment for survival.[176] Despite disagreeing on finance models, public funders have mostly accepted the empty pipeline metaphor with PPPs and PDPs designed to work within the presumed pipeline rather than rethink it. Meanwhile, delinkage has emerged as a key concept to reconcile stewardship and profitability concerns by expanding value-based reimbursement and satisfying investor demand for downstream earning potential (Figure 10 in Supplementary Appendix Page 3).[177]

Current HIC incentives will undoubtedly lead to a limited number of new compounds. However, the volume of existing R&D is unlikely to satisfy the global need for sustained and accessible antibiotic innovation.[178] Although most PPPs and PDPs incorporate access conditions, the prioritisation of HIC needs by global R&D appears to be increasing rather than decreasing.[179] Meanwhile, rising supply chain vulnerabilities for both old and new drugs remain unaddressed.[180] As global health funding and multilateralism falter, decision-makers have the chance to rethink and diversify core parts of their innovation and access strategies

[174] Mishra 2025; Glover et al. 2021.
[175] Abavisani et al. 2025; Cassir, Rolain, and Brouqui 2014; Klug et al. 2021; Singer, Kirchhelle, and Roberts 2020.
[176] Gleadle et al. 2014, 66–67.
[177] Abbott 2016, 37.
[178] Czaplewski et al. 2025; WHO 2024a.
[179] Adeoye et al. 2025; WHO 2024c.
[180] Skender and Zhang 2024.

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—including learning from non-HIC systems. A more diverse and equitable innovation era may lie beyond the self-imposed limits of the "empty antibiotic pipeline" imaginary.

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References

Abavisani, Mohammad, Alireza Khoshrou, Souzan Eshaghian, Sercan Karav, and Amirhossein Sahebkar. 2025. "Overcoming Antibiotic Resistance: The Potential and Pitfalls of Drug Repurposing." *Journal of Drug Targeting* 33 (3): 341–67. https://doi.org/10.1080/1061186x.2024.2424895.

Abbott, Frederick M. 2016. "Public–Private Partnerships as Models for New Drug Development: The Future as Now." In *The Cambridge Handbook of Public–Private Partnerships, Intellectual Property Governance, and Sustainable Development*, edited by Margaret Chon, Pedro Roffe, and Ahmed Abdel-Latif. Cambridge University Press, pp. 29–45.

Abbvie Investors. 2022. "Abbvie Reports Full Year and Fourth Quarter Financial Results." *Abbvie Investors.* https://investors.abbvie.com/news-releases/news-release-details/abbvie-reports-full-year-and-fourth-quarter-2022-financial. Accessed June 20, 2025.

Beam Alliance. 2025. https://beam-alliance.eu/overview/. Accessed June 20, 2025.

Adeoye, Marvellous O., Tochukwu C. Agboeze, Joseph A. Adegoke, and Iruka N. Okeke. 2025. "Beyond High Cost: Pharmaceutic Low-Resource Setting Barriers to Antibacterial Access." *PLOS Global Public Health* 5 (3): e0004280. https://doi.org/10.1371/journal.pgph.0004280.

Alas Portillo, Mirza. 2025. "How the Pipeline Ran Dry: Towards a Critical Historiography of the Antibiotic Pipeline (1980–2020)." PhD diss., School of History, University of Dublin.

Alas Portillo, Mirza, Isabel M. Gómez Rodríguez, Christoph Gradmann, Claas Kirchhelle, Jørgen J. Leisner, Laura D. Martinenghi, Erin L. Paterson, et al. 2024a. "Paradoxes of the Antibiotic Pipeline." *Humanities and Social Sciences Communications* 11 (1): 1–4. https://doi.org/10.1057/s41599-024-03211-1.

Alas Portillo, Mirza, Erin Lindsay Paterson, Nadya Wells, Frédéric Vagneron, and Claas Kirchhelle. 2024b. *Emerging Financial Models for Antibiotic Development (2000–2016). Witness Seminar Conducted by the Dryap Project and in Collaboration with the Global Health Centre, Geneva Graduate Institute*. Strasbourg: Dry AP Project. https://repository.graduateinstitute.ch/record/319326?ln=en&v=pdf. Accessed June 20, 2025.

Althobaiti, Hana, Enrique Seoane-Vazquez, Lawrence M. Brown, Marc L. Fleming, and Rosa Rodriguez-Monguio. 2023. "Disentangling the Cost of Orphan Drugs Marketed in the United States." *Healthcare* 11 (4): 558. https://doi.org/10.3390/healthcare11040558.

Amabile-Cuevas, Carlos F. 2010. "Global Perspectives of Antibiotic Resistance." In *Antimicrobial Resistance in Developing* Countries, edited by Aníbal de J. Sosa, Denis K. Byarugaba, Carlos F. Amábile-Cuevas, Po-Ren Hsueh, Samuel Kariuki, and Iruka N. Okeke. Springer, pp. 3–13.

AMR Industry Alliance. 2020. *AMR Industry Alliance—2020 Progress Report*. AMR Industry Alliance. https://www.amrindustryalliance.org/wp-content/uploads/2020/01/AMR-2020-Progress-Report.pdf. Accessed June 20, 2025.

AMR Review. 2015. *Securing New Drugs for Future Generations: The Pipeline of Antibiotics. The Review on Antimicrobial Resistance. Chaired by Jim O'neill*. The Review on Antimicrobial Resistance. https://amr-review.org/sites/default/

files/SECURING%20NEW%20DRUGS%20FOR%20FUTURE%20GENERATIONS%20FINAL%20WEB_0.pdf. Accessed June 20, 2025.

AMR Review. 2016. *Tackling Drug-Resistant Infections Globally: Final Report and Recommendations*. The Review on Antimicrobial Resistance. https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf. Accessed June 20, 2025.

Anderson, Michael, Dimitra Panteli, and Elias Mossialos. 2023. *How Can the EU Support Sustainable Innovation and Access to Effective Antibiotics? Policy Options for Existing and New Medicines*. World Health Organization EURO. https://iris.who.int/bitstream/handle/10665/369638/Policy-brief-51-1997-8073-eng.pdf?sequence=2. Accessed June 20, 2025.

Anon. 2004a. "Infectious Diseases." *Nature Reviews Drug Discovery* 3 (7): S26–32. https://doi.org/10.1038/nrd1409.

Anon. 2004b. "Data Show Zyvox Is More Effective Compared to Vancomycin for the Treatment of Presumed MRSA Skin Infections." *Infection Control Today*, October 4. https://www.infectioncontroltoday.com/view/data-show-zyvox-more-effective-compared-vancomycin-treatment-presumed-mrsa. Accessed June 20, 2025.

