Integrated Approaches for Addressing Antimicrobial Resistance in Human, Animal, and Environmental Health

Authors

Bilal Deniz[1], Ayşe Sona Karakuş[2], Vural Denizhan[2], Gülay Seher Başböyük[1], Mehmet Mamay[3], Muhammet Ali Daşkın[1], Mine Sönmez[1], Ronayı Coşkun[4]

Affiliations

[1] Gaziosmanpaşa Training and Research Hospital, Istanbul, Turkey
[2] Van Yüzüncü Yıl University, Faculty of Veterinary Medicine, Van, Turkey
[3] Harran University, Faculty of Agriculture, Şanlıurfa, Turkey
[4] University of Health Sciences, Faculty of Pharmacy, Istanbul, Turkey

Corresponding Author

Bilal Deniz
Gaziosmanpaşa Training and Research Hospital, Istanbul, Turkey
Email: bilal.deniz3@saglik.gov.tr
ORCID: 0009-0003-6307-8745

Cite as, Deniz B, Karakuş AS, Denizhan V, et al. (2026). Integrated Approaches for Addressing Antimicrobial Resistance in Human, Animal, and Environmental Health. *Journal of Global Medicine*, 6(1), e385. Retrieved from https://globalmedicine.co.uk/index.php/jogm/article/view/385

Abstract
Antimicrobial resistance (AMR) is a major public health problem that is making infections increasingly difficult to treat and increasing the global burden of disease. Its effects are not limited to clinical outcomes; they also directly affect health systems, the economy, livestock production, agriculture, and the environment. This review examines the main factors involved in the emergence and spread of AMR, as well as the limitations of existing antibiotics. It also reviews current options, including new antibiotics, bacteriophages, endolysins, anti-virulence approaches, monoclonal antibodies, vaccines, and microbiota-based therapies. The role of rapid diagnostic methods in the timely initiation of appropriate treatment, the contribution of antimicrobial stewardship programs, and the importance of the One Health approach are also discussed. In conclusion, combating AMR requires more than the development of new drugs alone; it requires a comprehensive approach based on global collaboration, effective regulatory and oversight mechanisms, and strengthened data sharing across institutions.

Submitted: 25 June 2026; Revision Received: 4 August 2026; Accepted: 9 August 2026; Published: xx.xx.xxxx

Keywords

antimicrobial resistance; rapid diagnostics; antimicrobial stewardship; One Health; infectious diseases; antimicrobial therapy

1. Introduction

Antimicrobial agents play a critical role in the treatment and prevention of infectious diseases observed across different living organisms.[1] Antimicrobial resistance (AMR) arises when bacteria, viruses, fungi, and parasites no longer respond effectively to antimicrobial medicines. Consequently, antimicrobial drugs become ineffective, making infections difficult to treat and increasing the risk of disease spread, severe illness, and death.[1–3]

AMR was directly responsible for 1.27 million deaths, while the total number of deaths indirectly associated with resistance exceeded 4.95 million.[4] It has been reported that AMR-related mortality has surpassed that of infectious diseases such as HIV/AIDS and malaria.[4] The economic burden of AMR is also substantial. It is estimated that AMR could impose an additional economic burden of USD 1–3·4 trillion on the global economy by 2050.[5]

Although several solutions, i.e., rationalising clinical antimicrobial use, regulating use in livestock and crop production, controlling resistance genes in environmental reservoirs, implementing rapid diagnostic tests, and developing alternative biological therapies exist, the global burden of AMR has not decreased. This suggests that scientific and technological solutions have not been implemented adequately across health systems, environmental management, agriculture, and policy. This review addresses this lack of integration by examining clinical outcomes, the current antibiotic development pipeline, non-antibiotic alternative approaches, rapid diagnostic methods, antimicrobial stewardship programs, and the

One Health approach. The One Health approach is an integrated framework that recognises the close interconnection between human, animal, and environmental health.[1,93] The review also highlights priority policy and research areas that could strengthen integration in the fight against AMR.

2. Methodology

This study was conducted as a narrative review to provide an integrated overview of current evidence on antimicrobial resistance across human, animal, and environmental health. The review aimed to synthesise evidence on the determinants of antimicrobial resistance, emerging therapeutic approaches, rapid diagnostic methods, antimicrobial stewardship programs, and the One Health framework.

The literature included in this review was identified through searches of PubMed and Google Scholar, supplemented by screening the reference lists of relevant articles and reviews, as well as reports published by international organisations. The search strategy included combinations of keywords related to antimicrobial resistance, novel therapeutic approaches, rapid diagnostic methods, antimicrobial stewardship programs, and the One Health approach.

Priority was given to recent original studies, systematic reviews, meta-analyses, and major policy documents published primarily between 2012 and 2026. A limited number of earlier publications were included where necessary to provide historical context and conceptual background. Studies that were not directly relevant to the objectives of this review were excluded.

Relevant information from eligible sources was extracted and narratively synthesised. The evidence was then organised into thematic sections covering the major dimensions of antimicrobial resistance, including its determinants in human, animal, and environmental health, clinical outcomes, the antibiotic development pipeline, non-antibiotic therapeutic strategies, rapid diagnostic methods, antimicrobial stewardship programs, and the One Health approach.

3. Multisectoral Determinants of Antimicrobial Resistance

3.1. Determinants of AMR in Human Healthcare

Patients' knowledge regarding antimicrobial use plays an important role in antimicrobial use patterns, a pattern frequently observed in low- and middle-income countries.[6] In India, primary healthcare providers prescribed antibiotics to half (49·9%) of patients presenting with clinical complaints that did not require them during 2020.[7] In addition, non-prescription dispensing of antibiotics in pharmacies is more common in low-income countries than in high-income countries, with particularly higher prevalence in Sub-Saharan Africa, East Asia and the Pacific, and Latin America and the Caribbean.[8] Hence, clinical decisions are shaped not only by medical necessity but also by knowledge levels, patient expectations, and the policy dynamics and regulatory oversight mechanisms of a country's health system.

3.2. Determinants of AMR in Agriculture and Food Production

Antibiotics are a cornerstone of animal health; however, their increasing use at subtherapeutic doses to promote growth and prevent disease, in place of hygiene practices, creates substantial selection pressure for the evolution of resistance.[9] Globally, 73% of all antimicrobials sold are used in animals raised for food.[10] The high volumes of antibiotic use in industrial livestock systems promote the emergence and persistence of resistant bacterial strains.[11] Antibiotics used in veterinary settings further contribute to the dissemination of AMR by facilitating the transfer of plasmid-mediated resistance genes from the animal microbiota to environmental bacteria and human pathogens.[12] Consequently, the animal production chain becomes a major predisposing context in which resistance determinants are shared across humans, animals, and the environment.

Although increasing evidence suggests agroecosystems significantly contribute to resistance gene selection and exchange, AMR remains elusive in crop production systems. Crop production systems redistribute resistance across environmental interfaces.

Several economically important diseases in agricultural production systems are managed by antibiotics, including streptomycin and oxytetracycline. These are sprayed to the soil and affect non-target microbiota, insects, and water systems. Hence, the use of antibiotics in agriculture sector establishes broader microbial interaction networks.

Natural occurrence of antibiotic-producing microorganisms gives rise to resistance determinants. Nevertheless, exogenous application of these compounds may intensify selection pressure and mobilisation of antimicrobial resistance genes (ARGs).[12,13] Although the Food and Agriculture Organisation of the United Nations (FAO) and the World Health Organisation (WHO) stress that antimicrobial stewardship must include crop systems, surveillance mechanisms remain limited compared with those in the veterinary and clinical domains. Plant-associated antibiotic use is lower than livestock use, yet the ecological diffusion potential per application is comparatively higher due to environmental exposure and runoff.

