

Antimicrobial Resistance: Global Threat and Solutions

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Abstract

Antimicrobial resistance (AMR) signifies a critical global health issue that erodes decades of treatment progress. Resistant microorganisms diminish the effectiveness of available treatments, leading to longer disease courses, higher fatality rates, and escalating healthcare expenditures. The phenomenon is driven by inappropriate antibiotic use in humans and animals, weak infection-control practices, and limited innovation in drug discovery.

Furthermore, the environmental dissemination of resistant genes through untreated waste and agricultural runoff creates a self-reinforcing cycle of resistance that transcends clinical settings. Addressing AMR requires coordinated international strategies that integrate a One Health paradigm linking environmental health, animal, and human, to ensure robust surveillance, stewardship, regulatory oversight, and investment in novel interventions. Raising public awareness, ensuring rational prescribing, and fostering cross-sectoral collaboration are essential to safeguard future generations. This review outlines the magnitude of the problem and explores sustainable approaches across healthcare, agriculture, and policy. Beyond primary infections, the rise of AMR threatens the safety of routine surgical procedures and cancer treatments, potentially transforming manageable medical interventions into high-risk endeavors.

Keywords: Antimicrobial resistance, Global health, Stewardship, Drug development, Policy solutions

1. Introduction

Antimicrobial resistance (AMR) has become one of the leading prominent health threats of the present age. It is defined as the capacity of microorganisms including viruses, bacteria, parasites and fungi to survive exposure to antimicrobial agents that previously suppressed or eliminated them. This phenomenon erodes decades of advancement in medicine and undermines the reliability of modern healthcare systems ^[1]. The World Health Organization (WHO) has repeatedly classified AMR as a global priority, cautioning that without immediate intervention, even minor injuries and routine infections could over again prove lethal ^[2]. The scale of the crisis is alarming. In 2019, bacterial AMR was directly responsible for an estimated 1.27 million mortalities and connected with approximately 5 million worldwide ^[3]. Forecasts suggest thereby 2050, AMR could account for up to 10 million mortalities yearly, exceeding cancer as a predominant cause of mortality ^[4]. Beyond human health, AMR also jeopardizes food security, economic stability, and sustainable development, given its impact on agriculture, veterinary medicine, and international trade ^[5].

The economic repercussions are profound. The World Bank projects that AMR could decrease global GDP by 1.1% to 3.8% by 2050, with minimum-income countries disproportionately affected ^[6].

Healthcare costs rise sharply due to prolonged hospital stays, reliance on costly second-line therapies, and increased morbidity ^[7]. Moreover, AMR threatens the safety of medical procedures such as organ transplantation, chemotherapy, and major surgeries, all of which depend on effective prophylactic antimicrobials ^[8]. Although the discovery of penicillin in 1928 revolutionized medicine, resistance was reported within a decade of its widespread use ^[9]. Since then, improper and excessive utilization of antimicrobials in human health services, agriculture, and aquaculture has accelerated the emergence of resistant strains ^[10]. The globalization of trade and travel has further facilitated the rapid dissemination of resistance genes across borders ^[11]. Table 1 shows Global burden of antimicrobial resistance.

Table 1. Global burden of antimicrobial resistance

Region	Estimated AMR deaths (2019)	Projected deaths (2050)	Economic impact (GDP loss %)
Global ^[10]	1.27 million	10 million	1.1–3.8%
Europe ^[10]	133,000	390,000	1.6%
South Asia ^[11]	389,000	2.5 million	2.0%
Sub-Saharan Africa ^[12]	255,000	4.1 million	3.0%

Microorganisms utilize a wide range of strategies to resist antimicrobial activity, including enzymatic breakdown of drugs, structural modifications at target sites, activation of efflux systems, and the formation of biofilms ^[12]. The exchange of genetic material through horizontal gene transfer additionally speeds up the distribution of resistance traits over different species and ecological niches ^[13]. The emergence of multidrug-resistant pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, and methicillin-resistant *Staphylococcus aureus* (MRSA) illustrates the serious clinical consequences of these mechanisms ^[14]. Several interconnected factors drive the rapid development and spread of resistance. In human medicine, inappropriate prescribing practices and poor patient adherence remain major contributors ^[15]. At the same time, widespread use of antimicrobials in agriculture and aquaculture encourages the evolution of resistant strains that can reach humans through environmental exposure and food chains ^[16]. Weak infection-control measures in healthcare facilities intensify the problem, enabling resistant organisms to spread more easily ^[17]. Additionally, contamination from pharmaceutical production and improper waste disposal creates reservoirs of resistance genes in soil and aquatic environments, sustaining their persistence and circulation ^[18].

Effective surveillance is essential for tracking antimicrobial resistance (AMR) patterns, yet many regions still lack robust monitoring frameworks ^[19]. Programs such as the Global Antimicrobial Resistance Surveillance System (GLASS) were developed to standardize data collection, but differences in laboratory infrastructure and reporting capacity remain significant obstacles ^[20]. Advances in genomic sequencing and specialized AMR databases now offer promising avenues for earlier detection and targeted interventions ^[21].

The economic consequences of AMR are severe. According to World Bank estimates, global GDP could reduce by 1.1% to 3.8% by 2050, with low-income nations facing the greatest impact ^[22]. Healthcare systems are burdened by extended hospital admissions, reliance on costly second-line treatments, and increased rates of morbidity ^[23]. In addition, AMR undermines the safety of critical medical procedures

including organ transplants, chemotherapy, and major surgeries that depend on reliable prophylactic antimicrobials ^[24].

Addressing AMR requires a coordinated and multifaceted global strategy. Core measures include:

- Implementation of antimicrobial stewardship programs to ensure rational prescribing ^[25].
- Investment in innovative therapeutics, including new antibiotics, vaccines, and alternatives such as bacteriophage therapy.
- Strengthening infection prevention and control practices in hospitals and communities.
- Public education campaigns to encourage responsible antimicrobial use.
- International cooperation and policy frameworks that guarantee equitable access to diagnostics and medicines.

Mechanisms of Resistance

Antimicrobial resistance emerges through a variety of biochemical and molecular processes that permit microorganisms to withstand exposure to therapeutic substances. These mechanisms are shaped by microbial physiology, evolutionary pressures, selective environments, and horizontal gene transfer. A clear understanding of these pathways is crucial for designing effective interventions, advancing drug discovery, and guiding stewardship initiatives.