Anon. 2020. "'A Crisis': Why Do Antibiotics Companies Keep Going 'Belly Up'?" *Advisory Board*. https://www.advisory.com/daily-briefing/2020/01/15/new-antibiotics. Accessed June 20, 2025.

Årdal, Christine, Enrico Baraldi, Reinhard Busse, Rosa Castro, Francesco Ciabuschi, José Miguel Cisneros, Inge C. Gyssens et al. 2024. "Transferable Exclusivity Voucher: A Flawed Incentive to Stimulate Antibiotic Innovation." *The Lancet* 403 (10422): e2–4. https://doi.org/10.1016/s0140-6736(23)00282-9.

Årdal, Christine, David Findlay, Miloje Savic, Yehuda Carmeli, Inge Gyssens, Ramanan Laxminarayan, Kevin Outterson, and John H. Rex. 2018. *Revitalizing the Antibiotic Pipeline: Stimulating Innovation While Driving Sustainable Use and Global Access*. Drive-AB. https://drive-ab.eu/wp-content/uploads/2018/01/CHHJ5467-Drive-AB-Main-Report-180319-WEB.pdf. Accessed June 20, 2025.

Årdal, Christine, Yohann Lacotte, Suzanne Edwards, Marie-Cécile Ploy, and European Union Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI). 2021. "National facilitators and barriers to the implementation of incentives for antibiotic access and innovation." *Antibiotics* 10 (6): 749. https://doi.org/10.3390/antibiotics10060749

Årdal, Christine, John-Arne Røttingen, Aleksandra Opalska, Arjon J. Van Hengel, and Joseph Larsen. 2017. "Pull Incentives for Antibacterial Drug Development: An Analysis by the Transatlantic Task Force on Antimicrobial Resistance." *Clinical Infectious Diseases* 65 (8): 1378–82. https://doi.org/10.1093/cid/cix526.

Atkinson, Paul, and Sally Sheard. 2025. *NICE: A Contemporary History of the National Institute for Health and Care Excellence*. Routledge.

Banić Tomišić, Z. 2011. "The Story of Azithromycin." *Kemija u industriji: Časopis kemičara i kemijskih inženjera Hrvatske* 60 (12): 603–17.

Baxerres, C., and M. Cassier, eds. 2021. *Understanding Drugs Markets: An Analysis of Medicines, Regulations and Pharmaceutical Systems in the Global South*, 1st ed. Routledge.

Birch, Kean, and Fabian Muniesa. 2020. *Assetization: Turning Things into Assets in Technoscientific Capitalism*. MIT Press.

Birn, Anne-Emanuelle. 2014. "Philanthrocapitalism, Past and Present: The Rockefeller Foundation, the Gates Foundation, and the Setting(s) of the International/Global Health Agenda." *Hypothesis* 12 (1): e8. https://doi.org/10.5779/hypothesis.v12i1.229.

Blume, Stuart, and Baptiste Baylac-Paouly, eds. 2021. *Immunization and States: The Politics of Making Vaccines*. Routledge.

Bozdogan, Bülent, and Peter C. Appelbaum. 2004. "Oxazolidinones: Activity, Mode of Action, and Mechanism of Resistance." *International Journal of Antimicrobial Agents* 23 (2): 113–19. https://doi.org/10.1016/j.ijantimicag.2003.11.003.

Brazelton, Mary Augusta. 2019. "The Production of Penicillin in Wartime China and Sino-American Definitions of 'Normal Microbiology.'" *Journal of Modern Chinese History* 13 (1): 102–23. https://doi.org/10.1080/17535654.2019.1632563.

Bud, Robert. 2007. *Penicillin: Triumph and Tragedy*. Oxford University Press.

Capocci, Mauro. 2014. "Cold Drugs. Circulation, Production and Intelligence of Antibiotics in Post-WWII Years." *Medicina nei Secoli: Journal of History of Medicine and Medical Humanities* 26 (2): 401–22.

CARBX. 2021. *Stewardship & Access Plan (SAP) Development Guide*. Combating Antibiotic-Resistant Bacteria Accelerator. www.carb-x.org/about/stewardship-and-access. Accessed June 15, 2025.

CARBX. 2022. "UA Government and Wellcome Commit up to an Additional $370 Million to Carb-X." *CARBX Website*, May 19. https://carb-x.org/carb-x-news/u-s-government-and-wellcome-commit-an-additional-us370-million-to-carb-x/. Accessed June 15, 2025.

Cars, Otto, Liselotte Diaz Högberg, Mary Murray, Olle Nordberg, Satya Sivaraman, Cecilia Stålsby Lundborg, Anthony D. So, and Göran Tomson. 2008. "Meeting the challenge of antibiotic resistance." *BMJ* 337, https://doi.org/10.1136/bmj.a1438

https://doi.org/10.1017/pub.2025.10067 Published online by Cambridge University Press

Casadevall, Arturo. 1996. "Crisis in Infectious Diseases: Time for a New Paradigm?." *Clinical Infectious Diseases* 23 (4): 790–94. https://doi.org/10.1093/clinids/23.4.790.

Cassir, Nadim, Jean-Marc Rolain, and Philippe Brouqui. 2014. "A New Strategy to Fight Antimicrobial Resistance: The Revival of Old Antibiotics." *Frontiers in Microbiology* 5: 551. https://doi.org/10.3389/fmicb.2014.00551.

Chabrol, Fanny, and Jean-Paul Gaudillière. 2023. *Introduction À La Santé Globale*. La Découverte.

Chandler, Clare I. R. 2019. "Current Accounts of Antimicrobial Resistance: Stabilisation, Individualisation and Antibiotics as Infrastructure." *Palgrave Communications* 5 (1): 1–13. https://doi.org/10.1057/s41599-019-0263-4.

Chatham House Working Group on New Antibiotic Business Models. 2015. *Towards a New Global Business Model for Antibiotics. Delinking Revenues from Sales*. Royal Institute of International Affairs. https://www.chathamhouse.org/sites/default/files/field/field_document/20151009NewBusinessModelAntibioticsCliftGopinathanMorelOuttersonRottingenSo.pdf. Accessed June 6, 2025.

Chu, Y.-M. 1974. "Achievements in Applied Microbiology." In *China Medicine as We Saw It*, edited by J. R. Quinn. National Institutes of Health, pp. 372–73.

CIPLA. 2024. "Cipla Strengthens Fight against AMR, Secures Approval to Introduce ZEMDRI® (Plazomicin) Injection in India." *CIPLA News Release*, February 26. https://www.cipla.com/press-releases-statements/Cipla-strengthens-fight-against-AMR-secures-approval-to-introduce-ZEMDRI-injection-in-India. Accessed June 6, 2025.