3.3. Environmental and Wastewater Determinants of AMR

The environment is recognised as a key component in the selection, dissemination, and transport of antimicrobial resistance. Wastewater, healthcare facilities, pharmaceutical manufacturing plants, inadequate sanitation, and antimicrobial use in crop production are among the vectors that introduce antibiotics and antimicrobial resistance genes into the environment.[13] Concentrations of 22 antibiotics, including fluoroquinolones, sulfonamides, and macrolides, were detected in river water and fish muscle from the Haihe River in China. Ciprofloxacin and erythromycin in particular showed a marked tendency to bioaccumulate in fish muscle.[14] Persistent antibiotic residues in the environment may facilitate the selection of resistant bacterial strains and accelerate both the emergence and environmental dissemination of antibiotic resistance genes.[14] Uncontrolled wastewater mixing with aquatic ecosystems that are actively used by communities can serve as both a reservoir and a distribution node for the spread of antimicrobials and resistance genes.

3.4. Diagnostic and Surveillance Gaps

Population-based surveillance data on cases of community-acquired pneumonia requiring hospitalisation show that respiratory viruses (27%) are detected more frequently than bacterial pathogens (14%).[15] This implies that empiric antibacterial therapy initiated in this setting

often lacks a microbiological basis.[15] Without bacterial confirmation, empiric antibiotic use may provide no clinical benefit and may potentially result in antibiotic-associated harm.[16]

Rapid identification of the causative pathogen and its resistance profile is a key determinant of success in antimicrobial therapy, enabling timely initiation of appropriate treatment.[17–19] However, standard culture-based methods for organism identification require 48–72 hours to produce a definitive result, whereas rapid diagnostic tests can provide definitive identification within hours.[20] This delay creates a major gap by increasing both mortality risk and unnecessary use of broad-spectrum antibiotics in severe infections. Moreover, it predisposes to prolonged hospital stays; delayed initiation of appropriate therapy results in economic losses and can strain hospital bed capacity.

3.5. Governance, Policy, and Economic Determinants of AMR

Obtaining antibiotics without a prescription and inappropriate dosing often arise not simply from a lack of knowledge but from responses to competitive, commercial environments in which ethical practice is economically penalised.[21–24] Historical experience shows that the sequential introduction of multiple antibiotics with similar spectra of activity has led to rapidly diminishing returns on investment and market collapses, suppressing corporate investment in the antimicrobial space.[25–27] Subscription models proposed under legislative frameworks such as the United States PASTEUR (Pioneering Antimicrobial Subscriptions to End Upsurging Resistance) Act aim to address the low return-on-investment problem for antibiotics by decoupling industry revenue from sales volume.[28] Nevertheless, this approach alone may not be sufficient to ensure long-term financial sustainability.[28] Antibiotics are also framed as a "societal trust" because each use can affect the treatment options available to others in the community; therefore, their stewardship requires shared responsibility.[29] This is especially salient when institutions are profit-driven, strong ministerial policies are absent, and regulatory oversight mechanisms are functionally inadequate—conditions that can render the health system increasingly unsafe.

4. Clinical Outcomes and the Limitations of Current Antibiotics

In this review, clinical outcomes refer to measures such as mortality, treatment success, length of hospital stay, hospital readmissions, microbiological eradication, and healthcare utilisation associated with antimicrobial resistance. Resistant bacterial infections have become one of the most challenging conditions to manage in clinical practice, primarily due to the progressive decline in effective antibiotic options. This not only complicates treatment but also increases mortality and imposes a substantial burden on health systems.[4,30] Bloodstream infections account for a considerable share of this burden and were associated with approximately 2·91 million deaths in 2019.[31]

The impact of antimicrobial resistance extends beyond clinical outcomes alone. Resistant infections are typically associated with longer hospital stays, more frequent readmissions, and increased treatment costs. In addition, the need for adjunctive therapies and greater healthcare utilisation further exacerbates the overall burden. Taken together, these data clearly indicate that resistant infections pose a serious threat to both individual patient outcomes and the sustainability of healthcare systems.[32–34] Given that antibiotic development has not kept pace with resistance, accelerating antibiotic discovery and development is essential.

5. New Molecules

One of the major challenges posed by antibiotic resistance is the slow pace of new antibiotic development relative to clinical needs. Many pharmaceutical companies have withdrawn entirely from antibiotic research and development because of the low profitability of antibiotics.[35,36] The drivers of AMR are multifactorial; however, excessive antimicrobial use, inappropriate prescribing, and misuse due to incorrect treatment indications are widely recognised as key factors that increase the burden of AMR.[37]

WHO has published a global analysis of antibacterial agents in clinical and preclinical development, providing an up-to-date assessment of the current antibacterial pipeline.[38] Several novel agents in the current pipeline, with diverse target pathogen spectra and mechanisms of action, are summarised in Table 1.

The agents included in Table 1 were selected to provide representative examples of antibacterial candidates currently under clinical development, based on their relevance to antimicrobial resistance and the availability of published information.

Table 1: Some new molecules

Antibiotic	Target Pathogen	Mode of Action	References
SCH-79797	Broad-spectrum, including MDR pathogens	Folate metabolism and membrane disruption	39
Plazomicin	Broad-spectrum	Inhibits binding at the aminoacyl site of bacterial 16S ribosomal RNA	40
PA-69180	Pseudomonas aeruginosa	Cell shape-determining protein MreB	41
Halicin	Broad-spectrum, including multidrug-resistant bacterial pathogens	Disturbs the maintenance of the proton gradient, resulting in reduced ATP production	42
Evybactin	Mycobacterium tuberculosis	The antibiotic targets DNA gyrase and enters the bacterial cell through the BacA transporter	43
Clovibactin	Gram-positive pathogens	Blocks cell wall formation by binding to pyrophosphate peptidoglycan intermediates	44
Abaucin	Acinetobacter baumannii	Lipoprotein trafficking through a LolE-dependent pathway	45
Zosurabalpin	Acinetobacter baumannii	Inhibits lipopolysaccharide transport	46

Corbomycin	Gram-positive pathogens	Inhibits autolysin function	47

In the post-antibiotic era, the pace of new antibiotic discovery has fallen behind the steadily growing problem of resistance, rendering even common infections potentially fatal and highlighting the urgent need for alternative therapeutic strategies.[48] Unless novel agents are developed judiciously and used strategically, any gains they offer may prove transient in the face of continuing resistance evolution.

6. Non-antibiotic Strategies

6.1. Bacteriophage Therapy

Bacteriophages are viruses that can infect and kill specific pathogenic bacteria upon encountering them. After lysing bacteria, phages release new phage particles, which can disseminate to different sites of infection. Among antibacterial agents, phages are unique in their ability to replicate in the presence of their target bacteria. Moreover, they have minimal effects on non-target bacteria and human tissues.[49]

A cohort study of 100 patients showed clinical improvement in 77.2% of infections and bacterial eradication in 61.3% of infections.[50] In the same study, eradication of the targeted bacteria was 70% less likely when bacteriophage therapy was administered without concomitant antibiotics (odds ratio, 0.3; 95% confidence interval, 0.127–0.749), suggesting that adjunctive antibiotic therapy may improve bacterial eradication.[50] However, higher-quality studies are needed to generate reliable predictions about the effectiveness of bacteriophage therapies. Currently, some companies are developing and commercialising broad-spectrum phage products in accordance with contemporary standards, including preclinical studies focused on toxicity and pharmacology, as well as randomised controlled trials (RCTs).[51] Nevertheless, substantial uncertainties remain regarding optimal dosing, frequency, and duration; pharmacokinetics (distribution and elimination in the body); effects on the host immune system; the dynamics of phage–bacterium interactions over time; and the regulatory frameworks required to govern these aspects.

