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Review Article

Reviving the Remedy: Global Action against Antimicrobial Resistance through Stewardship

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ABSTRACT

Antimicrobial Resistance (AMR) has become a significant healthcare problem worldwide, claiming an estimated 1.27 million lives in 2019, and the situation is projected to worsen by 2050. This threat arises from the improper use of antibiotics, particularly during surgeries and the treatment of common infections. Some of the mechanisms of bacterial resistance are drug target changes, enzyme breakdown, hampered absorption, and efflux of drugs, commonly aided by changes in genes through mutation or horizontal gene transfer. These translate into chronic infection, raised medical expenditure, long hospitalizations, and raised morbidity and mortality. Antimicrobial Stewardship Programs (ASPs) are a pillar in the fight against AMR because they provide direction in the rational use of antibiotics, audit prescriptions, place formulary restrictions, and endorse evidence-based measures. ASP implementation, however, in LMICs is hard because of a lack of infrastructure, low laboratory capacity, poor administrative management, and scarce interaction between healthcare professionals and the population. In addition to stewardship, the process of returning antibiotics' efficacy needs international collaboration in antibiotics research, a reappraisal of pharmaceutical R&D, and an incentive to produce antibiotics. The global health community should work together to create a holistic defense against AMR so that future generations can still use life-saving drugs. Unless it is checked, AMR poses a risk of reversing decades of medical advances, as infections become more and more incurable and even more lethal.

Keywords: Antimicrobial Resistance (AMR), Antibiotic misuse, Bacterial resistance mechanisms, Antimicrobial Stewardship Programs (ASPs), Global collaboration.

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INTRODUCTION

The worldwide health hazard of AMR has been occasioned by the fact that most individuals and organizations are misusing antimicrobial remedies and also utilizing them in abundance. The recent decades have witnessed an alarming increase in the number of resistant infections that have eventually escalated the number of patient deaths, lengthy hospital stays, and high costs. The authors predict that in 2019, approximately 1.27 million people died due to bacterial antibiotic resistance, with even more than 4.95 million deaths caused by bacterial antibiotic resistance all over the world. If present tendencies keep their course, by the year 2050, AMR is likely to kill 10 million people per annum, which is more than cancer and diabetes combined. The main cause of this alarming statistic is the improper distribution of antibiotics, which may be caused by ignorance, under-regulation, and the absence of a health infrastructure (Kraker *et al*., 2016; Murray *et al*., 2022; O'Neill, 2016; Ventola, 2015; World Health Organization, 2014). There is no treatment of infectious diseases without antibiotics, as well as major procedures such as organ transplants, chemotherapy, and robotic surgery, and also in preventing infections after surgical procedures. Their misuse threatens the entire ecosystem of modern healthcare, risking a return to the pre-antibiotic era where minor infections could prove fatal (World Health Organization, 2017). That's why dealing with AMR goes beyond science; it is important for the health of the entire world.

One of the most strategic solutions in this fight is the implementation of Antimicrobial Stewardship Programs (ASPs). Very often, the term "stewardship" is used, and yet its meaning is not always clear. According to Dyar *et al*., antimicrobial stewardship means performing certain actions to ensure proper use of antibiotics (Dyar *et al*., 2017). ASPs include evidence-based measures to help optimize the use of antibiotics, track prescribing routines, examine trends in resistance, and help advance educational activities with healthcare professionals (Barlam *et al*., 2016). The review describes the complexity of the AMR drivers and explains why global stewardship in high- and low-resource environments is important to maintain the effectiveness of

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antimicrobial agents. It also talks about policy frameworks, mass education campaigns, and the expected role of stewardship in bringing forth a more secure future.

