

The Next Pandemic? Antimicrobial Resistance and Its Societal Implications - A Comprehensive Review

Abstract: This comprehensive review examines the critical issue of antimicrobial resistance (AMR), a growing global concern with profound societal implications. This article presents an overview of the causes of AMR, including the misuse and overuse of antibiotics in healthcare, agriculture, and veterinary practices. Various conventional and advanced detection methodologies have been explored, highlighting the importance of the accurate and timely identification of resistant strains. The challenges associated with tackling AMR, encompassing scientific, economic, and regulatory aspects have been discussed in depth. In addition, this article sheds light on the far-reaching societal implications of AMR, including increased healthcare costs, treatment complexities, and potential disruptions to healthcare systems. This emphasizes the urgency of adopting proactive strategies to combat AMR and underscores the need for global cooperation, policy interventions and public awareness campaigns. By unraveling the multifaceted dimensions of AMR, this review aims to enhance our understanding, stimulate further research, and promote concerted efforts to mitigate the threat of antimicrobial resistance.

Keywords: Antimicrobial Resistance (AMR), Societal Implications, Healthcare, Global Cooperation.

1. Background

Microorganisms have existed on Earth for more than 3.5 billion years and play a significant role in maintaining the balance of various ecosystems including human species ¹. Most microbes are harmless or even beneficial, very few of them are pathogenic which are responsible for diseases ². To combat these pathogens, antimicrobial agents have been developed. They include antibiotics, fungicides, antiviral agents, and parasiticides. Additionally certain heavy metals, disinfectants, antiseptics, and natural products may also possess antimicrobial properties ^{3,4}. Antimicrobials found useful in healthcare systems. Bring significant benefits to humans, animals, and agriculture by reducing the burden of infectious diseases for many years. However, the effectiveness of antimicrobial treatments is currently threatened by the emergence of antimicrobial resistance ^{5,6}. AMR refers to the phenomenon where microorganisms such as bacteria, viruses, parasites, or fungi develop resistance to the effects of drugs. Consequently, numerous treatments that were once effective against infections are now becoming less potent ⁵⁻⁷. AMR has been listed as one of the top 10 global health and development threats to humanity by the World Health Organization (WHO). Up to 10 million deaths per year are projected by 2050, impacting economies and pushing more people into poverty ^{8,9}. AMR can also have a substantial impact on agricultural production,

further impacting economies and food security. Most of this burden is anticipated to fall on low-income and lower middle-income nations ^{9,10}. The majority of global attention regarding AMR has focused on human health and agriculture sectors, but there is emerging evidence highlighting the critical involvement of the environment in the evolution, transmission, and spread of AMR ¹¹. Effective handling of AMR can be accomplished by adopting the 'One Health' strategy, acknowledging the interconnectedness of human well-being, animal welfare, plant health, and the environment ¹⁴.

2. Causes of Antimicrobial Resistance:

The inappropriate use of antimicrobial drugs in humans, animals, and agriculture significantly contributes to the development and spread of AMR. There are several causes and contributing factors to antimicrobial resistance include:

2.1 Natural or Biological Causes

The natural causes of antimicrobial resistance arise from the inherent characteristics and adaptability of microorganisms. These causes include:

2.1.1 Selective Pressure

Selective pressure refers to the survival and replication advantage of microorganisms that carry resistance genes when exposed to antimicrobial agents ¹⁵. When antimicrobials are used, susceptible microorganisms are either killed or inhibited, allowing resistant strains to survive and multiply ¹⁶. These resistant strains become the dominant type within the microbial population. Over time, this selective pressure can lead to the proliferation of antimicrobial-resistant microorganisms ^{17,18}.

2.1.2 Mutation

Microorganisms have a remarkable ability to reproduce rapidly, allowing them to adapt and evolve quickly in response to changing environmental conditions, including exposure to antimicrobial agents ^{19,20}. During replication, genetic mutations can occur spontaneously, resulting in changes in the DNA of the microorganism. Some of these mutations may confer resistance to specific antimicrobial agents, providing a survival advantage to the mutated microorganism ^{21,22}.

2.1.3 Gene Transfer

Microorganisms, particularly bacteria, have the capability to acquire resistance genes from other microorganisms, including those of the same or distinct species ²³⁻²⁵. Gene transfer can occur through different mechanisms, such as horizontal gene transfer (HGT). In HGT, genetic material, including resistance genes, can be transferred between bacteria, even if they are not closely related. This transfer can happen through three processes: conjugation, transformation, and transduction. ²⁵⁻²⁸. Gene transfer allows bacteria to rapidly acquire resistance genes, which can make them resistant to antimicrobial agents. ^{27,29}.

