International Journal of Research and Review
[Indexed, Peer-Reviewed Journal]
Volume 12; Issue: 10; October 2025
Website: www.ijrrjournal.com
Review Paper *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Incentivizing Antibiotic Innovation: A Narrative Review of Push and Pull Economic Models for Antimicrobial Resistance (AMR)

Veda Dua[1], Dr. Adarsh Keshari[2], Dr. Rhea Aggarwal[3]

[1]Independent Researcher, Delhi Public School, R.K. Puram, New Delhi, India
[2]Senior Research Fellow, APAR Health, Gurugram, India
[3]Co-Founder, APAR Health, Gurugram, India

Corresponding Author: Dr. Adarsh Keshari

DOI: https://doi.org/10.52403/ijrr.20251049

ABSTRACT

Antimicrobial resistance (AMR) is one of the most pressing global health and economic challenges of the 21st century. It is projected to cause up to 10 million deaths annually by 2050 if unchecked, with severe health and economic consequences. The diminishing effectiveness of traditional antibiotics has created an urgent need for new therapies, but the economic environment for antibiotic innovation remains fragile.

This narrative review explores economic models designed to incentivize antibiotic innovation, focusing on "push" and "pull" mechanisms. Push mechanisms fund early-stage research, while pull mechanisms reward successful drug development. This review compares their efficiency, sustainability, and challenges. Ultimately, hybrid strategies combining push and pull elements may provide the most effective pathway forward to balance innovation, stewardship, and access.

Keywords: Antimicrobial resistance (AMR); economic incentives; push–pull models; hybrid funding mechanisms; global health economics; stewardship; access and equity.

INTRODUCTION

Antimicrobial resistance (AMR) is projected to cause up to 10 million deaths annually by 2050 if unchecked, with severe health and economic consequences [1, 2]. The World Health Organization (WHO) and other global bodies warn that AMR threatens to undermine modern medicine, including surgery, cancer therapy, and neonatal care [3, 4]. Despite the urgency, the antibiotic development pipeline has slowed due to scientific, regulatory, and economic challenges [5].

Unlike chronic disease drugs, antibiotics are used sparingly, limiting revenue potential [6]. Consequently, major pharmaceutical firms have scaled back antibiotic research, leaving a fragile innovation ecosystem [7]. Addressing this requires economic incentive models that encourage sustained investment in antibiotic development [8].

METHODS

To investigate the comparative economic efficiency of "push" and "pull" incentive models in promoting antibiotic innovation, we conducted a structured literature review using online academic databases. The primary databases searched were Google Scholar and PubMed, focusing on peer-reviewed documents, policy analyses, and economic studies related to antimicrobial resistance (AMR) and antibiotic innovation.

Search Strategy and Scope

The review concentrated on publications between 2019 and 2025 to ensure the most up-to-date findings reflecting recent trends in health economics and pharmaceutical innovation. However, seminal studies from previous years, dating back as far as 2002, were included if they offered key historical or conceptual background to AMR-associated economic policy.

The search employed the following keywords and phrases:

- Health economics
- Antimicrobial resistance
- Antibiotics waste management
- Push antibiotic development
- Pull antibiotic development

Selection Criteria

Papers were chosen based on their application to the research question, the quality of findings, and how comprehensively they covered the economic effect of AMR or the performance of incentive mechanisms. We specifically focused on literature reviews, observational studies, and economic studies that examined innovation funding models, misuse of antibiotics, and global policy architectures. This allowed us to delineate key themes, gaps, and evidence regarding how various incentive structures affect antibiotic innovation and public health outcomes.

DISCUSSION

Push Mechanisms

Push mechanisms provide early-stage financing of R&D for antibiotics, typically as grants, tax credits, or public-private partnerships [9]. Initiatives like CARB-X and the Innovative Medicines Initiative are examples that provide financing for preclinical and early-stage projects [10]. Push mechanisms effectively reduce economic risk for researchers and firms, particularly in academia, enabling research into novel drug targets [11]. However, push funding alone does not ensure market entry or long-term supply, as many prospects fail during later-stage clinical trials [2, 6]. Data suggest push mechanisms are particularly strong at inducing innovation in small biotech firms, which now dominate the antibiotic pipeline [12].

