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Antimicrobial resistance: Impacts, challenges, and future prospects

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ABSTRACT

Antimicrobial resistance (AMR) is a critical global health issue driven by antibiotic misuse and overuse in various sectors, leading to the emergence of resistant microorganisms. The history of AMR dates back to the discovery of penicillin, with the rise of multidrug-resistant pathogens posing significant challenges to healthcare systems worldwide. The misuse of antibiotics in human and animal health, as well as in agriculture, contributes to the spread of resistance genes, creating a "Silent Pandemic" that could surpass other causes of mortality by 2050. AMR affects both humans and animals, with resistant pathogens posing challenges in treating infections. Various mechanisms, such as enzymatic modification and biofilm formation, enable microbes to withstand the effects of antibiotics. The lack of effective antibiotics threatens routine medical procedures and could lead to millions of deaths annually if left unchecked. The economic impact of AMR is substantial, with projected losses in the trillions of dollars and significant financial burdens on healthcare systems and agriculture. Artificial intelligence is being explored as a tool to combat AMR by improving diagnostics and treatment strategies, although challenges such as data quality and algorithmic biases exist. To address AMR effectively, a One Health approach that considers human, animal, and environmental factors is crucial. This includes enhancing surveillance systems, promoting stewardship programs, and investing in research and development for new antimicrobial options. Public awareness, education, and international collaboration are essential for combating AMR and preserving the efficacy of antibiotics for future generations.

1. Introduction

Antimicrobial resistance (AMR) has emerged as one of the most pressing global public health threats of the 21st century [1–3]. AMR manifests when microorganisms, encompassing bacteria, fungi, parasites, and viruses, undergo evolutionary processes leading to their resistance against antimicrobial medications, such as antibiotics, commonly employed for treating such infections [1,4–6]. The prevalent issue is largely attributed to the repercussions of antibiotic overuse or irresponsible utilization across diverse contexts, predominantly in clinical treatment, agricultural practices, animal healthcare, war crisis and the food system [7–10]. Often dubbed the "Silent Pandemic", AMR necessitates immediate and efficacious intervention rather than being relegated to a future scenario [11]. In the absence of preventive measures, projections indicate that by 2050, AMR could potentially supersede all other causes of mortality worldwide [12]. Globally, estimates indicate that the direct fatalities linked to AMR surpassed 1.2 million in 2019, with a foreseen escalation to approximately 10 million deaths annually by 2050 if inadequate measures are implemented to curb AMR [4,13].

The aim of this study is to comprehensively investigate antimicrobial resistance (AMR), delineating its historical context, elucidating the mechanisms involved, and assessing its profound impact on human and animal populations. Additionally, it aims to analyze past and current

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prevalence rates, project future burdens, explore the role of artificial intelligence in combating AMR, address associated challenges, and provide actionable recommendations for effective mitigation strategies and further research endeavors.

2. AMR- definition and history

The issue of AMR presents a substantial risk to the overall well-being of the global population and is increasingly becoming a matter of great apprehension on a worldwide scale [14]. AMR pertains to the capacity of microorganisms, encompassing bacteria, viruses, fungi, and parasites, to withstand the therapeutic impact of previously efficacious drugs in combating them. This phenomenon undermines the efficacy of antibiotics, antivirals, and other pharmaceuticals, resulting in heightened morbidity, mortality, and healthcare expenditures. Addressing AMR has emerged as a pivotal global health imperative, necessitating prompt and synchronized endeavors from governmental bodies, healthcare practitioners, scholars, and the general populace [15]. AMR occurs when microorganisms like bacteria, viruses, fungi, and parasites resist antimicrobial drugs, making standard treatments ineffective and increasing the risk of infection [16]. The evolution of AMR is a natural phenomenon; however, human influences have dramatically accelerated and exacerbated its progression over recent decades.

Microbes are under selective pressure to become resistant and acquire adaptive mutations or genes when antimicrobial agents are misused or overused in healthcare, veterinary, and agricultural settings [17]. This then enables their survival and persistence in environments saturated with antibiotics and antiseptics that would previously have readily destroyed them. Bacteria and other microbes have a remarkable ability to rapidly adapt, mutate, and share adaptive genetic elements via horizontal gene transfer mechanisms allowing them to develop diverse resistance mechanisms. Microorganisms that develop AMR may make human and animal diseases challenging to cure. Resistance prolongs sickness, increases spread risk, lengthens hospital stays, requires more costly therapies, and raises fatality rates. This escalating cycle of resistance development is not only a contemporary concern but has roots deeply embedded in the history of antimicrobial use.