A. Enzymatic Degradation and Modification: One of the most recognized mechanisms involves enzymatic inactivation of drugs. β -lactamases, for instance, break down the β -lactam ring in penicillins and cephalosporins, rendering them ineffective ^[26]. Carbapenemases and Extended-spectrum β -lactamases (ESBLs) are of significant concern, as they impart resistance to last-line antibiotics ^[27]. Aminoglycoside-modifying enzymes including acetyltransferases, nucleotidyltransferases, and phosphotransferases alter drug structures, preventing them from binding to ribosomal targets ^[28].

B. Target Site Alteration: Resistance can also arise through mutations or modifications in drug-binding sites. For example, changes in penicillin-binding proteins [PBPs] lead to β -lactam resistance in *Streptococcus pneumoniae* ^[29]. Alterations in DNA gyrase and topoisomerase IV are central to fluoroquinolone resistance ^[30]. In *Mycobacterium tuberculosis*, mutations in the *rpoB* gene encoding RNA polymerase result in rifampicin resistance, a hallmark of multidrug-resistant tuberculosis ^[31].

C. Efflux Pumps: Efflux systems actively transport antimicrobial drugs out of the cell, decreasing intracellular drug concentrations below therapeutic thresholds. The AcrAB-TolC efflux pump in *Escherichia coli* is a classic example, capable of expelling β -lactams, tetracyclines, fluoroquinolones, and chloramphenicol ^[32]. These pumps are often controlled by global transcriptional regulators, allowing bacteria to adapt quickly to environmental stress ^[33]. Schematic diagram of efflux pump activity in Gram-negative bacteria is shown in figure 1.

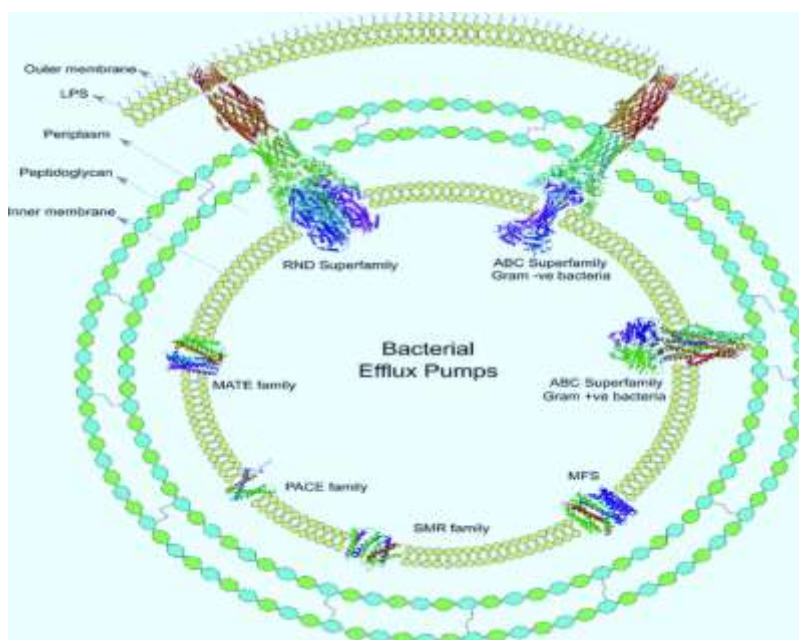


Figure 1: Schematic diagram of efflux pump activity in Gram-negative bacteria.

A. Reduced Permeability: Alterations in microbial membrane permeability can restrict the entry of antimicrobial agents. In Enterobacteriaceae, the loss or modification of porin proteins such as OmpF and OmpC reduces sensitivity to β -lactams and fluoroquinolones [34]. Gram-positive bacteria, by contrast, often develop thicker cell walls and altered lipid structures, which further impede drug penetration [35].

B. Biofilm Formation: Biofilms create a specialized environment that enhances microbial survival against antimicrobials. Within these communities, reduced metabolic activity, limited drug diffusion, and the persistence of dormant cell populations contribute to resistance [36]. Infections linked to biofilms, particularly those associated with indwelling medical devices—are notoriously difficult to treat and eradicate [37].

C. Horizontal Gene Transfer Resistance: Genes are consistently spread through mobile genetic elements such as transposons, integrons and plasmids, enabling rapid dissemination across species and ecosystems [38]. Processes like conjugation, transformation, and transduction facilitate the acquisition of these genes, often clustering multiple resistance determinants together [39]. The global spread of NDM-1 carbapenemase exemplifies the epidemiological importance of plasmid-mediated transfer [40].

D. Adaptive and Intrinsic Resistance: Some microorganisms naturally resist antimicrobials due to inherent structural or metabolic traits. For example, *Pseudomonas aeruginosa* demonstrates innate resistance through efflux systems and reduced membrane permeability [41]. Adaptive resistance, however, is transient and arises under stress conditions, such as exposure to sub-inhibitory antibiotic concentrations [42].

E. Resistance in Fungi, Viruses, and Parasites: Although bacterial resistance dominates discussions, other pathogens also exhibit resistance. In fungi, mutations in ERG11 confer azole resistance in *Candida* species [43]. Viral resistance often results from mutations in polymerase enzymes, as seen with HIV reverse transcriptase inhibitors [44]. In parasites, resistance to antimalarials such as chloroquine and artemisinin is linked to transporter gene mutations and altered drug metabolism [45]. Table 2 depicts major mechanisms of antimicrobial resistance.

F. Clinical Implications: The coexistence of multiple resistance mechanisms within a single pathogen can cause multidrug-resistant (MDR) and widely drug-resistant (XDR) phenotypes ^[46]. These strains severely restrict therapeutic options and are related with higher mortality, morbidity and higher health services costs ^[47].

G. Future Perspectives: Advances in genomics, proteomics, and structural biology continue to reveal the complexity of resistance pathways. These insights provide opportunities for novel drug development, efflux pump inhibitors, β -lactamase inhibitors, and anti-biofilm strategies ^[48]. Integrating molecular knowledge with surveillance systems and stewardship programs is essential to mitigate the AMR crisis ^[49,50].