Anderson et al. (2023) propose that high initial investment is needed to stimulate early antibiotic development and that late-stage failure rates remain a substantial barrier in the absence of adequate early support [13]. Årdal et al. (2020) emphasize that push strategies can enhance scientific understanding and increase the scope of antibiotic development, but grants must be designed so that they prioritize research that can be translated into effective therapies. They contend that investments in early-stage collaborations are especially important in low-resource environments, where private capital is limited [14].

Pull Mechanisms

Pull mechanisms create incentives when an antibiotic successfully reaches the market [15]. These incentives include market entry rewards, transferable exclusivity vouchers, and subscription schemes [5]. The UK's subscription model, in which the state pays a flat annual rate for access regardless of use, has been identified as a potential global model [16]. Pull incentives effectively tie the financial reward to social value rather than the quantity of sales, which helps ensure stewardship [17]. Challenges persist, however, in calculating the reward value, ensuring fair global involvement, and avoiding high costs to national healthcare systems [18].

Anderson et al. (2024) add that outcome-based measures must be integrated when calculating reward structures, stressing that global coordination is essential to avoid unequal benefits [13]. Årdal et al. (2020) highlight the difficulties in ensuring equitable access while structuring rewards to make late-stage development economically effective without inadvertently promoting over-consumption [14]. Outterson (2021) further suggests that global governance frameworks need to be paired with pull incentives to avoid market fragmentation and

ensure uniform regulation across borders [19].

Hybrid Models

Given the limitations of both push and pull mechanisms alone, hybrid models integrating both have become increasingly popular [20]. One common type combines advance grants (push) for initial research with market entry incentives (pull) for late-stage development and commercialization [7]. Laxminarayan et al. (2016) emphasize that only hybrid approaches can effectively drive innovation, stewardship, and access equity in parallel [5]. Simulation studies suggest hybrid models are efficient and resilient [15]. More recent research by Glover et al. (2023) and Brogan and Mossialos (2013) investigates subscription models linked with outcome-based funding to maximize sustainability and innovation [15, 16].

Towse et al. (2017) elaborate on how insurance-based models balance risk, ensuring that antibiotic R&D remains a viable investment for stakeholders at every level [10]. Outterson (2021) suggests a two-tiered incentive mechanism, with push and pull incentives dynamically scaled by project stage and geographic need [19].

Global Health and Equity Considerations

AMR disproportionately affects low- and middle-income countries (LMICs), where the burden of infectious disease is highest and access to existing antibiotics is most restricted [3, 8]. Economic models must therefore balance the trade-off between stimulating innovation and ensuring affordability and access. Global coordination is essential, as unilateral national incentives risk duplication or unfairness [21]. The WHO and G20 have emphasized the importance of international cooperation to coordinate incentives and establish antibiotics as global public goods [9]. Without this cooperation, new antibiotics may never be available to vulnerable populations [13].

Anderson et al. (2024) point out how inclusive financing arrangements can facilitate stakeholder participation, ensuring that deprived areas reap the benefits of innovation pipelines [13]. In the same vein, Årdal et al. (2020) posit that international pooled funds are necessary to balance out access and stabilize financial risk, particularly where investment incentives are weak [14]. Kållberg et al. (2018) refer to the need to integrate stewardship and access frameworks so that conservation does not inadvertently block the supply of life-saving medicines in areas of high need [18]. Glover et al. (2023) address how subscription contracts can be designed to secure fair distribution of antibiotics while driving innovation [15].

Economic and Policy Challenges

The "valley of death" problem plagues antibiotic markets, wherein early-stage research is relatively well funded compared to late-stage development, which lacks sufficient funding [6]. Moreover, stewardship initiatives that limit the application of antibiotics further decrease revenues, making antibiotics less attractive for investors [18]. Policy innovations, such as transferable exclusivity vouchers, provide strong pull incentives but are controversial because of potential negative spillovers in other disease areas [11]. Likewise, the complexity of developing sustainable economic incentives is compounded by the reliance of subscription models on significant government involvement and robust health technology assessment frameworks [16].

Renwick et al. (2018) point out that novel market structures must incorporate both push and pull components and address market failures to provide long-term sustainability [9]. Bandara et al. (2022) support regulatory changes that simplify approval procedures while maintaining stewardship objectives [21]. Outterson (2021) suggests that financial incentives need to be integrated into a global governance system to provide uniform

implementation and avoid fragmentation [19].