Clancy, Cornelius J., Brian A. Potoski, Deanna Buehrle, and M. Hong Nguyen. 2019. "Estimating the Treatment of Carbapenem-Resistant Enterobacteriaceae Infections in the United States Using Antibiotic Prescription Data." *Open Forum Infectious Diseases* 6 (8): ofz344. https://doi.org/10.1093/ofid/ofz344.

Condrau, Flurin, and Robert G. W. Kirk. 2011. "Negotiating Hospital Infections: The Debate between Ecological Balance and Eradication Strategies in British Hospitals, 1947–1969." *Dynamis* 31 (2): 385–404. https://doi.org/10.4321/S0211-95362011000200007.

Cubist Pharmaceuticals, Inc. 2005. *Second Quarter 2005 Earnings Conference Call*. U.S. Securities and Exchange Commission. https://www.sec.gov/Archives/edgar/data/912183/000110465905034008/a05-13525_1ex99d2.htm. Accessed June 6, 2025.

Cubist Pharmaceuticals, Inc.—Form 10-K. 2014. U.S. Securities and Exchange Commission. https://www.sec.gov/Archives/edgar/data/912183/000104746914001280/a2218356z10-k.htm#dc49501_overview. Accessed June 6, 2025.

Cueto, Marcos, Theordore M. Brown, and Elizabeth Fee. 2019. *The World Health Organization: A History*. Cambridge University Press.

Culotta, Elizabeth. 1994. "Funding Crunch Hobbles Antibiotic Resistance Research." *Science* 264 (5157): 362–63. https://doi.org/10.1126/science.8153617.

Custos, Dominique, and John Reitz. 2010. "Public–Private Partnerships." *American Journal of Comparative Law* 58 (Suppl 1): 555–84. https://doi.org/10.5131/ajcl.2009.0037.

Czaplewski, L., U. Lamichhane, R. Sudbrak, A. Hennessy, L. Ogilivie, and L. J. Piddock. 2025. "Follow the Money! A Review of Global Public and Philanthropic Investments into Antibacterial Therapeutics (2017–2023)." Preprint. https://www.scilit.com/publications/495a1d7881fb4342bfa232fe3106afc3. Accessed June 6, 2025.

Daemmrich, Arthur. 2009. "Synthesis by Microbes or Chemists? Pharmaceutical Research and Manufacturing in the Antibiotic Era." *History and Technology* 25 (3): 237–56. https://doi.org/10.1080/07341510903083237.

Darrow, Jonathan J., and Aaron S. Kesselheim. 2020. "Incentivizing Antibiotic Development: Why Isn't the Generating Antibiotic Incentives Now (Gain) Act Working?" *Open Forum Infectious Diseases* 7 (1): ofaa001. https://doi.org/10.1093/ofid/ofaa001.

Davies, Sally C. 2011. "Chief Medical Officer's Summary." In *Annual Report of the Chief Medical Officer. Volume Two, 2011: Infections and the Rise of Antimicrobial Resistance*. https://assets.publishing.service.gov.uk/media/5a7a1cb9e5274a34770e456d/CMO_Annual_Report_Volume_2_2011.pdf. Accessed June 6, 2025.

de Bengy Puyvallée, Antoine. 2024. "The Rising Authority and Agency of Public–Private Partnerships in Global Health Governance." *Policy and Society* 43 (1): 25–40. https://doi.org/10.1093/polsoc/puad032.

Deeg, Richard. 2012. "Financialisation and Models of Capitalism: A Comparison of the UK and Germany." In *Capitalist Diversity and Diversity within Capitalism*, edited by Richard Deeg, Christel Lane, and Geoffrey T. Wood. Routledge, pp. 121–49.

Doganova, Liliana, and Vololona Rabeharisoa. 2024. "The Temporalities of Prices: 'Value-Based Pricing' in Pharmaceutical Markets." *Economy and Society* 53 (2): 183–204. https://doi.org/10.1080/03085147.2024.2346037.

Drews, Jürgen. 1998. *Die Verspielte Zukunft. Wohin Geht Die Arzneimittelforschung*. Birkenhäuser.

Duddy, Claire. 2024. *"Netflix" for Antimicrobials: The Antimicrobial Products Subscription Model*. UK House of Commons Library. https://commonslibrary.parliament.uk/netflix-for-antimicrobials-the-antimicrobial-products-subscription-model/. Accessed June 6, 2025.

Duke-Margolis Center. 2016. *Exploring Practical Implementation of Economic Incentives for Antimicrobial Development in the U.S.* Duke-Margolis Center for Health Policy. https://healthpolicy.duke.edu/sites/default/files/2020-03/abxmeetingssummary_final_0.pdf. Accessed June 6, 2025.

Dutescu, Ilinca A., and Sean A. Hillier. 2021. "Encouraging the Development of New Antibiotics: Are Financial Incentives the Right Way Forward? A Systematic Review and Case Study." *Infectious Drug Resistance* 14: 415–34. https://doi.org/10.2147/idr.s287792.

Edwards, Jim. 2009. "Pfizer Rep Describes Pushing Zyvox with Flawed Data." *CBS News*, September 4. https://www.cbsnews.com/news/pfizer-rep-describes-pushing-zyvox-with-flawed-data/. Accessed June 6, 2025.

EFPIA. 2022. "A New EU Pull Incentive to Address Anti-Microbial Resistance (AMR)." European Federation of Pharmaceutical Industries and Associations. https://www.efpia.eu/media/sdqp5gbi/a-new-eu-pull-incentive-to-address-anti-microbial-resistance-amr.pdf. Accessed June 6, 2025.

Eisenstein, Barry I., Frederick B. Oleson Jr., and Richard H. Baltz. 2010. "Daptomycin: From the Mountain to the Clinic, with Essential Help from Francis Tally, MD." *Clinical Infectious Diseases* 50 (Suppl 1): S10–15. https://doi.org/10.1086/647938.

European Investment Bank. 2020. "New AMR Action Fund Steps in to Save Collapsing Antibiotic Pipeline with Pharmaceutical Investment of US $1 Billion." *European Investment Bank*, July 9. https://www.eib.org/en/press/all/2020-190-new-amr-action-fund-steps-in-to-save-collapsing-antibiotic-pipeline-with-pharmaceutical-industry-investment-of-ususd1-billion. Accessed June 6, 2025.

Fairclough, Norman. 2013. *Language and Power*. Routledge.

Farrar, Jeremy. 2019. "We Ignore the Disaster in the Antibiotics Market at Our Peril." *Financial Times*, April 21. https://www.ft.com/content/4da1c6e4-603d-11e9-9300-0becfc937c37. Accessed June 6, 2025.

FDA. 2020. "Limited Population Pathway for Antibacterial and Antifungal Drugs—the LPAD Pathway." *US Food and Drugs Administration*, May 8. https://www.fda.gov/drugs/development-resources/limited-population-pathway-antibacterial-and-antifungal-drugs-lpad-pathway. Accessed June 6, 2025.