Table 2. Major mechanisms of antimicrobial resistance

Mechanism	Example Pathogen	Molecular Basis	Clinical Impact
Enzymatic degradation ^[27]	Klebsiella pneumoniae	β -lactamase production	Carbapenem resistance
Target site alteration ^[28]	Streptococcus pneumoniae	Mutations in PBPs	Penicillin resistance
Efflux pumps ^[36]	E. coli	AcrAB-TolC system	Multidrug resistance
Reduced permeability ^[84]	Enterobacter cloacae	Loss of OmpF/OmpC porins	Fluoroquinolone resistance
Biofilm formation ^[89]	Pseudomonas aeruginosa	Persister cells, matrix protection	Device-associated infections

1. Drivers of Antimicrobial Resistance

Human Misuse: Improper use of antimicrobials in clinical practice remains the leading factor driving resistance. Excessive prescribing, patient expectations, and the absence of rapid diagnostic tools often result in unnecessary antibiotic administration ^[51]. Self-medication and incomplete treatment courses further intensify the problem, as pathogens are exposed to sub-therapeutic drug levels that encourage adaptation ^[52]. In many low- and middle-income countries, unrestricted access to antibiotics without prescription has led to widespread misuse ^[53].

Veterinary and Agricultural Use: Heavy reliance on antimicrobials in agriculture and aquaculture promotes the emergence of resistant strains that can be transmitted to humans through food chains and environmental exposure ^[54]. Despite international recommendations to limit such practices, antibiotics continue to be used for growth promotion and prophylaxis in livestock ^[55]. Resistant organisms, including ESBL-producing E. coli, have been identified in food animals, underscoring the zoonotic dimension of AMR ^[56].

Environmental Contamination: Pharmaceutical production, hospital effluents, and agricultural runoff contribute to reservoirs of resistance in the environment ^[57]. Residual antibiotics in soil and water exert selective pressure, enabling resistant organisms to persist ^[58]. Wastewater treatment facilities have been identified as hotspots for genetic exchange, facilitating the spread of resistance genes into broader ecosystems ^[59].

Globalization and Travel: The interconnected nature of modern societies accelerates the global dissemination of resistant pathogens. International travel and trade allow resistance traits to cross borders rapidly ^[60]. Outbreaks of carbapenemase-producing Enterobacteriaceae and NDM-1 have been linked to

medical tourism and global mobility^[61]. Migration patterns and international food supply chains further complicate containment strategies^[62]. Table 3 includes key drivers of antimicrobial resistance.

Table 3. Key drivers of antimicrobial resistance

Driver	Example Context	Impact on Resistance Spread
Human misuse ^[50-54]	Overprescription, self-medication	Selection of resistant strains
Veterinary/agricultural ^[55-57]	Growth promotion in livestock	Zoonotic transmission of resistant bacteria
Environmental ^[58-60]	Wastewater contamination	Reservoirs of resistance genes
Globalization/travel ^[61,62]	Medical tourism, trade	Rapid international dissemination

2. Impact of Antimicrobial Resistance

Clinical Outcomes: Antimicrobial resistance undermines the effectiveness of therapies for common infections such as urinary tract infections, sepsis and pneumonia^[63]. Resistant pathogens are linked to prolonged illness, elevated mortality rates, and a greater likelihood of complications^[64]. Conditions such as multidrug-resistant tuberculosis and extensively drug-resistant Gram-negative infections highlight the severe clinical consequences of AMR^[65].

Economic Burden: The financial impact of AMR is substantial. Resistant infections drive healthcare costs upward due to extended hospital stays, reliance on expensive second-line treatments, and increased admissions to intensive care units^[66]. The World Bank has cautioned that AMR could decrease global GDP by trillions of dollars by 2050, with low-income nations bearing the greatest losses^[67]. Productivity declines caused by prolonged illness and premature deaths further intensify the economic strain^[68].

Projections of global mortality: Due to AMR by 2050 emphasize that low- and middle-income countries will be most severely affected. Asia is expected to account for approximately 4.73 million deaths [47.3%], followed by Africa with 4.15 million deaths (41.5%). In contrast, Europe and Latin America are projected to face around 390,000–392,000 deaths (about 3.9%), North America about 317,000 [3.1%], and Oceania the lowest at 22,000 (<0.5%). Together, Asia and Africa are anticipated to bear nearly 90% of the global burden^[66].

Threats to Modern Medicine: AMR poses a serious risk to the safety of medical interventions such as chemotherapy, organ transplantation, and major surgical procedures, all of which depend on effective prophylactic antimicrobials^[69]. Without reliable drugs, routine medical practices could become life-threatening^[70]. The emergence of pan-resistant organisms raises the possibility of a “post-antibiotic era,” where even little infections could once again prove fatal^[71]. Clinical and economic impacts of AMR are shown in Table 4.

Table 4. Clinical and economic impacts of AMR

Impact Area	Example Outcome	Evidence/Statistic
Clinical outcomes ^[63-65]	Increased mortality in sepsis	2–3× higher mortality with resistant strains
Economic burden ^[66-68]	Longer hospital stays	+8–20 days per patient
Threats to medicine ^[69-71]	Unsafe surgeries, chemotherapy risks	WHO warning of “post-antibiotic era”

3. Surveillance and Data Gaps

Global Initiatives (GLASS, EARS-Net, etc.)

Surveillance as a Foundation: Monitoring systems are central to effective management of antimicrobial resistance (AMR). The World Health Organization's Global Antimicrobial Resistance Surveillance System (GLASS) was established to provide standardized approaches for data collection and reporting across participating nations ^[72]. GLASS prioritizes harmonization of laboratory practices and integration of clinical and epidemiological information. In Europe, the European Antimicrobial Resistance Surveillance Network (EARS-Net) has played a vital role in tracking resistance trends and shaping policy responses ^[73]. Together, these initiatives underscore the importance of coordinated global action to produce reliable and comparable datasets.

The WHO's GLASS enrollment map (September 2022) illustrates the global distribution of participation. Countries are color-coded by their enrollment status: dark blue indicates involvement in both AMR (antimicrobial resistance) and AMC (antimicrobial consumption), purple reflects AMR-only participation, orange denotes AMC-only, while light gray marks non-enrolled nations and dark gray those not applicable. This visualization highlights regions actively contributing to surveillance efforts, contrasted with areas still outside the program ^[72].

