

Review Article

A Global Syndemic: The Interwoven Roles of Climate Change and Socioeconomic Disparities in Driving Antimicrobial Resistance

Yasir Alhassan Ahmad ^{1*}

1. Department of Public Health, Symbiosis Institute of Health Sciences, Symbiosis International (Deemed University), Pune, India

* Correspondence: ahmadyasir@gmail.com

Abstract: Antimicrobial resistance (AMR) represents an escalating, multifactorial crisis that threatens to undermine modern medicine. The World Health Organization (WHO) has identified AMR as a top global public health and development threat. Recent data estimates that AMR was directly responsible for 1.27 million deaths and associated with nearly 5 million deaths in 2019 alone. This is not merely a clinical challenge but a complex “syndemic” driven by the convergence of a changing climate and persistent socioeconomic disparities. This review synthesized recent findings to elucidate the intricate, often synergistic, pathways through which these two macro-level forces accelerate the development and spread of AMR. The report examines how rising temperatures and extreme weather events, fueled by climate change, create conditions ripe for microbial adaptation and environmental dissemination of resistant pathogens. Concurrently, it explores how socioeconomic factors—including poverty, inadequate healthcare infrastructure, and weak governance—perpetuate the misuse of antimicrobials and amplify the risk of infection, with the burden disproportionately impacting low- and middle-income countries (LMICs). Crucially, the report highlights a vicious cycle where climate-related crises exacerbate pre-existing socioeconomic vulnerabilities, leading to a compounding effect on AMR. Finally, it reviews global response strategies, emphasizing that siloed, drug-centric approaches are insufficient. Drawing on the “One Health” framework, the review argues that effective mitigation requires integrated, multi-sectoral policies focused on sustainable development initiatives like universal access to water, sanitation, and hygiene (WASH) services and robust public health infrastructure, alongside the pursuit of innovative non-traditional therapies.

Keywords: interwoven, roles, climate change, socioeconomic disparities, antimicrobial resistance

1. THE UNPRECEDENTED THREAT OF ANTIMICROBIAL RESISTANCE

The ability of microorganisms to resist drugs designed to kill them, a phenomenon known as antimicrobial resistance (AMR), has emerged as one of the most significant public health and development threats of the 21st century [1]. The scale of this crisis is staggering, challenging the very foundation of modern medicine. Infections that were once easily treatable with a short course of antibiotics are now becoming increasingly difficult and, in some cases, impossible to manage. This reality jeopardizes the safety of routine medical procedures, such as surgery and cancer chemotherapy, and threatens to return the world to a “post-antibiotic era” where common infections could once again be deadly [2]. The human toll of AMR is immense. A report from The Lancet estimated that in 2019, bacterial AMR was directly responsible for 1.27 million deaths globally and was associated with a staggering 4.95 million deaths [5]. To put this in perspective, this makes AMR one of the leading causes of death, surpassing the number of deaths from HIV/AIDS and roughly doubling the deaths from malaria

in the same year [6]. This health burden is not distributed equally, with the vast majority of deaths occurring in low- and middle-income countries (LMICs). For children under five, the disparity is particularly grim, as 99.65% of AMR-related deaths in this age group occur in LMICs, highlighting a profound global inequality in the crisis [6]. Beyond the human cost, AMR imposes a severe economic burden on health systems and national economies. A collaborative CDC study estimated the annual cost to treat infections from just six antimicrobial-resistant germs in the U.S. at over 4.6 billion [5]. Globally, the economic impact is projected to be far more extensive. The World Bank estimates that AMR could lead to an additional US\$1 trillion in healthcare costs by 2050, and other analyses project a potential decline in global gross domestic product (GDP) of US\$1.67 trillion by 2050 if resistance rates continue to accelerate [2]. This economic pressure stems from the need for more expensive and intensive care, longer hospital stays, and reduced workforce productivity due to illness and disability [4]. To effectively address this complex and multifaceted problem, a new conceptual framework is required. The "One Health" approach, which recognizes the interconnectedness of human health, animal health, plant health, and the environment, provides the necessary perspective [1]. It posits that AMR is not an isolated problem confined to clinical settings but a systemic issue that requires coordinated policy action across all these sectors. This review adopts the One Health framework to explore how two primary macro-level forces—a changing climate and deep-seated socioeconomic disparities—act as major drivers of the AMR crisis, often in a synergistic and mutually reinforcing manner.