This review is subject to several constraints. Methodologically, its nature as a narrative review carries an inherent risk of selection bias and literature omission, compounded by restricting the search to Google Scholar and PubMed. Conceptually, the depth of this synthesis is constrained by the general scarcity of detailed economic research on AMR compared to other global challenges. Finally, policy assessment is complicated by inherent uncertainties: outcome-based funding models lack clear metrics for equitable risk-sharing, and the vast diversity of global health systems (HICs vs. LMICs) limits the generalizability and replicability of successful incentive mechanisms across different contexts.

Future research must shift from conceptual analysis to empirical verification. Priority should be given to developing cost-effectiveness models for hybrid incentive systems to establish concrete financial benchmarks. Concurrently, policy research must design robust global governance frameworks to harmonize stewardship and financing, specifically investigating tiered pricing strategies to ensure access equity in LMICs. Finally, technical studies are required to define and validate standardized metrics for the 'social value' necessary for outcome-based funding mechanisms.

CONCLUSION

Antibiotic innovation is critical to combating AMR, but traditional market forces have failed to incentivize sufficient investment. Push mechanisms support early research, while pull mechanisms reward successful products. Both have strengths and limitations, but hybrid approaches appear most promising for balancing innovation, stewardship, and access. Future progress will require sustained political will, global coordination, and ongoing evaluation of incentive models. Without decisive action, the world risks entering a post-antibiotic era with devastating health and economic consequences.

Declaration by Authors

Ethical Approval: Not applicable

Acknowledgement: The authors would like to acknowledge TEAM APAR Health, Gurugram for the continuous mentorship. (SPARK PROGRAM)

Source of Funding: None

Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Abraham, I., Hiligsmann, M., Lee, K. K. C., Citrome, L., Colombo, G. L., & Gregg, M. (2023). What to expect in 2024: important health economics and outcomes research (HEOR) trends. Current Medical Research and Opinion, 40(2), 185–192. https://doi.org/10.1080/03007995.2023.2291603
2. Baker, S. J., Payne, D. J., Rappuoli, R., & De Gregorio, E. (2018). Technologies to address antimicrobial resistance. Proceedings of the National Academy of Sciences, 115(51), 12887–12895. https://doi.org/10.1073/pnas.1717160115
3. Dadgostar, P. (2019). Antimicrobial Resistance: Implications and Costs. Infection and Drug Resistance, Volume 12, 3903–3910. https://doi.org/10.2147/idr.s234610
4. Holmes, A. H., Moore, L. S. P., Sundsfjord, A., Steinbakk, M., Regmi, S., Karkey, A., Guerin, P. J., & Piddock, L. J. V. (2016). Understanding the mechanisms and drivers of antimicrobial resistance. The Lancet, 387(10014), 176–187. https://doi.org/10.1016/s0140-6736(15)00473-0
5. Laxminarayan, R., Sridhar, D., Blaser, M., Wang, M., & Woolhouse, M. (2016). Achieving global targets for antimicrobial resistance. Science, 353(6302), 874–875. https://doi.org/10.1126/science.aaf9286
6. Lipsitch, M., & Samore, M. H. (2002). Antimicrobial Use and Antimicrobial Resistance: A Population Perspective. Emerging Infectious Diseases, 8(4), 347–354. https://doi.org/10.3201/eid0804.010312
7. Morrison, L., & Zembower, T. R. (2020). Antimicrobial Resistance. Gastrointestinal Endoscopy Clinics of North America, 30(4), 619–635. https://doi.org/10.1016/j.giec.2020.06.004
8. Okeke, I. N., de Kraker, M. E. A., Van Boeckel, T. P., Kumar, C. K., Schmitt, H.,

Gales, A. C., Bertagnolio, S., Sharland, M., & Laxminarayan, R. (2024). The scope of the antimicrobial resistance challenge. The Lancet, 403(10442), 2426–2438. https://doi.org/10.1016/s0140-6736(24)00876-6

