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The mounting hazard of drug-resistant infections, its impact and global action

Abstract

The rise of drug-resistant infections poses a significant global health threat, undermining decades of medical progress. Antimicrobial resistance (AMR) occurs when bacteria, viruses, fungi, and parasites evolve to withstand the effects of drugs designed to kill them, rendering treatments ineffective. This phenomenon is primarily driven by the overuse and misuse of antibiotics in human medicine, agriculture, and animal husbandry. Poor infection control, inadequate sanitation, and limited access to new antibiotics further exacerbate the crisis. Drug-resistant infections complicate routine medical procedures, such as surgeries, chemotherapy, and organ transplants, increasing the risk of complications and mortality. Pathogens like methicillin-resistant *Staphylococcus aureus* (MRSA), multidrug-resistant *Mycobacterium tuberculosis* (MDR-TB), and carbapenem-resistant Enterobacteriaceae (CRE) are among the most concerning. The World Health Organization (WHO) warns that without urgent action, AMR could cause 10 million deaths annually by 2050, surpassing cancer-related fatalities. Combating drug-resistant infections requires a multifaceted approach, including the development of new antibiotics, alternative therapies, and improved diagnostics. Strengthening global surveillance, promoting responsible antibiotic use, and enhancing infection prevention strategies are essential to mitigating the crisis. Public awareness and policy interventions, such as antibiotic stewardship programs and investment in research, are crucial in slowing resistance. Without immediate and coordinated action, drug-resistant infections will continue to threaten public health, economic stability, and the future of modern medicine.

Keywords: drug resistance, antibiotic, control and prevention, infection, rational usage

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Introduction

Drug-resistant infections have emerged as one of the most serious public health threats of the 21st century. Microorganisms, including bacteria, viruses, fungi, and parasites, are increasingly developing resistance to the drugs used to treat them, making infections harder to cure. This growing resistance threatens the effectiveness of life-saving treatments, leading to prolonged illnesses, higher healthcare costs, and increased mortality rates.[1] The World Health Organization (WHO) has warned that if urgent action is not taken, the world may face a post-antibiotic era where even common infections become untreatable. The rise of drug-resistant infections is primarily driven by the overuse and misuse of antimicrobial drugs in human medicine, veterinary practices, and agriculture. In many countries, antibiotics and other antimicrobial agents are readily available over the counter, leading to their inappropriate use.[1,2] Patients frequently self-medicate, do not complete their prescribed courses, or use antibiotics for viral infections where they have no effect. These practices contribute to the survival and spread of drug-resistant microorganisms.[3] Additionally, poor infection control in healthcare settings, lack of sanitation, and excessive use of antibiotics in livestock farming further accelerate the problem. The burden of drug-resistant infections is especially severe in developing nations, where limited healthcare infrastructure makes it difficult to diagnose and treat resistant infections effectively.[4,5] Countries with high rates of infectious diseases, such as India, face unique challenges in controlling antimicrobial resistance due to overcrowded healthcare facilities, lack of access to proper medications, and poor awareness of the dangers of antibiotic misuse. Furthermore, resistant bacteria and viruses can spread across borders through international travel and trade, making drug resistance a global concern. Beyond health implications, drug resistance has significant economic consequences.[5] Patients suffering from resistant infections require longer hospital stays, additional diagnostic tests, and more expensive second-line treatments.[6] This increases the financial burden on healthcare systems and families. The loss of productivity due to prolonged illness and premature deaths further impacts economies worldwide. Addressing the growing threat of drug-resistant infections requires a coordinated global response. Strategies such as improving antimicrobial stewardship, investing in new drug development, strengthening infection prevention measures, and raising public awareness are essential.[7] Without immediate action, the effectiveness of modern medicine will continue to decline, pushing humanity toward a future where even minor infections could become life-threatening once again. Response of major organizations like WHO and UNICEF to the growing worldwide threat of antimicrobial resistance (AMR) to adult and child survival, growth, and development.[2,4,5]

A global concern

Antimicrobial medicines are the cornerstone of modern medicine.[6] The emergence and spread of drug-resistant pathogens threaten our ability to treat common infections and to perform life-saving procedures including cancer chemotherapy and caesarean section, hip replacements, organ transplantation and other surgeries.[7] In addition, drug-resistant infections impact the health of animals and plants, reduce productivity in farms, and threaten food security. AMR has significant costs for both health systems and national economies overall. For example, it creates need for more expensive and intensive care, affects productivity of patients or their caregivers through prolonged hospital stays, and harms agricultural productivity. AMR is a problem for all countries at all income levels. Its spread does not recognize country borders.[6-8] Contributing factors include lack of access to clean water, sanitation and hygiene (WASH) for both humans and animals; poor infection and disease prevention and control in homes, healthcare

facilities and farms; poor access to quality and affordable vaccines, diagnostics and medicines; lack of awareness and knowledge; and lack of enforcement of relevant legislation.[8] People living in low-resource settings and vulnerable populations are especially impacted by both the drivers and consequences of AMR.[8,9]