Table 01: Global Burden and Economic Impact of Antimicrobial Resistance (2019-2050)

Metric	Value (2019)	Source
Direct Deaths from AMR	1.27 million	[7]
Deaths Associated with AMR	4.95 million	[7]
U.S. Annual Healthcare Costs (6 germs)	>US\$4.6 billion	[5]
China Annual Healthcare Costs	US\$42 billion	[11]
Projected Global GDP Decline (by 2050)	US\$1.67 trillion	[8]
Projected Global GDP Gain (by 2050)	US\$990 billion	[9]
Projected Global Healthcare Cost Increase (by 2050)	US\$1 trillion	[2]

2. MECHANISMS AND EPIDEMIOLOGY OF ANTIMICROBIAL RESISTANCE

Understanding the global burden of AMR requires a foundational knowledge of the mechanisms by which microbes evade antimicrobial drugs. These mechanisms can be innate to the organism or acquired from other microorganisms, often through horizontal gene transfer [12]. There are four primary cellular and molecular strategies that confer resistance. The first is limiting drug uptake, where bacteria modify their cell wall or outer membrane to physically block or reduce the entry of antimicrobial agents. Gram-negative bacteria, for example, have an outer LPS layer that acts as a barrier to certain molecules, giving them intrinsic resistance to large antimicrobial agents. Similarly, mutations in porin channels, which normally allow hydrophilic molecules to enter the cell, can either decrease the number of channels or alter their selectivity, thereby restricting drug access [13]. A second mechanism involves modifying a drug target, where microorganisms alter the specific site to which a drug binds. This change prevents the drug from recognizing and attaching to its target, rendering it ineffective. A classic example is the resistance of *Staphylococcus aureus* to vancomycin, where the bacteria produce a thickened cell wall that makes it difficult for the drug to reach its target [13]. The third major

mechanism is inactivating a drug through the production of enzymes that chemically destroy or modify the antibiotic. A well-known example is the production of beta-lactamases, which break down the beta-lactam ring of drugs like penicillin, neutralizing their effect. Finally, AMR can arise from active drug efflux, where bacteria develop protein pumps that actively transport antimicrobial agents out of the cell before they can reach a concentration sufficient to kill the microbe [12]. These mechanisms are not mutually exclusive and can operate in combination, creating a formidable defense against a wide range of drugs. The spread of AMR is further amplified by the formation of biofilms. These are thick, sticky communities of bacteria encased in a matrix of polysaccharides, proteins, and DNA. Within a biofilm, microbes are protected from the host immune system and antimicrobial agents. The dense, slow-metabolizing nature of the bacterial cells in a biofilm means that drugs targeting growing and dividing cells are less effective. Most importantly, the close proximity of bacterial cells within a biofilm facilitates the horizontal transfer of antimicrobial resistance genes, enabling the rapid sharing of genetic material and accelerating the evolution of resistance across a community of organisms [13]. The epidemiology of AMR demonstrates significant geographical disparities, with the greatest burden concentrated in LMICs. Sub-Saharan Africa, for instance, had the highest mortality rate attributable to AMR in 2019, at 23.5 deaths per 100,000, far exceeding rates in other regions [14]. These disparities highlight that while the mechanisms of resistance are microbiological, the underlying drivers are rooted in human systems and behaviors, which are heavily influenced by climate and socioeconomic factors.