Challenges in Resource-Limited Settings: Despite progress, surveillance capacity remains uneven. Many low- and middle-income countries lack sufficient laboratory infrastructure, skilled personnel, and financial resources to maintain long-term monitoring programs ^[74]. Limited diagnostic capabilities contribute to underreporting and delays in identifying emerging resistance ^[75]. Additionally, fragmented health systems and weak regulatory oversight hinder effective data sharing and integration ^[76]. Table 5 shows global surveillance initiatives and challenges.

Role of Genomics and Big Data: Recent advances in whole-genome sequencing [WGS] and bioinformatics have transformed AMR surveillance. Genomic tools allow rapid detection of resistance genes, mapping of transmission pathways, and support for outbreak investigations ^[77]. Big data platforms and global repositories such as the Comprehensive Antibiotic Resistance Database [CARD] enable real-time monitoring and predictive modeling ^[78]. However, fair access to these technologies persist as a significant issue, particularly in resource-constrained regions ^[79].

Table 5. Global surveillance initiatives and challenges

Initiative	Coverage Region	Strengths	Challenges in LMICs
GLASS [WHO] [72,73]	Global	Standardized methodology	Limited lab capacity
EARS-Net [EU] [74-76]	Europe	Harmonized EU data	Resource disparities
National plans [77-79]	UK, India, GCC	Policy integration	Weak enforcement, fragmented systems

4. Solutions and Strategies

A. Antimicrobial Stewardship (25%)

Antimicrobial stewardship programs [ASPs] are designed to ensure the judicious use of antimicrobials, thereby enhancing patient outcomes and slowing the development of resistance. These initiatives focus on

refining prescribing practices, minimizing inappropriate drug use, and enhancing overall treatment effectiveness. Evidence indicates that stewardship programs play a substantial role in reducing resistance rates, contributing approximately 25% to the overall success of AMR containment strategies ^[80].

Key elements of ASPs include adherence to evidence-based prescribing guidelines, timely de-escalation of therapy when appropriate, and structured audit-and-feedback mechanisms to monitor and improve clinical practice ^[81]. Successful implementation of these programs has consistently demonstrated reductions in unnecessary antibiotic prescriptions and improved patient outcomes across a variety of healthcare settings ^[82].

B. Infection Prevention and Control (30%)

Infection Prevention and Control (IPC) Strengthening infection prevention and control measures is vital to curbing the transmission of resistant organisms. Practices such as rigorous hand hygiene, environmental sanitation, and patient isolation protocols are proven to reduce hospital-acquired infections. Preventive strategies—including vaccination programs—extend beyond clinical settings, lowering transmission in communities and collectively accounting for about 30% of the overall effectiveness in AMR containment ^[83]. The implementation of bundled IPC interventions in intensive care units has been shown to significantly decrease multidrug-resistant infection rates ^[84]. Vaccines also play a crucial role by reducing bacterial disease incidence, thereby indirectly lowering antibiotic consumption ^[85].

C. Novel Therapeutics (New Antibiotics, Vaccines, Phage Therapy) (20%)

The slowdown in antibiotic discovery has prompted exploration of alternative therapeutic approaches. New agents targeting resistant Gram-negative pathogens are under development, though challenges in clinical translation persist ^[86]. Vaccines, such as pneumococcal conjugate formulations, have successfully reduced disease burden and indirectly mitigated resistance. Emerging strategies—including phage therapy, which employs bacteriophages to selectively target resistant bacteria—are gaining renewed attention, with clinical trials reporting encouraging outcomes. Collectively, these innovations contribute around 20% to global AMR containment efforts ^[87,88].

D. Policy Frameworks and Global Collaboration (25%)

Policy-driven interventions are essential for sustaining long-term progress against AMR. The WHO Global Action Plan provides a framework for national strategies, emphasizing surveillance, stewardship, and innovation ^[89]. Collaborative initiatives such as the Transatlantic Taskforce on Antimicrobial Resistance [TATFAR] promote knowledge exchange and harmonization of policies across regions ^[90]. Economic incentives—including market entry rewards and public-private partnerships—are being explored to stimulate antibiotic development. International action plans, regulatory alignment, and adoption of the One Health approach are critical for sustainable management, accounting for roughly 25% of effectiveness in long-term AMR control ^[91]. Ultimately, integrating human, animal, and environmental health perspectives is indispensable for a comprehensive response ^[92]. Figure 2 depicts pie chart on % global solutions and relative contributions to AMR. Table 6 shows key strategies to combat AMR.

% Global Solutions and Relative Contributions to AMR

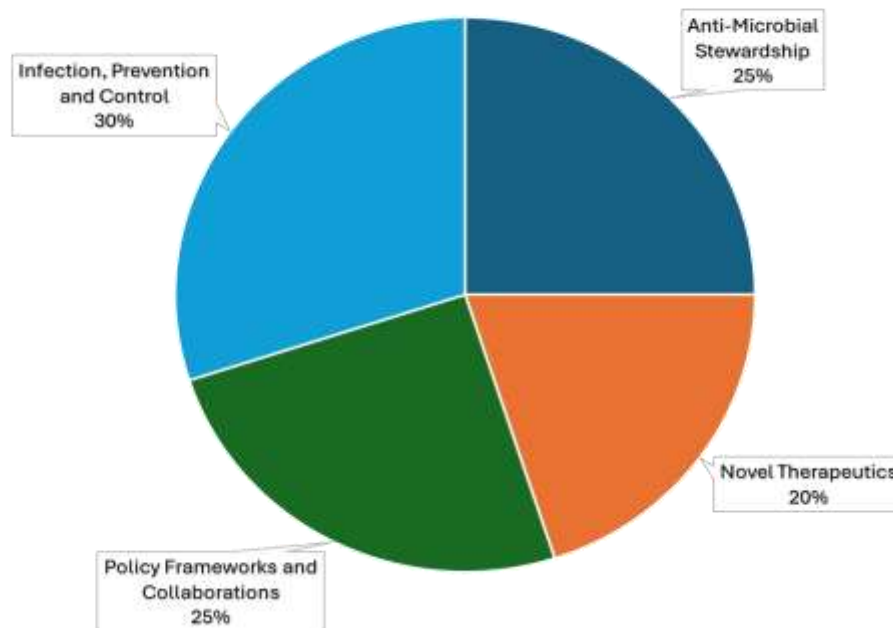


Figure 2: Pie chart on % global solutions and relative contributions to AMR

Table 6. Key strategies to combat AMR

Strategy	Example Intervention	Outcome
Stewardship ^[82]	Audit-feedback programs	Reduced broad-spectrum use
Infection prevention ^[83-85]	Hand hygiene bundles	Lower nosocomial infection rates
Novel therapeutics ^[86-88]	Phage therapy trials	Promising clinical outcomes
Policy frameworks ^[89-92]	WHO Global Action Plan	Coordinated global response