The history of AMR traces back to the discovery of penicillin in 1928 by Alexander Fleming [18] and the subsequent mass production and utilization of antibiotics in the 1940 s. However, resistant organisms emerged almost immediately thereafter. The first cases of penicillin-resistant *Staphylococcus aureus* were reported in 1942 [19], along with tetracycline resistance by 1953 [20]. The widespread agricultural use of antibiotics in the 1950–60 s also accelerated resistance. The MRSA was reported in 1961, followed by resistance to multiple antibiotic classes [21,22]. The 1980 s saw a global epidemic of MDR tuberculosis [23]. In the 1990 s, gram-negative pathogens such as *Escherichia coli* and *Klebsiella pneumonia* developed ESBL resistance [24]. The rise of MDR diminished the number of available effective antibiotics and resulted in the withdrawal of pharmaceutical companies from antibiotic research. This perfect storm of increasing resistance and lack of new drug development continues to strain healthcare systems today. We have now entered a dangerous post-antibiotic era where common infections and minor injuries can once again become lethal. If solutions are not urgently implemented, it is expected that millions of people may die annually from AMR infections.

3. Mechanisms of AMR and microbes involved

Natural selection, antibiotic overuse and misuse, insufficient access to safe water and sanitation, and substandard and counterfeit drugs are a few causes of AMR [25]. Antibiotic overuse and misuse include but are not limited to incomplete treatment, inappropriate prescription, and self-medication. Bacteria that survive a partial antibiotic course may acquire resistance. Additionally, prescribing medicines for viral infections, self-prescribing, or utilizing leftover antibiotics without medical supervision can contribute to AMR. Insufficient sanitation and poor hygiene practices contribute to the proliferation of infectious diseases, resulting in heightened reliance on antibiotics and subsequent development of resistance. Finally, low-quality medications may not have enough active substances or the correct dose, resulting in insufficient therapy and the development of resistance. Microorganisms have developed various and ingenious strategies to withstand the antibacterial effects of previously effective medications in treating illnesses. These systems enable microorganisms to endure attacks from antibiotics and other antimicrobial chemicals that often hinder their development or cause their complete demise. Bacteria and other parasites demonstrate remarkable adaptive mechanisms by making structural modifications and employing strategic metabolic pathways, enabling them to disregard or neutralize antimicrobial substances that pose a threat.

Typical resistance mechanisms involve enzymatic modification or degradation of antibiotics, limiting the entry of antibiotics into cells to prevent their build-up, alterations to metabolic pathways, modifying binding sites like ribosomes to reduce drug effectiveness, and increasing the activity of efflux pumps that remove antibiotics from cells before they can reach adequate levels [26,27]. Bacteria may also create biofilms, surface-bound communities with varying nutrition levels and limited antibiotic penetration [28]. These resistant mechanisms are summarized in Fig. 1. These biofilms provide further protection for the bacteria. In addition, bacteria are proficient in obtaining resistance genes from nearby cells or even distinct species through horizontal gene transfer facilitated by plasmids and other mobile genetic components [29]. These acquired genes frequently include several intricate resistance mechanisms inside a single unit, enabling the fast spread of MDR throughout microbial populations. The capacity for efficient horizontal transfer of genetic information grants microorganisms a wide array of resistance strategies that may be adapted as necessary to ensure survival against ongoing advancements and utilization of antimicrobial treatments by the medical field.

Several microorganisms have developed AMR through different mechanisms in the past few decades [30]. Methicillin-resistant *Staphylococcus aureus* is resistant to numerous antibiotics, including methicillin, through mutations in *mecA and mecC* genes and horizontal gene transfer [31]. Carbapenem-resistant Enterobacteriaceae, such as *Klebsiella pneumoniae* and *Escherichia coli*, have gained resistance to carbapenem drugs by acquiring carbapenemase genes [32]. These genes are often carried on plasmids, facilitating their transmission across bacteria. The ESBL-producing *E. coli* is resistant to a broad spectrum of antibiotics, including penicillins and cephalosporins, by obtaining ESBL genes, commonly through plasmids. Mutations in the DNA of MDR *Mycobacterium tuberculosis* have rendered them resistant to many anti-tuberculosis medications [33]. *Acinetobacter baumannii* has developed resistance to several antibiotics due to a combination of mutations and the acquisition of resistance genes [34]. Multidrug-resistant *Neisseria gonorrhoeae* defies front-line antibiotics for treating the sexually transmitted illness of gonorrhea [35]. Fluconazole-resistant Candida fungi, which cause opportunistic oral and genital infections, have burdened high-risk groups [36]. Last but not least, viral infections like HIV and influenza also routinely develop resistance mutations to available antiviral medications [37]. The alarming surge of these MDR microbial strains underscores the ability of pathogenic bacteria, viruses, fungi, and protozoa to rapidly circumvent chemical agents aimed at destroying them.