Fox, Erin R., Burgunda V. Sweet, and Valerie Jensen. 2014. "Drug Shortages: A Complex Health Care Crisis." *Mayo Clinic Proceedings* 89 (3): 361–73. https://doi.org/10.1016/j.mayocp.2013.11.014.

GARDP. 2023. "Critical Agreement Paves Way for New Model to Accelerate Access to Important Antibiotics for Serious Bacterial Infections." *Global Antibiotic Research and Development Partnership*, September 12. https://gardp.org/critical-agreement-paves-way-for-new-model-to-accelerate-access-to-important-antibiotics-for-serious-bacterial-infections/. Accessed June 7, 2025.

Gaudilliere, Jean-Paul. 2021. "Pharmaceutical Innovation and Its Crisis: Drug Markets, Screening, and the Dialectics of Value." *BioSocieties* 16 (3): 411–32. https://doi.org/10.1057/s41292-021-00235-7.

Gleadle, Pauline, Stuart Parris, Alan Shipman, and Roberto Simonetti. 2014. "Restructuring and Innovation in Pharmaceuticals and Biotechs: The Impact of Financialisation." *Critical Perspectives on Accounting* 25 (1): 67–77. https://doi.org/10.1016/j.cpa.2012.10.003.

Global AMR R&D Hub. 2025. "Dynamic Dashboard—Investments in AMR R&D." https://dashboard.globalamrhub.org/reports/investments/overview. Accessed June 20, 2025.

Glover, Rebecca E., Andrew C. Singer, Adam P. Roberts, and Claas Kirchhelle. 2021. "Nimble Innovation—a Networked Model for Public Antibiotic Trials." *The Lancet Microbe* 2 (11): e637–44. https://doi.org/10.1016/S2666-5247(21)00182-8.

Glover, Rebecca E., Andrew Singer, Adam P. Roberts, and Claas Kirchhelle. 2023. "Why Is the UK Subscription Model for Antibiotics Considered Successful?" *The Lancet Microbe* 4 (11): e852–53. https://doi.org/10.1016/S2666-5247(23)00250-1.

Goh, Maple, Matt McEnany, Rachel Freeman, Max Newton, Aaron S. Kesselheim, and Kevin Outterson. 2025. "Bridging the fair share gap for antibacterial innovation: an observational analysis of antibacterial revenues in the G7 and EU27." *EClinicalMedicine* 88. https://doi.org/10.1016/j.eclinm.2025.103485.

Gotham, Dzintars, Lorenzo Moja, Maarten van der Heijden, Sarah Paulin, Ingrid Smith, and Peter Beyer. 2021. "Reimbursement Models to Tackle Market Failures for Antimicrobials: Approaches Taken in France, Germany, Sweden, the United Kingdom, and the United States." *Health Policy* 125 (3): 296–306. https://doi.org/10.1016/j.healthpol.2020.11.015.

Gradmann, Christoph. 2016. "Re-Inventing Infectious Disease: Antibiotic Resistance and Drug Development at the Bayer Company 1945–1980." *Medical History* 60 (2): 155–80. https://doi.org/10.1017/mdh.2016.2.

Gradmann, Christoph. 2017. "From Lighthouse to Hothouse: Hospital Hygiene, Antibiotics and the Evolution of Infectious Disease, 1950–1990." *History and Philosophy of the Life Sciences* 40: 8. https://doi.org/10.1007/s40656-017-0176-8.

Gradmann, Christoph, and Claas Kirchhelle. 2023. "Pills and Politics." In *Steering against Superbugs: The Global Governance of Antimicrobial Resistance*, edited by Oliver Rubin, Erik Baekkeskov, and Louise Munkholm. Oxford University Press, pp. 19–29.