2.2 Misuse and Overuse of Antibiotics

The misuse and overuse of antibiotics represent an alarming challenge that drives the emergence and propagation of antimicrobial resistance (AMR), a phenomenon in which microorganisms, notably bacteria, develop resistance to once-effective drugs ³⁰⁻³². Within the context of human medicine, antibiotics are frequently employed inappropriately, particularly for viral infections, despite their ineffectiveness against non-bacterial pathogens ³³. This misguided practice exposes bacteria needlessly, creating opportunities for the development of resistance mechanisms, thereby diminishing the efficacy of antibiotics ³⁴. The incomplete adherence to prescribed antibiotic treatment regimens allows surviving bacteria to potentially acquire resistance to the initially effective drugs ³⁵. In agriculture, excessive use of antibiotics for livestock growth promotion and disease prevention contributes to the proliferation of antibiotic-resistant bacteria ^{36,37}. The transmission of these resilient pathogens to humans through the food chain and environmental pathways represents a serious and imminent threat to public health ³⁸. To address the complex issue of antimicrobial resistance (AMR), we need to take a comprehensive and collaborative approach that includes educating healthcare professionals and the public about the importance of using antibiotics appropriately ³⁹. The implementation of rigorous measures across healthcare and agriculture sectors can effectively combat the growing threat of antimicrobial resistance (AMR) by preserving the efficacy of antibiotics ⁴⁰.

2.3 Lack of New Antibiotics

In recent times, the creation of new drugs to fight against harmful microorganisms is decreasing, and this poses a significant problem ^{41,42}. These drugs play a crucial role in treating infections caused by bacteria, viruses, and other microbes. However, the number of new antibiotics being developed is declining rapidly ⁴¹⁻⁴³. The consequences of this decline are worsened by the fact that many microorganisms are becoming resistant to existing antimicrobial drugs ^{44,45}. The number of new drugs entering the market decreases and the prevalence of drug resistance continues to rise, there is a growing concern about the possibility of a future shortage of effective treatments ⁴⁶. The shortage of effective treatments is a cause for concern because it means that infections that were once easily treated may become more difficult to control ⁴⁷. Simple infections could become life-threatening, and medical procedures such as surgeries, organ transplants, and cancer treatments could become riskier due to the lack of effective antimicrobials to prevent and treat infections ^{48,49}. Solving this issue requires a coordinated effort from the scientific community, pharmaceutical companies, and policymakers to promote the research and development of new antimicrobial drugs. ⁵⁰ Finding innovative solutions is crucial to combat antimicrobial resistance and ensure a continuous supply of effective treatments to fight against harmful infections ^{51,52}.

2.4 Global Travel and Trade

Global travel and trade play a significant role in the spread of AMR worldwide ^{53,54}. When people travel internationally, they can unknowingly carry resistant bacteria with them. These bacteria can be present in their bodies without causing any symptoms. As a result, when infected individuals visit other countries, they can introduce these resistant strains of bacteria to new populations ⁵³⁻⁵⁶. AMR can also be transmitted through contaminated food, water, or other goods traded between countries. If these items are contaminated with resistant

bacteria, they can act as carriers, spreading the bacteria to various parts of the world ⁵⁶⁻⁵⁸. The global dissemination of resistant strains is a significant concern. It means that once a particular strain of bacteria becomes resistant to antibiotics in one location, it can quickly spread to other regions. This can make it challenging to control and treat infections, as the available drugs may no longer be effective against these resistant strains ⁵⁹. To tackle this problem effectively, it is crucial to raise awareness about AMR and implement preventive measures. This includes improving infection control practices, promoting responsible use of antibiotics, and implementing strict regulations on the trade and transportation of goods to minimize the risk of transmitting resistant bacteria ⁶⁰.

2.5 Agricultural Use of Antibiotics

The use of antibiotics in agriculture has raised significant concerns regarding their potential impact on human health ⁶¹. Antibiotics are commonly administered to livestock for two main reasons: growth promotion and disease prevention. This widespread practice carries significant risks ^{61,62}. The utilization of antibiotics in agriculture has been strongly associated with the emergence and dissemination of antibiotic-resistant bacteria ⁶³. When animals are treated with these drugs, the bacteria present in their bodies can develop mechanisms to resist the effects of the antibiotics. Over time, this can give rise to the development of superbugs that are challenging to treat, posing a threat to both animal and human health ^{64,65}. The consequences of antibiotic-resistant bacteria are extensive and extend to various aspects. Resistant bacteria have the potential to contaminate meat and other animal-derived products, effectively entering the human food chain ⁶⁶. These bacteria can spread through environmental contamination, affecting soil, water, and crops. This poses a substantial threat to human health, as infections caused by antibiotic-resistant bacteria are more challenging to treat and can result in increased morbidity and mortality rates ⁶⁷. The use of antibiotics in agriculture is a growing concern due to the potential for antibiotic resistance. There is a need for stricter regulations and oversight to ensure that antibiotics are used appropriately and that the risk of antibiotic resistance is minimized. It is also important to find sustainable practices that reduce the need for antibiotics in agriculture, while still meeting the demands of food production ⁶⁸.