Current situation

Major drug-resistant pathogens

Several pathogens have been identified as critical threats due to their resistance to multiple antibiotics. Such as Carbapenem-resistant Enterobacteriaceae (CRE) bacteria are resistant to carbapenems, one of the last-resort antibiotics, making infections extremely difficult to treat.[11,13-16] Methicillin-resistant Staphylococcus aureus (MRSA) (Figure 1) infections are other common in hospitals and can cause severe bloodstream infections, pneumonia, and skin infections. Tuberculosis (TB) remains a leading cause of death worldwide, with resistant strains complicating treatment efforts. In 2023, 1.25 million people died from tuberculosis (TB), including 161,000 HIV-positive individuals.[15] Following three years of being supplanted by coronavirus disease (COVID-19), tuberculosis is likely to reclaim its position as the largest cause of death from a single infectious agent globally. Fluconazole-resistant *Candida auris* is fungal pathogen is responsible for hospital outbreaks and is resistant to multiple antifungal drugs.[17-21] Extended-spectrum beta-lactamase (ESBL)-producing bacteria inactivate beta-lactam antibiotics, making infections harder to treat. The identification of innovative pharmaceuticals from plants or bacteria such as Streptomyces sp. is urgently required.[22-24]

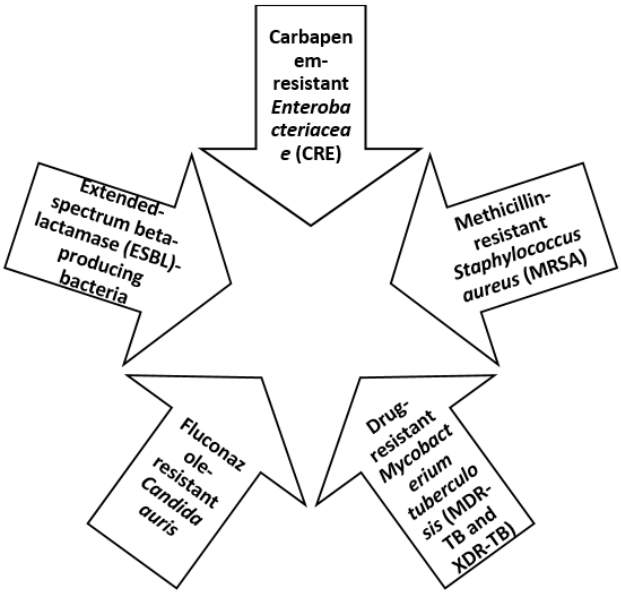

Figure 1 Major drug-resistant pathogens.

The global increase in antibiotic resistance poses a serious threat to public health, reducing the effectiveness of commonly used antibiotics against widespread bacterial infections. The 2022 report from the Global Antimicrobial Resistance and Use Surveillance System (GLASS) revealed alarming resistance levels in several key bacterial pathogens. Among 76 countries, the median reported resistance rate was 42% for third-generation cephalosporin-resistant *Escherichia coli* and 35% for methicillin-resistant Staphylococcus aureus (MRSA), raising significant concerns.[9] In cases of urinary tract infections caused by *E. coli*, approximately 1 in 5 infections in 2020 showed decreased susceptibility to standard antibiotics such as ampicillin, co-trimoxazole, and fluoroquinolones, complicating treatment strategies for these common conditions. *Klebsiella pneumoniae*, a frequent gut bacterium, also demonstrated high resistance rates to critical antibiotics.[8,9] This growing resistance often necessitates the use of last-resort treatments like carbapenems. Alarmingly, resistance to carbapenems is now being reported in multiple regions, threatening the efficacy of even these powerful antibiotics. According to the Organization for Economic Cooperation and Development (OECD), resistance to last-resort antibiotics is projected to double by 2035 compared to 2005 levels. This underscores the urgent need for strengthened antimicrobial stewardship programs and expanded global surveillance to combat the spread of resistant bacterial infections.[9,10]