Greenwood, David. 2007. *Antimicrobial Chemotherapy*. Oxford University Press.
Gringarten, Hagai, 2019. "Bayer, Ethics, and the Anthrax Scare: Leveraging National Crisis for a Public Relations Bonanza." In *Ethical Branding and Marketing: Cases and Lessons*, edited by Hagai Gringarten and Raúl Fernández-Calienes, Routledge, pp. 69–79.
H.R. 8920—116th Congress. 2020. *The PASTEUR Act*. GovTrack.us. https://www.govtrack.us/congress/bills/116/hr8920. Accessed June 6, 2025.
Harbarth, Stephan. 2007. "Should the Development of New Antibiotics Be a Public Health Priority?" *Current Opinion in Critical Care* 13 (5): 554–56. https://doi.org/10.1097/mcc.0b013e3282efc3af.
Hilgartner, Stephen. 2000. *Science on Stage. Expert Advice as Public Drama*. Stanford University Press.
Hoare, Quintin, and Geoffrey Nowell Smith, eds. [1971] 2010. *Selections from the Prison Notebooks of Antonio Gramsci*. International Publishers.
Hoen, Ellen't, Jonathan Berger, Alexandra Calmy, and Suerie Moon. 2011. "Driving a Decade of Change: HIV/AIDS, Patents and Access to Medicines for All." *Journal of the International AIDS Society* 14: 1–12. https://doi.org/10.1186/1758-2652-14-15.
Holmes, David. 2014. "Report Urges Controversial "Delinkage" to Foster New Antibiotics." *Nature Medicine* 20 (4): 320. https://doi.org/10.1038/nm0414-320.
Hunt, Avery, and Donald R. Kirsch. 2020. "Decision Making in the Pharmaceutical Industry—a Tale of Three Antibiotics." *International Journal of Pharmaceutics* 581): 119251. https://doi.org/10.1016/j.ijpharm.2020.119251.
Hüntelmann, Axel C. 2010. "Seriality and Standardization in the Production of '606.'" *History of Science* 48 (3–4): 435–60. https://doi.org/10.1177/007327531004800307.
Husain, L., Y. Hu, and Y. Huang. 2024. "Towards Mission-Driven Investment in New Antimicrobials? What Role for Chinese Strategic Industrial Financing Vehicles in Responding to the Challenge of Antimicrobial Resistance?" *Global Health* 20 (1): 26. https://doi.org/10.1186/s12992-024-01030-2.
IDSA. 2004. *Bad Bugs, No Drugs: As Antibiotic Discovery Stagnates, ... a Public Health Crisis Brews*. Infectious Diseases Society of America. https://www.idsociety.org/globalassets/idsa/policy–advocacy/current_topics_and_issues/antimicrobial_resistance/10x20/statements/070104-as-antibiotic-discovery-stagnates-a-public-health-crisis-brews.pdf. Accessed June 20, 2025.
IDSA. 2020. "PASTEUR Act Will Build Antibiotic Arsenal, Protect Existing Medicines." *Infectious Diseases Society of America*, October 1. https://www.idsociety.org/news–publications-new/articles/2020/pasteur-act-will-build-antibiotic-arsenal-protect-existing-medicines/. Accessed June 20, 2025.
Institute of Medicine. 1992. *Emerging Infections: Microbial Threats to Health in the United States*. Institute of Medicine. https://www.ncbi.nlm.nih.gov/books/NBK234855.
Jasanoff, Sheila. 2006. "Ordering Knowledge, Ordering Society." In *States of Knowledge: The Co-Production of Science and Social Order*, edited by Sheila Jasanoff. Routledge, pp. 13–45.
Jolliffe, D. M. 1993. "A History of the Use of Arsenicals in Man." *Journal of the Royal Society of Medicine* 86 (5): 287–89. https://doi.org/10.1177/014107689308600515.
KEI-Online. 2012a. *The De-Linkage of R&D Costs and Drug Prices through the Prize Fund for HIV/AIDS Will Cost Less, Expand Access, Accelerate and Improve Innovation. Hearing before the US Senate Committee on Health Education, Labor and Pensions, Subcommittee on Primary Health and Agency on the High Cost of High Prices for HIV/AIDS Drugs and the Prize Fund Alternative*. Knowledge Ecology International. https://www.keionline.org/sites/default/files/testimony_JamesLove_15May2012_prizes_HELP_subject2revision.pdf. Accessed June 20, 2025.
KEI-Online. 2012b. *Wellcome Trust Tells Who It Opposes R&D Treaty and the De-Linkage of R&D Costs from Drug Prices (26.11.2012)*. Knowledge Ecology International. https://www.keionline.org/22073. Accessed June 20, 2025.
Kirchhelle, Claas. 2018. "Pharming Animals: A Global History of Antibiotics in Food Production (1935–2017)." *Palgrave Communication* 4: 96. https://doi.org/10.1057/s41599-018-0152-2.
Kirchhelle, Claas, Paul Atkinson, Alex Broom, Komatra Chuengsatiansup, Jorge Pinto Ferreira, Nicolas Fortané, Isabel Frost, et al. 2020. "Setting the Standard: Multidisciplinary Hallmarks for Structural, Equitable and Tracked Antibiotic Policy." *BMJ Global Health* 5 (9): e003091. https://doi.org/10.1136/bmjgh-2020-003091.
Klug, Dana M., Fahima I. M. Idiris, Mark A. T. Blaskovich, Frank von Delft, Christopher G. Dowson, Claas Kirchhelle, Adam P. Roberts, Andrew C. Singer, and Matthew H. Todd. 2021. "There Is No Market for New Antibiotics: This Allows an Open Approach to Research and Development." *Wellcome Open Research* 6: 146. https://doi.org/10.12688/wellcomeopenres.16847.1.
Kong, Linghui, Qiu Li, Kenneth I. Kaitin, and Liming Shao. 2023. "Innovation in the Chinese Pharmaceutical Industry." *Nature Reviews Drug Discovery* 22 (1): 12–13. https://doi.org/10.1038/d41573-022-00167-2.
Kunin, Calvin M., Helene L. Lipton, Thelma Tupasi, Theodore Sacks, William E. Scheckler, Amir Jivani, Aleksander Goic, et al. 1987. "Social, Behavioral, and Practical Factors Affecting Antibiotic Use Worldwide: Report of Task Force 4." *Reviews of Infectious Diseases* 9 (Suppl 3): S270–85, https://doi.org/10.1093/clinids/9.Supplement_3.S270.
Lachenal, Guillaume. 2017. *The Lomidine Files: The Untold Story of a Medical Disaster in Colonial Africa*. Johns Hopkins University Press.

LaFrance, David B. 2024. "Pricing: Cost of Service versus Value of Water." *Journal—American Water Works Association* 116 (6): 112. https://doi.org/10.1002/awwa.2309.

Latour, Bruno, 2007. *Reassembling the Social: An Introduction to Actor-Network Theory*. Oxford University Press.

Latour, Bruno, Jonas Salk, and Steve Woolgar. 2013. *Laboratory Life: The Construction of Scientific Facts*. Princeton University Press.

Laxminarayan, Ramanan, Isabella Impalli, Radha Rangarajan, Jennifer Cohn, Kavi Ramjeet, Betsy Wonderly Trainor, Steffanie Strathdee, et al. 2024. "Expanding Antibiotic, Vaccine, and Diagnostics Development and Access to Tackle Antimicrobial Resistance." *The Lancet* 408 (10443): 2534–50. https://doi.org/10.1016/s0140-6736(24)00878-x.

Lazonick, William, and Öner Tulum. 2011. "US Biopharmaceutical Finance and the Sustainability of the Biotech Business Model." *Research Policy* 40 (9): 1170–87. https://doi.org/10.2139/ssrn.2257932.

Leach, Karen L., Steven J. Brickner, Mark C. Noe, and Paul F. Miller. 2011. "Linezolid, the First Oxazolidinone Antibacterial Agent." *Annals of the New York Academy of Sciences* 1222 (1): 49–54. https://doi.org/10.1111/j.1749-6632.2011.05962.x.

Leach, Melissa, Ian Scoones, and Andrew Stirling. 2010. "Governing Epidemics in an Age of Complexity: Narratives, Politics and Pathways to Sustainability." *Global Environmental Change* 20 (3): 369–77. https://doi.org/10.1016/j.gloenvcha.2009.11.008.

Leisner, Jørgen J. 2020. "The Diverse Search for Synthetic, Semisynthetic and Natural Product Antibiotics from the 1940s and up to 1960 Exemplified by a Small Pharmaceutical Player." *Frontiers in Microbiology* 11: 976. https://doi.org/10.3389/fmicb.2020.00976.

Lesch, John E. 2007. *The First Miracle Drugs: How the Sulfa Drugs Transformed Medicine*. Oxford University Press.

Lezaun, Javier. 2018. "The Deferred Promise of Radical Cure: Pharmaceutical Conjugations of Malaria in the Global Health Era." *Economy and Society* 47 (4): 547–71. https://doi.org/10.1080/03085147.2018.1528075.

Li, Yanchang. 2024. "Antibiotic Cold War and Ernst Chain's Visit to China in 1961." *Social History of Medicine* 38 (2): 205–26, https://doi.org/10.1093/shm/hkae030.

Lloyd, I. 2023. "Pharma R&D Annual Review." https://www.citeline.com/-/media/citeline/resources/pdf/citeline-rd-review-white-paper.pdf. Accessed June 6, 2025.