FACTORS INFLUENCING ANTIMICROBIAL RESISTANCE (AMR)

The development of AMR goes hand-in-hand with the obsessive use and inadequate use of antibiotics since their birth. Already in the 1940s, Sir Alexander Fleming, the discoverer of penicillin, stated that its inappropriate use might result in resistance, an issue that has eventually swept the globe (Bin *et al*., 2017; Langford and Morris, 2017). In most low- and Middle-Income Countries (LMICs), access to correct diagnostics is limited, and therefore empirical treatment with broad-spectrum antibiotics, unless required, is common (Chaw *et al*., 2018). To add to this is the occurrence of the availability of low-quality or fake antibiotics as well as Over-the-Counter (OTC) sales of antibiotics in most countries, with the Indian and Vietnamese countries being particularly lax in their regulation or enforcement of the regulation (Chokshi *et al*., 2019; Nguyen *et al*., 2013). Such uncontrolled accessibility contributes to self-medication, whereby the patients self-treat conditions that do not necessarily need the intervention of antimicrobials, further hastening the emergence of resistance (Bin *et al*., 2017; Chokshi *et al*., 2019). Besides, the use of antibiotics is widespread in mammal husbandry and plant production, in addition to application to humans, leading to a substantial share of AMR in the environment. Recent projections concluded that, given the changes in overall veterinary antibiotic usage, countries like Indonesia, Myanmar, Nigeria, and Peru will record the largest relative increases by the year 2030, and for Vietnam, the rise will still be moderate but significant (Boeckel *et al*., 2019). One Health is the approach that proposes to look at the interrelationship of human and animal health and environmental health, and this is crucial in creating comprehensive stewardship policies that include all these fields. It is possible to cope with these problems with the help of a coordinated and global approach. As illustrated in Figure 1, the overuse and misuse of antibiotics can lead to several adverse effects on host health, including disruption of the gut microbiota, increased susceptibility to infections, and the emergence of antibiotic-resistant strains. To restore the remedy and maintain the overall health developments in the world, it is crucial to empower the ASPs, implement strict regulations, and make quality diagnostics and therapeutics available equally to all. In addition to looking at human behavior, the state of the environment also plays a big role. Despite their advantages, antibiotics often reach the environment through the wastewater system, farm water, and medical locations. The constant presence of antibiotics in these settings acts as a constant source of selection pressure, which promotes the growth of bacteria that are resistant to them (Yousuf *et al*., 2023). Figure 2 demonstrates the transmission pathways of resistant bacteria between farm animals, environmental sources, and humans (Rawpixel, n.d.; Vecteezy, n.d.).

ANTIMICROBIAL RESISTANCE MECHANISM (AMR)

It is required to obtain knowledge concerning the processes of AMR to help further the fight against resistance globally. To avoid the impact of antibiotics, there are numerous survival strategies used by bacteria, which undermine the outcome of treatment and also lead to AMR in various parts of the world. All these mechanisms can be reduced to four main groups: 1. Limited Intake of Drugs, 2. Modification of Drug Targets 3. Drug Inactivation 4. Active Drug Efflux The mechanisms that include diffusion barriers to limited uptake of antibiotics, enzymes, and activation of efflux pumps are generally regarded to be a part of the inner resistance mechanism inherently found in some bacterial species. Contrastingly, altered drug targets, learned enzyme barriers, and efflux gene acquisition tend to symbolize acquired obstruction, more often deciphered via horizontal gene transmission or as a result of altering (Chancey *et al*., 2012; Mahon *et al*., 2014). Mode and level of resistance also occur as a result of structural differences between gram-positive bacteria and gram-negative bacteria. Gram-positive bacteria, which contain no outer membrane made of Lipopolysaccharides (LPS), are typically less prepared to barricade antibiotics with the help of an external layer. In the meantime, gram-negative bacteria, as they have a double-membrane structure and are covered with LPS, employ all four resistance strategies, namely decreased permeability, target defense mechanisms, and enhancement of many more efflux pumps; they are hard to treat. In the global stewardship context, the awareness of these mechanisms offers a scientific basis to customize strategies on antimicrobial policies, prescriptions, and the development of the next-generation antibiotics. It also denotes the necessity to talk about diagnostic stewardship to guarantee that resistance mechanisms can be diagnosed quickly and treatment adjusted. An alternative to the development of new drugs that can subsequently help in the combat of antimicrobial resistance, therefore, lies in applying evidence-based stewardship programs that specifically oppose these resistance pathways at the single-patient and system level. Figure 3 illustrates the historical development of antibiotics and the parallel emergence of resistance mechanisms among bacteria (Mahizhchi *et al*., 2024).