4. The impact of AMR on human and animal populations

AMR has arisen as a multifaceted issue that impacts the health of both humans and animals. The excessive and improper utilization of antibiotics in various domains, such as healthcare facilities, agricultural practices, and veterinary medicine, has expedited the emergence of drug-resistant strains of microorganisms. The excessive dependence on antibiotics has resulted in the emergence of antibiotic-resistant bacteria,

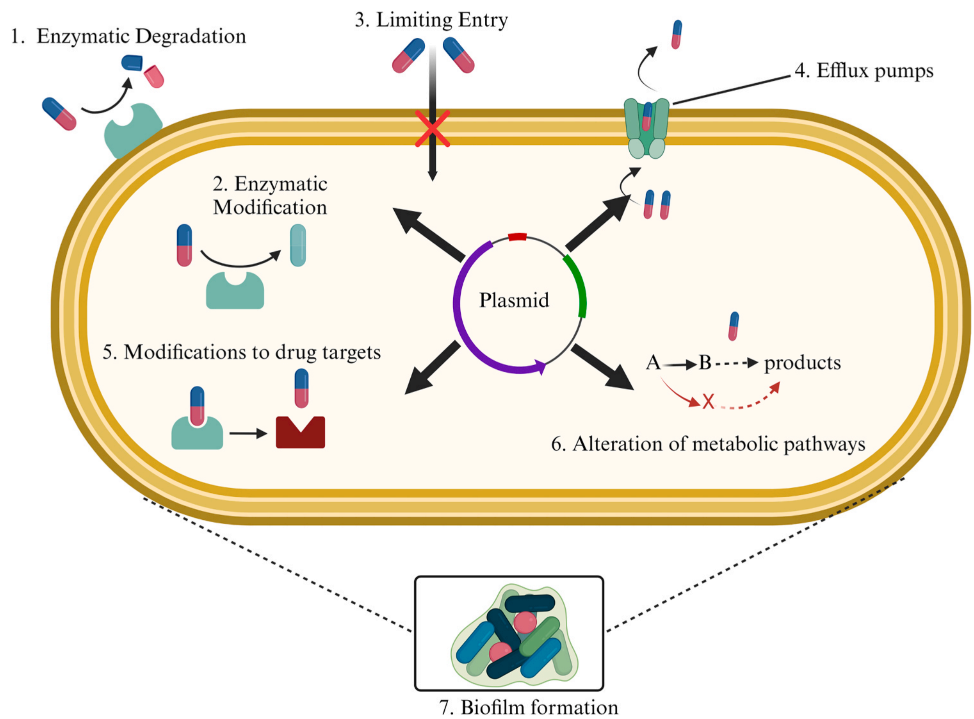

Fig. 1. Mechanisms of antimicrobial resistance in bacteria.

commonly known as superbugs, which pose significant challenges in treatment efficacy and can lead to severe infections. Furthermore, the inadequate progress in developing novel antimicrobial medications exacerbates the issue, as the rate at which resistance develops surpasses the rate at which effective therapies are being identified [38].

AMR has emerged as one of the most significant threats to human health in the 21st century. Previously treatable infections are becoming increasingly intractable, posing substantial clinical challenges. The loss of effective first-line antimicrobials has driven growing reliance on second and third-line therapies, which are often more expensive, more toxic, and require longer treatment durations [39]. Prolonged illnesses drain individual and healthcare system resources due to extended hospitalizations. Lengthier recoveries also impact economic productivity, giving more excellent time off work. AMR infections similarly necessitate increased outpatient clinic visits, laboratory testing, and isolation precautions [40]. The mortality attributed directly to AMR pathogens claims over a million lives annually [40]. The absence of effective antibiotics, routine procedures like surgery, organ transplantations, chemotherapy, and neonatal care could become exponentially more dangerous due to the limited capacity to control infections [41]. Some pathogens described as "ESKAPE" bacteria, including resistant forms of *Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* spp., represent the most troublesome MDR threats facing hospitals today [42]. Common scratch-borne infections or minor injuries could be fatal in a post-antibiotic era.