Drug resistance in fungi

The growing threat of drug-resistant fungal infections has prompted the World Health Organization (WHO) to closely monitor their scale and impact on public health. Treating fungal infections is often challenging, particularly in patients with co-existing conditions such as HIV, due to potential drug-drug interactions.[15] Of special concern is the emergence and global spread of *Candida auris*, a multidrug-resistant and invasive fungal pathogen. In response to these developments, WHO conducted a comprehensive review of drug-resistant fungi and fungal infections worldwide, which contributed to the formulation of the Fungal Priority Pathogens List (WHO, 2022).[16]

Drug resistance in HIV, tuberculosis, and malaria

HIV

HIV drug resistance (HIVDR) arises from mutations in the HIV genome that reduce the efficacy of antiretroviral (ARV) drugs. Resistance can be transmitted at the time of infection or acquired later due to suboptimal adherence, drug-drug interactions, or improper treatment regimens.[16] HIVDR contributes to increased rates of infection and HIV-related illness and death. To combat this, WHO recommends that countries routinely conduct HIVDR surveillance to support the selection of effective ARV drug regimens for both treatment and prevention (WHO, 2022).[16,17]

Tuberculosis (TB)

TB continues to be a major driver of antimicrobial resistance. Multidrug-resistant TB (MDR-TB), caused by strains resistant to isoniazid and rifampicin- the two most potent first-line TB medications-poses a significant health threat. Although MDR-TB can be treated with second-line drugs, these alternatives are often more toxic, costly, and less effective. In severe cases, further resistance may limit treatment options entirely.[16,17] In 2022, only about 40% of individuals diagnosed with drug-resistant TB received appropriate treatment, highlighting a significant treatment gap (WHO, 2022).

Malaria

The rise of drug-resistant Plasmodium parasites poses a critical threat to malaria control efforts. Artemisinin-based combination therapies (ACTs) remain the first-line treatment for uncomplicated *Plasmodium falciparum* malaria across endemic regions. However, resistance- either to artemisinin or its partner drugs -has been reported since 2001, particularly in the Greater Mekong Subregion. Resistance to sulfadoxine-pyrimethamine in parts of the WHO Eastern Mediterranean Region has led to treatment failures, necessitating changes in national drug policies.[16,17] In Africa, mutations associated

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with partial resistance to artemisinin have been detected in several countries. While tested ACTs continue to be effective, ongoing spread of resistance could pose a significant public health challenge. Enhanced surveillance is therefore crucial (WHO, 2022).

Drug resistance in neglected tropical diseases (NTDs)

The development of drug resistance in treatments for neglected tropical diseases (NTDs) poses a serious threat to global efforts aimed at controlling, eliminating, and eradicating these conditions. NTDs primarily affect vulnerable and marginalized populations, making the impact of resistance particularly severe in low-resource settings.[18] Resistance has been documented in several key NTD treatments. This includes resistance to leprosy drugs such as dapsone, rifampicin, and clofazimine in multiple countries. There are also growing concerns over resistance to various anti-helminthic drugs. While most resistance has so far been observed in veterinary applications, many of these medications are also used in human treatments, raising significant public health concerns.[9,18] Additionally, resistance has emerged to melarsoprol- used for treating human African trypanosomiasis- and to antileishmanial drugs such as pentavalent antimonials and miltefosine. To address this threat, it is critical to implement robust systems for monitoring drug resistance and efficacy, develop strategies to prevent or slow the spread of resistance, and invest in the development of second-line treatment options.[18,19] The World Health Organization (WHO) supports these efforts by providing guidance for resistance surveillance, such as through the Global Leprosy Elimination Programme. WHO also plays a key role in regulating the distribution and ensuring the standardized use, safety, and efficacy of medicines- particularly those provided through donation programs in NTD control initiatives.[19]

Reasons of drug resistance

The widespread and inappropriate use of antibiotics is the leading cause of resistance. Common resistance mechanisms include breaking down or altering antibiotics enzymatically, preventing antibiotics from building up inside cells, changing metabolic pathways, altering binding sites like ribosomes to lessen the effectiveness of drugs, and boosting the activity of efflux pumps that remove antibiotics from cells before their levels are sufficient.[9] Patients often misuse antibiotics by taking them without prescriptions, using incorrect dosages, or failing to complete prescribed courses. Hospitals and clinics are hotspots for drug-resistant infections due to inadequate hygiene, overcrowding, and improper sterilization of medical equipment.[7,8] Farmers frequently administer antibiotics to livestock for growth promotion and disease prevention, leading to the development of resistant bacteria that can spread to humans through food consumption. Pharmaceutical waste, untreated sewage, and industrial pollutants contribute to the spread of resistant microorganisms in water sources, soil, and food chains.[9] In many developing countries, lack of proper diagnostic tools leads to the unnecessary prescription of antibiotics, while the availability of substandard or counterfeit drugs further drives resistance.

