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Antimicrobial Resistance Patterns in Clinical Pathogens and Implications for Public Health

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Abstract

Antimicrobial resistance (AMR) has emerged as one of the most pressing global health threats of the 21st century, with bacterial AMR directly responsible for 1.27 million deaths and associated with nearly 5 million fatalities in 2019 alone. This review provides a comprehensive analysis of current resistance patterns among clinical pathogens, with particular emphasis on the ESKAPE group (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp.), which dominate healthcare-associated and community-acquired infections worldwide. Drawing on data from the WHO GLASS surveillance system and recent regional studies, the analysis reveals alarmingly high rates of multidrug resistance (MDR), extensively drug-resistant (XDR), and difficult-to-treat resistance (DTR) phenotypes, particularly to β-lactams, carbapenems, and fluoroquinolones. Gram-negative pathogens exhibit the most concerning trends, with carbapenem-resistant Klebsiella pneumoniae and Acinetobacter baumannii reaching 55–100% resistance in many settings. South Asia, including Pakistan, stands out as a major hotspot for XDR Salmonella Typhi and high rates of ESBL- and carbapenemase-producing Enterobacterales. The review elucidates key molecular mechanisms (enzymatic inactivation, target modification, efflux pumps, reduced permeability, and biofilm formation) and underscores the critical role of the One Health interface in resistance dissemination. Public health implications include increased mortality, prolonged hospital stays, higher treatment costs, and threats to modern medicine (surgery, chemotherapy, transplantation). Effective containment requires strengthened antimicrobial stewardship, rapid diagnostics, enhanced surveillance, and accelerated development of novel therapeutics. Without urgent, coordinated global action, AMR will continue to undermine healthcare systems and sustainable development goals.

Keywords: Antimicrobial Resistance (AMR), Multidrug-Resistant Bacteria, ESKAPE Pathogens, Carbapenem-Resistant Enterobacterales (CRE), Methicillin-Resistant Staphylococcus Aureus (MRSA), Extended-Spectrum B-Lactamases (ESBL), One Health, Antimicrobial Stewardship, Clinical Specimens, Global Surveillance (GLASS), XDR Salmonella Typhi, Public Health Implications

1. Introduction

The emergence and dissemination of antimicrobial resistance (AMR) represent a paradigmatic shift in the landscape of global infectious diseases, threatening to render the most fundamental tools of modern medicine obsolete (Coque et al., 2023). Often described as a "silent pandemic," the phenomenon of resistance is characterized by the adaptive evolution of microorganisms bacteria, fungi, viruses, and parasites enabling them to survive exposure to the very drugs designed to eliminate them (World Health Organization, 2023). The scale of the crisis is substantiated by recent epidemiological data; in 2019 alone, bacterial AMR was directly responsible for 1.27 million deaths and was associated with nearly 5 million fatalities globally (Habib et al., 2025). Projections based on current trajectories warn that if left unaddressed, AMR could cause 10 million deaths annually by 2050, resulting in a global economic loss of approximately USD 100 trillion (United Nations General Assembly, 2024). The clinical implications of this trend are profound, as the efficacy of major surgeries, cancer chemotherapy, and organ transplantation is fundamentally contingent upon the availability of effective prophylactic and therapeutic antimicrobials (Mora-Brito, 2025). The global burden and projected mortality associated with antimicrobial resistance are illustrated in Figure 1.

2. Global Epidemiology and the Evolution of Surveillance

The global understanding of AMR has been significantly refined through the expansion of the World Health Organization (WHO) Global Antimicrobial Resistance and Use Surveillance System (GLASS) (Cantón et al., 2023). Launched to standardize data collection and reporting, GLASS has seen a four-fold increase in country participation since 2016, with 104 countries reporting data for 2023 (Knight, 2025). This expanded footprint covers over 70% of the global population, yet significant surveillance gaps remain, particularly in low- and middle-income countries (LMICs)