5. Case Studies

Success Stories in Stewardship Programs: Antimicrobial stewardship programs [ASPs] have shown clear success in curbing inappropriate prescribing and improving patient outcomes. In the United States, hospital-based ASPs achieved notable reductions in broad-spectrum antibiotic use, which in turn lowered rates of *Clostridioides difficile* infections ^[93]. Australia's nationwide stewardship initiatives have contributed to a measurable decline in fluoroquinolone resistance among Gram-negative pathogens ^[94]. Likewise, pediatric stewardship programs in Canada have reduced unnecessary antibiotic prescriptions for respiratory tract infections, all while maintaining patient safety ^[95].

National Action Plans (UK, India, EU, GCC): Several countries and regions have adopted comprehensive national strategies to address AMR. The United Kingdom introduced its AMR plan in 2013, focusing on stewardship, surveillance, and innovation, which has led to reduced antibiotic consumption in primary care ^[96]. Within the European Union, coordinated efforts through the European Commission and the ECDC have harmonized surveillance systems and promoted responsible antimicrobial use ^[97]. India launched its National Action Plan on AMR in 2017, emphasizing awareness, surveillance, and infection prevention, though implementation challenges remain ^[98]. In the Gulf Cooperation Council (GCC), collaborative frameworks have been established to enhance laboratory

capacity and align stewardship practices across member states^[99]. National action plans and Stewardship successes are shown in Table 7.

Table 7. National action plans and Stewardship successes

Country/Region	Key Components	Reported Outcomes
UK ^[96]	Stewardship, surveillance	Decline in primary care antibiotic use
EU ^[97]	Harmonized reporting	Improved cross-border data sharing
India ^[98]	Awareness, IPC, surveillance	Early implementation challenges
GCC ^[99]	Regional collaboration	Strengthened lab capacity

6. Future Directions

Research Priorities: Future research must focus on advancing rapid diagnostic tools, developing new antimicrobials, and exploring alternative therapies. Point-of-care diagnostics are particularly important, as they enable clinicians to distinguish bacterial infections from viral ones, thereby reducing unnecessary antibiotic prescriptions^[100]. Continued investment in antimicrobial discovery pipelines, especially those targeting Gram-negative pathogens, remains a critical priority for global health^[101].

One Health Approach: The One Health framework demonstrates the interdependence of animal, human, and environmental health in tackling AMR. Coordinated surveillance across these domains is essential for tracking resistance determinants and designing effective interventions^[102]. Incorporating veterinary and environmental data into public health systems will enhance preparedness and strengthen global capacity to respond to emerging resistance threats^[103].

Sustainable Innovation Models: Long-term innovation in combating antimicrobial resistance requires both economic incentives and collaborative frameworks. Approaches such as public-private partnerships, market entry rewards, and subscription-based payment systems are currently being explored to encourage the development of new antibiotics^[104]. Global actions, including the Global Antibiotic Research and Development Partnership (GARDP), serve as strong examples of cooperative models that drive progress in this field^[105]. Ensuring that new therapies are distributed equitably while upholding stewardship principles will be essential for achieving sustainable outcomes in the fight against AMR^[106,107]. Table 8 shows research priorities and innovation models.

Table 8. Research priorities and innovation models

Priority Area	Example Focus	Potential Impact
Rapid diagnostics ^[100-102]	Point-of-care tests	Reduced inappropriate prescribing
Novel antimicrobials ^[102-103]	Gram-negative targets	Expanded treatment options
One Health integration ^[104]	Veterinary/environmental surveillance	Holistic containment of AMR
Innovation models ^[105-106]	GARDP, CARB-X partnerships	Sustainable drug development

8. Conclusion

Antimicrobial resistance (AMR) stands as one among the most critical challenges confronting global health, food security, and sustainable development. The evidence reviewed across mechanisms, drivers,

impacts, surveillance gaps, and mitigation strategies highlights both the complexity of the problem and the urgent need for coordinated international action. Resistant pathogens undermine the efficacy of existing therapies, elevate mortality rates, prolong hospital admissions, and substantially increase healthcare expenditures. Beyond clinical outcomes, AMR threatens the very foundations of modern medicine, placing routine interventions such as surgery, chemotherapy, and organ transplantation at risk. Encouraging examples from stewardship programs and national action plans demonstrate that meaningful progress is achievable when evidence-based policies, surveillance systems, and innovation converge. Nevertheless, disparities in infrastructure, resources, and governance remain major obstacles, particularly in low- and middle-income countries. Looking ahead, future strategies must fully embrace the One Health perspective, integrating human, animal, and environmental health, while advancing sustainable innovation models that incentivize the development of new therapeutics and diagnostics.

Ultimately, confronting AMR requires global solidarity: harmonized surveillance, responsible antimicrobial use, investment in novel solutions, and equitable access to healthcare. Without decisive and sustained action, the world risks entering a post-antibiotic era where even little infections could once again prove fatal. With continued commitment, innovation, and collaboration, however, AMR can be contained, preserving the achievements of modern medicine for generations to come.