AMR threatens human health and food production by enabling animal-to-human transfer of resistant zoonotic pathogens [43]. Overuse of antibiotics in livestock to treat illness and promote livestock growth has precipitated reservoirs of resistance. This facilitates enhanced transmission risks of MDR bacteria like *Salmonella* and *Campylobacter* via the food chain or animal handlers [44]. Resistant bacterial strains spread readily between species. Wildlife similarly develops AMR from indirect environmental exposures driving additional pathogen transmission. Resistant microbes extend into the broader environment through fertilizers made from manure, contaminating waterways and produce that reaches consumer tables. They additionally exchange AMR genes with normal environmental and human commensal microflora. Restricted treatment options for animal infections resulting from resistance promote outbreak escalation among cattle, poultry, and sheep, necessitating culling and generating significant economic losses while threatening food supplies. Approximations indicate AMR could impose a $3–4 billion financial burden through livestock alone in the coming decades [45]. Detrimental resistance impacts across agriculture and economic systems also spur disruptive ripple effects for national security and trade. Hence, a proper One Health approach encompassing human, animal, and environmental health surveillance and interventions remain necessary to fully address AMR's substantial existing and prospective adverse impacts on animals that, in turn, heighten human exposure risks further [46–50].

5. Past and current prevalence of AMR

Early instances of resistance were noted shortly after the widespread use of penicillin. This era marked the beginning of a continuous battle against evolving bacterial resistance. By the mid-20th century, the emergence of MRSA and other resistant pathogens signaled a growing public health concern. The prevalence of AMR was further exacerbated by the indiscriminate use of antibiotics in agriculture and livestock, contributing to the spread of resistance genes. These developments underscored a clear trend: the more antibiotics were used, the more resistance emerged, leading to a constant need for new antimicrobials. Previously, the annual incidence of infections related to antibiotic resistance exceeded 2 million cases in North America, leading to a mortality rate of 23,000 individuals [51]. In the European region, it has been observed that there are over 700,000 instances of infections that have developed resistance to antibiotics. These infections have been found to directly contribute to over 33,000 deaths on an annual basis [52]. Furthermore, it has been estimated that the economic burden associated with these infections amounts to over €1.5 billion [53]. In light of a notable 36% surge in the utilization of antibiotics by the human population between 2000 and 2010 [54], it is worth noting that about 20% of global mortality is presently attributed to infectious diseases [55]. The situation further deteriorated as nosocomial infections emerged as a prominent cause of morbidity and mortality [56], leading to prolonged hospitalizations and escalated healthcare expenditures [57]. In addition, it is worth noting that more than 15% of nosocomial infections are presently attributed to MDR organisms [58], some of which lack effective antimicrobial treatments [59].

Based on the findings of the 2019 Antibiotic Resistance Threats Report by the Center for Disease Control (CDC), it has been determined that the United States experiences an annual occurrence of over 2.8 million infections resistant to antibiotics. As a consequence of these infections, the number of deaths exceeds 35,000 [60]. Based on a report, it has been observed that in India, the occurrence of child mortality resulting from bacterial infections resistant to antibiotics takes place at a frequency of once every nine minutes. Additionally, it is estimated that over 50,000 infants in India are at risk of succumbing to sepsis due to the presence of antibiotic-resistant microorganisms, which renders commonly used treatments ineffective [61]. Based on the findings of the European Antimicrobial Resistance Surveillance Network (EARS-Net) study spanning from 2015 to 2019 [62], variations in the prevalence of AMR were seen across the European Union. These variations were observed concerning the specific bacterial species, classes of drugs, and geographical locations. The microorganisms that were extensively investigated in this report included *Escherichia coli* (44.2%), *Staphylococcus aureus* (20.6%), *Klebsiella pneumoniae* (11.3%), *Enterococcus faecalis* (6.8%), *Pseudomonas aeruginosa* (5.6%), *Streptococcus pneumoniae* (5.3%), *Enterococcus faecium* (4.5%), and *Acinetobacter spp*. (1.7%).