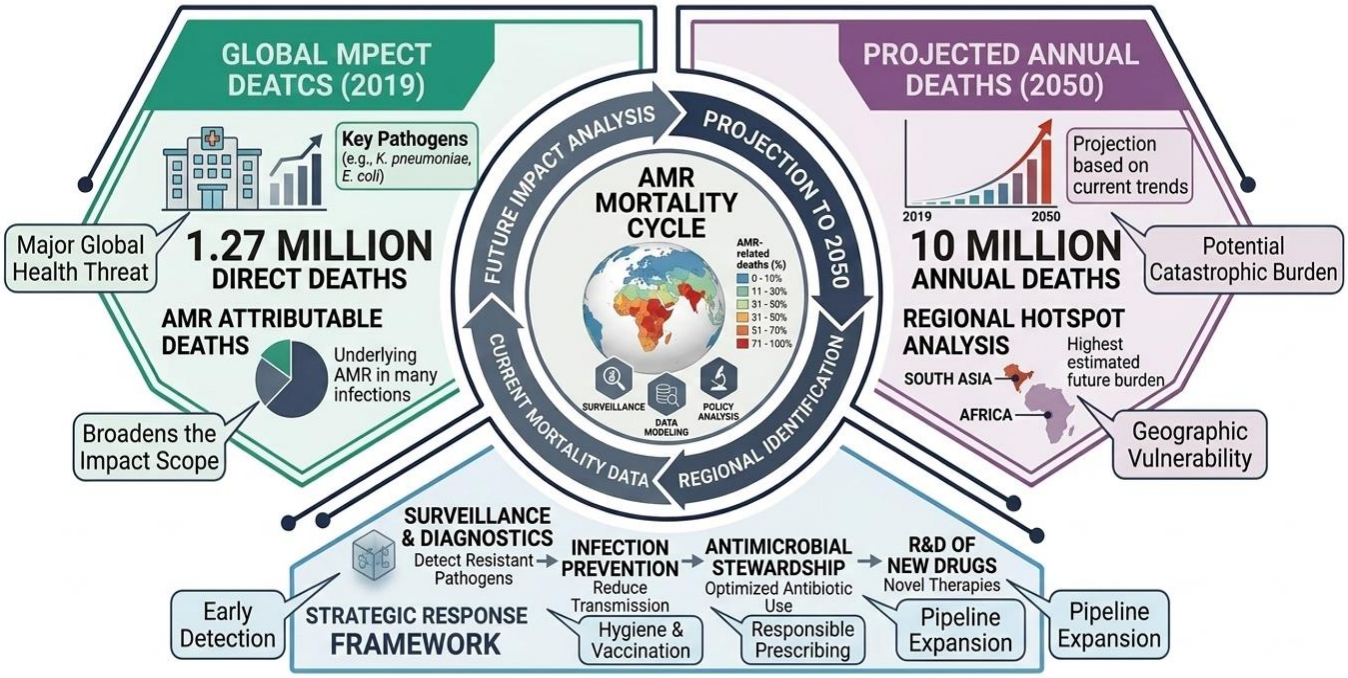

Figure 1. Global burden of antimicrobial resistance showing current mortality and projected deaths by 2050 with regional hotspots.

where laboratory infrastructure and data completeness are often compromised (World Health Organization, 2025).

2.1. Global Resistance Trends and Key Findings

The Global Antibiotic Resistance Surveillance Report 2025 provides a sobering analysis of resistance prevalence across 22 antibiotics used to treat infections of the bloodstream, urinary tract, gastrointestinal tract, and urogenital system. Data indicates that one in six laboratory-confirmed bacterial infections globally is now resistant to standard treatments (Ferraz, 2024). Between 2018 and 2023, resistance to essential antibiotics rose by an average of 5% to 15% annually (Rana et al., 2025).