3. THE IMPACT OF A CHANGING CLIMATE ON AMR

The climate crisis and its effects on the natural environment are increasingly recognized as critical drivers of AMR. The impact is not limited to a passive increase in disease spread; a changing climate actively contributes to the development of drug resistance at a microbial level. This intricate relationship operates through multiple pathways, all of which underscore the necessity of a One Health approach. Studies have established a direct, positive correlation between rising global and local temperatures and increased rates of antimicrobial resistance. For instance, a 2018 study found that a 10°C increase in local temperature was associated with a 2.2% to 4.2% rise in antibiotic resistance for common bacterial pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, and *Staphylococcus aureus* [15]. Research published in *Nature Ecology & Evolution* reinforced this finding, showing that warmer temperatures make soil bacteria more resilient and better equipped to survive in the presence of antimicrobial agents. Laboratory experiments with *E. coli* confirmed a molecular basis for this phenomenon: elevated temperatures lead to increased expression of antibiotic resistance genes, including those responsible for efflux pumps and stress response proteins [16]. This finding suggests that climate change is not merely a passive environmental backdrop but an active evolutionary force. The physiological stress imposed by a warmer environment appears to trigger a bacterial survival response that includes the upregulation of defense mechanisms. This means that even in the absence of increased antibiotic use, climate change is actively generating new resistance. The effect is a self-perpetuating feedback loop where rising temperatures create an environment that encourages microbial adaptation, accelerating the evolutionary arms race between pathogens and our therapeutic interventions. The increasing frequency and severity of extreme weather events, such as floods, storms, and heavy rainfall, represent a significant mechanism for the environmental dissemination of AMR. These natural disasters can damage crucial water, sanitation, and hygiene (WASH) infrastructure and wastewater management systems [15]. When sewage and agricultural waste systems are compromised, they release a mix of pollutants and antimicrobial-resistant microbes into waterways, air, and soil.¹⁵ Since wastewater is a known reservoir for resistance genes, this environmental pollution acts as a conduit for the spread of resistant bacteria into broader ecosystems, where they can encounter and infect humans and animals. The implications of this environmental spread are profound. The environment effectively becomes an incubator for resistance, facilitating the transfer of resistance

genes between environmental bacteria and human pathogens. The problem is no longer confined to hospitals or clinics but is a pervasive threat present in our water and food systems. This physical pathway for the spread of AMR highlights the critical need for a One Health perspective, as a failure in one sector (environmental infrastructure) directly compromises another (human health). A changing climate may also be responsible for the emergence of new pathogens that pose a threat to human health. Evidence suggests that the deadly fungal pathogen *Candida auris*, which is often multi-drug resistant, may have evolved to become pathogenic in humans as a direct result of the climate crisis [5]. The hypothesis is that a warmer climate provides the selective pressure needed for environmental microbes to adapt to higher temperatures, making the transition to a human host's stable body temperature a more viable evolutionary step. Furthermore, the thawing of permafrost in the Arctic, a direct consequence of global warming, is believed to be releasing ancient, long-dormant pathogens. A 2016 anthrax outbreak in Siberia, for example, has been linked to the thawing permafrost and the exposure of a reindeer carcass infected with anthrax many years ago [15]. These events suggest that climate change is not only accelerating the resistance of known pathogens but is also creating entirely new infectious threats from the vast microbial diversity of the planet. This adds another layer of urgency to the AMR crisis, as we are facing not only a battle against drug-resistant microbes but also the potential emergence of novel infectious agents for which we have no treatments.