2.6 Lack of Diagnostic Tools

The lack of diagnostic tools in healthcare settings presents a significant challenge when it comes to timely and accurate diagnosis of infections ⁶⁹. This issue can have profound consequences, as delayed or incorrect diagnosis often leads to the inappropriate use of antibiotics ^{69,70}. In the absence of efficient diagnostic tests, healthcare providers may opt for broad-spectrum antibiotics as a precautionary measure rather than administering targeted therapy ⁷¹. Broad-spectrum antibiotics are effective against a wide range of bacteria but do not target the microorganism causing the infection ⁷². This approach increases the likelihood of unnecessary antibiotic use, which in turn contributes to the development and spread of antibiotic resistance ^{72,73}. Rapid and accurate diagnostic tools are essential for identifying the specific pathogens that cause infections. This information allows healthcare professionals to prescribe the most effective treatment, including targeted antibiotics, which can help to improve patient outcomes and reduce the spread of antibiotic resistance ⁷⁴. With accurate

diagnostics, the choice of antibiotics can be tailored to the specific infection, reducing the unnecessary use of broad-spectrum drugs, and mitigating the risk of antibiotic resistance ^{74,75}. Improved diagnostic tools, such as point-of-care tests or molecular diagnostics, offer healthcare providers real-time information, enabling them to make well-informed decisions regarding treatment options ⁷⁶. By ensuring precise diagnoses, these tools have the potential to optimize antibiotic use, minimize resistance, and improve patient outcomes ^{76,77}.

2.7 Poor Public Awareness and Education

Poor public awareness and education regarding the proper use of antibiotics and the consequence of antimicrobial resistance is a significant factor contributing to the development and spread of this global health crisis ⁷⁸. The lack of understanding about the appropriate use of antibiotics leads to misuse and overuse of these drugs, which accelerates the emergence of drug-resistant bacteria ⁷⁹. A significant challenge lies in the common misconception among many individuals who believe that antibiotics are effective in treating viral infections like the common cold or flu. This misconception leads to unnecessary antibiotic prescriptions and contributes to the development of antibiotic resistance ^{80,81}. Additionally, patients often fail to complete the full course of antibiotics as prescribed, further promoting the survival of drug-resistant bacteria ^{82,83}. Insufficient knowledge about the consequences of antimicrobial resistance also hampers efforts to control its spread ⁸⁴. When individuals are unaware of the potential dangers, they may neglect taking preventive measures, such as practicing good hygiene and infection control. This lack of awareness allows resistant bacteria to thrive and spread in communities, healthcare settings, and the environment ⁸⁵. Efforts to address poor public awareness and education should focus on increasing knowledge about the appropriate use of antibiotics, emphasizing the importance of completing prescribed courses, and promoting alternatives to antibiotics where possible ⁸⁶. By improving public awareness and education on these critical issues, we can empower individuals to make informed decisions about antibiotic use and take proactive measures to prevent the spread of antimicrobial resistance ^{86,87}.

3. Detection Methodologies for Antimicrobial Resistance

Detection methodologies for antimicrobial resistance have evolved to address the growing public health concern of antimicrobial resistance. Detecting AMR is crucial for effective treatment and containment of resistant infections. Here are some methodologies used for detecting AMR:

3.1 Phenotypic Methods

Phenotypic techniques for identifying antimicrobial resistance are essential tools used in microbiology to determine the susceptibility of bacterial or fungal pathogens to various antimicrobial agents ⁸⁸. These techniques involve growing the microorganisms in the presence of specific antibiotics or antifungal drugs and observing their growth response to assess their susceptibility or resistance ⁸⁹. Here are some common phenotypic techniques used for identifying antimicrobial resistance:

3.1.1 Disk Diffusion

The Disk Diffusion Test, also known as the Kirby-Bauer Test, is a fundamental method employed in clinical microbiology to assess the susceptibility of bacteria to various antibiotics ⁹⁰. This technique involves placing paper disks, impregnated with specific antibiotics of known concentrations, onto an agar plate inoculated with the target bacteria. Over time, the antibiotics diffuse from the disks into the surrounding agar medium. After incubation, a clear "zone of inhibition" appears around each disk, representing the area where bacterial growth is inhibited due to the antibiotic's action. Larger zones indicate greater susceptibility of the bacteria to the antibiotic, suggesting effective inhibition of their growth ⁹¹. This rapid and cost-effective test is a valuable tool for clinicians to select the most appropriate antibiotic therapy for bacterial infections. However, it is important to complement this method with other techniques to get a comprehensive understanding of antimicrobial resistance patterns. By using a combination of approaches, we can get a more in-depth analysis of resistance profiles, which will help us to make better treatment decisions and effectively manage infections ^{91,92}.

3.1.2 Broth Dilution

The Broth Dilution Method is a fundamental technique used in microbiology to determine the Minimum Inhibitory Concentration (MIC) of antibiotics against a specific microorganism. In this method, the antibiotic of interest is serially diluted in liquid growth medium, creating a range of concentrations. The test organism is then exposed to these dilutions and incubated for a defined period. MIC is defined as the lowest concentration of the antibiotic that completely inhibits visible growth of the microorganism. A higher MIC value suggests reduced susceptibility or resistance, indicating that higher concentrations of the antibiotic are required to inhibit the growth of the microorganism effectively ⁹¹⁻⁹³. The Broth Dilution Method provides essential quantitative data for clinicians and researchers, enabling the selection of appropriate antibiotic dosages to combat infections effectively and contribute to the management of antimicrobial resistance ⁹⁴.