Based on a report, it has been observed that MRSA is responsible for a range of 13–74% of *Staphylococcus aureus* infections on a global scale. *Staphylococcus aureus* impacted approximately 119,247 individuals in the United States, leading to 19,832 fatalities [63]. The most recent Global Antimicrobial Surveillance System (GLASS) by the World Health Organization (WHO) reveals a significant prevalence of AMR among a population of 500,000 individuals diagnosed with bacterial illnesses in 22 different countries [64]. *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, and *Klebsiella pneumoniae* were the bacterial strains most frequently detected exhibiting resistance [65]. The prevalence of resistance to ciprofloxacin, a commonly prescribed antibiotic for urinary tract infections, varied significantly across different countries. For *Escherichia coli*, resistance rates ranged from 8.4% to 92.9%, while for *Klebsiella pneumoniae*, the range was 4.1–79.4%. Penicillin resistance was reported to be as high as 51% among countries participating in GLASS. In 2019, GLASS collected data about MRSA bloodstream infections from a total of 25 nations, regions, and zones. Additionally, data on *Escherichia coli* bloodstream infections obtained from 49 countries. According to the study conducted by Kraker et al. [66], the median prevalence of MRSA was found to be 12.11% with an interquartile range (IQR) of 6.4–26.4%. Additionally, the study reported a median resistance rate of *E. coli* to third-generation cephalosporins at 36%, with an IQR of 15.2–63%.

6. Future projections of AMR burden and associated issues

The future outlook is not optimistic, as evidenced by research commissioned by the government in the United Kingdom. This study projected that by the year 2050, there might be approximately 10 million deaths annually attributed to illnesses that are resistant to antibiotics [67]. Uncomplicated infections and minor injuries could once again become life-threatening, while major procedures like organ transplants, chemotherapy, or hip replacements may become overwhelmingly risky. The economic losses associated with AMR will reach $100 trillion USD by 2050 [67]. Low- and middle-income countries are expected to witness the most tremendous burden as bacterial resistance growth outpaces the development of new antimicrobial options. At the same time, resource constraints obstruct access to existing premium-priced therapies. Global coordination is critically lacking, with piecemeal containment efforts unable to match the evolutionary capacity of pathogenic bacteria continually exposed to humanity's extensive antimicrobial use across healthcare, agriculture, and the environment.

Compounding direct mortality and economic impacts, the increasing inefficacy of antimicrobials could profoundly handicap modern medicine while enabling the resurgence of bacterial infections that had become historically rare thanks to antibiotic therapies. Cancer patients, the immunocompromised, and those requiring surgical interventions constitute populations especially vulnerable to emerging extensively- or pan-drug-resistant bacterial strains [68]. Additionally, the collective burden of common infectious diseases like pneumonia, tuberculosis, and gastrointestinal illnesses may swell considerably in a post-antibiotic era. Ultimately, the rapid depletion of effective antimicrobial options jeopardizes decades of medical progress while portending reconvergence with humanity's past, where bacterial infections constituted dominant environ-medical threats.

7. Artificial intelligence in combating AMR

Currently, artificial intelligence is used in various healthcare fields, demonstrating its broad implementation in modern medical procedures [69–77]. Several studies that have been published on artificial intelligence demonstrate its effectiveness in combating antimicrobial resistance by rapidly identifying patterns in bacterial behavior and optimizing treatment strategies accordingly [78–100]. These advancements hold great promise for the development of more effective and personalized approaches in addressing the global health threat posed by antimicrobial-resistant pathogens. The emergence of artificial intelligence (AI) and machine learning approaches presents promising opportunities to strengthen antimicrobial stewardship and precision medicine strategies addressing the pressing crisis of AMR [84–86,100]. As AMR undermine the efficacy of standard antibiotic regimens against increasingly pervasive "superbugs", AI tools able to enhance diagnostics, optimize prescribing patterns, and replenish depleted drug pipelines will become invaluable. Within healthcare delivery, AI integration constitutes an evolutionary step building upon traditional antibiotic stewardship programs reliant on specialized staff oversight and formulary restriction policies. Advanced neural networks and predictive analytics may identify positive cultures or high-probability infections earlier based on clinical presentations, allowing faster targeted therapy. Similarly, AI prescription assistants can integrate hospital metadata on local microbiology, individual patient factors, and treatment guidelines to recommend optimal antibiotic selection.