6.2. Endolysins

Endolysins are bacteriophage (phage)-encoded enzymes that can specifically hydrolyse the bacterial cell wall and rapidly kill bacteria. The development of bacterial resistance to endolysins is thought to be relatively low; therefore, endolysins are considered a promising alternative approach to the growing resistance problem.[52,53] When applied externally against Gram-positive bacteria, they rapidly degrade the cell wall and induce cell death. However, their activity against Gram-negative bacteria is largely limited due to the outer membrane barrier.[54] Certain endolysins have been reported to act synergistically with some antibiotics.[55]

Whereas antibiotics often eradicate bacteria indiscriminately due to their broad-spectrum effects—potentially harming the commensal microbiota—endolysins exhibit high specificity, enabling preservation of the microbiota by targeting specific pathogens.[56] Phage–endolysin systems have been reported to eliminate large bacterial populations rapidly when

appropriately matched, and endolysins can kill both actively dividing and non-dividing cells by directly targeting peptidoglycan.[56,57] However, their short half-lives and insufficient clinical studies represent important disadvantages.[54]

Current evidence is largely based on in vitro experiments and animal models; therefore, more comprehensive pharmacokinetic, safety, and dose-finding studies are needed to define the real-world role of endolysins in the treatment of resistant infections.

6.3. Anti-virulence and Biofilm Targeting

Anti-virulence therapy is an emerging approach that aims to reduce the selective pressure driving resistance by targeting a pathogen's disease-causing factors rather than directly killing the organism.[58] Biofilm formation represents another major contributor to bacterial infections. A biofilm is a thin, gel-like matrix that harbours bacterial communities and facilitates bacterial adherence to host cells. This evolutionary strategy enables bacteria to better withstand antibiotics and host immune defences. Consequently, biofilm formation on surfaces can lead to persistent infections and increased antibiotic resistance. [59]

Pseudomonas aeruginosa and *Staphylococcus aureus* are among the clearest examples of pathogens in which biofilm formation contributes to increased resistance and enhanced persistence in bacterial infections. Biofilms have also been shown to facilitate processes such as horizontal gene transfer, thereby supporting the acquisition and spread of resistance traits in bacteria.[60]

Biofilms act as barriers that protect bacteria from antibiotics. Quorum-sensing inhibitors (QSIs), such as eugenol, curcumin, and furanones, disrupt biofilm formation by interfering with quorum-sensing (QS) signalling pathways, rendering bacteria embedded within biofilms more vulnerable to antibiotics.[61,62] Moreover, because QSIs target virulence rather than bacterial viability, they reduce selective pressure for the development of antibiotic resistance; when used alongside antibiotics, they may also decrease horizontal gene transfer, suggesting that antibiotics and QSIs can act synergistically.[63–66] However, due to the complexity of bacterial pathogenesis, despite hundreds of potential anti-virulence candidates being documented, no anti-virulence molecule has yet been approved for clinical use.[58] Overall, current evidence suggests that anti-virulence and biofilm-targeting strategies are theoretically strong, but further translational work and well-designed clinical studies are required before these approaches can be incorporated into routine clinical practice for the treatment of resistant infections. Overall, the main advantages and disadvantages of anti-virulence therapy are summarised in Table 2.

Table 2. Advantages and Disadvantages of Anti-virulence Therapy

Advantages	**Disadvantages**
It exerts weaker evolutionary pressure than antibiotics.	It is likely to have more limited therapeutic efficacy than antibiotics.
The pathogen can be incapacitated without killing it.	After treatment is discontinued, the remaining bacteria are likely to persist.

Quorum-sensing inhibitors can help reduce the production of several virulence factors by regulating the expression of virulence genes.	It may not be effective against all forms of disease caused by the same pathogen.

6.4. Monoclonal Antibodies

Monoclonal antibodies are biologic molecules produced and engineered in laboratory settings to mimic the immune system's capacity to combat pathogens and diseased cells.[67] They are highly important in modern medicine because they offer effective therapeutic options across a wide range of conditions, including cancer, autoimmune disorders, infectious diseases, and many others. Owing to their high specificity, monoclonal antibodies have become indispensable tools in both diagnosis and treatment, providing clinicians with powerful means to address complex health problems.[68] In addition, their narrow-spectrum activity is thought to be associated with a lower propensity for the development of resistance.[69] However, some monoclonal antibodies can cause serious adverse reactions, including multiple organ failure, capillary leak syndrome, and cytokine release syndrome.[67]

Because they can target specific pathogens or toxins, monoclonal antibodies represent a complementary option that may help reduce the need for antibiotics. Nevertheless, high costs, the requirement for parenteral administration, and the potential for severe adverse effects limit their widespread adoption as a first-line, broadly used solution in the fight against AMR.

6.5. Vaccines and Immunoprophylactic Strategies

Vaccines reduce the incidence of both drug-susceptible and drug-resistant bacterial infections, secondary infections, and viral infections for which antibiotics are frequently prescribed inappropriately.[70] According to a WHO modelling report published in 2024, if 44 vaccines—available, in development, or at the hypothetical stage—targeting 23 of 24 pathogens were implemented comprehensively, approximately 2·5 billion defined daily doses (DDD) of antibiotic use could be averted annually. This reduction corresponds to roughly 22% of human antibiotic consumption for the pathogens assessed, underscoring how vaccination can serve as a highly impactful public health tool at the global level to reduce the burden of AMR.[70]

However, the real-world impact of vaccines on AMR is shaped not only by vaccine availability but also by "field" conditions, including access to vaccination, the coverage and regularity of immunisation programs, vaccine hesitancy in the community, and—particularly in low- and middle-income countries—the sustainability of cold-chain logistics. Therefore, while vaccines are a powerful population-level tool against AMR by reducing the need for antibiotics, realising their full expected benefit requires comprehensive immunisation strategies that strengthen health systems and promote global equity.

6.6. Microbiota-Based Approaches

Disruption of microbiome balance has been linked to increased susceptibility to many conditions, including cancer, diabetes, allergies, obesity, and infections.[71] However, microbiome transplantation remains in its early stages of development and, aside from a few

notable exceptions, has achieved limited success in most clinical studies.[71] Microbiome research is expanding rapidly, but translation into clinical practice and marketable products requires alignment not only among regulators but also between researchers and industry. Such alignment is crucial for developing effective pathways to address the diverse health problems associated with the gut microbiota, along with the technological challenges that accompany them. [72]

In this context, microbiota-based approaches are considered complementary options that could reduce the need for antibiotics by strengthening colonisation resistance and preventing certain infections at the outset. Nevertheless, this approach is not yet sufficiently robust to be implemented safely and standardised in routine clinical practice as part of the fight against AMR. The main alternative strategies to antibiotics, together with their advantages and limitations, are summarised in Table 3.