3.1.3 Etest

Epsilon testing, commonly known as Etest, has emerged as a versatile and reliable method for assessing the minimum inhibitory concentration (MIC) of antibiotics against bacterial strains. Combining elements of the traditional disk diffusion and broth dilution techniques, the Etest involves the placement of an Etest strip impregnated with a continuous gradient of the antibiotic on an agar plate inoculated with the test organism ⁹⁵. As the antibiotic diffuses into the agar, an elliptical zone of inhibition forms, and the point at which the ellipse intersects the Etest strip represents the MIC value. This approach offers a quantitative assessment of antibiotic susceptibility, aiding in the identification of resistant pathogens and the determination of optimal treatment regimens. The Etest's simplicity, accuracy, and ability to evaluate multiple antibiotics simultaneously make it an invaluable tool in clinical laboratories and research settings for combating antimicrobial resistance ^{95,96}.

3.2 Genotypic Methods

Molecular diagnostics for genotypic detection of antibiotic resistance has revolutionized the field of antimicrobial susceptibility testing. These methods leverage

advanced molecular techniques to identify specific antibiotic resistance genes rapidly and accurately in microorganisms, aiding in the precise characterization of antimicrobial resistance (AMR) profiles ⁹⁷.

Polymerase Chain Reaction (PCR) is a well-established molecular method used in genotypic detection. It amplifies specific DNA sequences, including known resistance genes, allowing for the targeted identification of resistance determinants. PCR is a rapid and reliable technique, commonly used in clinical laboratories to detect a wide range of resistance genes ⁹⁸.

DNA microarrays are another powerful tool for genotypic detection. These microarrays contain immobilized DNA probes that can hybridize with DNA samples, enabling simultaneous detection of multiple resistance genes ⁹⁹. By analyzing the hybridization patterns, researchers can identify the presence of known resistance markers in a single test, making DNA microarrays a high-throughput option for AMR detection ¹⁰⁰.

Next-generation sequencing (NGS) represents an innovative technology in genotypic detection. NGS allows for the complete sequencing of microbial genomes, providing a comprehensive view of all genetic elements, including resistance genes and mutations ¹⁰¹. This technology enables the identification of both known and novel resistance mechanisms, enhancing our understanding of AMR and supporting the development of new antimicrobial therapies ^{101,102}.

Commercially available molecular diagnostic platforms have streamlined the detection of antibiotic resistance genes, making it faster and more accurate than traditional methods. These approaches play a crucial role in guiding appropriate antibiotic therapy, preventing the spread of resistant infections, and informing infection control measures. They are invaluable tools in the ongoing fight against antimicrobial resistance ¹⁰³.

3.3 Innovative and Rapid Antimicrobial Susceptibility Testing (AST) Systems

In recent years, innovative and rapid antimicrobial susceptibility testing (AST) systems have emerged to address the urgent need for faster and more efficient ways to combat antimicrobial resistance. These innovative approaches aim to significantly reduce testing time and quickly identify bacterial susceptibility to antibiotics, enabling timely and targeted treatment decisions ^{104,105}. One class of rapid AST systems utilizes phenotypic analysis, where the growth characteristics of bacteria are assessed in the presence of antibiotics ¹⁰⁶. Some methods, like the Accelerate Pheno™ system, employ rapid phenotypic analysis combined with automated imaging and artificial intelligence algorithms to detect bacterial growth inhibition within hours. Such systems offer substantial time savings compared to conventional culture-based methods, which can take up to 24-48 hours or longer for results ¹⁰⁷. Other innovative AST systems incorporate microfluidic technology, where bacteria are exposed to a panel of antibiotics in tiny, controlled chambers ¹⁰⁸. The growth or inhibition of bacteria is continuously monitored, providing real-time data on susceptibility patterns, and enabling quicker identification of effective antibiotic options ¹⁰⁹. Some AST systems leverage advanced molecular techniques, such as DNA-based methods or mass spectrometry, to rapidly detect specific resistance genes or protein markers ¹¹⁰. Novel approaches in AST can provide valuable information on antibiotic resistance within a matter of hours by analyzing the genetic or proteomic profiles of bacteria. These new approaches

represent a significant advancement in the fight against antimicrobial resistance. They enhance patient care by expediting the identification of effective treatments, support antibiotic stewardship efforts, and contribute to global efforts in tackling the challenge of antimicrobial resistance [111](#).

3.4 Bioinformatics' Approaches

It plays a pivotal role in the identification and analysis of antibiotic resistance genes in clinical samples using metagenomic next-generation sequencing [112](#). Metagenomic sequencing involves the direct sequencing of genetic material extracted from complex microbial communities present in the clinical sample. This powerful technique provides a comprehensive view of the diverse microbial populations, including potential pathogens and antibiotic-resistant strains [112,113](#). After metagenomic sequencing, vast amounts of sequencing data are generated, requiring sophisticated bioinformatics tools for analysis. Alignment and assembly methods are employed to match the sequencing reads to reference databases of known antibiotic resistance genes. These tools allow researchers to identify specific resistance genes present in microbial communities [114,115](#). Bioinformatics also enable the characterization of novel or previously undiscovered resistance genes. By comparing the sequencing data to comprehensive databases, researchers can detect genetic variations and mutations that might confer antibiotic resistance [116,117](#). Bioinformatics approaches are indispensable for extracting meaningful insights from metagenomic NGS data, contributing significantly to our understanding of antimicrobial resistance in clinical settings. They offer powerful tools to inform clinicians and public health officials in making informed decisions regarding antibiotic use, infection control strategies, and the development of novel antimicrobial therapies to combat the threat of antibiotic resistance [118](#).