GLOBAL BURDEN OF ANTIMICROBIAL RESISTANCE (AMR)

Antimicrobial Resistance (AMR) poses a dual threat to global health and economic stability, increasingly undermining the foundations of modern medicine. As resistant infections continue to rise, the consequences are becoming more pronounced in

terms of both patient outcomes and systemic costs (Stewardson *et al*., 2016).

Health-Related Burden

AMR significantly amplifies the complexity of disease management. Patients with resistant infections often experience longer hospital stays, require isolation precautions, and demand greater specialist intervention, all of which strain healthcare resources (Limmathurotsakul *et al*., 2019). Seeing the increasing concern, the government of the United Kingdom asked economist Jim O'Neill to carry out a wide-ranging review on AMR. His landmark report drew international attention to the crisis, estimating that 700,000 people die annually due to drug-resistant infections-most notably drug-resistant Tuberculosis (TB)-with projections rising to 10 million deaths per year by 2050 if urgent action is not taken (O'Neill, 2016).

A real-world clinical case illustrates the critical nature of this threat: on March 28, 2025, an 82-year-old woman presented with a Urinary Tract Infection (UTI). Laboratory findings identified Enterococcus species as the causative agent, yet the isolate showed resistance to all tested antibiotics, including gentamicin, penicillin, nitrofurantoin, and norfloxacin. This alarming resistance profile rendered standard treatment ineffective and highlighted the severe limitations faced by healthcare providers in managing such infections.

This is not an isolated event. Countless similar cases are being reported across India and globally, reflecting the widespread and escalating nature of AMR. If not addressed promptly, AMR could result in the collapse of standard infection control practices, severely compromising surgeries, cancer treatment, neonatal care, and other medical interventions that rely on effective antibiotics.

Economic Burden

Beyond health, the economic ramifications of AMR are far-reaching. Resistant infections increase healthcare costs, require more expensive or prolonged treatments, and reduce the productivity of both patients and caregivers. Entire families may face emotional and financial distress due to recurrent infections, prolonged recovery, and limited treatment options.

Countries already grappling with limited healthcare budgets are especially vulnerable. Resources that should be allocated to essential services are often diverted to manage outbreaks of resistant infections. This redirection can cause social imbalance, particularly in communities with limited financial resilience. Compounded by inequities in banking, healthcare access, and infrastructure, the economic strain of AMR deepens social vulnerabilities.

Additionally, global factors like climate change and international travel exacerbate the spread and persistence of resistant organisms. This underlines the need for collaborative, transnational efforts to mitigate AMR through integrated stewardship programs, sustainable pharmaceutical innovation, and fair access to diagnostics and therapeutics (Patel *et al*., 2023).

RATIONALE FOR ANTIBIOTIC STEWARDSHIP

The increase in AMR underlines how important it is to follow AMS supported by evidence. Without updated clinical guidance and local resistance data, inappropriate antibiotic use may escalate, leading to devastating public health and economic consequences. Antibiotic stewardship ensures that healthcare providers are empowered to make informed, timely, and targeted prescribing decisions, which form the first line of defense against AMR and unnecessary medical interventions.

AMR significantly complicates and increases the cost of patient treatment, placing a burden on healthcare infrastructure. Interestingly, studies reveal that without structured stewardship, even well-meaning physicians may unintentionally contribute to antimicrobial overuse. Furthermore, public advertisements and awareness campaigns have helped bring responsible antibiotic use to the forefront, especially in the wake of Clostridium difficile outbreaks and rising safety concerns in clinical settings.