References

1. Ho CS, Wong CT, Aung TT, Lakshminarayanan R, Mehta JS, Rauz S, et al. Antimicrobial resistance: a concise update. *Lancet Microbe*. 2025;6^[1]:100947.
2. WHO. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015.
3. Murray CJL, Ikuta KS, Sharara F, Swetschinski L, Robles Aguilar G, Gray A, et al. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*. 2022;399[10325]:629-55.
4. GBD 2021 Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance 1990–2021: forecasts to 2050. *Lancet*. 2024;404[10459]:1199-226.
5. Aljeldah MM. Antimicrobial resistance and its spread is a global threat. *Antibiotics*. 2022;11^[8]:1082.
6. World Bank. Drug-resistant infections: a threat to our economic future. Washington DC: World Bank; 2017.
7. Smith R, Coast J. The economic burden of antimicrobial resistance: why it is more serious than current estimates. *Appl Health Econ Health Policy*. 2013;11^[3]:325-36.
8. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis*. 2006;42[S2]:S82-9.
9. Fleming A. Penicillin. *Br J Exp Pathol*. 1929;10^[3]:226-36.
10. Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen JA, Klugman K, et al. Access to effective antimicrobials: a worldwide challenge. *Lancet*. 2016;387[10014]:168-75.
11. Holmes AH, Moore LSP, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet*. 2016;387[10014]:176-87.
12. Blair JMA, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJV. Molecular mechanisms of antibiotic resistance. *Nat Rev Microbiol*. 2015;13^[1]:42-51.
13. Davies J, Davies D. Origins and evolution of antibiotic resistance. *Microbiol Mol Biol Rev*. 2010;74^[3]:417-33.

14. Tacconelli E, Carrara E, Savoldi A, Harbarth S, Mendelson M, Monnet DL, et al. WHO priority list of antibiotic-resistant bacteria. *Lancet Infect Dis.* 2018;18^[3]:318-27.
15. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis.* 2003;36^[11]:1433-7.
16. Van Boeckel TP, Brower C, Gilbert M, Grenfell BT, Levin SA, Robinson TP, et al. Global trends in antimicrobial use in food animals. *Proc Natl Acad Sci USA.* 2015;112^[18]:5649-54.
17. Allegranzi B, Pittet D. Role of infection control in combating antimicrobial resistance. *Clin Infect Dis.* 2009;49^[4]:575-9.
18. Larsson DGJ, Flach CF. Antibiotic resistance in the environment. *Nat Rev Microbiol.* 2022;20^[5]:257-69.
19. Holmes AH, Moore LSP, Sundsfjord A, Steinbakk M, Regmi S, Karkey A, et al. Understanding the mechanisms and drivers of antimicrobial resistance. *Lancet.* 2016;387[10014]:176-87.
20. WHO. Global antimicrobial resistance surveillance system [GLASS] report. Geneva: WHO; 2021.
21. Centner CM, Di Gregorio S, Argimón S, Brankin A, Dean A, Zamora DM, et al. Antimicrobial resistance databases: opportunities and challenges for public health. *npj Antimicrobials and Resistance.* 2026;4:1.
22. Bush K, Bradford PA. β -lactams and β -lactamase inhibitors: an overview. *Cold Spring Harb Perspect Med.* 2016;6^[8]:a025247.
23. Logan LK, Weinstein RA. The epidemiology of carbapenem-resistant Enterobacteriaceae: the impact and evolution of a global menace. *J Infect Dis.* 2017;215[Suppl 1]:S28-36.
24. Ramirez MS, Tolmasky ME. Aminoglycoside modifying enzymes. *Drug Resist Updat.* 2010;13^[6]:151-71.
25. Hakenbeck R, Brückner R, Denapaite D, Maurer P. Molecular mechanisms of β -lactam resistance in *Streptococcus pneumoniae*. *Future Microbiol.* 2012;7^[3]:395-410.
26. Hooper DC, Jacoby GA. Mechanisms of fluoroquinolone resistance. *Clin Infect Dis.* 2015;41^[2]:S113-22.
27. Telenti A, Imboden P, Marchesi F, Lowrie D, Cole S, Colston MJ, et al. Molecular basis of rifampicin resistance in *Mycobacterium tuberculosis*. *Lancet.* 1993;341[8846]:647-50.
28. Nikaido H, Pagès JM. Broad-specificity efflux pumps and their role in multidrug resistance of Gram-negative bacteria. *FEMS Microbiol Rev.* 2012;36^[2]:340-63.
29. Li XZ, Plésiat P, Nikaido H. The challenge of efflux-mediated antibiotic resistance in Gram-negative bacteria. *Clin Microbiol Rev.* 2015;28^[2]:337-418.
30. Delcour AH. Outer membrane permeability and antibiotic resistance. *Biochim Biophys Acta.* 2009;1794^[5]:808-16.
31. Cui L, Murakami H, Kuwahara-Arai K, Hanaki H, Hiramatsu K. Contribution of a thickened cell wall to vancomycin resistance in *Staphylococcus aureus*. *Antimicrob Agents Chemother.* 2000;44^[9]:2276-85.
32. Hall CW, Mah TF. Molecular mechanisms of biofilm-based antibiotic resistance and tolerance in pathogenic bacteria. *FEMS Microbiol Rev.* 2017;41^[3]:276-301.
33. Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. *Clin Microbiol Rev.* 2002;15^[2]:167-93.
34. Partridge SR, Kwong SM, Firth N, Jensen SO. Mobile genetic elements associated with antimicrobial resistance. *Clin Microbiol Rev.* 2018;31^[4]:e00088-17.