Table 3. Alternative strategies to antibiotics

Strategy	**Advantages (benefits)**	**Disadvantages**	**References**
Bacteriophage therapy	High specificity, synergistic potential, and low side effects	Lack of standardisation, absence of randomised controlled trials	49,50,73
Endolysin therapy	Rapid effect, low risk of resistance development	Mainly effective against Gram-positive bacteria	52,53,54
Anti-virulence therapy	Low selective pressure preserves microbiota	Limited efficacy as monotherapy	61,63,74
Monoclonal antibody therapy	Specific targets, low resistance risk	Production is time-consuming and costly	67,68,69
Microbiota therapy	Restoration of natural flora	Limited success in human clinical studies	71,72
Vaccines	Protective effect, reduced resistance pressure, decreased need and use of antibiotics	Complex process, distribution challenges of cold-chain vaccines in regions without electricity	9,75,76

7. Rapid Diagnostic Methods

One of the most critical components of effective antimicrobial therapy is identifying the causal pathogen and its resistance profile as rapidly as possible. Because classical culture-

based methods often require prolonged turnaround times, a range of rapid diagnostic methods has been developed in recent years to shorten the time to diagnosis and enable earlier, more targeted treatment decisions.

7.1. Multiplex Polymerase Chain Reaction (PCR) Panels

Multiplex PCR panels enable the rapid identification of pathogens and resistance genes in patients with positive blood cultures.[77–79] In addition, they integrate nucleic acid extraction, amplification, detection, and analysis, delivering results in approximately 65 minutes.[80] This can allow empiric therapy in severe sepsis and septic shock to be narrowed early or appropriately modified.

7.2. Matrix-Assisted Laser Desorption/Ionisation Time-of-Flight Mass Spectrometry (MALDI-TOF MS)

MALDI-TOF MS can identify bacteria and fungi to the species level within minutes.[81] While the high accuracy and short turnaround times of MALDI-TOF MS systems provide a major advantage, they demonstrate superior performance for the identification of direct colony isolates.[82] However, it is insufficient on its own to determine resistance profiles as MALDI-TOF MS cannot directly detect antimicrobial resistance genes.

7.3. Next-Generation Sequencing (NGS)

Next-generation sequencing (NGS) is an efficient technology that enables high-throughput, massively parallel sequencing of millions of DNA or RNA molecules within hours.[83,84] Beyond identifying the causative agent at the species level, NGS can simultaneously reveal a broad spectrum of genetic information, including resistance genes and virulence factors. However, the complexity of data analysis, high costs, and the need for advanced bioinformatics infrastructure limit its widespread implementation in routine clinical practice.

7.4. Scattered Light Integrated Collector (SLIC)

The Scattered Light Integrated Collector (SLIC) is regarded as a major step forward in antimicrobial susceptibility testing (AST). Owing to its high sensitivity, SLIC facilitates the detection of subtle changes in microbial populations. While the current limit of detection (LoD) of existing photonic technologies is approximately 10,000 microbial cells per millilitre, SLIC has an LoD of 25 cells/mL. Its capacity to determine antimicrobial resistance in real time, in under 30 minutes, represents a major shift for microbiological healthcare services.[85]

Each method has distinct advantages and limitations; it should be kept in mind that selecting the appropriate method can collectively improve clinical outcomes and enable faster treatment decisions.[86] The main rapid diagnostic techniques, together with their turnaround times, strengths, and limitations, are summarised in Table 4.

Table 4. Rapid diagnostic techniques

Technique	Turnaround time	Advantage (Strengths)	Disadvantage	References

Multiplex PCR panels	A few hours	Allows rapid detection of resistance genes	Expensive, limited panel	77,79,80
MALDI-TOF MS	Within minutes	Very rapid and accurate diagnosis	Cannot detect antimicrobial resistance genes	81,82
NGS	A few hours	The most comprehensive data	Data analysis is complex and costly	83,84
SLIC	<30 min	Very low LoD (25 cells/mL), real-time	New in clinical practice	85

8. Antimicrobial Stewardship Programs

Hospitals implement antimicrobial stewardship programs (ASPs) to reduce antibiotic resistance, prevent adverse drug reactions and treatment failures, and decrease costs arising from inappropriate prescribing and prolonged lengths of stay. These programs encompass appropriate drug selection, optimisation of dose and treatment duration, surveillance of antimicrobial use and resistance patterns, and the provision of regular education and feedback to prescribers.[87] Studies have shown that ASPs significantly reduce inappropriate antimicrobial use. [88,89]

ASPs are currently considered one of the cornerstone strategies for controlling antimicrobial resistance.[90] By promoting more rational antibiotic use, these programs not only improve patient care but also make an important contribution to the fight against AMR.[91] Evidence from different centres indicates that ASP implementation can markedly reduce antibiotic consumption and, in some settings, achieve reductions of up to 91%, while improving adherence to treatment guidelines.[92] While the effectiveness of ASPs in conferring an advantage against resistance is clear, the failure to develop and implement ASPs broadly contributes to delays in addressing this pandemic-scale resistance problem.

9. One Health

The One Health approach represents an integrated and unifying framework, developed through collaboration among the WHO, FAO, World Organisation for Animal Health (WOAH) and United Nations Environment Programme (UNEP), aimed at reducing the impact of current and future challenges arising from interactions among humans, animals, plants, and the environment, and at achieving optimal and sustainable health outcomes.[1,93] Building on this premise, it recognises that the health of humans, domestic and wild animals, plants, and the broader environment is not independent but closely interconnected.[1]

While AMR is widely regarded as one of the most significant challenges in global public health, it also constitutes a critical threat to animal and plant health, food security, and economic development.[13] This is largely because uncontrolled and inappropriate antimicrobial use across sectors such as agriculture, livestock production, and human medicine directly affects each of these interconnected domains. Inadequate antimicrobial governance facilitates the spread of resistance mechanisms through uncontrolled infections, agricultural residues, environmental contamination, and the movement of humans and animals carrying resistant bacteria.[94]

Environmental factors also play a pivotal role in the dissemination of AMR. Antibiotic residues originating from hospitals, communities, and agricultural activities can enter waste sites and sewage systems, creating conditions that favour the selection and spread of resistant microorganisms; water, soil, and air then serve as media that facilitate the transport of resistant bacteria and resistance genes.[95] In this context, the One Health approach to AMR is not limited to mitigating resistance-related risks and burdens in human populations; it also provides a framework that may contribute to addressing the "triple planetary crisis", which refers to the interconnected challenges of climate change, biodiversity loss, and pollution and waste.[13] Although One Health appears theoretically robust, implementation often falls short in practice due to a lack of mechanisms to mandate and enforce cross-sector accountability and data sharing, resulting in health, agriculture, and environmental institutions operating largely within their own silos.