By investing in education, feedback mechanisms, and continual professional development, we not only preserve the effectiveness of current antimicrobials but also safeguard future generations from the catastrophic consequences of unchecked resistance (World Health Organization, 2021).

CORE STRATEGIES OF ANTIMICROBIAL STEWARDSHIP

Educating Healthcare Providers

Never-ending education of clinicians is a main principle in AMS. Physicians must stay abreast of emerging resistance patterns, new antibiotics, and appropriate treatment protocols to ensure optimal care. Hospital administrators and healthcare leaders play a critical role in supporting these efforts by allocating resources for diverse educational formats-including online modules, seminars, clinical workshops, and interdisciplinary conferences (World Health Organization, 2021). Evidence indicates that educational interventions can significantly reduce inappropriate antibiotic prescribing. In one study, intervention groups receiving training via phone consultations, electronic messaging, seminars, and in-person lectures demonstrated sustained reductions in antibiotic use over four months compared to control groups (Doron and Davidson, 2011).

Educating Patients and the Public

Public awareness is a vital pillar in the fight against AMR. Many individuals remain unaware of the dangers of improper antibiotic use, such as self-medication, non-adherence to prescriptions, or

expecting antibiotics for viral infections. Education efforts should focus on emphasizing the importance of:

- Completing prescribed antibiotic courses,
- Following medical advice strictly,
- Knowing that antibiotics are not helpful when treating viral infections (Ayukekbong *et al*., 2017; Abushaheen *et al*., 2020).

Campaigns promoting public literacy, enhancing patient-doctor communication, and dispelling myths around antibiotics are essential in shaping long-term behavioral change and reinforcing the global effort to reduce AMR (Ayukekbong *et al*., 2017).

Prescription Audits and Feedback

A proactive approach to stewardship includes regular prescription audits and real-time feedback. Stewardship teams evaluate the

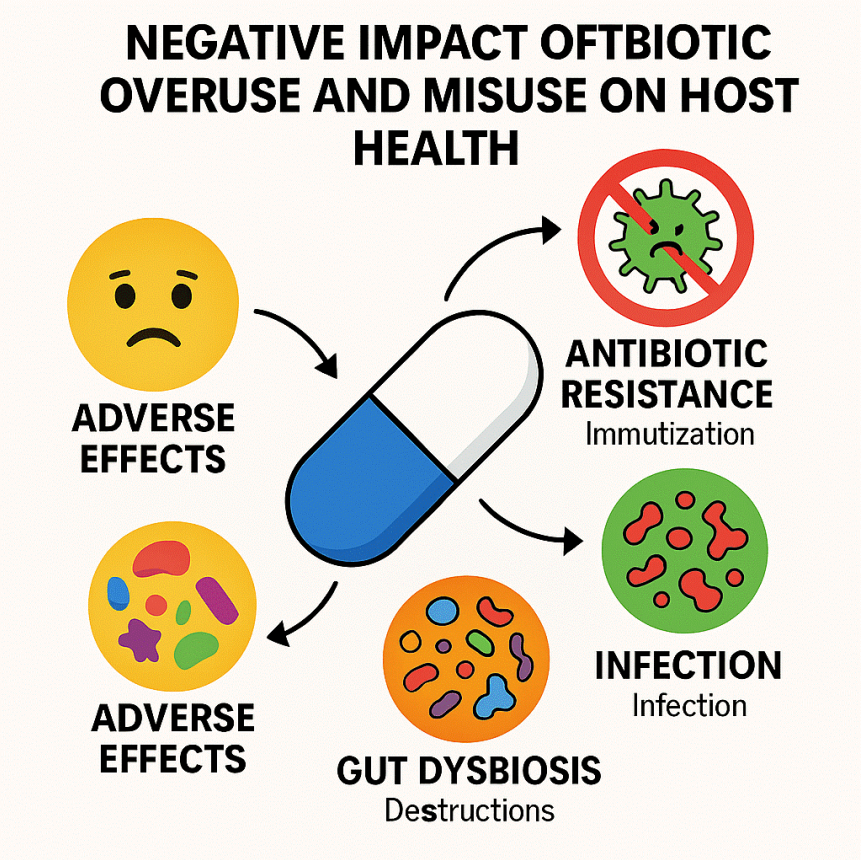

Figure 1: The overuse and misuse of antibiotics can lead to several adverse effects on host health, including disruption of the gut microbiota, increased susceptibility to infections, and the emergence of antibiotic-resistant strains.