4. SOCIOECONOMIC DRIVERS OF AMR

The AMR crisis is fundamentally a matter of equity, with socioeconomic factors playing a critical role in its perpetuation and disproportionate burden on the most vulnerable populations. Poverty, inadequate infrastructure, and weak governance create a complex environment that accelerates the development and spread of drug-resistant infections. Poverty acts as a profound barrier to effective infection treatment and prevention, thereby fueling AMR. In many parts of the world, particularly in LMICs, financial constraints can prevent individuals from accessing basic medical care, leading to delayed diagnoses and treatment for bacterial infections [20]. Even when treatment is sought, the high cost of medicines can lead to inappropriate behaviors, such as self-medication, purchasing cheaper and often less effective or substandard drugs, and prematurely stopping a course of antibiotics to save money [20]. The use of substandard or falsified antibiotics, which contain suboptimal levels of active ingredients, fails to kill pathogens and instead exposes them to a sub-lethal dose, creating the ideal conditions for the selection and propagation of resistant strains [10]. This problem is not confined to LMICs; a U.S. study found a higher incidence of invasive MRSA and ESBL-producing *Enterobacter* *ales* infections in lower-income and medically underserved areas, demonstrating the link between poverty and AMR in high-income countries as well [21]. Inadequate public health infrastructure, particularly in sanitation and hygiene, is a major driver of AMR. Only 43% of the population in LMICs has access to safely managed water, and only 30% has access to sanitation. These deficiencies are exacerbated in urban areas, where high population density amplifies the risk of bacterial transmission not only between humans but also between humans and animals. Studies have found that bacterial isolates from urban settings are almost always more resistant than those from rural areas [22]. This is due to a perfect storm of factors: overcrowding, poor hygiene, and a higher prevalence of infectious diseases that necessitate antibiotic use. A lack of effective WASH services leads to a high prevalence of diseases like diarrhea that are often treated with antibiotics, creating a continuous cycle of infection, antibiotic use, and resistance development. The profound impact of this is highlighted by the fact that universal access to WASH services is projected to reduce antibiotic-treatable diarrheal illnesses by 60%, a powerful argument for infrastructural investment as a primary AMR strategy [21]. The mismanagement and misuse of antimicrobials are primary drivers of resistance; a problem often rooted in weak governance and regulatory failure. Political instability, corruption, and a lack of enforcement allow for the unregulated sale of antibiotics without a prescription, a common practice in many LMICs [10].

Furthermore, the agricultural sector, which accounts for a substantial volume of global antimicrobial use, often operates with minimal oversight. Antibiotics are frequently used for growth promotion in livestock and aquaculture, not just for treating disease, creating a massive selective pressure on bacterial populations. The volume of antimicrobials used in animals worldwide is estimated to be greater than in humans, and this extensive use in the food supply chain is a significant reservoir for resistance [23]. These resistant microbes can then be transmitted to humans through food contamination, occupational exposure, and environmental pathways, blurring the lines between human, animal, and environmental health. The lack of surveillance and coordination between government sectors—such as health and agriculture ministries—is a critical failure that allows this problem to persist and grow [10].

Table 02: Key Socioeconomic and Climate-Related Drivers of AMR

Driver Category	Specific Factor	Mechanism of Action	Impact on AMR
Climate	Rising Temperatures	Increases expression of resistance genes; makes bacteria more adaptable and active.	Accelerates microbial evolution and proliferation of resistant strains [16]
	Extreme Weather Events	Damages WASH infrastructure, leading to sewage overflow and agricultural runoff.	Disseminates resistant microbes from known reservoirs into the environment [15]
	Emerging Pathogens	Puts selective pressure on environmental microbes, aiding their adaptation to human hosts.	Creates novel, multi-drug-resistant threats to human health (<i>Candida auris</i>) [15]
Socioeconomic	Poverty	Creates financial barriers to healthcare and high-quality drugs; leads to self-medication and shortened treatment courses.	Increases the misuse of antibiotics, creating a selection pressure for resistance [20]
	Inadequate Infrastructure	Lack of clean water and sanitation in dense urban areas.	Amplifies bacterial transmission and infection rates, increasing demand for antibiotics [21]
	Weak Governance	Poor regulation of antibiotic sales and agricultural use.	Perpetuates the use of substandard drugs and the non-therapeutic use of antimicrobials in food production [10]

5.THE SYNERGISTIC VICIOUS CYCLE: CLIMATE, SOCIOECONOMICS, AND AMR

The analysis of climate and socioeconomic factors reveals that they are not independent drivers of AMR; rather, they are locked in a devastating positive feedback loop that creates a complex "syndemic" of interconnected crises. A pivotal study by Chinese researchers provides a quantitative projection of this synergy, demonstrating that the combined effects of climate change and socioeconomic