Such AI antibiotic advisors limit empirical overuse of broad agents. As human clinicians often excessively prescribe antibiotics in the absence of definitive diagnostics, intelligent safeguards balancing infection risks versus resistance generation can prove invaluable. AI integration may also expand stewardship programs' capacity for continuous patient monitoring on appropriate antibiotic discontinuation post-cultures [101]. Outside direct care, AI-powered epidemiology surveillance detecting local resistance outbreaks can better inform dynamic formulary policies. Computational approaches mining -omics datasets, published literature, and molecular libraries may also reveal novel drug targets or chemical scaffolds for antibiotic development pipelines increasingly abandoned by pharmaceutical companies. Overall, AI stewardship augmenting traditional antimicrobial governance and precision medicine efforts constitute a key evolutionary step toward preserving antibiotic efficacy.

A number of limitations still constrain contemporary artificial intelligence's ability to combat AMR, centered on data quality, algorithmic biases, and real-world implementation barriers [88,102]. Most healthcare AI remain narrow artificial neural networks trained on limited clinical datasets vulnerable to inherent biases. Careless application risks exacerbating antimicrobial overuse and toxicities if inaccurate predictions erode clinician trust or introduce new usage drivers. The majority of antibiotic prescription data also originates from developed nations, risking reduced model generalizability. Furthermore, most AI antibiotic advisors still lack sufficient transparency and explainability of underlying logic for clinician users. Gain of user trust requires explainable models so recommendations considered can be clinically validated based on available metadata. On the drug development end, despite successes in scaffold prediction or mechanism elucidations, experimental validation remains quite sparse [103]. Beyond technical limitations, the majority of AI antimicrobial tools still remain confined to academic research without clear translation pathways toward clinical and policy integration. Still, with prudent development and application, AI constitutes a promising avenue amidst the pressing AMR crisis.

8. Challenges in addressing AMR

Tackling the emergence of AMR presents complex challenges with no facile resolutions. Efforts to reduce humanity's vast utilization of antimicrobials are obstructed by their widespread integration into medical care and food animal production economics [104]. Lacking rapid point-of-care diagnostics, physicians often depend on empiric antibiotic prescribing to safeguard against bacterial infections, while modern farming systems predicate the regular administration of antimicrobials to livestock for infection prevention and growth promotion. Implementation of antimicrobial stewardship programs in healthcare and updated animal husbandry policies lag considerably despite awareness of resistance risks associated with antibiotic overuse. Compounding these issues, the antibiotic drug development pipeline cannot keep pace with the continuous evolution of MDR pathogens. Pharmaceutical companies increasingly abandon costly antimicrobial research with limited profit incentives. And while policy expansions financing antibiotic development mark progress, near-term solutions seem unlikely considering phase trial durations.

Further frustrating containment efforts, international coordination on AMR surveillance and stewardship guidelines remains piecemeal despite organizations like the WHO, CDC, and UN recognizing its borderless risks. Variable access to quality diagnostics and antibiotic oversight across countries enables local emergence and global spread of novel resistance factors. Patches of weak stewardship may continually undermine and negate localized progress. Ultimately, the unique 'tragedy of the commons' nature of antibiotic resistance demands equitable, cooperative global action and shared responsibility. However, geopolitical complexities continue obstructing consensus on binding international policies and funding channels needed to strengthen antimicrobial stewardship and innovation worldwide [105].

AMR transcends geographical boundaries and has a global impact on populations. In recent times, formerly manageable infections have evolved into significant health concerns. The absence of efficacious antimicrobial agents renders routine medical procedures, such as surgeries, chemotherapy, and organ transplants, more precarious. In addition to the adverse impact on human health, AMR also presents substantial economic challenges for healthcare systems, governments, and societies as a whole [106,107]. The financial burden associated with managing resistant infections is significantly elevated as a result of extended hospitalizations, escalated healthcare consultations, and the necessity for costly medications as a last line of defense.

9. Recommendations for research

The mitigation of AMR necessitates a comprehensive strategy that encompasses multiple sectors and involves various stakeholders. Primarily, there exists a necessity for improved surveillance systems to effectively observe and trace the occurrence and dissemination of resistant pathogens [108]. Furthermore, it is crucial to emphasize the importance of employing antimicrobials responsibly and prudently in order to effectively mitigate the selective pressure that contributes to the development of resistance. The promotion of antimicrobial stewardship programs within healthcare facilities, as well as the implementation of regulations about the use of antibiotics in agriculture and veterinary medicine, can effectively mitigate the excessive consumption of these drugs [109–112].