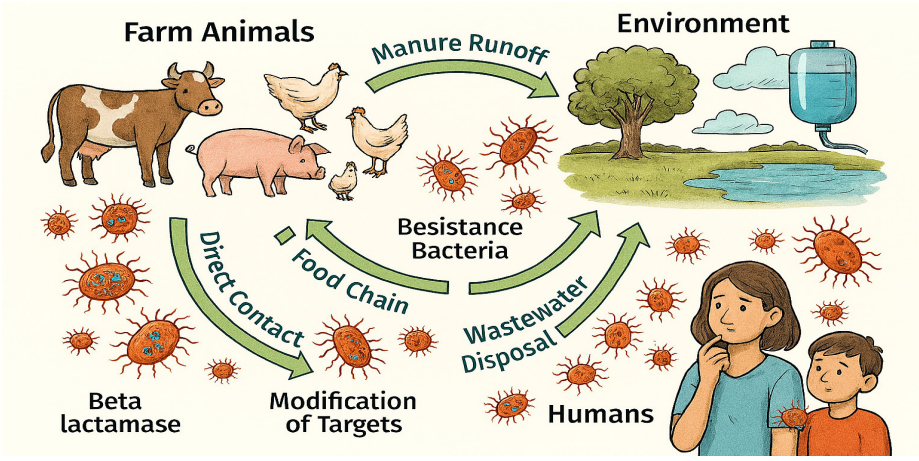

Figure 2: The transmission pathways of resistant bacteria between farm animals, environmental sources, and humans.

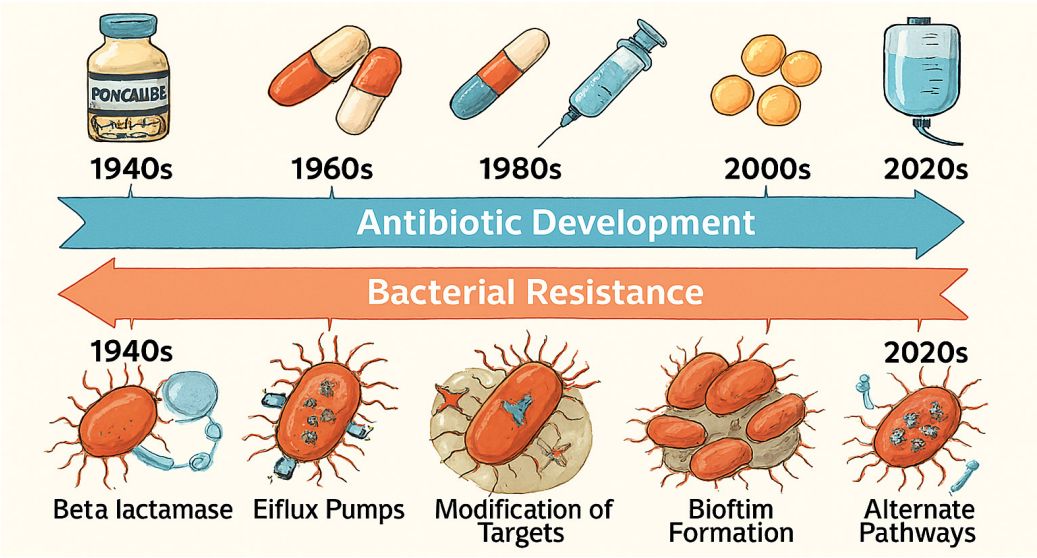

Figure 3: The historical development of antibiotics and the parallel emergence of resistance mechanisms among bacteria.

use of high-risk or broad-spectrum antibiotics shortly after they are prescribed-typically within 48-72 hr-and provide recommendations to continue, adjust, or discontinue therapy based on the patient's clinical response and microbiology reports.