9. Renwick, M. J., Brogan, D. M., & Mossialos, E. (2015). A systematic review and critical assessment of incentive strategies for discovery and development of novel antibiotics. The Journal of Antibiotics, 69(2), 73–88. https://doi.org/10.1038/ja.2015.98
10. Towse, A., Hoyle, C. K., Goodall, J., Hirsch, M., Mestre-Ferrandiz, J., & Rex, J. H. (2017). Time for a change in how new antibiotics are reimbursed: Development of an insurance framework for funding new antibiotics based on a policy of risk mitigation. Health Policy, 121(10), 1025–1030. https://doi.org/10.1016/j.healthpol.2017.07.011
11. Analytical framework for examining the value of antibacterial products. (2014, April 14). ASPE. https://aspe.hhs.gov/reports/analytical-framework-examining-value-antibacterial-products
12. Rex, J. H., & Outterson, K. (2016). Antibiotic reimbursement in a model delinked from sales: a benchmark-based worldwide approach. The Lancet Infectious Diseases, 16(4), 500–505. https://doi.org/10.1016/s1473-3099(15)00500-9
13. Anderson, M., Panteli, D., van Kessel, R., Ljungqvist, G., Colombo, F., & Mossialos, E. (2023). Challenges and opportunities for incentivising antibiotic research and development in Europe. The Lancet Regional Health - Europe, 33, 100705. https://doi.org/10.1016/j.lanepe.2023.100705
14. Årdal, C., Lacotte, Y., & Ploy, M.-C. (2020). Financing Pull Mechanisms for Antibiotic-Related Innovation: Opportunities for Europe. Clinical Infectious Diseases, 71(8), 1994–1999. https://doi.org/10.1093/cid/ciaa153
15. Glover, R. E., Singer, A., Roberts, A. P., & Kirchhelle, C. (2023). Why is the UK subscription model for antibiotics considered successful? The Lancet Microbe, 4(11), e852–e853. https://doi.org/10.1016/s2666-5247(23)00250-1
16. Brogan, D. M., & Mossialos, E. (2013). Incentives for new antibiotics: the Options Market for Antibiotics (OMA) model. Globalization and Health, 9(1), 58. https://doi.org/10.1186/1744-8603-9-58
17. Årdal, C., Balasegaram, M., Laxminarayan, R., McAdams, D., Outterson, K., Rex, J. H., & Sumpradit, N. (2019). Antibiotic development - economic, regulatory and societal challenges. Nature Reviews Microbiology, 18(5), 267–274. https://doi.org/10.1038/s41579-019-0293-3
18. Kållberg, C., Årdal, C., Salvesen Blix, H., Klein, E., M. Martinez, E., Lindbæk, M., Outterson, K., Røttingen, J.-A., & Laxminarayan, R. (2018). Introduction and geographic availability of new antibiotics approved between 1999 and 2014. PLOS ONE, 13(10), e0205166. https://doi.org/10.1371/journal.pone.0205166
19. Outterson, K. (2021). Estimating The Appropriate Size Of Global Pull Incentives For Antibacterial Medicines. Health Affairs, 40(11), 1758–1765. https://doi.org/10.1377/hlthaff.2021.00688
20. Årdal, C., Røttingen, J.-A., Opalska, A., Van Hengel, A. J., & Larsen, J. (2017). Pull Incentives for Antibacterial Drug Development: An Analysis by the Transatlantic Task Force on Antimicrobial Resistance. Clinical Infectious Diseases, 65(8), 1378–1382. https://doi.org/10.1093/cid/cix526
21. Bandara, S., Baral, P., Joshi, A., Muhia, J., Rahman-Shepherd, A., Adhikari, P., Bayingana, A., Bookholane, H., Changyit-Levin, Y., Dada, S., Dutta, R., Essar, M. Y., Evaborhene, N. A., Krugman, D., Kumar, R., Manoj, M., Mathewos, K., Olson, N., Osborne, R., … Wong, B. L. H. (2022). Open Letter to G7 and G20 leaders: resolve global crises to secure our future. Nature Medicine, 28(10), 1974–1975. https://doi.org/10.1038/s41591-022-01944-7

How to cite this article: Veda Dua, Adarsh Keshari, Rhea Aggarwal. Incentivizing antibiotic innovation: a narrative review of push and pull economic models for antimicrobial resistance (AMR). *International Journal of Research and Review*. 2025; 12(10): 468-472. DOI: *https://doi.org/10.52403/ijrr.20251049*

******