10. Discussion

Antimicrobial resistance is no longer merely a microbiological phenomenon. It is fundamentally shaped by how health systems, economic incentives, and agricultural and environmental governance are designed and implemented. Unless current trends change, the post-antibiotic era should be viewed as an increasingly visible societal risk.[1,4,5] This situation reflects not only a lack of new molecules, but also the continued uncontrolled and inappropriate use of antibiotics in many countries, the persistence of growth-oriented antimicrobial, pesticide, and herbicide practices in agriculture and livestock production, and the inadequacy of regulatory and oversight frameworks to correct these dynamics.[9,13]

Both the clinical and preclinical antibacterial pipelines struggle to keep pace with the global burden of AMR in terms of the number of candidates and the breadth of targeted pathogen spectra.[35,38] The high costs and long timelines of developing new agents, combined with relatively low returns, have pushed the private sector away from this field.[96,97] These observations support the view that, while indispensable, new molecules do not constitute a stand-alone solution under current conditions. At this juncture, non-antibiotic approaches emerge as important tools, but they are often mispositioned. Bacteriophages, endolysins, anti-virulence agents, monoclonal antibodies, vaccines, and microbiota-based strategies may offer meaningful benefits for specific pathogens and clinical scenarios; however, the evidence base is still largely derived from in vitro studies, animal models, and limited human data, and the number of large-scale, well-designed clinical trials remains small.[49,73,71] For this reason, it is more accurate to frame these approaches not as "alternatives" that replace antibiotics, but as complementary tools that—when used appropriately—can support therapy and help reduce antibiotic selection pressure.[52,70]

From a clinical perspective, what ultimately determines the quality of care is not only which drug is selected, but also how rapidly a diagnosis can be clarified and how effectively that information is translated into prescribing behaviour. The multi-day turnaround times of conventional culture-based methods often force clinicians to rely on broad-spectrum empiric therapy in severe infections, with substantial downstream consequences for both mortality and resistance dynamics.[15,20] The impact of rapid diagnostic technologies becomes most apparent when they operate alongside antimicrobial stewardship programs. Although ASPs have been shown to substantially reduce antibiotic consumption, stewardship implementation remains limited in many health systems, and rapid diagnostic capacity often cannot be scaled due to cost, infrastructure constraints, and misaligned incentives.[92,98]

These tensions within human healthcare, when combined with animal health, food production, and environmental reservoirs, make the One Health approach a practical necessity. In many countries, the total volume of antibiotics used in livestock can reach approximately four times that used in humans, and the extensive use of these agents for growth promotion or prophylaxis—rather than treatment—expands the reservoir of resistant bacteria.[11,94] In parallel, intensive use of pesticides, herbicides, and other chemicals, together with the transfer of agricultural and urban waste into water and soil systems, facilitates the accumulation and recirculation of resistance genes in the environment.[13,99] This landscape suggests that the fragmentation of health, agriculture, and food policies creates AMR risk, and that the One Health framework must be translated into concrete action that also encompasses pesticide policy and waste management. [93]

Globally, solution capacity is as unevenly distributed as the burden itself. High-income countries are relatively better positioned to institutionalise rapid diagnostics, ASPs, and vaccination programs, whereas in low- and middle-income countries, access to effective antibiotics, diagnostic tests, and basic vaccines is both limited and often poorly regulated.[13,100] In settings where cold-chain systems cannot be sustained, barriers to vaccine access increase the burden of preventable infections and further fuel uncontrolled and inappropriate antibiotic use.[70,76] These inequities influence not only access to treatment but also the geographical distribution and pace of resistance emergence, with the heaviest burden falling on vulnerable, low-income communities. In a world characterised by extensive international travel and trade—and ecosystems that do not respect national borders—AMR cannot be treated as a problem solvable within individual countries alone.

Accordingly, the fight against AMR depends less on the strength of any single tool than on how these tools are integrated. New antibiotics, non-antibiotic strategies, rapid diagnostic technologies, ASPs, and One Health approaches are often implemented as separate programs; yet institutions require an integrated, guideline-level framework that specifies where each tool should be deployed, how responsibilities should be allocated, and which pathways to follow.

From a research agenda perspective, priority areas include RCTs that clarify dosing, pharmacokinetics, and safety profiles for phage and endolysin therapies; clinical and cohort studies that track the long-term effects of anti-virulence and microbiota-based interventions on resistance; and implementation research that evaluates the real-world impact of rapid diagnostic–ASP integration using field data.[19,52,73] At the policy level, surveillance systems that jointly monitor use and resistance in human and animal health, financing reforms that incentivise appropriate prescribing and deter misuse, and national action plans that make One Health genuinely binding across ministries of health, agriculture, and environment should be viewed as core instruments capable of generating sustained impact against AMR.[29,92]

This review has some limitations. It was not conducted as a systematic review, and the included sources were identified through database searches, reference screening, and review of reports from international organisations. Because antimicrobial resistance is a rapidly evolving field, some recently published studies may not have been included. Nevertheless, current studies, relevant policy documents, and international reports were included to reflect the broad scope of the topic.

Author Contributions

Conceptualisation: B Deniz. Methodology: B Deniz, A Sona Karakuş, V Denizhan, and M Mamay. Investigation and literature search: B Deniz, A Sona Karakuş, V Denizhan, M Mamay, M Sönmez, GS Başböyük, MA Daşkın, and R Coşkun. Evidence synthesis and interpretation: all authors. Writing—original draft: B Deniz. Writing—review and editing: all authors. Supervision: A Sona Karakuş, V Denizhan, and M Mamay. Project administration: B Deniz. All authors approved the final version of the manuscript and agreed to its submission.

Declaration of interests

The authors declare no competing interests.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Authorship Statement

All authors meet the authorship criteria and have approved the final version of the manuscript.

References

1. World Health Organization. Antimicrobial resistance [Internet]. Geneva: World Health Organization; 2023 Nov 21 [cited 2025 Oct 24]. Available from: https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance

2. Tzialla C. Microbial infections and antimicrobial use in neonates and infants. Trop Med Infect Dis. 2025 Mar 18;10(3):80. doi:10.3390/tropicalmed10030080.

3. Thomas R, Ondongo-Ezhet C, Motsoaledi N, Sharland M, Clements M, Velaphi S. Incidence and all-cause mortality rates in neonates infected with carbapenem resistant organisms. Front Trop Dis. 2022;3:832011. doi:10.3389/fitd.2022.832011.
4. Antimicrobial Resistance Collaborators. Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Lancet. 2022;399(10325):629-55. doi:10.1016/S0140-6736(21)02724-0.

5. World Bank. Drug-resistant infections: a threat to our economic future [Internet]. Washington (DC): World Bank; 2017 Mar [cited 2025 Nov 13]. Available from: https://documents1.worldbank.org/curated/en/323311493396993758/pdf/final-report.pdf

6. Otaigbe II, Elikwu CJ. Drivers of inappropriate antibiotic use in low- and middle-income countries. JAC Antimicrob Resist. 2023;5(3):dlad062. doi:10.1093/jacamr/dlad062.

7. Sulis G, Daniels B, Kwan A, et al. Antibiotic overuse in the primary health care setting: a secondary data analysis of standardised patient studies from India, China and Kenya. BMJ Glob Health. 2020 Sep;5(9):e003393. doi:10.1136/bmjgh-2020-003393.

8. Li J, Zhou P, Wang J, et al. Worldwide dispensing of non-prescription antibiotics in community pharmacies and associated factors: a mixed-methods systematic review. Lancet Infect Dis. 2023 Sep;23(9):e361-70.

9. Laxminarayan R, Matsoso P, Pant S, et al. Access to effective antimicrobials: a worldwide challenge. Lancet. 2016 Jan 9;387(10014):168-75. doi:10.1016/S0140-6736(15)00474-2.

10. Van Boeckel TP, Pires J, Silvester R, et al. Global trends in antimicrobial resistance in animals in low- and middle-income countries. Science. 2019 Sep 20;365(6459):eaaw1944. doi:10.1126/science.aaw1944.
11. World Health Organization. Antimicrobial resistance: the food chain [Internet]. Geneva: World Health Organization; 2017 Nov 1 [cited 2025 Dec 19]. Available from: https://www.who.int/news-room/questions-and-answers/item/antimicrobial-resistance-in-the-food-chain

12. Hallal Ferreira Raro O, Poirel L, Tocco M, Nordmann P. Impact of veterinary antibiotics on plasmid-encoded antibiotic resistance transfer. J Antimicrob Chemother. 2023 Sep 5;78(9):2209-16. doi:10.1093/jac/dkad226.