35. von Wintersdorff CJH, Penders J, van Niekerk JM, Mills ND, Majumder S, van Alphen LB, et al. Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer. *Front Microbiol.* 2016;7:173.
36. Yong D, Toleman MA, Giske CG, Cho HS, Sundman K, Lee K, et al. Characterization of a new metallo- β -lactamase gene, NDM-1, in Enterobacteriaceae. *Antimicrob Agents Chemother.* 2009;53^[7]:2529-35.
37. Poole K. *Pseudomonas aeruginosa*: resistance to the max. *Front Microbiol.* 2011;2:65.
38. Levin BR, Rozen DE. Non-inherited antibiotic resistance. *Nat Rev Microbiol.* 2006;4^[7]:556-62.
39. Sanglard D, Coste AT. Mechanisms of azole resistance in *Candida albicans*. *Future Microbiol.* 2016;11^[3]:255-71.
40. Wright GD. The antibiotic resistome: the nexus of chemical and genetic diversity. *Nat Rev Microbiol.* 2007;5^[3]:175-86.
41. Munita JM, Arias CA. Mechanisms of antibiotic resistance. *Microbiol Spectr.* 2016;4^[2]:10.1128/microbiolspec.VMBF-0016-2015.
42. Piddock LJV. Multidrug-resistance efflux pumps—not just for resistance. *Nat Rev Microbiol.* 2006;4^[8]:629-36.
43. Blair JM, Richmond GE, Piddock LJV. Multidrug efflux pumps in Gram-negative bacteria and their role in antibiotic resistance. *Future Microbiol.* 2014;9^[10]:1165-77.
44. Doi Y, Paterson DL. Carbapenemase-producing Enterobacteriaceae. *Semin Respir Crit Care Med.* 2015;36^[1]:74-84.
45. Martínez JL. Environmental pollution by antibiotics and by antibiotic resistance determinants. *Environ Pollut.* 2009;157^[11]:2893-902.
46. Andersson DI, Hughes D. Antibiotic resistance and its cost: is it possible to reverse resistance? *Nat Rev Microbiol.* 2010;8^[4]:260-71.
47. Wood TK, Knabel SJ, Kwan BW. Bacterial persister cell formation and dormancy. *Appl Environ Microbiol.* 2013;79^[23]:7116-21.
48. Balaban NQ, Helaine S, Lewis K, Ackermann M, Aldridge B, Andersson DI, et al. Definitions and guidelines for research on antibiotic persistence. *Nat Rev Microbiol.* 2019;17^[7]:441-8.
49. Fajardo A, Martínez JL. Antibiotics as signals that trigger specific bacterial responses. *Curr Opin Microbiol.* 2008;11^[2]:161-7.
50. Van Hoek AHAM, Mevius D, Guerra B, Mullany P, Roberts AP, Aarts HJM. Acquired antibiotic resistance genes: an overview. *Front Microbiol.* 2011;2:203.
51. Ventola CL. The antibiotic resistance crisis: part 1. *P T.* 2015;40^[4]:277-83.
52. Morgan DJ, Okeke IN, Laxminarayan R, Perencevich EN, Weisenberg S. Non-prescription antimicrobial use worldwide. *Lancet Infect Dis.* 2011;11^[9]:692-701.
53. Auta A, Hadi MA, Oga E, Adewuyi EO, Abdu-Aguye SN, Adeloye D, et al. Global access to antibiotics without prescription: a systematic review. *J Infect.* 2019;78^[1]:8-18.
54. Landers TF, Cohen B, Wittum TE, Larson EL. A review of antibiotic use in food animals: perspective, policy, and potential. *Public Health Rep.* 2012;127^[1]:4-22.
55. Marshall BM, Levy SB. Food animals and antimicrobials: impacts on human health. *Clin Microbiol Rev.* 2011;24^[4]:718-33.
56. Madec JY, Haenni M, Nordmann P, Poirel L. Extended-spectrum β -lactamase-producing *E. coli* in livestock: a threat to human health. *Clin Microbiol Infect.* 2017;23^[11]:826-33.

57. Kümmerer K. Antibiotics in the aquatic environment—a review. *Chemosphere*. 2009;75^[4]:417-34.
58. Wellington EM, Boxall AB, Cross P, Feil EJ, Gaze WH, Hawkey PM, et al. The role of the natural environment in the emergence of antibiotic resistance. *Environ Microbiol*. 2013;15^[11]:3070-92.
59. Rizzo L, Manaia C, Merlin C, Schwartz T, Dagot C, Ploy MC, et al. Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes. *Sci Total Environ*. 2013;447:345-60.
60. Tängdén T, Giske CG. Global dissemination of extensively drug-resistant carbapenemase-producing Enterobacteriaceae: clinical perspectives on detection, treatment and infection control. *J Intern Med*. 2015;277^[5]:501-12.
61. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism in India, Pakistan, and the UK: NDM-1. *Lancet Infect Dis*. 2010;10^[9]:597-602.
62. Collignon P, Beggs JJ, Walsh TR, Gandra S, Laxminarayan R. Anthropological and socioeconomic factors contributing to global antimicrobial resistance: a univariate and multivariable analysis. *Lancet Planet Health*. 2018;2^[9]:e398-405.
63. Cosgrove SE, Carmeli Y. The impact of antimicrobial resistance on health and economic outcomes. *Clin Infect Dis*. 2003;36^[11]:1433-7.
64. Schwaber MJ, Carmeli Y. Mortality and delay in effective therapy associated with extended-spectrum β -lactamase production in Enterobacteriaceae bacteremia. *J Antimicrob Chemother*. 2007;60^[5]:913-20.
65. Gandhi NR, Nunn P, Dheda K, Schaaf HS, Zignol M, van Soolingen D, et al. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. *Lancet*. 2010;375[9728]:1830-43.
66. Roberts RR, Hota B, Ahmad I, Scott RD, Foster SD, Abbasi F, et al. Hospital and societal costs of antimicrobial-resistant infections in a Chicago teaching hospital. *Clin Infect Dis*. 2009;49^[8]:1175-84.
67. Jonas OB, Irwin A, Berthe FCJ, Le Gall FG, Marquez PV. Drug-resistant infections: a threat to our economic future. Washington DC: World Bank; 2017.
68. Smith R, Coast J. The true cost of antimicrobial resistance. *BMJ*. 2013;346:f1493.
69. Cosgrove SE. The relationship between antimicrobial resistance and patient outcomes: mortality, length of hospital stay, and health care costs. *Clin Infect Dis*. 2006;42[S2]:S82-9.
70. Cassini A, Högberg LD, Plachouras D, Quattrocchi A, Hoxha A, Simonsen GS, et al. Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and EEA, 2015. *Lancet Infect Dis*. 2019;19^[1]:56-66.
71. Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M. Achieving global targets for antimicrobial resistance. *Science*. 2020;367[6483]:146-8.
72. WHO. Global antimicrobial resistance surveillance system [GLASS] report. Geneva: World Health Organization; 2021.
73. European Centre for Disease Prevention and Control. EARS-Net report: antimicrobial resistance surveillance in Europe. Stockholm: ECDC; 2020.
74. Omulo S, Thumbi SM, Lockwood S, Verani JR, Bigogo G, Meara W, et al. Surveillance of antimicrobial resistance in low-income countries: challenges and opportunities. *Clin Infect Dis*. 2015;61[Suppl 2]:S159-S164.
75. Okeke IN, Laxminarayan R, Bhutta ZA, Duse AG, Jenkins P, O'Brien TF, et al. Antimicrobial resistance in developing countries. *Lancet Infect Dis*. 2005;5^[8]:481-93.