For instance, approval for the use of vancomycin or other critical antibiotics often requires initial authorization followed by a reassessment after two days. This method has shown success in both adult and pediatric settings by reducing unnecessary usage and promoting targeted therapy (Metjian *et al*., 2008; Patel and Saiman, 2012).

Such structured feedback loops foster accountability, precision, and safety in prescribing practices while preserving antimicrobial efficacy.

Formulary Restriction and Preauthorization

Antimicrobials or drugs included in a formulary are approved by a regulatory body working at either the institution, health network, or national level. These formulary systems help regulate the use of antimicrobial agents and promote consistency in prescribing practices (Australian Commission on Safety and Quality in Health Care, 2018). A common practice in hospitals and NICUs alike is to use formulary restrictions and require preauthorization before giving certain medications (Patel *et al*., 2010). By limiting the availability of high-risk or broad-spectrum antibiotics, hospitals aim to encourage rational prescribing. However, such restrictions may unintentionally shift prescribing behavior toward a few permitted drugs, increasing pressure on those agents. Once a prescriber gains approval for a restricted drug, they often receive little follow-up guidance or decision support on its continued use, which may limit the effectiveness of such controls (Cabana *et al*., 1999). Table 1 illustrates other strategies for effective antimicrobial stewardship (Patel and Saiman, 2012).

ADDITIONAL ANTIMICROBIAL STEWARDSHIP STRATEGIES

Challenges in Implementing Antibiotic Stewardship

Resource Constraints in LMICs

Antimicrobial resistance and healthcare-associated infections are a bigger problem for low- and middle-income countries. Barriers include a lack of infrastructure, limited diagnostic facilities, absence of trained personnel, poor financing, and inadequate access to IT tools and antimicrobial data. Increased political problems and higher turnover of staff make applying AMS programs more problematic. These systemic gaps leave such regions vulnerable to the unchecked spread of resistant pathogens (Abbas, 2024).

Diagnostic Limitations

In LMICs, infectious diseases remain widespread, especially among immunocompromised populations affected by HIV, malnutrition, and malaria (Feikin *et al*., 2011). Hospital-based microbiology labs are scarce, and those that exist often face challenges related to staffing, equipment, and standardization (Petti *et al*., 2006). Robust diagnostic stewardship demands adherence to quality protocols covering sample collection, facility design, waste management, water access, and quality control, which are frequently absent (Barbé *et al*., 2016; Barbé *et al*., 2017).

Lax policy enforcement

One more topic of main concern is about pharmacy practices. Even in situations where the hospitals will embrace the use of AMS guidelines and protocols, patients will be able to purchase antibiotics without prescriptions. This interferes with the hospital policies, and this is the reason why the community-based one is required. This is, as one of the pharmacists described it, when the

Table 1: Other strategies for effective antimicrobial stewardship (Patel and Saiman, 2012).

Strategy	Examples
Guidelines and Clinical Pathways	Develop consensus protocols for the treatment duration of culture-negative sepsis.
Antimicrobial Order Forms	Implement automatic stop orders to ensure appropriate perioperative prophylaxis.
Dose Optimization	Titrate vancomycin levels to 15-20 mg/L for persistent MRSA bacteremia.

hospital declines to administer antibiotics to the patient, the latter will just walk down the block and get them in a neighborhood drugstore (Shah *et al*., 2024).

Inadequate Training and Consciousness

A majority of the health care workers, including the physicians, nurses, pharmacists, or even the informal care providers in LMICs, lack any training in antimicrobial stewardship (García *et al*., 2011; Thriemer *et al*., 2013; Quet *et al*., 2015; Viberg *et al*., 2010; Morgan *et al*., 2011). Although there is awareness concerning AMR, they are rarely translated into clinical decisions (Thriemer *et al*., 2013; Quet *et al*., 2015). The important concepts in antimicrobial resistance are not given much consideration in the current medical programs. ABR education has to be integrated into the undergraduate training and professional training (World Health Organization, 2015; Pulcini and Gyssens, 2013). The availability of locally derived evidence-based statistics, in general, is also low, which means that personalized rules cannot be created or utilized (Agweyu *et al*., 2012; Nabyonga Orem *et al*., 2012).