Lopez, Paula Palanco, Salome Manyau, Justin Dixon, Eleanor MacPherson, Susan Nayiga, John Manton, Claas Kirchhelle, and Clare I. R. Chandler. 2022. "Antibiotic Arrivals in Africa: A Case Study of Yaws and Syphilis in Malawi, Zimbabwe and Uganda." *Medicine Anthropology Theory* 9 (3): 1–31. https://doi.org/10.17157/mat.9.3.5633.

Lowe, D. 2015. "What Became of Cubist?" *Science*, August 4. https://www.science.org/content/blog-post/what-became-cubist. Accessed June 20, 2025.

Mackintosh, Maureen, Geoffrey Banda, Paula Tibandebage, and Wata Wamae, eds. 2016. *Making Medicines in Africa: The Political Economy of Industrializing for Local Health*. Palgrave Macmillan.

Maggon, Krishan. 2005. "Best-Selling Human Medicines 2002–2004." *Drug Discovery Today* 10 (11): 739–42. https://doi.org/10.1016/S1359-6446(05)03468-9.

McEnany, Matt, and Kevin Outterson. 2024. "Changes in Revenues Associated with Antimicrobial Reimbursement Reforms in Germany." *Humanities and Social Sciences Communications* 11 (1): 1–12. https://doi.org/10.1057/s41599-024-03374-x.

McKenna, Maryn. 2010. *Superbug: The Fatal Menace of MRSA*. Free Press.

McMillen, Christian W. 2015. *Discovering Tuberculosis: A Global History 1900 to the Present*. Yale University Press.

Mindry, Deborah. 2008. "Neoliberalism, Activism, and HIV/AIDS in Postapartheid South Africa." *Social Text* 26 (1): 75–93. https://doi.org/10.1215/01642472-2007-020.

Mishra, Vibhu. 2025. "Countries Finalise Historic Pandemic Agreement after Three Years of Negotiations." *UN News Release*, April 16. https://news.un.org/en/story/2025/04/1162301.

Monnet, Dominique L. 2005. "Antibiotic Development and the Changing Role of the Pharmaceutical Industry." *International Journal of Risk & Safety in Medicine* 17 (3–4): 133–45. https://doi.org/10.3233/JRS-2005-349.

MSF Access Campaign. 2024. "The PASTEUR Act Is Not the Way for the US Government to Address Antimicrobial Resistance." *Médecins Sans Frontières Access Campaign.* https://www.msfaccess.org/sites/default/files/2024-02/MSF_PASTEUR%20Act%20position_Feb2024_Final_ENG.pdf. Accessed June 20, 2025.

Murphy, Flynn. 2025. "How Trump's Trade War Will Break Global Medicine Supply Chains." *BMJ* 389: r648. https://doi.org/10.1136/bmj.r648.

Novo Nordisk. 2023. *Novo Nordisk Investor Presentation Full Year 2023*. https://investor.novonordisk.com/q4full-presentation2023/. Accessed June 20, 2025.

Oehler, R. L., and S. G. Gompf. 2020. Shortcomings in the US Pharmaceutical Supply Chain: Potential Risks Associated with International Manufacturing and Trade-Related Tariffs. *JAMA* 324 (2): 143. https://doi.org/10.1001/jama.2020.1634.

Oleson Jr., F. B., C. L. Berman, J. B. Kirkpatrick, K. S. Regan, J.-J. Lai, and F. P. Tally. 2000. "Once-Daily Dosing in Dogs Optimizes Daptomycin Safety." *Antimicrobial Agents and Chemotherapy* 44 (11): 2948–53. https://doi.org/10.1086/420818.

Outterson, Kevin. 2022. "*Estimating the EU 'Fair Share' of a Global Antibacterial Pull Incentive." Presentation. ISPOR, November 8.* https://www.ispor.org/docs/default-source/euro2022/2022.pdf?sfvrsn=4f27512a_0. Accessed June 20, 2025.

Outterson, Kevin, Unni Gopinathan, Charles Clift, Anthony D. So, Chantal M. Morel, and John-Arne Røttingen. 2016. "Delinking Investment in Antibiotic Research and Development from Sales Revenues: The Challenges of Transforming a Promising Idea into Reality." *PLoS Medicine* 13 (6): e1002043. https://doi.org/10.1371/journal.pmed.1002043.

Outterson, Kevin, Ebiowei S. F. Orubu, John Rex, Christine Årdal, and Muhammad H. Zaman. 2022. "Patient Access in 14 High-Income Countries to New Antibacterials Approved by the US Food and Drug Administration, European Medicines Agency, Japanese Pharmaceuticals and Medical Devices Agency, or Health Canada, 2010–2020." *Clinical Infectious Diseases* 74 (7): 1183–90. https://doi.org/10.1093/cid/ciab612.

Overbye, Karen M., and John F. Barrett. 2005. "Antibiotics: Where Did We Go Wrong?" *Drug Discovery Today* 10 (1): 45–52. https://doi.org/10.1016/S1359-6446(04)03285-4.

Overton, Kristen, Nicolas Fortané, Alex Broom, Stephanie Raymond, Christoph Gradmann, Ebiowei Samuel F. Orubu, Scott H. Podolsky, et al. 2021. "Waves of Attention: Patterns and Themes of International Antimicrobial Resistance Reports, 1945–2020." *BMJ Global Health* 6 (11): e006909. https://doi.org/10.1136/bmjgh-2021-006909.

Paterson, Erin. 2025. "A Crumbling Infrastructure: Challenging the Use of the Dry Antibiotic Pipeline in the Framework of Access to Antibiotics New and Old." PhD diss., Université de Strasbourg. https://theses.hal.science/tel-05328559.

Pfotenhauer, Sebastian M., Joakim Juhl, and Erik Aarden. 2019. "Challenging the 'Deficit Model' of Innovation: Framing Policy Issues under the Innovation Imperative." *Research Policy* 48 (4): 895–904. https://doi.org/10.1016/j.respol.2018.10.015.

PhIRDA. 2021. "Fostering China Pharmaceutical Innovation System. Report 1: 2015–2020 Review and Future Outlook." *China Pharmaceutical Innovation and Research Development Association* Report No. 1. http://enadmin.rdpac.org/upload/upload_file/1637846943.pdf. Accessed June 6, 2025.

Piddock, Laura J. V., Yewande Alimi, James Anderson, Damiano de Felice, Catrin E. Moore, John-Arne Røttingen, Henry Skinner, and Peter Beyer. 2024. "Advancing Global Antibiotic Research, Development and Access." *Nature Medicine* 30 (9): 2432–43. https://doi.org/10.1038/s41591-024-03218-w.

Podolsky, Scott H. 2015. *The Antibiotic Era: Reform, Resistance and the Pursuit of a Rational Therapeutics*. Johns Hopkins Press.