Table 1. Global Resistance Prevalence and Median National Resistance Levels for Priority Pathogens (2023-2025)

Pathogen	Infection Type	Resistance Context	Median National Resistance (%)
Escherichia coli	Bloodstream/UTI	Third-generation Cephalosporins	> 40% (World Health Organization, 2025)
Klebsiella pneumoniae	Bloodstream/Respiratory	Third-generation Cephalosporins	> 55% (World Health Organization, 2025)
Klebsiella pneumoniae	Bloodstream	Carbapenems (Imipenem)	15% Annual Increase (World Health Organization, 2025)
Staphylococcus aureus	Skin/Soft Tissue/Blood	Methicillin (MRSA)	25% - 60% (Regionally) (Habib et al., 2025; Noreen et al., 2025)
Acinetobacter baumannii	Healthcare-associated	Carbapenems	85% - 100% (Guzek et al., 2025; De Oliveira et al., 2020)
Neisseria gonorrhoeae	Urogenital	Various First-line Agents	Critically High (World Health Organization, 2025)

Gram-negative pathogens remain the most urgent concern, particularly carbapenem-resistant Enterobacterales (CRE) and Acinetobacter baumannii. Carbapenem resistance, once a rare clinical occurrence, is now frequent, forcing reliance on last-resort antibiotics that are often toxic, expensive, and unavailable in resource-limited settings (Hansen, 2021).

2.2. Impact of the COVID-19 Pandemic on AMR

The COVID-19 pandemic served as a catalyst for the acceleration of resistance in many regions. In the United States, dedicated prevention and infection control efforts had successfully reduced deaths from resistant infections by 18% overall and by 30% in hospitals until 2020 (Ansari et al., 2021). However, the strain on healthcare systems during the pandemic led to longer hospital stays, challenges in maintaining infection control practices, and an increase in inappropriate antibiotic use (Gulumbe et al., 2023). Consequently, six bacterial antimicrobial-resistant hospital-onset infections increased by a combined 20% compared to pre-pandemic levels, peaking in 2021 (Lai et al., 2021). Furthermore, clinical cases of Candida auris, an emerging multidrug-resistant fungus, increased nearly five-fold from 2019 to 2022 (Centers for Disease Control and Prevention, 2025).

3. The ESKAPE Pathogens: Primary Drivers of Clinical Resistance

The ESKAPE group comprising Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species represents the highest priority for clinical surveillance and drug development (De Oliveira et al., 2020). These organisms are characterized by their high potential for multidrug resistance (MDR) and their significant contribution to the burden of healthcare-associated infections (HAIs) (Guzek et al., 2025).

3.1. Enterococcus faecium: The Resilience of VRE

Enterococcus faecium is a frequent cause of HAIs in immunocompromised patients, particularly those undergoing prolonged hospitalization or chemotherapy. The dissemination of vancomycin-resistant Enterococci (VRE) occurred in distinct waves, often driven by the selection pressure of broad-spectrum cephalosporins (Oyenuga et al., 2024). Contemporary studies show persistently high resistance to vancomycin, although linezolid remains a highly effective therapeutic option in most settings. E. faecium exhibits a remarkable ability to survive in hospital environments, including wastewater systems, where it acts as a reservoir for resistance genes (Jannati et al., 2023).

3.2. Staphylococcus aureus and the Challenge of MRSA

Staphylococcus aureus remains a dominant pathogen in clinical microbiology, accounting for a large proportion of bloodstream and surgical site infections. Methicillin resistance (MRSA) is the primary clinical concern, with rates varying significantly by geographic region. In Northern Punjab, Pakistan, approximately 25% of S. aureus isolates are methicillin-resistant, while other reports across South Asia suggest rates as high as 40% to 60% (Hussain et al., 2018). Despite the prevalence of MRSA, glycopeptides such as vancomycin and oxazolidinones like linezolid have largely retained high efficacy, exceeding 90% susceptibility in most reported cohorts (Noreen et al., 2025).

3.3. Klebsiella pneumoniae: The Rise of Carbapenemases

Klebsiella pneumoniae is a leading cause of severe pneumonia and bloodstream infections, particularly in intensive care units (ICUs). Resistance in K. pneumoniae is often driven by the production of extended-spectrum beta-lactamases (ESBLs) and, increasingly, carbapenemases such as NDM-1 and OXA-48 (Santajit & Indrawattana, 2016). A particularly alarming trend is the emergence of dual carbapenemase-producing strains, which exhibit near-universal resistance to available beta-lactams (Ahmad et al., 2025). Global estimates indicate that mortality rates for carbapenem-resistant K. pneumoniae (CRKP) bloodstream infections can range from 40% to 70% (Muhammad et al., 2026).