4. Challenges in Addressing Antimicrobial Resistance

Antimicrobial resistance is a pressing global health challenge that threatens the effectiveness of antimicrobial drugs used to combat infections in humans, animals, and plants. The rise of AMR has led to limited treatment options, the development of multidrug-resistant organisms, inadequate surveillance and data collection, issues with antibiotic stewardship and prescribing practices, and a need for improved global coordination and collaboration.

4.1 Limited Treatment Options

Limited treatment options remain a major challenge in combating AMR. The increasing ineffectiveness of once-reliable antimicrobial treatments has left medical practitioners grappling with a reduced arsenal against infectious diseases [119](#). Pathogens, in their relentless evolution, have developed mechanisms to withstand the effects of previously successful antimicrobials, rendering them less potent or even entirely ineffective [120](#). Compounding this problem is the alarming scarcity of new antimicrobial drugs in the clinical development pipeline. Pharmaceutical companies and researchers face significant challenges in discovering and bringing new drugs to market, resulting in a stagnation of potential solutions to combat AMR [121](#). To effectively confront this crisis, urgent action is necessary in the form of intensified research and innovation. The scientific community must unite to

explore novel antimicrobial agents, harnessing innovative technologies and interdisciplinary approaches ¹²². Genomics, nanotechnology, and other emerging fields offer promising avenues for developing targeted and efficient antimicrobial treatments. Prioritizing the development of new antimicrobial agents and implementing comprehensive strategies, we can hope to stem the tide of AMR and safeguard the future of modern medicine ¹²³.

4.2 Development of Multidrug-Resistant Organisms

The misuse and overuse of antimicrobial drugs in various sectors, including human medicine, animal husbandry, and agriculture have contributed significantly to the development and dissemination of drug-resistant pathogens ^{124,125}. When antibiotics are used indiscriminately or prescribed inappropriately, bacteria can evolve and develop resistance, rendering these once-effective drugs powerless against infections ¹²⁶. In human medicine, the inappropriate prescription and improper use of antibiotics have fueled the evolution of resistant bacteria, making once-treatable infections much harder to manage ¹²⁷. The agricultural industry's routine use of antimicrobials in livestock and crops has also facilitated the proliferation of resistant strains, as these drugs can enter the environment and food chain ¹²⁸. Collaborative initiatives between healthcare, veterinary, and agricultural sectors are crucial to implementing effective interventions. Safeguarding the effectiveness of antimicrobials requires a collective commitment to combat the misuse of these life-saving drugs. By adopting a comprehensive approach, we can work towards mitigating the rapid rise of resistance and preserving the effectiveness of our antimicrobial arsenal for future generations ¹²⁹.

4.3 Inadequate Surveillance and Data Collection

In the battle against AMR, one major obstacle is the lack of adequate surveillance and data collection systems. Without accurate and up-to-date information on the prevalence of resistant pathogens, it becomes challenging to devise effective management strategies and monitor the impact of interventions ¹³⁰. Timely and precise data play a pivotal role in guiding healthcare professionals' treatment decisions ¹³¹. Understanding which antibiotics remain effective in specific regions and against certain pathogens is crucial to avoid the misuse of antibiotics and prevent the further development of resistance ¹³². Additionally, having access to comprehensive data allows researchers and policymakers to identify emerging trends and patterns of AMR, facilitating the development of targeted solutions ¹³³. It is essential to bolster surveillance networks and data collection efforts on a global scale to address this critical issue. By establishing robust surveillance systems, we can gather comprehensive information on antimicrobial resistance in different healthcare settings, veterinary practices, and communities ¹³⁴. Fostering collaboration among countries and organizations to share data can provide a more comprehensive understanding of AMR's global impact and allow for the implementation of coordinated strategies ¹³⁵.

4.4 Antibiotic Stewardship and Prescribing Practices

Antibiotic stewardship and responsible prescribing practices are pivotal in the fight against antimicrobial resistance. To effectively curb the rise of drug-resistant microbes, it is crucial to optimize the use of antibiotics through evidence-based prescribing guidelines ¹³⁶.

Healthcare professionals must be judicious in their prescription decisions, prescribing antibiotics only when necessary and ensuring appropriate dosages and treatment durations ¹³⁷. Avoiding unnecessary antibiotic use reduces selective pressure on microbes, minimizing the chances of resistance development ¹³⁸. Patient education on the proper use of antibiotics, including the importance of completing prescribed courses and not sharing or using leftover antibiotics, is vital ¹³⁹. Encouraging patients to consult their healthcare providers before demanding antibiotics for illnesses that do not require them is also essential in preserving the effectiveness of these life-saving drugs ¹⁴⁰. Beyond healthcare professionals and patients, policymakers also have a critical role to play. They must enact and enforce policies that support antibiotic stewardship initiatives, incentivize research into new antimicrobial agents, and promote the development of diagnostic tools to better target antibiotic treatments. A collaborative effort involving healthcare professionals, policymakers, and the public is essential in promoting prudent antibiotic use. By adopting these responsible practices, we can slow down the development of AMR, extend the lifespan of existing antibiotics and safeguard their effectiveness in treating infectious diseases ^{141,142}.