13. United Nations Environment Programme. Bracing for superbugs: strengthening environmental action in the One Health response to antimicrobial resistance [Internet]. Nairobi: United Nations Environment Programme; 2023 [cited 2025 Oct 24]. Available from: https://wedocs.unep.org/items/e06380a1-453c-4a77-811f-9bfcced60018

14. Gao LH, Shi YL, Li WH, Liu JM, Cai YQ. Occurrence, distribution and bioaccumulation of antibiotics in the Haihe River in China. J Environ Monit. 2012;14(4):1248-55. doi:10.1039/C2em10916f.
15. Jain S, Self WH, Wunderink RG, et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. N Engl J Med. 2015 Jul 30;373(5):415-27. doi:10.1056/NEJMoa1500245.

16. Park K, Park S, Choi JY, et al. Comparative safety of empirical antibiotic classes in newly hospitalized COVID-19 patients. Pharmaceuticals. 2025;18(10):1588. doi:10.3390/ph18101588.

17. Yamin D, Uskoković V, Wakil AM, et al. Current and future technologies for the detection of antibiotic-resistant bacteria. Diagnostics (Basel). 2023 Oct 18;13(20):3246. doi:10.3390/diagnostics13203246.

18. Bouzid D, Zanella MC, Kerneis S, et al. Rapid diagnostic tests for infectious diseases in the emergency department. Clin Microbiol Infect. 2021 Feb;27(2):182-91. doi:10.1016/j.cmi.2020.02.024.

19. Peri AM, Chatfield MD, Ling W, Furuya-Kanamori L, Harris PNA, Paterson DL. Rapid diagnostic tests and antimicrobial stewardship programs for the management of bloodstream infection: what is their relative contribution to improving clinical outcomes? A systematic review and network meta-analysis. Clin Infect Dis. 2024 Aug

16;79(2):502-15. doi:10.1093/cid/ciae234.

20. Vineeth VK, Nambi PS, Gopalakrishnan R, et al. Clinical utility of blood culture identification 2 panel in flagged blood culture samples from the intensive care unit of a tertiary care hospital. Indian J Crit Care Med. 2024 May;28(5):461-6. doi:10.5005/jp-journals-10071-24709.

21. Nahar P, Unicomb L, Lucas PJ, et al. What contributes to inappropriate antibiotic dispensing among qualified and unqualified healthcare providers in Bangladesh? A qualitative study. BMC Health Serv Res. 2020 Jul 15;20(1):656. doi:10.1186/s12913-020-05512-y.

22. Haile KT, Yabeyu AB. Knowledge, attitude and practice of pharmacy professionals against dispensing antibiotics without prescription in Ethiopia. Integr Pharm Res Pract. 2022;11:167-76. doi:10.2147/IPRP.S383709.

23. Damisie G, Hambisa S, Yimam M. Over the counter sale of antibiotics at drug stores found in Mizan-Aman Town, southwest Ethiopia: a cross-sectional simulated client visit study. J Pharm. 2019;2019:3510659. doi:10.1155/2019/3510659.

24. Muhammed OS, Serbessa MK, Fenta TG. Exploring behavioral determinants of antimicrobial dispensing in drug retail outlets of Addis Ababa, Ethiopia: a mixed methods study. Sci Rep. 2025 Oct 17;15(1):36423. doi:10.1038/s41598-025-20558-w.
25. Spellberg B. The antibacterial pipeline: why is it drying up, and what must be done about it? In: Choffnes ER, Relman DA, Mack A, editors. Antibiotic resistance: implications for global health and novel intervention strategies: workshop summary. Washington (DC): National Academies Press; 2010. p. 299–332. doi: 10.17226/12925.

26. Nielsen TB, Brass EP, Gilbert DN, Bartlett JG, Spellberg B. Sustainable discovery and development of antibiotics: is a nonprofit approach the future? N Engl J Med. 2019 Aug 8;381(6):503-5. doi:10.1056/NEJMp1905589.

27. Spellberg B, Nielsen TB, Gilbert DN, Shorr AF, Brass EP. Ensuring sustainability of needed antibiotics: aiming for the DART Board. Ann Intern Med. 2019 Oct 15;171(8):580-2. doi:10.7326/M19-1893.

28. Spellberg B, Gilbert DN, Baym M, et al. Sustainable solutions to the continuous threat of antimicrobial resistance. Health Aff Sch. 2025 Feb;3(2):qxaf012. doi:10.1093/haschl/qxaf012.

29. Spellberg B, Srinivasan A, Chambers HF. New societal approaches to empowering antibiotic stewardship. JAMA. 2016;315(12):1229-30. doi:10.1001/jama.2016.1346.

30. Naghavi M, Vollset S, Ikuta K, et al. Global burden of bacterial antimicrobial resistance 1990-2021: a systematic analysis with forecasts to 2050. Lancet. 2024;404:1199-226. doi:10.1016/S0140-6736(24)01867-1.

31. Zha L, Li S, Guo J, et al. Global and regional burden of bloodstream infections caused by carbapenem-resistant Gram-negative bacteria in 2019: a systematic analysis from the MICROBE database. Int J Infect Dis. 2025;153:107769.

doi:10.1016/j.ijid.2024.107769.

32. Poudel AN, Zhu S, Cooper N, et al. The economic burden of antibiotic resistance: a systematic review and meta-analysis. PLoS One. 2023;18(5):e0285170. doi:10.1371/journal.pone.0285170.

33. Naylor NR, Hasso-Agopsowicz M, Kim C, et al. The global economic burden of antibiotic-resistant infections and the potential impact of bacterial vaccines: a modelling study. BMJ Glob Health. 2025;10:e016249. doi:10.1136/bmjgh-2024-016249.

34. Siaba S, Casal B, López-Martínez I. The economics of antibiotic resistance: a systematic review and meta-analysis based on global research. Appl Health Econ Health Policy. 2025 Aug 30. doi:10.1007/s40258-025-01001-7.

35. Muteeb G, Rehman MT, Shahwan M, et al. Origin of antibiotics and antibiotic resistance, and their impacts on drug development: a narrative review. Pharmaceuticals. 2023 Nov 15;16(11):1615. doi:10.3390/ph16111615.

36. Kariuki S. Global burden of antimicrobial resistance and forecasts to 2050. Lancet. 2024 Sep 28;404(10459):1172-3. doi:10.1016/S0140-6736(24)01885-3.

37. Tang KWK, Millar BC, Moore JE. Antimicrobial resistance. Br J Biomed Sci. 2023 Jun 28;80:11387. doi:10.3389/bjbs.2023.11387.

38. World Health Organization. *Analysis of antibacterial agents in clinical and preclinical development: overview and analysis 2025* [Internet]. Geneva: World Health Organization; 2025 [cited 2026 Aug 3]. Available from: https://www.who.int/publications/i/item/9789240113091

39. Martin JK 2nd, Sheehan JP, Bratton BP, et al. A dual-mechanism antibiotic kills Gram-negative bacteria and avoids drug resistance. Cell. 2020 Jun 25;181(7):1518-32.e14. doi:10.1016/j.cell.2020.05.005.

40. Golkar T, Bassenden AV, Maiti K, Arya DP, Schmeing TM, Berghuis AM. Structural basis for plazomicin antibiotic action and resistance. Commun Biol. 2021 Jun 11;4(1):729. doi:10.1038/s42003-021-02261-4.