3.4. Acinetobacter baumannii: The Ultimate Escape Artist

Acinetobacter baumannii is frequently described as the most challenging ESKAPE pathogen to manage clinically due to its rapid acquisition of resistance and its environmental hardiness. In many tertiary care facilities, A. baumannii isolates have moved from multidrug-resistant to extensively drug-resistant (XDR) or even pan-drug-resistant (PDR) status (Ayoub Moubareck et al., 2020). In a Polish study, resistance rates in A. baumannii rose from 85% in 2018 to 100% by 2024, leaving colistin as the only remaining therapeutic option (Nguyen & Joshi, 2021). The organism's ability to form robust biofilms further complicates treatment by protecting bacterial cells from both antibiotics and the host immune system (Vrancianu et al., 2021).

3.5. Pseudomonas aeruginosa and Enterobacter species

Pseudomonas aeruginosa utilizes a combination of low outer membrane permeability and highly efficient efflux pumps to resist multiple classes of antibiotics, including aminoglycosides and carbapenems. While it often demonstrates lower overall resistance rates than Acinetobacter, its intrinsic resistance mechanisms make it a formidable pathogen in surgical and pulmonary infections (Lorusso et al., 2022). Enterobacter species, meanwhile, frequently possess chromosomal AmpC beta-lactamases that can be induced or derepressed during therapy, leading to treatment failure with cephalosporins (Langendonk et al., 2021).

4. Molecular Mechanisms of Antimicrobial Resistance

The ability of clinical pathogens to resist antimicrobial action is rooted in diverse biochemical and genetic strategies. These mechanisms are typically classified into four broad categories reduction of intracellular drug concentrations, enzymatic inactivation, modification of the drug target, and metabolic bypass (Belay et al., 2024). The principal molecular mechanisms through which bacteria resist antimicrobial agents are summarized in Figure 2.

4.1. Reduction of Drug Uptake and Active Efflux

In Gram-negative bacteria, the outer membrane acts as a primary barrier to antibiotic entry. Small hydrophilic molecules, such as beta-lactams, must pass through protein channels called porins. The loss or mutation of specific porins, such as OmpA or CarO in Acinetobacter baumannii, significantly reduces the permeability of the membrane to carbapenems (Ghai, 2023). Complementing this barrier are active efflux pumps, which utilize energy to expel antibiotics from the periplasmic space before they reach their targets (Winterhalter, 2021). The MexAB-OprM system in P. aeruginosa is a classic example of an RND-family pump capable of extruding diverse agents, including fluoroquinolones and beta-lactams (Prajapati et al., 2021).

4.2. Enzymatic Inactivation and Degradation

The production of enzymes that chemically modify or degrade antibiotics remains the most prevalent mechanism of resistance. Beta-lactamases are the most diverse group, including penicillinases, cephalosporinases, and carbapenemases. These enzymes catalyze the hydrolysis of the beta-lactam ring, rendering the drug inactive (Akhtar et al., 2022). Furthermore, aminoglycoside-modifying enzymes (AMEs) add chemical groups (acetyl, adenyl, or phosphoryl) to aminoglycosides, interfering with their ability to bind to the 30S ribosomal subunit (Gambo et al., 2023).

4.3. Modification of Drug Targets

Bacteria can evade antimicrobial action by altering the structure of the antibiotic's molecular target. In MRSA, the acquisition of the mecA gene leads to the production of PBP2a, a penicillin-binding protein with a very low affinity for almost all beta-lactams (Lade & Kim, 2023). Similarly, resistance to fluoroquinolones often arises from mutations in the gyrA and parC genes, which encode DNA gyrase and topoisomerase IV, respectively, preventing the drugs from inhibiting DNA replication (Ambade et al., 2023).