Quadri, Farha, Maryann Mazer-Amirshahi, Erin R. Fox, Kristy L. Hawley, Jesse M. Pines, Mark S. Zocchi, and Larissa May. 2015. "Antibacterial Drug Shortages from 2001 to 2013: Implications for Clinical Practice." *Clinical Infectious Diseases* 60 (12): 1737–42. https://doi.org/10.1093/cid/civ201.

Quirke, Viviane. 2012. *Collaboration in the Pharmaceutical Industry: Changing Relationships in Britain and France, 1935–1965*. Routledge.

Quirke, Viviane, and Jean-Paul Gaudillière. 2008. "The Era of Biomedicine: Science, Medicine, and Public Health in Britain and France after the Second World War." *Medical History* 52 (4): 441–52. https://doi.org/10.1017/s002572730000017x.

Rajan, Kaushik Sunder. 2017. *Pharmocracy: Value, Politics, and Knowledge in Global Biomedicine*. Duke University Press.

Rasmussen, Nicolas. 2014. *Gene Jockeys: Life Science and the Rise of Biotech Enterprise*. Johns Hopkins University Press.

ReACT. 2021. "The World Needs New Antibiotics—So Why Aren't They Developed?" *ReACT Group*, October 28. https://www.reactgroup.org/news-and-views/news-and-opinions/year-2021/the-world-needs-new-antibiotics-so-why-arent-they-developed/. Accessed June 20, 2025.

Repair Impact Fund. 2025. "Repair Impact Fund—About." *Repair Impact Fund.* https://www.repair-impact-fund.com/about/. Accessed June 20, 2025.

Reubi, David. 2018. "Epidemiological Accountability: Philanthropists, Global Health and the Audit of Saving Lives." *Economy and Society* 47 (1): 83–110. https://doi.org/10.1080/03085147.2018.1433359.

Roy, Victor. 2020. "A Crisis for Cures? Tracing Assetization and Value in Biomedical Innovation." In *Assetization: Turning Things into Assets in Technoscientific Capitalism*, edited by Kean Birch and Fabian Muniesa. The MIT Press, pp. 97–124.

Roy, Victor. 2023. *Capitalizing a Cure: How Finance Controls the Price and Value of Medicines*. University of California Press.

Rubin, Oliver, and Erik Baekkeskov. 2023. "Policy Entrepreneurship and Problem Brokering in the Global Governance of AMR." In *Steering against Superbugs: The Global Governance of Antimicrobial Resistance*, edited by Oliver Rubin, Erik Baekkeskov, and Louise Munkholm. Oxford University Press, pp. 191–204.

Sagonowsky, E. 2019. "Years after Cubist Buyout, Merck Scores a New Zerbaxa Indication. Can It Jump-Start Sales." *Fierce Pharma*, June 3. https://www.fiercepharma.com/pharma/merck-scores-zerbaxa-label-expansion-years-after-cubist-buyout. Accessed June 20, 2025.

Santesmases, Mariá Jesús. 2018. *The Circulation of Penicillin in Spain: Health, Wealth and Authority*. Palgrave Macmillan.

Schramm, Manuel. 2008. *Wirtschaft Und Wissenschaft in Ddr Und Brd. Die Kategorie Vertrauen in Innovationsprozessen*. Böhlau Verlag.

Schwab, Tim. 2021. "COVID-19, Trust, and Wellcome: How Charity's Pharma Investments Overlap with Its Research Efforts." *BMJ* 372: 556. https://doi.org/10.1136/bmj.n556.

Sertkaya, Aylin, and Calvin Franz. 2022. *Antimicrobial Market Returns Analysis: Final Report*. Office of the Assistant Secretary for Planning and Evaluation. https://www.ncbi.nlm.nih.gov/books/NBK603193/.

Sheller, P.C. 2009. "$2.3 Billion Settlement." News Release. https://sheller.com/2-3-billion-settlement-pfizer-zyvox/. Accessed June 20, 2025.

Shlaes, David, Stuart Levy, and Gordon Archer. 1991. "Antimicrobial Resistance: New Directions." *ASM American Society for Microbiology News* 57 (9): 455–58.

Shlaes, David M. 2003. "The Abandonment of Antibacterials: Why and Wherefore?" *Current Opinion in Pharmacology* 3 (5): 470–73. https://doi.org/10.1016/j.coph.2003.04.003.

Shlaes, David M. 2019. "The Economic Conundrum for Antibacterial Drugs." *Antimicrobial Agents and Chemotherapy* 64 (1). https://doi.org/10.1128/aac.02057-19.

Silverman, M., P. R. Lee, and M. P. Lydecker. 1982. *Prescriptions for Death: The Drugging of the Third World*. University of California Press.

Singer, Andrew C., Claas Kirchhelle, and Adam P. Roberts. 2020. "(Inter)Nationalising the Antibiotic Research and Development Pipeline." *Lancet Infectious Disease* 20 (2): e54–62. https://doi.org/10.1016/S1473-3099(19)30552-3.

Skender, Belma. 2024. "The Demise of the Antibiotic Pipeline: The Bayer Case." *Humanities and Social Sciences Communications* 11 (1): 1–10. https://doi.org/10.1057/s41599-024-03584-3.

Skender, Belma, and Mingyuan Zhang. 2024. "From Local Issue to Global Challenge: A Brief Overview of Antibiotic Shortages since the 1970s." *Humanities and Social Sciences Communications* 11 (1): 1–6. https://doi.org/10.1057/s41599-024-03759-y.

Sorenson, Corinna, and Kalipso Chalkidou. 2012. "Reflections on the Evolution of Health Technology Assessment in Europe." *Health Economics, Policy and Law* 7 (1): 25–45. https://doi.org/10.1017/S1744133111000296.

Spilker, Bert. 1989. *Multinational Drug Companies: Issues in Drug Discovery and Development*. Raven Press.

Staton, T. 2014. "Updated: Did Merck Pay $3b Too Much for Cubist? Weighing the Impact of Cubicin Patent Loss." *Fierce Pharma*, December 9. https://www.fiercepharma.com/m-a/updated-did-merck-pay-3b-too-much-for-cubist-weighing-impact-of-cubicin-patent-loss. Accessed June 20, 2025.

Swann, John Patrick. 1988. *Academic Scientists and the Pharmaceutical Industry: Cooperative Research in Twentieth-Century America*. Johns Hopkins University Press.

Tansey, E.M., and L. A. Reynolds, eds. 2000. *Post Penicillin Antibiotics: From Acceptance to Resistance? A Witness Seminar Held at the Wellcome Institute for the History of Medicine, London, on 12 May 1998*. Vol. 6. Wellcome Trust. https://discovery.ucl.ac.uk/id/eprint/2074/1/wit6.pdf.