vulnerabilities will lead to a rise in AMR that is more severe than either factor alone. The study projected that if the world continues on a fossil fuel-intensive development pathway, global AMR prevalence would rise by 2.4% by 2050, with LMICs facing a disproportionate 4.1% increase [26]. This vicious cycle often begins with a climate event that disproportionately impacts low-income populations. For example, a severe flood, a consequence of extreme weather, is most likely to affect densely populated, urban areas with fragile infrastructure [10]. This event immediately creates a public health emergency. The flooding compromises sanitation systems, flushing sewage—a rich reservoir of antibiotic-resistance genes—into the environment and contaminating drinking water sources [15]. Concurrently, the displacement of populations into crowded, unsanitary emergency shelters creates ideal conditions for the rapid transmission of infections. The surge in infectious diseases places an overwhelming strain on local healthcare systems, which are often already under-resourced and ill-equipped to handle mass casualties [10]. In this environment of chaos and scarcity, the demand for antibiotics skyrockets. The lack of access to proper diagnostics and a scarcity of medical professionals lead to a greater reliance on empirical antibiotic use, much of which may be unnecessary or inappropriate [28]. This intense and often indiscriminate use of antibiotics creates a strong selective pressure, accelerating the evolution of resistance among a wide range of pathogens. These new, resistant strains then become more prevalent, making the next wave of infections harder to treat, more deadly, and more costly. The economic fallout of the disaster—including lost homes, businesses, and income—pushes more people into poverty, further limiting their access to future medical care and creating an even greater vulnerability to the next health crisis [7]. The crucial point here is that addressing these issues in isolation is insufficient. The same Chinese study found that simply reducing antimicrobial consumption would have a smaller effect (a 2.1% reduction in AMR by 2050) than a comprehensive strategy focused on achieving sustainable development goals (a 5.1% reduction) [26]. This demonstrates that the root causes of the AMR crisis are not just biological but are deeply social and environmental. A policy that focuses solely on limiting antibiotic prescriptions without addressing the underlying poverty, poor infrastructure, and climate change that drive the demand for those prescriptions is a strategy that is destined to fail.

6. GLOBAL STRATEGIES AND FUTURE DIRECTIONS

The systemic nature of the AMR crisis demands a multi-pronged, globally coordinated response that extends beyond the traditional medical sphere. While the challenge is immense, a combination of sustainable development, improved governance, and innovative therapeutic approaches offers a path forward. The evidence strongly indicates that sustainable development is the single most effective strategy for mitigating AMR. The Chinese forecasting study showed that a comprehensive effort to achieve sustainable development goals could reduce global AMR levels by 5.1% by 2050, an impact more than double that of a purely medical approach focused on reducing antibiotic consumption alone [26]. This finding fundamentally reframes the battle against AMR, shifting the focus from a perpetual game of "whack-a-mole" with resistant bacteria to a more strategic, preventative approach. The most impactful sustainable development initiatives, according to the study, include: Reducing out-of-pocket health expenses: This was found to be the most prominent factor, with a potential reduction of 3.6% in AMR prevalence [26]. By removing financial barriers to care, this initiative ensures that patients can afford full courses of quality medications and are not driven to self-medicate or use substandard drugs. Comprehensive immunization coverage: Universal vaccination is a critical tool for preventing infections that would otherwise require antibiotics. Increasing immunization coverage is projected to reduce AMR prevalence by 1.2% by 2050 [27]. Universal access to water, sanitation, and hygiene (WASH) services: This initiative, foundational to public health, contributes to a 0.1% reduction in AMR [27]. As discussed, improved sanitation prevents the transmission of infectious diseases and reduces the overall demand for antibiotics. These data make a powerful case that the most effective "antimicrobial" is not a new drug but a healthy, educated, and well-resourced population with access to essential infrastructure and