4.4. Genetic Transmission and Horizontal Gene Transfer

The rapid spread of resistance is facilitated by horizontal gene transfer (HGT), mediated by mobile genetic elements (MGEs) such as plasmids, transposons, and integrons. These elements allow resistance genes to move between different bacterial species and even across genera (Dimitriu, 2022). The mcr-1 gene, which confers resistance to colistin, is frequently localized on highly

transmissible plasmids, enabling its rapid global dissemination across human, animal, and environmental sectors (; Khalid et al., 2026).

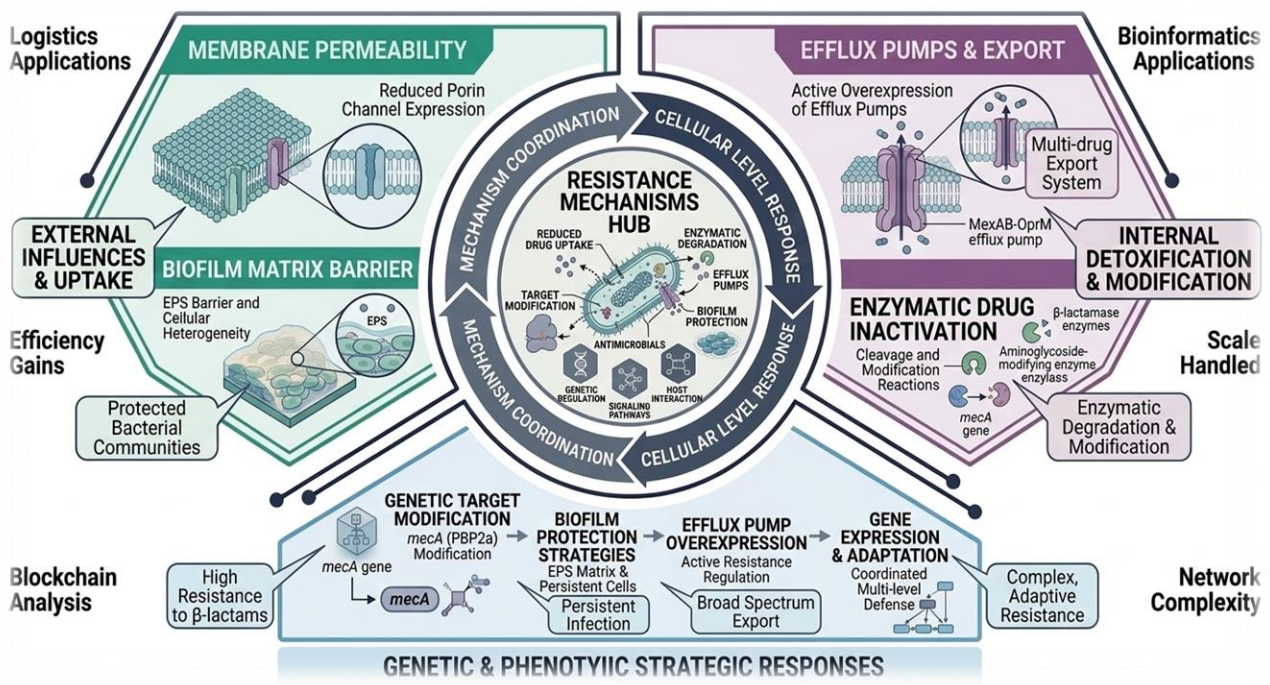

Figure 2: Major molecular mechanisms responsible for antimicrobial resistance in clinical pathogens.

5. Regional Perspectives: The Crisis in South Asia and Pakistan

Pakistan and the broader South Asian region have emerged as a global hotspot for AMR, driven by high population density, inadequate sanitation infrastructure, and unregulated antibiotic consumption (Noreen et al., 2025). Pakistan ranks among the highest antibiotic-consuming countries globally, with significant rates of inappropriate usage and self-medication (Maria, 2025).