Conducting research that focuses on taking action is crucial for creating and using successful strategies to reduce antimicrobial resistance (AMR) [16,107,113–118]. Initiatives should explore the intricate relationship between several elements that lead to the establishment of resistance. Studying antimicrobial prescribing practices, usage patterns in agriculture, horizontal gene transfer's role in resistance spread, and socio-cultural factors affecting antimicrobial consumption are crucial aspects of a thorough research plan [16,107,113–117]. Understanding microbial ecosystem dynamics, such as the resistome and the influence of environmental conditions, is crucial for developing comprehensive strategies. It is crucial to foster interdisciplinary cooperation among microbiologists, pharmacologists, epidemiologists, social scientists, and policymakers to enhance our understanding of antimicrobial resistance. Developing new antimicrobial drugs and alternative therapies is a crucial aspect in combating antibiotic resistance, alongside surveillance and diagnostic research. Advancements in drug development, including finding novel molecular targets, improving current antibiotics, and investigating non-traditional therapeutic methods such as bacteriophage therapy and immunomodulation, are crucial aspects of this field. It is crucial to promote translational research in order to accelerate the implementation of new interventions by connecting laboratory discoveries with clinical use. Collaboration among academics, pharmaceutical businesses, and regulatory agencies is crucial for accelerating the discovery, evaluation, and approval of new antimicrobial drugs.

In addition, it is imperative to enhance research and development endeavors in order to uncover novel antibiotics and explore alternative treatment modalities [119]. It is essential for governments, pharmaceutical companies, and research institutions to engage in collaborative efforts aimed at incentivizing and streamlining the process of developing innovative antimicrobial agents [15]. Furthermore, it should be noted that metal nanoparticles can potentially be one of the current therapeutic strategies employed to address the issue of AMR [120–123]. The utilization of artificial intelligence also holds the potential to address the issue of elevated rates of AMR [124]. Furthermore, it has been proposed that concurrently using antibiotics and antivirulence drugs may offer enhanced management of pathogenic microorganisms while minimizing the development of AMR [125]. Finally, it is imperative to allocate resources towards the advancement of vaccines and diagnostics in order to mitigate the reliance on antimicrobial agents and facilitate precise therapeutic interventions [126].

10. Priorities to public health action

Promoting public awareness and providing education are essential components to address AMR. It is imperative to provide the general population with comprehensive education regarding the proper utilization of antibiotics, the adverse outcomes associated with their excessive usage, and the significance of adhering to prescribed treatment regimens [127]. Healthcare professionals must possess current knowledge regarding antimicrobial stewardship, infection prevention, and control practices. Antibiotic stewardship in hospital settings encompasses the establishment of guidelines, provision of education to healthcare providers, and implementation of protocols to ensure the judicious utilization of antibiotics. Conversely, in outpatient settings, antibiotic stewardship centers on patient education, diagnostic testing, and promoting antibiotic usage solely when deemed necessary. By establishing a culture that promotes responsible utilization of antimicrobials, it is possible to mitigate the selection pressure exerted on microorganisms and consequently decelerate the progression of antimicrobial resistance. The details of various alternative strategies for addressing antimicrobial resistance are illustrated in Table 1.

International collaboration is crucial in addressing the global nature of AMR [115,128]. It is imperative for governments, international

Table 1
Shows various alternative approaches for mitigating global antimicrobial resistance.