76. Ayukekbong JA, Ntemgwa M, Atabe AN. The threat of antimicrobial resistance in developing countries: causes and control strategies. *Antimicrob Resist Infect Control*. 2017;6:47.
77. Didelot X, Bowden R, Wilson DJ, Peto TEA, Crook DW. Transforming clinical microbiology with bacterial genome sequencing. *Nat Rev Genet*. 2012;13^[9]:601-12.
78. Jia B, Raphenya AR, Alcock B, Waglechner N, Guo P, Tsang KK, et al. CARD 2017: expansion and model-centric curation of the comprehensive antibiotic resistance database. *Nucleic Acids Res*. 2017;45[D1]:D566-D573.
79. Hendriksen RS, Bortolaia V, Tate H, Tyson GH, Aarestrup FM, McDermott PF. Using genomics to track global antimicrobial resistance. *Front Public Health*. 2019;7:242.
80. Dyar OJ, Huttner B, Schouten J, Pulcini C. What is antimicrobial stewardship? *Clin Microbiol Infect*. 2017;23^[11]:793-8.
81. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the IDSA and SHEA. *Clin Infect Dis*. 2016;62^[10]:e51-77.
82. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic review and meta-analysis of clinical and economic outcomes of antimicrobial stewardship programs. *Antimicrob Agents Chemother*. 2016;60^[8]:4840-52.
83. Allegranzi B, Pittet D. Role of infection control in combating antimicrobial resistance. *Clin Infect Dis*. 2009;49^[4]:575-9.
84. Tacconelli E, Cataldo MA, Dancer SJ, De Angelis G, Falcone M, Frank U, et al. Infection control and hospital epidemiology: guidelines for preventing the spread of multidrug-resistant Gram-negatives. *Clin Microbiol Infect*. 2014;20[Suppl 1]:1-55.
85. Whitney CG, Farley MM, Hadler J, Harrison LH, Bennett NM, Lynfield R, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med*. 2003;348^[18]:1737-46.
86. Theuretzbacher U, Bush K, Harbarth S, Paul M, Rex JH, Tacconelli E, et al. Critical analysis of antibacterial agents in clinical development. *Nat Rev Microbiol*. 2020;18^[5]:286-98.
87. Klugman KP, Black S. Impact of vaccines on bacterial antimicrobial resistance. *Drug Resist Updat*. 2018;39:1-12.
88. Kortright KE, Chan BK, Koff JL, Turner PE. Phage therapy: a renewed approach to combat antibiotic-resistant bacteria. *Cell Host Microbe*. 2019;25^[2]:219-32.
89. WHO. Global action plan on antimicrobial resistance. Geneva: World Health Organization; 2015.
90. US CDC, European Commission. Transatlantic Taskforce on Antimicrobial Resistance [TATFAR] report. Atlanta: CDC; 2014.
91. Renwick MJ, Brogan DM, Mossialos E. A systematic review of incentives to stimulate antibiotic development. *Health Policy*. 2016;120^[8]:863-75.
92. Robinson TP, Bu DP, Carrique-Mas J, Fèvre EM, Gilbert M, Grace D, et al. Antibiotic resistance is the quintessential One Health issue. *Trans R Soc Trop Med Hyg*. 2016;110^[7]:377-80.
93. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the IDSA and SHEA. *Clin Infect Dis*. 2016;62^[10]:e51-77.
94. James R, Upjohn L, Cotta M, Luu S, Marshall C, Buising K. Measuring antimicrobial prescribing in Australian hospitals: development of a national surveillance system. *Med J Aust*. 2015;202^[7]:366-8.

95. Gerber JS, Prasad PA, Fiks AG, Localio AR, Grundmeier RW, Bell LM, et al. Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians. *JAMA*. 2013;309^[22]:2345-52.
96. Department of Health UK. UK five-year antimicrobial resistance strategy 2013–2018. London: DH; 2013.
97. European Commission. A European One Health action plan against antimicrobial resistance. Brussels: EC; 2017.
98. Ministry of Health and Family Welfare, Government of India. National action plan on antimicrobial resistance. New Delhi: MoHFW; 2017.
99. Zowawi HM, Balkhy HH, Walsh TR, Paterson DL. β -lactamase production in key Gram-negative pathogen isolates from the Gulf Cooperation Council states. *Clin Microbiol Rev*. 2013;26^[3]:361-80.
100. O'Neill J. Rapid diagnostics: stopping unnecessary use of antibiotics. London: Review on Antimicrobial Resistance; 2015.
101. Theuretzbacher U, Bush K, Harbarth S, Paul M, Rex JH, Tacconelli E, et al. Critical analysis of antibacterial agents in clinical development. *Nat Rev Microbiol*. 2020;18^[5]:286-98.
102. Robinson TP, Bu DP, Carrique-Mas J, Fèvre EM, Gilbert M, Grace D, et al. Antibiotic resistance is the quintessential One Health issue. *Trans R Soc Trop Med Hyg*. 2016;110^[7]:377-80.
103. Hernando-Amado S, Coque TM, Baquero F, Martínez JL. Defining and combating antibiotic resistance from One Health and global health perspectives. *Nat Microbiol*. 2019;4^[9]:1432-42.
104. Renwick MJ, Brogan DM, Mossialos E. A systematic review of incentives to stimulate antibiotic development. *Health Policy*. 2016;120^[8]:863-75.
105. Balasegaram M, Kolb P, McKee M, Wilcox M, Wertheim H, Laxminarayan R, et al. Global Antibiotic Research and Development Partnership [GARDP]: addressing AMR through public-private collaboration. *J Antibiot*. 2017;70^[9]:775-9.
106. Outterson K, Rex JH, Jinks T, Jackson P, Hallinan N, Karp S, et al. Accelerating global innovation to address antibacterial resistance: introducing CARB-X. *Nat Rev Drug Discov*. 2016;15^[9]:589-90.
107. Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M. Achieving global targets for antimicrobial resistance. *Science*. 2020;367[6483]:146-8.