preventative care. Global efforts to combat AMR have been guided by the WHO's Global Action Plan (GAP), established in 2015. The GAP outlines five key objectives: improving awareness and education, strengthening surveillance and research, reducing the incidence of infection, optimizing antimicrobial use, and developing the economic case for sustainable investment [3]. This framework provides the blueprint for countries to create their own National Action Plans (NAPs) [21]. However, the implementation of these plans faces significant challenges. The response to AMR is often inadequate due to a lack of political will, weak governance, and insufficient human and financial resources [20]. A lack of coordination and communication between the human, animal, and environmental health sectors—a fundamental tenet of the One Health approach—has resulted in fragmented and duplicated efforts [20]. The unregulated use of antibiotics in agriculture and the availability of substandard drugs, both symptoms of regulatory failure, continue to drive resistance on a massive scale [10]. To succeed, policy efforts must overcome these challenges by fostering cross-sectoral collaboration, strengthening surveillance systems, and ensuring adequate funding for implementation. A crucial component of any long-term AMR strategy is the development of new and innovative therapies. Unfortunately, the current antibacterial R&D pipeline is insufficient to meet the rising threat of resistance. While the number of antibacterial agents in the clinical pipeline increased from 80 to 97 between 2021 and 2023, there is a critical lack of innovation. Of the 32 antibiotics in development for high-priority pathogens, only 12 are considered truly innovative, and only four of these are effective against a WHO 'critical' pathogen [22]. This scientific and technical challenge, coupled with economic disincentives for pharmaceutical companies, has led to a significant gap in our ability to combat emerging superbugs. In response, research is increasingly focusing on non-traditional biological agents that exert limited selective pressure on bacteria, thus slowing the development of new resistance [22]. Several promising strategies are being explored:

- **Bacteriophages (Phages):** Phages are naturally occurring viruses that selectively infect and kill bacteria without harming human cells. They can be used as a "personalized medicine" to target specific antibiotic-resistant infections, either alone or in synergy with traditional antibiotics [13].
- **Anti-virulence Agents:** Instead of killing bacteria, these agents "disarm" them by blocking virulence factors, such as those used for adhesion or invasion [22]. This approach limits the damage caused by the pathogen while placing less selective pressure on it to develop resistance, as its growth is not directly inhibited.
- **CRISPR-Based Therapies:** Early-stage research is exploring the use of the CRISPR-Cas system as a precise gene-editing tool to eliminate resistance genes from bacterial genomes [17]. This technology could offer a highly targeted way to combat superbugs by stripping them of their resistance capabilities.

Table 03: Innovative Therapeutic Strategies in the Antimicrobial Pipeline

Therapy	Mechanism of Action	Advantages
Bacteriophages (Phages)	Viruses that specifically infect and destroy bacterial cells without affecting human cells.	High specificity to bacterial hosts; can be used as personalized medicine; can be synergistic with antibiotics [13].
Anti-virulence Agents	Block bacterial virulence factors (e.g., adhesion, invasion, colonization) rather than killing the bacteria.	Reduces selective pressure on bacteria to develop resistance; does not disrupt the body's normal microbiota [22].
CRISPR-based Systems	Utilize gene-editing tools to precisely remove antibiotic	Highly targeted approach to strip "superbugs" of their

	resistance genes from a bacterial genome.	resistance; offers potential for a definitive solution to genetic resistance [21].
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7. Conclusion

The global AMR crisis is a complex and urgent problem driven by the interconnected forces of climate change and socioeconomic disparities. This review has established that AMR is not a static threat but a dynamic evolutionary process fueled by a vicious cycle of environmental and social factors. Rising global temperatures accelerate microbial adaptation and increase resistance at a genetic level, while climate-related disasters like floods create environmental pathways for the widespread dissemination of resistant pathogens. These environmental shocks disproportionately impact low-income populations with inadequate infrastructure, amplifying infection rates and overwhelming fragile health systems. This stress on the system, in turn, leads to the inappropriate use of antibiotics, which further accelerates the development of resistance. A siloed, single-sector approach to this crisis is insufficient. The data clearly demonstrates that a purely medical strategy of developing new drugs or simply reducing antibiotic use is less effective than a holistic approach. The most impactful interventions are not always clinical; they are foundational public health measures. Investing in sustainable development, ensuring equitable access to healthcare, improving sanitation infrastructure, and promoting universal vaccination are now recognized as essential, frontline defenses against AMR. Looking forward, a robust global response must embrace a true "One Health" framework, breaking down the traditional barriers between human, animal, and environmental health. This includes strengthening international governance and surveillance, regulating antimicrobial use in agriculture, and supporting innovative, non-traditional therapies like bacteriophages and anti-virulence agents that bypass the evolutionary arms race with bacteria. The fight against AMR is ultimately a battle for global equity and environmental sustainability. By addressing the root causes of this syndemic, we can not only mitigate the threat of drug resistance but also build a more resilient and equitable world for all.

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