41. Romano KP, Bagnall J, Warrier T, et al. Perturbation-specific transcriptional mapping for unbiased target elucidation of antibiotics. Proc Natl Acad Sci U S A. 2024 Nov 5;121(45):e2409747121. doi:10.1073/pnas.2409747121.

42. Stokes JM, Yang K, Swanson K, et al. A deep learning approach to antibiotic discovery. Cell. 2020 Feb 20;180(4):688-702.e13. doi:10.1016/j.cell.2020.01.021.

43. Imai Y, Hauk G, Quigley J, et al. Evybactin is a DNA gyrase inhibitor that selectively kills Mycobacterium tuberculosis. Nat Chem Biol. 2022;18:1236-44. doi:10.1038/s41589-022-01102-7.

44. Shukla R, Peoples AJ, Ludwig KC, et al. An antibiotic from an uncultured bacterium binds to an immutable target. Cell. 2023 Sep 14;186(19):4059-73.e27. doi:10.1016/j.cell.2023.07.038.

45. Liu G, Catacutan DB, Rathod K, et al. Deep learning-guided discovery of an antibiotic targeting Acinetobacter baumannii. Nat Chem Biol. 2023 Nov;19(11):1342-50. doi:10.1038/s41589-023-01349-8.

46. Zampaloni C, Mattei P, Bleicher K, et al. A novel antibiotic class targeting the lipopolysaccharide transporter. Nature. 2024;625:566-71. doi:10.1038/s41586-023-06873-0.

47. Culp EJ, Waglechner N, Wang W, et al. Evolution-guided discovery of antibiotics that inhibit peptidoglycan remodelling. Nature. 2020;578:582-7. doi:10.1038/s41586-020-1990-9.

48. Cui X, Chai L, Zhang Y, et al. Next-generation antimicrobials: a review of phage lysins as precision weapons against drug-resistant pathogens. Virulence. 2025;16(1). doi:10.1080/21505594.2025.2562634.

49. Abedon ST, Kuhl SJ, Blasdel BG, Kutter EM. Phage treatment of human infections. Bacteriophage. 2011;1(2):66-85. doi:10.4161/bact.1.2.15845.

50. Pirnay JP, Djebara S, Steurs G, et al. Personalized bacteriophage therapy outcomes for 100 consecutive cases: a multicentre, multinational, retrospective observational study. Nat Microbiol. 2024;9:1434-53. doi:10.1038/s41564-024-01705-x.

51. Pirnay JP, Kutter E. Bacteriophages: it's a medicine, Jim, but not as we know it. Lancet Infect Dis. 2021 Mar;21(3):309-11. doi:10.1016/S1473-3099(20)30464-3.

52. Liu H, Hu Z, Li M, Yang Y, Lu S, Rao X. Therapeutic potential of bacteriophage endolysins for infections caused by Gram-positive bacteria. J Biomed Sci. 2023;30:29. doi:10.1186/s12929-023-00919-1.

53. Tesema MY. Outlooks of endolysins with innolysins therapeutic potentials against antimicrobial resistance. Discov Med. 2025;2:188. doi:10.1007/s44337-025-00424-4.

54. Sabur A, Khan A, Borphukan B, Razzak A, Salimullah M, Khatun M. The unique capability of endolysin to tackle antibiotic resistance: cracking the barrier. J Xenobiot. 2025;15(1):19. doi:10.3390/jox15010019.

55. Hong HW, Kim YD, Jang J, Kim MS, Song M, Myung H. Combination effect of engineered endolysin EC340 with antibiotics. Front Microbiol. 2022;13:821936. doi:10.3389/fmicb.2022.821936.

56. Fischetti VA. Development of phage lysins as novel therapeutics: a historical perspective. Viruses. 2018 Jun 7;10(6):310. doi:10.3390/v10060310.

57. Matsuzaki S, Rashel M, Uchiyama J, et al. Bacteriophage therapy: a revitalized therapy against bacterial infectious diseases. J Infect Chemother. 2005 Oct;11(5):211-

9. doi:10.1007/s10156-005-0408-9.

58. Zhou S, Liu B, Zheng D, et al. VFDB 2025: an integrated resource for exploring anti-virulence compounds. Nucleic Acids Res. 2025 Jan 6;53(D1):D871-7. doi:10.1093/nar/gkae968.

59. Costerton JW, Stewart PS, Greenberg EP. Bacterial biofilms: a common cause of persistent infections. Science. 1999 May 21;284(5418):1318-22. doi:10.1126/science.284.5418.1318.

60. Madsen JS, Burmølle M, Hansen LH, Sørensen SJ. The interconnection between biofilm formation and horizontal gene transfer. FEMS Immunol Med Microbiol. 2012 Jul;65(2):183-95. doi:10.1111/j.1574-695X.2012.00960.x.

61. Mirghani R, Saba T, Khaliq H, et al. Biofilms: formation, drug resistance and alternatives to conventional approaches. AIMS Microbiol. 2022 Jul 4;8(3):239-77. doi:10.3934/microbiol.2022019.

62. Konda M, Tippani R, Porika M, Banoth L. Quorum sensing: a new target for anti-infective drug therapy. In: Maddela NR, Reddy Kondakindi V, Pabbati R, editors. Quorum quenching. Cambridge: Royal Society of Chemistry; 2023. p. 250-81. doi:10.1039/BK9781837671380-00250.

63. Rodríguez-Urretavizcaya B, Vilaplana L, Marco MP. Strategies for quorum sensing inhibition as a tool for controlling Pseudomonas aeruginosa infections. Int J Antimicrob Agents. 2024 Nov;64(5):107323. doi:10.1016/j.ijantimicag.2024.107323.

64. Shamim A, Ali A, Iqbal Z, et al. Natural medicine a promising candidate in combating microbial biofilm. Antibiotics (Basel). 2023 Feb 2;12(2):299. doi:10.3390/antibiotics12020299.

65. Sunanta P, Kontogiorgos V, Pankasemsuk T, et al. The nutritional value, bioactive availability and functional properties of garlic and its related products during processing. Front Nutr. 2023 Jul 25;10:1142784. doi:10.3389/fnut.2023.1142784.

66. Alum EU, Gulumbe BH, Izah SC, et al. Natural product-based inhibitors of quorum sensing: a novel approach to combat antibiotic resistance. Biochem Biophys Rep. 2025;43:102111. doi:10.1016/j.bbrep.2025.102111.

67. National Cancer Institute. Monoclonal antibodies [Internet]. Bethesda (MD): National Cancer Institute; 2019 Sep 24 [cited 2025 Sep 11]. Available from: https://www.cancer.gov/about-cancer/treatment/types/immunotherapy/monoclonal-antibodies

68. Singh R, Chandley P, Rohatgi S. Recent advances in the development of monoclonal antibodies and next-generation antibodies. Immunohorizons. 2023 Dec 1;7(12):886-97. doi:10.4049/immunohorizons.2300102.

69. Zurawski DV, McLendon MK. Monoclonal antibodies as an antibacterial approach against bacterial pathogens. Antibiotics (Basel). 2020;9(4):155.

doi:10.3390/antibiotics9040155.

70. World Health Organization. Estimating the impact of vaccines in reducing antimicrobial resistance and antibiotic use [Internet]. Geneva: World Health Organization; 2024 Oct 10 [cited 2026 Jan 3]. Available from: https://www.who.int/publications/i/item/9789240098787

71. Alam MZ, Maslanka JR, Abt MC. Immunological consequences of microbiome-based therapeutics. Front Immunol. 2023 Jan 12;13:1046472. doi:10.3389/fimmu.2022.1046472.