Limited technological support

The use of manual processes in the pharmacy practice that exists in most primary and secondary health facilities leads to inefficient documentation of the antimicrobial usage. Generating antibiograms or reviewing culture sensitivity reports is time-intensive and rarely automated. Smaller hospitals often outsource diagnostic tests to external laboratories, leading to delayed clinical decisions and suboptimal antimicrobial use (Thriemer *et al*., 2013; Quet *et al*., 2015).

FUTURE PERSPECTIVES

Antimicrobial resistance presents an escalating threat to modern medicine. The pipeline of antibiotics that are yet to be developed is very low because pharmaceutical firms lack the motivation to invest in this field. The majority of the existing antibiotics are derivatives of previous broad-spectrum ones. There has been a developing trend, however, toward precision antimicrobials, also known as agents that specifically attack a certain type of infection with a new mechanism; these can potentially slow down resistance formation. New business models are needed to encourage the innovation of pharmaceuticals.

The attempts of the UK, by means of NHS and NICE, to consider the reimbursement issues concerning antibiotics with references to value, are a decent beginning. Earlier use of such targeted therapies, as a primary rather than a final alternative, might lead to clinical and commercial benefits, which may encourage study of such therapies in research and development (Kmietowicz, 2017).

CONCLUSION

The world faces a worldwide crisis of antimicrobial resistance, which increases, supported by excess use in human and veterinary curing, and aggravated by ecological contamination.

Bacteria evolve diverse resistance mechanisms, threatening the efficacy of existing treatments. While Antimicrobial Stewardship Programs (ASPs) offer hope through education, monitoring, and guideline enforcement, their success-especially in resource-constrained settings-is hindered by a lack of infrastructure, training, and institutional support.

Addressing AMR requires a collaborative global response: strengthening diagnostic capacity, reforming commercial incentives for antibiotic development, educating prescribers and the public, and implementing resilient policy frameworks. Without proper and speedy action, people may experience dangerous illnesses again, like those that were once very easy to treat.

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ABBREVIATIONS

AMR: Antimicrobial Resistance; **ASPs:** Antimicrobial Stewardship Programs; **LMICs:** Low- and Middle-Income Countries; **OTC:** Over-the-Counter; **LPS:** Lipopolysaccharides; **TB:** Tuberculosis; **UTI:** Urinary Tract Infection; **NICU:** Neonatal Intensive Care Unit; **NHS:** National Health Service; **NICE:** National Institute for Health and Care Excellence.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

SUMMARY

Antimicrobial Resistance (AMR) is accumulated owing to the improper use of antibiotics. The resistance has increased the difficulty of curing infections, which has meant prolonged hospital stays, higher costs, and 10 million dead each year, a projection that may reach 10 million annually by 2050. The authors identify some of the major factors that have contributed to the development of this crisis, such as inappropriate diagnostic equipment, unregulated selling of over-the-counter antibiotics, and their extensive use in human medicine as well as agriculture. To counter this, in the review paper, the significance of Antimicrobial Stewardship Programs (ASPs) is brought out, which provide a systematic review of antibiotic use by conducting continuous education of healthcare providers and the community, prescription audits, and stringent control of the formulary. Nevertheless, difficulties in the implementation of such programs, especially in low- and middle-income countries, are severe, as there are shortages in resources, limitations in diagnosis, and weak enforcement of policies and inefficient training. The authors summarize that a global, unilateral approach is crucial where new pharmaceutical inventions, enhanced diagnostic skills, and solid policy initiatives are all needed to avoid going back to the times when the world lived in the pre-antibiotic era.

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