4.5 Global Coordination and Collaboration

The global challenge of antimicrobial resistance demands a unified and collaborative response, transcending geographical and political boundaries. AMR knows no borders; therefore, effective solutions can only be achieved through shared knowledge, best practices, and resources among nations, international organizations, and research institutions ^{143,144}. Collaborative efforts foster a collective understanding of AMR's complexities, enabling a more comprehensive approach to combat this threat ¹⁴⁵. The One Health approach stands out as a crucial initiative in this regard, acknowledging the interdependence of human, animal, and environmental health in the spread of AMR. By recognizing these interconnected systems, we can address the various pathways through which AMR disseminates and formulate holistic strategies that encompass both human and veterinary medicine, agriculture, and environmental practices ¹⁴⁶. Global coordination in AMR research and response is essential for developing innovative solutions, identifying new antimicrobial agents, and improving diagnostic techniques. It also facilitates the sharing of data and expertise, enabling rapid response to emerging AMR threats. By working together, we can pool our collective strengths, experiences, and resources, forging a powerful alliance against AMR. A united front, grounded in global coordination and collaboration, offers the best chance to curb the spread of antimicrobial resistance and ensure a sustainable future for healthcare and disease management worldwide ¹⁴⁷.

5. Societal Implications of Antimicrobial Resistance

5.1 Increased healthcare costs

The emergence of antimicrobial resistance presents substantial hurdles to healthcare systems worldwide and carries extensive implications for society at large. One of the major consequences is the substantial increase in healthcare costs. As per recent estimates, AMR is projected to impose an enormous economic burden on the world economy, reaching an alarming \$100 trillion by the year 2050. These costs encompass several factors, such as the

expenses incurred in treating infections that are no longer responsive to standard antibiotics ¹⁴⁸. The development of new antimicrobial drugs involves substantial financial investments and research efforts, further adding to the economic strain. The impact of AMR on productivity cannot be overlooked, as it leads to extended hospital stays, delayed recovery periods, and increased absenteeism from work due to prolonged illness ¹⁴⁹. The consequences of AMR extend beyond economic ramifications and affect public health significantly. Healthcare delivery and infection control systems face immense challenges in managing and preventing the spread of resistant infections, resulting in compromised patient care and potentially overwhelming healthcare facilities ^{149,150}. AMR also has the potential to spark widespread infections and pandemics, posing a global health threat. Addressing these societal implications necessitates a concerted effort from governments, healthcare professionals, researchers, and the public to implement robust strategies for antimicrobial stewardship, infection prevention, and the development of new therapeutic approaches ¹⁵¹.

5.2 Higher morbidity and mortality rates

Antimicrobial resistance poses a significant threat to public health, and one of its key societal implications is the potential for higher morbidity and mortality rates. Currently, AMR is already responsible for causing millions of deaths annually, and this number is projected to surge if effective interventions are not implemented. The emergence of drug-resistant pathogens undermines the efficacy of existing antibiotics, rendering once-treatable infections untreatable, thus exacerbating the toll of infectious diseases on human lives ¹⁵². AMR not only affects individuals but also imposes significant burdens on healthcare systems and economies. Treating drug-resistant infections requires more extensive and costly interventions, leading to increased healthcare costs. AMR also impacts healthcare delivery and infection control measures, making it challenging to manage outbreaks and prevent the spread of resistant strains ^{119,153}. The rise of AMR also has severe economic implications, as the economic burden on society escalates due to prolonged illnesses, prolonged hospital stays and the need for more expensive treatments. The potential for widespread infections and pandemics looms large as AMR can facilitate the rapid dissemination of resistant microbes on a global scale ¹⁵⁴. The societal implication of AMR demands a multifaceted approach encompassing improved antimicrobial stewardship, infection prevention and control measures, development of novel antimicrobial agents and enhanced international collaboration ¹⁵⁵.

5.3 Potential for widespread infections and pandemics

AMR presents a critical concern for global public health due to its potential to foster widespread infections and pandemics. The increased resistance of microorganisms to antimicrobial drugs can facilitate the rapid transmission of infectious diseases among individuals and communities. As these pathogens become more resilient to conventional treatments, the likelihood of containing and controlling outbreaks diminishes significantly ^{152,156}. One of the major concerns with AMR is its ability to promote the spread of infections. Resistant microorganisms can proliferate rapidly and spread between individuals, communities, and even across borders, facilitated by travel and global connectivity. This means that infections that were once manageable can become difficult to control, leading to

larger outbreaks and potential pandemics ¹⁵⁷. The rise of AMR can increase morbidity and mortality rates significantly. When infections become resistant to frontline treatments, individuals are at greater risk of severe illnesses and complications, which can lead to higher death rates. This, in turn, puts additional strain on healthcare systems, resulting in increased healthcare costs and economic burdens on society. To combat the potential consequences of AMR, a multifaceted approach is required, including responsible use of antimicrobials, investment in research and development of new drugs, improved infection prevention and control measures, and international cooperation to address this global health challenge. Staying vigilant and updated on the latest scientific research and policies is crucial to mitigate the potential impact of AMR on society and public health ¹⁵⁸.