72. Sorbara MT, Pamer EG. Microbiome-based therapeutics. Nat Rev Microbiol. 2022 Jun;20(6):365-80. doi:10.1038/s41579-021-00667-9.

73. Uyttebroek S, Chen B, Onsea J, et al. Safety and efficacy of phage therapy in difficult-to-treat infections: a systematic review. Lancet Infect Dis. 2022 Aug;22(8):e208-20. doi:10.1016/S1473-3099(21)00612-5.

74. Ghazaei C. Anti-virulence therapy against bacterial infections: mechanisms of action and challenges. J Kermanshah Univ Med Sci. 2021;25(3):e111808. doi:10.5812/jkums.111808.

75. Tekle YI, Nielsen KM, Liu J, et al. Controlling antimicrobial resistance through targeted, vaccine-induced replacement of strains. PLoS One. 2012;7(12):e50688. doi:10.1371/journal.pone.0050688.

76. Médecins Sans Frontières. The right shot: bringing down barriers to affordable and adapted vaccines. 2nd ed [Internet]. New York: Médecins Sans Frontières; 2015 [cited 2026 Feb 18]. Available from: https://www.doctorswithoutborders.org/latest/right-shot-bringing-down-barriers-affordable-and-adapted-vaccines-2nd-edition

77. Xu Z, Chen D, Li T, et al. Microfluidic space coding for multiplexed nucleic acid detection via CRISPR-Cas12a and recombinase polymerase amplification. Nat Commun. 2022;13:6480. doi:10.1038/s41467-022-34086-y.

78. Xie Y, Chen Z, Cai D, et al. Rapid detection of uropathogens using an integrated multiplex digital nucleic acid detection assay powered by a digital-to-droplet microfluidic device. Anal Chem. 2024 Jul 17. doi:10.1021/acs.analchem.4c02578.

79. Zhao J, Wang Z, Yang K, Deng G, Liu Y, Zhu L. Breaking through PCR multiplexing barriers: a shared-label-tagged primer design enables high-efficiency single-reaction booster PCR (SLP-bPCR). Anal Chim Acta. 2026 Jan 15;1383:344869. doi:10.1016/j.aca.2025.344869.

80. Kim KJ, Yun SG, Cho Y, Lee CK, Nam MH. Rapid direct identification of microbial pathogens and antimicrobial resistance genes in positive blood cultures using a fully automated multiplex PCR assay. J Korean Med Sci. 2024 May 6;39(17):e157. doi:10.3346/jkms.2024.39.e157.

81. Patel R. MALDI-TOF MS for the diagnosis of infectious diseases. Clin Chem. 2015 Jan;61(1):100-11. doi:10.1373/clinchem.2014.221770.

82. Prakika A, Srisai P, Nithimongkolchai N, et al. Comparison of *Acinetobacter calcoaceticus-baumannii* complex identification by MALDI-TOF mass spectrometry and biochemical method, using whole-genome sequencing as the reference standard. Infect Drug Resist. 2025;18:6951-60. doi:10.2147/IDR.S576056.

83. Thermo Fisher Scientific. Next-generation sequencing information [Internet]. [cited 2026 Mar 18]. Available from: https://www.thermofisher.com/tr/en/home/life-science/sequencing/sequencing-learning-center/next-generation-sequencing-information.html

84. Akaçin İ, Ersoy Ş, Doluca O, et al. Comparing the significance of the utilization of next generation and third generation sequencing technologies in microbial metagenomics. Microbiol Res. 2022 Nov;264:127154. doi:10.1016/j.micres.2022.127154.

85. University of St Andrews. SLIC. Infection and Global Health Research Division [Internet]. 2020 [cited 2026 Feb 2]. Available from: https://medicine.st-andrews.ac.uk/igh/research/molecular-diagnostics/slic/

86. Arbefeville SS, Timbrook TT, Garner CD. Evolving strategies in microbe identification-a comprehensive review of biochemical, MALDI-TOF MS and molecular testing methods. J Antimicrob Chemother. 2024 Sep;79(Suppl 1):i2-8. doi:10.1093/jac/dkae275.

87. Ababneh MA, Nasser SA, Rababa'h AM. A systematic review of antimicrobial stewardship program implementation in Middle Eastern countries. Int J Infect Dis. 2021 Apr;105:746-52. doi:10.1016/j.ijid.2021.03.035.

88. Alawi MM, Tashkandi WA, Basheikh MA, et al. Effectiveness of antimicrobial stewardship program in long-term care: a five-year prospective single-center study. Interdiscip Perspect Infect Dis. 2022 Apr 12;2022:8140429. doi:10.1155/2022/8140429.

89. Alshehri AA, Aldali JA, Abdelhamid MA, et al. Implementation of antimicrobial stewardship programs in Saudi Arabia: a systematic review. Microorganisms. 2025;13(2):440. doi:10.3390/microorganisms13020440.

90. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. Antimicrob Agents Chemother. 2016 Jul 22;60(8):4840-52. doi:10.1128/AAC.00825-16.

91. Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs [Internet]. Atlanta (GA): Centers for Disease Control and Prevention; 2025 Sep 15 [cited 2026 Jan 28]. Available from: https://www.cdc.gov/antibiotic-use/hcp/core-elements/hospital.html

92. Krishnamoorthy Y, Govindan D, Karunakaran M, Parveen M, Manohar A, Al-Tawfiq JA. Global impact of antimicrobial stewardship programs in healthcare: an umbrella review of effectiveness, cost-efficiency, and implementation strategies. J Infect Chemother. 2025 Aug;31(8):102753. doi:10.1016/j.jiac.2025.102753.

93. World Health Organization, Food and Agriculture Organization of the United Nations, World Organisation for Animal Health, United Nations Environment Programme. One health joint plan of action (2022-2026): working together for the health of humans, animals, plants and the environment [Internet]. Geneva: World Health Organization; 2022 Oct 14 [cited 2025 Nov 3]. Available from: https://www.who.int/publications/i/item/9789240059139

94. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: One Health approach. Vet World. 2022;15(3):743-9. doi:10.14202/vetworld.2022.743-749.

95. Johns Hopkins Bloomberg School of Public Health. 5 takeaways from the UNEP report on AMR [Internet]. 2023 Feb 20 [cited 2025 Sep 19]. Available from: https://publichealth.jhu.edu/2023/5-takeaways-from-the-un-environmental-programme-report-on-antimicrobial-resistance

96. Plackett B. Why big pharma has abandoned antibiotics. Nature. 2020 Oct;586(7830):S50-2. doi:10.1038/d41586-020-02884-3.

97. Towse A, Hoyle CK, Goodall J, Hirsch M, Mestre-Ferrandiz J, Rex JH. 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. 2017 Oct;121(10):1025-30. doi:10.1016/j.healthpol.2017.07.011.

98. Vincent JL, Rello J, Marshall J, et al. International study of the prevalence and outcomes of infection in intensive care units. JAMA. 2009 Dec 2;302(21):2323-9. doi:10.1001/jama.2009.1754.

99. Zhou W, Li M, Achal V. A comprehensive review on environmental and human health impacts of chemical pesticide usage. Emerg Contam. 2025 Mar;11(1):100410. doi:10.1016/j.emcon.2024.100410.

100. Aslam B, Asghar R, Muzammil S, et al. AMR and Sustainable Development Goals: at a crossroads. Global Health. 2024;20:73. doi:10.1186/s12992-024-01046-8.