5.1. Extensive Drug Resistance in Salmonella Typhi

A landmark challenge in the region is the outbreak of extensively drug-resistant (XDR) Salmonella Typhi. XDR typhoid is defined by resistance to all first-line agents (ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole) as well as second-line agents like fluoroquinolones and third-generation cephalosporins (ceftriaxone) (Habib et al., 2025). In pediatric cohorts in Northern Punjab, ceftriaxone resistance has forced clinicians to rely heavily on azithromycin and carbapenems. However, recent surveillance data has begun to detect isolates with reduced susceptibility even to these last-line drugs (Fahlin, 2023). Clinical severity in these cases is often linked to delayed fever clearance, with "severe" disease defined by fever persisting beyond three days of appropriate therapy (Alsabri et al., 2025).

5.2. Community-Acquired Urinary Tract Infections

In community settings, urinary tract infections (UTIs) remain a significant public health concern. A study in the district of Dera Ismail Khan (D.I. Khan) found that 42.6% of urine cultures were positive for bacteria, with E. coli being the most prevalent pathogen at 59.6% (Gomal Medical College, 2024). Alarmingly, these pathogens exhibited 100% resistance to ampicillin and amoxicillin-clavulanic acid, highlighting the obsolescence of traditional first-line oral therapies in

the region (Chandra et al., 2021). Imipenem and nitrofurantoin remain among the few effective agents for these community-acquired cases (Craft, 2019).

5.3. Bloodstream Infections and ICU Resistance Patterns

Data from hospitals in Northern Punjab and Karachi reveal a high prevalence of resistance in bloodstream infections (BSIs). Gram-positive organisms account for approximately 60% of BSIs, with S. aureus and Streptococcus pneumoniae being the most relevant (Riaz et al., 2024). Among Gram-negative pathogens, E. coli and P. aeruginosa are significant causes. While meropenem and vancomycin maintain high efficacy (>90%) in many reports, the underlying trend is one of increasing resistance to third-generation cephalosporins and fluoroquinolones (Inam et al., 2023).

6. One Health: The Intersection of Humans, Animals, and the Environment

The containment of AMR requires a "One Health" approach that acknowledges the interconnectedness of human health, animal husbandry, agriculture, and the environment (World Health Organization, 2025). Resistant bacteria and their genetic determinants circulate freely between these sectors, creating a complex web of transmission (Santajit & Indrawattana, 2016).

6.1. Antibiotic Misuse in Agriculture and the Food Chain

The overuse of antibiotics in livestock for growth promotion and prophylaxis is a primary driver of resistance in the food supply. Resistant strains of E. coli, Salmonella, and Enterococcus can be transmitted to humans through the consumption of contaminated meat, dairy, and fresh produce (Oyenuga et al., 2024).

Table 2. Potential for Human Transmission of ESKAPE Pathogens via Food and Agricultural Reservoirs

Pathogen	Food/Agricultural Reservoir	Potential for Human Transmission
Enterococcus faecium	Beef, poultry, pork, dairy	High; common in animal origin products (Oyenuga et al., 2024)
Staphylococcus aureus	Raw/frozen/RTE meat, cheese	High; commonly found in dairy and meat (Oyenuga et al., 2024)
Klebsiella pneumoniae	Turkey, cattle, chicken, raw vegetables	Emerging; found in diverse food sources (Oyenuga et al., 2024)
Acinetobacter baumannii	Fruits, vegetables, raw milk, meat	Growing concern; persists in fresh produce (Oyenuga et al., 2024)
Pseudomonas aeruginosa	Milk, dairy, meat (cold chain)	Persistent in refrigerated food products (Oyenuga et al., 2024)

6.2. Environmental Reservoirs and Wastewater Systems

The environment serves as both a reservoir and a conduit for resistant bacteria. Hospital wastewater, in particular, contains high concentrations of both antibiotics and multidrug-resistant pathogens (Chia et al., 2020). Studies have demonstrated a high level of genetic relatedness between ESKAPE pathogens isolated from untreated hospital runoff and those found in clinical specimens from the same facility (Bansal, 2019). Rivers and aquatic systems further disperse these pathogens, posing risks to populations that rely on these water sources for drinking, irrigation, and recreation (Valzano et al., 2024).