6. Conclusion

This study extensively explored the vital concerns of Antimicrobial Resistance (AMR), revealing crucial insights that illuminate the origins, methods of detection, hurdles, and wider consequences for society. Our findings underscore the urgent need to address AMR using collaborative and multifaceted strategies. By harnessing the power of diverse disciplines, such as medicine, microbiology, policy, and public health, we can develop comprehensive solutions to this pressing problem. Addressing AMR demands collective action at various levels. Strengthening surveillance systems for early detection, promoting the judicious use of antibiotics, and enhancing public awareness are pivotal steps. Fostering research on novel antimicrobial agents and treatment alternatives is paramount. Policymakers should enact stringent regulations to curb misuse and incentivize pharmaceutical innovation. As we look ahead, a unified effort is essential to effectively combat AMR. By implementing the recommendations outlined in this study and fostering ongoing collaboration between scientists, healthcare professionals, policymakers, and the public, we can forge a path towards a future where the threat of AMR is mitigated, safeguarding both current and future generations.

References:

1. Blaser MJ, Cardon ZG, Cho MK, *et al.* Toward a predictive understanding of earth's microbiomes to address 21st century challenges. *mBio* 2016; **7**.
2. Kazi Madina Maraz, Ruhul Amin Khan. An overview on impact and application of microorganisms on human health, medicine and environment. *GSC Biological and Pharmaceutical Sciences* 2021; **16**: 089–104.
3. Di Martino P. Antimicrobial agents and microbial ecology. *AIMS Microbiol* 2022; **8**: 1–4.
4. Sánchez-López E, Gomes D, Esteruelas G, *et al.* Metal-based nanoparticles as antimicrobial agents: An overview. *Nanomaterials* 2020; **10**.
5. Pokharel S, Shrestha P, Adhikari B. Antimicrobial use in food animals and human health: time to implement 'One Health' approach. *Antimicrob Resist Infect Control* 2020; **9**.
6. Sandhya SM, RekhaAG S. *Issue:3 Citation.* 2019. Available at: www.ijppr.humanjournals.com.

7. Dadgostar P. Antimicrobial resistance: implications and costs. *Infect Drug Resist* 2019; **12**: 3903–10.
8. EClinicalMedicine. Antimicrobial resistance: a top ten global public health threat. *EClinicalMedicine* 2021; **41**.
9. Cheng G, Ning J, Ahmed S, *et al.* Selection and dissemination of antimicrobial resistance in Agri-food production. *Antimicrob Resist Infect Control* 2019; **8**.
10. Samtiya M, Matthews KR, Dhewa T, Puniya AK. Antimicrobial Resistance in the Food Chain: Trends, Mechanisms, Pathways, and Possible Regulation Strategies. *Foods* 2022; **11**.
11. Ogyu A, Chan O, Littmann J, *et al.* National action to combat AMR: A One-Health approach to assess policy priorities in action plans. *BMJ Glob Health* 2020; **5**.
12. Anon. *The Need for a One Health Approach to Zoonotic Diseases and Antimicrobial Resistance*. Available at: <https://cdn.who.int/media/>.
13. Velazquez-Meza ME, Galarde-López M, Carrillo-Quiróz B, Alpuche-Aranda CM. Antimicrobial resistance: One Health approach. *Vet World* 2022; **15**: 743–9.
14. McEwen SA, Collignon PJ. Antimicrobial Resistance: a One Health Perspective. *Microbiol Spectr* 2018; **6**.
15. Tello A, Austin B, Telfer TC. Selective pressure of antibiotic pollution on bacteria of importance to public health. *Environ Health Perspect* 2012; **120**: 1100–6.
16. Tenover FC. Mechanisms of Antimicrobial Resistance in Bacteria. *American Journal of Medicine* 2006; **119**.
17. Dougherty TJ, Pucci MJ, Bronson JJ, Davison DB, Barrett JF. Antimicrobial resistance - Why do we have it and what can we do about it? *Expert Opin Investig Drugs* 2000; **9**: 1707–9.
18. Pablos-Mendez A, Lessnau K. *Chapter 5 Clinical mismanagement and other factors producing antituberculosis drug resistance*. 2000.
19. Geisel N, Vilar JMG, Rubi JM. Optimal resting-growth strategies of microbial populations in fluctuating environments. *PLoS One* 2011; **6**.
20. Mozhayskiy V, Tagkopoulos I. Guided evolution of in silico microbial populations in complex environments accelerates evolutionary rates through a step-wise adaptation. *BMC Bioinformatics* 2012; **13**.
21. Babic M, Bonomo RA. Mutations as a Basis of Antimicrobial Resistance. In: *Antimicrobial Drug Resistance*. Humana Press, 2009; 65–74.
22. Schrader SM, Botella H, Jansen R, *et al.* *Multiform antimicrobial resistance from a metabolic mutation*. 2021. Available at: <https://www.science.org>.