Strategy	Description	Advantages	Challenges
1. Antibiotic Stewardship	Rational use of antibiotics, prescribing only when necessary and appropriate dosage.	Preserves antibiotic effectiveness, reduces resistance emergence.	Requires behavior change in healthcare professionals and patients. Monitoring compliance is essential.
2. Development of New Antibiotics	Research and development of novel antibiotics targeting new bacterial mechanisms.	Addresses resistance to existing drugs.	High cost, lengthy development process, potential for cross-resistance.
3. Combination Therapies	Using multiple antibiotics with different mechanisms of action to treat infections.	Synergy can enhance effectiveness, reduce resistance.	Complex dosing regimens, increased risk of side effects, potential for antagonism.
4. Phage Therapy	Using bacteriophages (viruses that infect bacteria) to target specific bacterial strains.	Highly targeted approach, can be rapidly adapted.	Limited knowledge of phage-bacteria interactions, regulatory challenges, variable effectiveness.
5. Probiotics and Prebiotics	Promoting the growth of beneficial bacteria to outcompete harmful strains.	Supports healthy microbiota, reduces space for pathogens.	Limited knowledge of optimal strains, challenges in colonization and persistence.
6. Immunotherapy	Enhancing the body's immune response to fight infections.	Diverse targets, potential for long-lasting protection.	Specific to certain infections, risk of autoimmunity, complex development.
7. Repurposing Existing Drugs	Identifying non-antibiotic drugs with antimicrobial properties.	Faster development, potentially lower costs.	Limited candidates, potential for off-target effects, dose optimization required.
8. Alternatives to Antibiotics	Developing non-antibiotic treatments, like antimicrobial peptides, bacteriocins, or metal nanoparticles.	Reduced risk of resistance, diverse mechanisms.	Limited clinical data, potential for toxicity, delivery challenges.
9. Education and Public Awareness	Promoting proper hygiene, antibiotic use, and understanding of resistance.	Reduces unnecessary antibiotic demand and misuse.	Behavior change is gradual, hard to measure impact, requires ongoing efforts.
10. Surveillance Systems	Monitoring and tracking resistance patterns to inform treatment guidelines.	Provides real-time data, guides treatment decisions.	Resource-intensive, challenges in data sharing and harmonization.
11. Environmental Regulations	Reducing antibiotic use in agriculture and industry to limit resistance spread.	Mitigates selection pressure for resistance.	Regulatory enforcement, global coordination, economic implications.
12. One Health Approach	Coordinating efforts across human, animal, and environmental health to tackle resistance.	Addresses complex sources of resistance spread.	Requires interdisciplinary collaboration, challenges in communication and policy alignment.

organizations, and stakeholders to collaborate in order to achieve regulatory harmonization, exchange optimal methodologies, and synchronize endeavors to effectively combat AMR. Collaborative endeavors, exemplified by GLASS, serve to facilitate the exchange of data and enhance the worldwide response. The exchange of knowledge, resources, and experiences has the potential to facilitate the formulation of comprehensive strategies aimed at addressing AMR at a global level. The prevailing consensus among scientists and healthcare professionals is that AMR represents a substantial and pressing the global health issue. However, it is worth noting that within the scientific community, a small number of dissenting perspectives or ongoing disputes exist on this matter. These opinions do not necessarily contradict the notion that AMR is a problem. Instead, they provide distinct viewpoints on specific facets of the issue or suggest other strategies for addressing it. There exist conflicting perspectives and discussions regarding various aspects of AMR. These include the deliberations on the influence of environmental factors on AMR development, the viability of alternative therapies like bacteriophages, the need to ensure equitable access to essential antibiotics, and the implementation of programs aimed at reducing unnecessary antibiotic utilization. For instance, bacteriophage treatment has been beneficial in treating antibiotic-resistant Acinetobacter baumannii infections [129]. *Clostridium difficile* is another example of an AMR bacterium treated with monoclonal antibodies such as bezlotoxumab [130].

11. Conclusions

The capacity of bacteria and other microbes to rapidly evolve resistance threatens a pillar of modern medicine - effective antimicrobial therapies. Humanity's rampant overuse of antibiotics in healthcare and agriculture has applied immense selective evolutionary pressure, enabling pathogenic bacteria to develop diverse mechanisms undermining previously potent antimicrobials. With antibiotic discovery failing to keep pace as multidrug resistance proliferates globally, we have entered a dangerous post-antibiotic era. Implementing stewardship programs limiting inappropriate antibiotic use and bolstering infection control provides vital first steps. However, the unique 'tragedy of the commons' nature of antimicrobial resistance, transcending borders and sectors, necessitates binding cooperative action worldwide. Through synchronized surveillance, access equity, conservation policies, and innovation funding enacted under a One Health approach, we can curb resistance transmission and preserve antimicrobial efficacy. Further delays risk forecasted reversals to the pre-antibiotic susceptibility patterns underpinning infectious disease mortality's historical dominance - an outcome threatening modern medical capabilities and global health security.

Ethical approval

The ethical approval was not required, as the study conducted did not involve any ethical concerns or issues.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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