7. Public Health Implications and Clinical Consequences

The impact of AMR extends far beyond the difficulty of treating individual infections; it threatens

the very viability of specialized medical disciplines and the economic stability of healthcare systems (Aslam et al., 2024).

7.1. Impact on Oncology and High-Risk Surgery

In oncology, the safety of chemotherapy, stem cell transplants, and immune-based therapies is fundamentally dependent on effective infection management. Both the underlying malignancy and the cytotoxic treatments leave patients profoundly immunosuppressed, making survival contingent on timely access to effective antimicrobials (Asian Journal of Research in Medical and Pharmaceutical Sciences, 2024). The rise of MDR Gram-negative pathogens and VRE in heavily pre-treated populations can lead to "unstoppable" infections that compromise the success of cancer treatments (Mora-Brito, 2025).

Similarly, routine surgical procedures such as cesarean sections, hip replacements, and organ transplantations would become high-risk endeavors without effective prophylactic antibiotics (Menz al., 2021). The risk of surgical site infections (SSIs) by resistant pathogens increases patient morbidity, mortality, and the length of hospital stay (Guzek et al., 2025).

7.2. Economic Burden and Healthcare Costs

The economic consequences of AMR are substantial. Patients with HAIs caused by ESKAPE pathogens have significantly longer hospital stays averaging 20.3 days compared to 8.7 days for non-infected patients (Zjajo, 2024). This prolonged hospitalization, combined with the need for more expensive second- and third-line antibiotics and intensive care, imposes a significant financial burden on healthcare systems and individuals (Abban et al., 2023).

Table 3. Economic Burden and Prolonged Hospital Stays Associated with Healthcare-Associated Infections (HAIs)

Infection Type	Prolonged Stay (Days)	Estimated Additional Cost (USD)
CLABSI (Central Line)	13.4	$43,975 (Guzek et al., 2025)
CAUTI (Catheter)	8.9	$31,253 (Guzek et al., 2025)
Daily Isolation Cost	-	950.65 Euros (Guzek et al., 2025)

In the United States alone, the annual cost to treat infections caused by six common antimicrobial-resistant germs found in healthcare settings is estimated to exceed $4.6 billion (Centers for Disease Control and Prevention, 2024).

8. Antimicrobial Stewardship: Challenges and Implementation Strategies

Antimicrobial stewardship (ASP) programs are essential for promoting the rational use of antibiotics, improving patient outcomes, and slowing the emergence of resistance. However, the implementation of these programs faces significant hurdles, particularly in LMICs (Habib et al., 2025)

8.1. Roadblocks in Pakistan and LMICs

In Pakistan, despite high awareness of the importance of ASPs among healthcare professionals, formal training and institutional infrastructure remain limited. Key barriers include:

- Administrative Constraints: A lack of national policy enforcement and administrative ownership at the hospital level
- Professional Dynamics: A "prescriber-dominant" system where doctors may resist input from pharmacists or clinical microbiologists
- Laboratory Limitations: Insufficient microbiological testing facilities, which leads to a reliance on empirical therapy without sensitivity data

- Human Resources: Significant shortages of qualified infectious disease pharmacists and microbiologists (Maria, 2025).

8.2. Success Stories and Future Directions

During the COVID-19 pandemic, some institutions in Pakistan leveraged virtual platforms to continue ASP meetings, developed hospital-specific guidelines and protocols, and conducted drug utilization reviews (DURs) (Hansen, 2021). The National Antimicrobial Stewardship Plan (NASP) and the Drug Regulatory Authority of Pakistan (DRAP) guidelines on responsible antimicrobial use represent important steps toward a standardized national response (Gambo et al., 2023). Successful implementation often relies on targeting "low-hanging fruits" such as optimizing surgical prophylaxis before moving to more complex interventions like antibiotic restriction policies (Riaz et al., 2024).

9. The Therapeutic Pipeline and Regulatory Landscape

Addressing the innovation gap is critical, as the discovery of new antibiotic classes has slowed significantly since the 1980s. However, recent years have seen the approval of several novel agents and combinations designed to combat highly resistant clinical pathogens (U.S. Food and Drug Administration, 2025).