Tansey, E. M., and L. A. Reynolds, eds. 2008. *Superbugs and Superdrugs: A History of MRSA. The Transcript of a Witness Seminar Held by the Wellcome Trust Centre for the History of Medicine at UCL, on 11 July 2006*. Wellcome Trust Centre for the History of Medicine. https://histmodbiomed.history.qmul.ac.uk/sites/default/files/44862.pdf.

Thomas, Jayan Jose. 2008. *Innovation in India and China: Challenges and Prospects in Pharmaceuticals and Biotechnology*. Madras School of Economics.

Timmermann, Carsten. 2019. *Moonshots at Cancer: The Roche Story*. Editiones Roche.

Timmermann, Carsten. 2025. "From Chemotherapy to Biotechnology: The Transformation of the Cancer Research Pipeline at Hoffmann-La Roche." *Humanities and Social Sciences Communications* 12: 574. https://doi.org/10.1057/s41599-025-04812-0.

Tobbell, Dominique A. 2009. "'Who's Winning the Human Race?' Cold War as Pharmaceutical Political Strategy." *Journal of the History of Medicine and Allied Sciences* 64 (4): 429–73. https://doi.org/10.1093/jhmas/jrp012.

Todd, Matthew H. 2019. "Six Laws of Open Source Drug Discovery." *ChemMedChem* 14 (21): 1804–9. https://doi.org/10.1002/cmdc.201900565.

U.S. Justice Department. 2009. "Justice Department Announces Largest Health Care Fraud Settlement in Its History." U.S. Justice Department News Release, September 2. https://www.justice.gov/archives/opa/pr/justice-department-announces-largest-health-care-fraud-settlement-its-history. Accessed June 20, 2025.

U.S. Senate Committee on Homeland Security & Governmental Affairs. 2023. *Short Supply: The Health and National Security Risks of Drug Shortages*. Majority Report. US Senate. https://www.hsgac.senate.gov/wp-content/uploads/2023-06-06-HSGAC-Majority-Draft-Drug-Shortages-Report.-FINAL-CORRECTED.pdf. Accessed June 20, 2025.

Varadan, Sheila Rose, Clare I.R. Chandler, Kym Weed, Syed Masud Ahmed, Caesar Atuire, Deepshikha Batheja, Susan Jane Bull, et al. 2024. "A Just Transition for Antimicrobial Resistance: Planning for an Equitable and Sustainable Future with Antimicrobial Resistance." *The Lancet* 403 (10446): 2766–67. https://doi.org/10.1016/s0140-6736(23)01687-2.

Washer, Peter, and Helene Joffe. 2006. "The 'Hospital Superbug': Social Representations of MRSA." *Social Science & Medicine* 63 (8): 2141–52. https://doi.org/10.1016/j.socscimed.2006.05.018.

Wells, Nadya, Vinh-Kim Nguyen, and Stephan Harbarth. 2024a. "Novel Insights from Financial Analysis of the Failure to Commercialise Plazomicin: Implications for the Antibiotic Investment Ecosystem." *Humanities and Social Sciences Communications* 11 (1): 1–13. https://doi.org/10.1057/s41599-024-03452-0.

Wells, Nadya, Vinh-Kim Nguyen, and Stephan Harbarth. 2024b. "A Pharmaceutical Policy Accident: Collision of Shareholder Capitalism and Chinese State Capitalism Driving the Shortage of an Essential Antibiotic." *Journal of Pharmaceutical Policy and Practice* 17 (1): 2430441. https://doi.org/10.1080/20523211.2024.2430441.

WHO. 2001. *Global Strategy for Containment of Antimicrobial Resistance*. World Health Organization. https://iris.who.int/bitstream/handle/10665/66860/WHO_CDS_CSR_DRS_2001.2.pdf. Accessed June 20, 2025.

WHO. 2015. *Global Action Plan on Antimicrobial Resistance*. World Health Organization. https://www.who.int/publications/i/item/9789241509763. Accessed June 20, 2025.

WHO. 2017. "Who Publishes List of Bacteria for Which New Antibiotics Are Urgently Needed." News Release, February 27. https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed. Accessed June 20, 2025.

WHO. 2018. *Antibacterial Products in Clinical Development for Priority Pathogens*. World Health Organization. https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/antibacterial-products-in-clinical-development-for-priority-pathogens-Oct-2018. Accessed June 20, 2025.

WHO. 2024a. *Antibacterial Agents in Clinical and Preclinical Development: An Overview and Analysis*. World Health Organization. https://www.who.int/publications/i/item/9789240021303. Accessed June 20, 2025.

WHO. 2024b. *Review of Preclinical Antibacterial Products/Programs in the Pipeline Worldwide 2023*. World Health Organization. https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/who-antibacterial-preclinical-pipeline-review. Accessed June 20, 2025.

WHO. 2024c. *Clinical Pipeline Analysis for Antibacterial Products, Trends from 2017 to Current*. World Health Organization. https://www.who.int/observatories/global-observatory-on-health-research-and-development/monitoring/trend-analysis-of-antibacterial-agents-in-the-pipeline-(2017—2023). Accessed June 20, 2025.

Williams, Keith J., and Richard P. Bax. 2009. "Challenges in Developing New Antibacterial Drugs." *Current Opinion in Investigational Drugs* 10 (2): 157–63. https://doi.org/10.13109/9783666530951.157.

Williams, Keith J., and Bryan C. Hurst. 2013. "Virtual Drug Development: Vision, Oversight and Risk Management." *International Pharmaceutical Industry* 5 (2): 32–35.

Yang, X., C. Li, X. Wang, Z. Zheng, P. Sun, C. Xu, et al. 2024. An Update on the Clinical Pipelines of New Antibacterial Drugs Developed in China. *Engineering* 38: 52–68. https://doi.org/10.1016/j.eng.2024.02.009.

Yi, Doogab. 2015. *The Recombinant University. Genetic Engineering and the Emergence of Stanford Biotechnology*. University of Chicago Press.

Zhang, C., X. Fu, Y. Liu, H. Zhao, and G. Wang. 2024. "Burden of Infectious Diseases and Bacterial Antimicrobial Resistance in China: A Systematic Analysis for the Global Burden of Disease Study 2019." *The Lancet Regional Health—Western Pacific* 43: 100972. https://doi.org/10.1016/j.lanwpc.2023.100972.

Zhang, Mingyuan. 2023. "In Shortage: Understanding Global Antibiotic Supply Chains through Pharmaceutical Trade Fairs." *Anthropologica* 65 (1): 1–16. https://doi.org/10.18357/anthropologica65120232605.

Zhou, Xun. 2023. "Antibiotic Culture: A History of Antibiotic Use in the Second Half of the 20th and Early 21st Century in the People's Republic of China." *Antibiotics* 12 (3): 510. https://doi.org/10.3390/antibiotics12030510.

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