The worldwide impact of drug-resistant infections

Drug-resistant infections result in prolonged illnesses and higher death rates. According to estimates, AMR causes nearly 1.27 million deaths annually, with projections indicating it could surpass cancer as a leading cause of death by 2050.[10] Modern medical practices, including surgeries, organ transplants, and cancer treatments, rely on effective antibiotics to prevent and treat infections. Drug resistance jeopardizes these procedures, increasing the risk of fatal complications.[11] Multi-drug-resistant bacteria, commonly referred to as "superbugs," such as methicillin-resistant *Staphylococcus aureus* (MRSA) and carbapenem-resistant Enterobacteriaceae (CRE), are becoming increasingly difficult to treat. Additionally Antimicrobial resistance (AMR) has a significant and quickly increasing economic cost. Patients with resistant infections require longer hospital stays, additional diagnostic tests, and more expensive second- and third-line treatments.[12,13] Prolonged illnesses and premature deaths reduce workforce productivity, leading to economic downturns. Drug resistance affects animal health, reducing agricultural productivity and threatening food security. Moreover, in an interconnected world, drug-resistant infections do not remain confined to one region.[14] International travel, trade, and migration facilitate the rapid spread of resistant pathogens across borders.[30-35] This makes AMR a global crisis requiring urgent international collaboration.[14,15]

Global action against antimicrobial resistance (AMR)

In 2015, the Global Action Plan (GAP) on AMR was adopted at the World Health Assembly, urging countries to implement national action plans using a One Health approach.[36,37] This was backed by WHO, FAO, UNEP, and WOAH- together known as the Quadripartite. To lead global coordination, WHO hosts the Quadripartite Joint Secretariat, which supports initiatives like the Global Leaders Group on AMR (since 2020) and the Multi-Stakeholder Partnership Platform (launched in 2022).[38-41] A High-Level UN Meeting on AMR is scheduled for 2024, building on earlier ministerial conferences in the Netherlands and Oman. Another is planned in Saudi Arabia. These forums help drive national commitments and set global AMR targets. World AMR Awareness Week (WAAW), held annually from 18–24 November, promotes awareness and best practices across sectors. By late 2023, 178 countries had national AMR action plans. Implementation involves multisectoral governance, resource mobilization, and monitoring via the TrACSS survey, launched in 2016.[42-46] WHO promotes a people-centred approach with a core package of interventions, focusing on access to quality care, diagnosis, and treatment.[47,48]

These are integrated into broader health coverage and emergency plans. Antimicrobial stewardship ensures evidence-based prescribing and improves outcomes. WHO also developed the AWaRe classification to guide appropriate antibiotic use for common infections. WHO's GLASS system (since 2015) tracks AMR trends and antimicrobial use across human, animal, and environmental sectors, supporting especially low- and middle-income countries in data collection and decision-making.[48,49] Despite efforts, the antibiotic pipeline is limited, with only 6 of 27 new drugs in development being innovative. To address this, WHO has released priority pathogen lists and partners with GARDP, CARB-X, and others to support research and development. WHO emphasizes the need for investment and innovation in AMR research, having outlined 40 priority research areas and a One Health research agenda to drive future progress.[50] The report by Ganguly et al., highlights the need for reducing antibiotic use, lowering resistance-enhancing drug pressure, and eliminating antibiotic use for growth promotion in agriculture. Prioritizing national surveillance, increasing diagnostic tests, strengthening infection control committees, and restricting antibiotic use for non-therapeutic uses are key actions. Increased childhood vaccine coverage could also reduce the disease burden and spare antibiotics.[30]

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Conclusion

The growing threat of drug-resistant infections poses a serious challenge to public health, economies, and modern medicine. The misuse of antibiotics, poor healthcare infrastructure, and environmental contamination have accelerated the spread of resistance, making many infections harder to treat. If left unchecked, AMR could lead to a future where common infections become deadly, and medical procedures become too risky. Addressing this crisis requires a comprehensive approach, including antibiotic stewardship, infection control, research investment, regulatory measures, and public awareness. Global cooperation and immediate action are essential to safeguarding the effectiveness of antimicrobial treatments and protecting future generations from the devastating consequences of drug-resistant infections.

Author contributions

Nikita Sherwani, Neha Singh and Khushboo Bange are equally contribution in conceptualization, draft writing, review, data validation and editing.

Data accessibility

Data information will be provided upon request.

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None.

Conflicts of interest

The authors declare that there are no conflicts of interest.

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