9.1. Novel Antimicrobials Approved (2023–2025)

Table 4. Recent Novel Antimicrobial Agent Approvals and Clinical Indications (2023-2025)

Drug Name	Active Ingredient	FDA/EMA Context	Primary Indication
Xacduro	Sulbactam + Durlobactam	Approved 2023 (U.S. Food and Drug Administration, 2023)	HABP/VABP (Acinetobacter)
Pivya	Pivmecillinam	Approved (US) 2024 (U.S. Food and Drug Administration, 2024)	Uncomplicated UTIs
Orlynvah	Sulopenem etzadroxil	Approved 2024 (U.S. Food and Drug Administration, 2024)	Uncomplicated UTIs
Rezzayo	Rezafungin	Approved 2023 (U.S. Food and Drug Administration, 2023)	Candidemia/Invasive Candidiasis
Nuzolvence	Zoliflodacin	Approved 2025 (U.S. Food and Drug Administration, 2025)	Urogenital Gonorrhea
Vaborem	Meropenem + Vaborbactam	Pre-2023 (De Oliveira et al., 2020)	Carbapenem-resistant Enterobacterales
Recarbrio	Imipenem/Relebactam	Pre-2023 (De Oliveira et al., 2020)	Complicated UTI/Intra-abdominal

The approval of sulbactam-durlobactam (Xacduro) is particularly significant, as it provides a targeted therapy for the Acinetobacter baumannii-calcoaceticus complex, an organism previously considered nearly untreatable in many settings Similarly, the US approval of pivmecillinam (Pivya) introduces a co-first-line option for UTIs, particularly those caused by ESBL-producing pathogens (U.S. Food and Drug Administration, 2023).

10. Global Targets and Public Health Recommendations

The Political Declaration on AMR adopted at the UN General Assembly in 2024 has set ambitious global targets for 2030, aiming to catalyze action across all sectors (Akhtar et al., 2022). **10.1. Targets for 2030**

- Mortality: Reduce global deaths associated with bacterial AMR by 10% from 2019 levels
- AWaRe Stewardship: Ensure that at least 70% of human antibiotic use globally comes from the "Access" group to preserve the efficacy of "Watch" and "Reserve" agents
- Diagnostic Capacity: Ensure at least 80% of countries can test for resistance in all bacterial and fungal pathogens covered by GLASS
- Infection Prevention: Accelerate access to clean water, sanitation, and hygiene (WASH) and strengthen infection prevention and control (IPC) programs to reduce the incidence of HAIs (United Nations General Assembly, 2024).

10.2. Conclusions

Antimicrobial resistance has evolved from a manageable clinical challenge into a profound and accelerating global health crisis that threatens to unravel decades of progress in modern medicine. The widespread dissemination of multidrug-resistant, extensively drug-resistant, and difficult-to-treat pathogens particularly within the ESKAPE group has rendered many first- and second-line antibiotics ineffective, leading to increased mortality, prolonged hospitalizations, escalated healthcare costs, and compromised outcomes in surgery, oncology, and critical care. Regional data underscore the severity of the situation in low- and middle-income countries, with South Asia and parts of Africa emerging as major epicenters of resistance evolution and transmission. The molecular versatility of resistant bacteria, amplified by horizontal gene transfer, biofilm formation, and selective pressure from inappropriate antibiotic use across human, animal, and environmental sectors, demands a paradigm shift toward a true One Health response. Strengthening surveillance systems such as GLASS, implementing robust antimicrobial stewardship programs, expanding access to rapid diagnostics, and investing in the development of novel antimicrobials and alternative therapies are no longer optional but essential for containment. The window for effective action is narrowing. The 2024 United Nations Political Declaration on AMR and the 2030 global targets provide a critical roadmap, but success will depend on political commitment, sustainable financing, and equitable implementation, particularly in high-burden regions. Failure to act decisively will result in a post-antibiotic era where common infections once again become life-threatening and routine medical procedures carry unacceptable risks. Coordinated, multisectoral, and sustained efforts are imperative to preserve the efficacy of existing antimicrobials and safeguard public health for future generations.

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