23. Djordjevic SP, Stokes HW, Chowdhury PR. Mobile elements, zoonotic pathogens and commensal bacteria: Conduits for the delivery of resistance genes into humans, production animals and soil microbiota. *Front Microbiol* 2013; **4**.
24. Kristiansson E, Fick J, Janzon A, *et al.* Pyrosequencing of antibiotic-contaminated river sediments reveals high levels of resistance and gene transfer elements. *PLoS One* 2011; **6**.
25. Gandon S, Vale PF. The evolution of resistance against good and bad infections. *J Evol Biol* 2014; **27**: 303–12.
26. Nazarian P, Tran F, Boedicker JQ. Modeling multispecies gene flow dynamics reveals the unique roles of different horizontal gene transfer mechanisms. *Front Microbiol* 2018; **9**.
27. Milka M, Awkew A. *Role of Horizontal Gene Transfer in Bacteria*. Online; 2018. Available at: www.iiste.org.
28. Burmeister AR. Horizontal Gene Transfer. *Evol Med Public Health* 2015; **2015**: 193–4.
29. Wang Y, Batra A, Schulenburg H, Dagan T. Gene sharing among plasmids and chromosomes reveals barriers for antibiotic resistance gene transfer. *Philosophical Transactions of the Royal Society B: Biological Sciences* 2022; **377**.
30. Bright-Ponte SJ. Antimicrobial use data collection in animal agriculture. *Zoonoses Public Health* 2020; **67**: 1–5.
31. Shallcross LJ. Editorials: Antibiotic overuse: A key driver of antimicrobial resistance. *British Journal of General Practice* 2014; **64**: 604–5.
32. Manohar P, Loh B, Leptihn S. Will the Overuse of Antibiotics during the Coronavirus Pandemic Accelerate Antimicrobial Resistance of Bacteria? *Infectious Microbes and Diseases* 2020; **2**: 87–8.
33. Richards J. Emergence & spread of Multiresistant Organisms - Can Infection Control measures help? *Int J Infect Control* 2009; **5**.
34. Munita JM, Arias CA. Mechanisms of Antibiotic Resistance Kudva IT, Zhang Q, eds. *Microbiol Spectr* 2016; **4**. Available at: <https://journals.asm.org/doi/10.1128/microbiolspec.VMBF-0016-2015>.
35. Windels EM, Michiels JE, Van Den Bergh B, Fauvart M, Michiels J. Antibiotics: Combatting Tolerance To Stop Resistance. 2019. Available at: <https://doi.org/10.1128/mBio>.
36. Economou V, Gousia P. Agriculture and food animals as a source of antimicrobial-resistant bacteria. *Infect Drug Resist* 2015; **8**: 49–61.
37. Karimi A, Shulman C, Tchoudnovski D, Tobis M. An Agricultural Perspective for Combating Antibiotic Resistance: A Literature Review. *Undergraduate Research in Natural and Clinical Science and Technology (URNCST) Journal* 2020; **4**: 1–10.
38. Antunes P, Novais C, Peixe L. Food-to-Humans Bacterial Transmission. *Microbiol Spectr* 2020; **8**.

39. Sartelli M, Hardcastle TC, Catena F, *et al.* Antibiotic use in low and middle-income countries and the challenges of antimicrobial resistance in surgery. *Antibiotics* 2020; **9**: 1–12.
40. Harbarth S, Balkhy HH, Goossens H, *et al.* Antimicrobial resistance: One world, one fight! *Antimicrob Resist Infect Control* 2015; **4**.
41. Wei Zheng C, Zheng W, Sun W, Simeonov A. Themed Section: Inventing New Therapies Without Reinventing the Wheel: The Power of Drug Repurposing REVIEW ARTICLE Drug repurposing screens and synergistic drug-combinations for infectious diseases. *BJP British Journal of Pharmacology British Journal of Pharmacology* 2018; **175**: 181. Available at: <http://onlinelibrary.wiley.com/doi/10.1111/bph.v175.2/issuetoc>.
42. Spellberg B, Powers JH, Brass EP, Miller LG, Edwards JE. *Trends in Antimicrobial Drug Development: Implications for the Future*. 2004. Available at: <https://academic.oup.com/cid/article/38/9/1279/317267>.
43. Overbye KM, Barrett JF. Antibiotics: Where did we go wrong? *Drug Discov Today* 2005; **10**: 45–52.
44. Kalayci S. Antimicrobial Properties of Various Non-Antibiotic Drugs against Microorganisms. *J Bioanal Biomed* 2016; **8**.
45. Ross-Gillespie A, Kümmerli R. ‘Evolution-Proofing’ Antibacterials. *Evol Med Public Health* 2014; **2014**: 134–5.
46. Costantino L, Barlocco D. Challenges in the design of multitarget drugs against multifactorial pathologies: A new life for medicinal chemistry? *Future Med Chem* 2013; **5**: 5–7.
47. Leviton I. Commentary on ‘the impact of anti-infective drug shortages on hospitals in the United States: Trends and causes’. *Clinical Infectious Diseases* 2012; **54**: 692–3.
48. Bow EJ. There should be no ESKAPE for febrile neutropenic cancer patients: The dearth of effective antibacterial drugs threatens anticancer efficacy. *Journal of Antimicrobial Chemotherapy* 2013; **68**: 492–5.
49. Lesho EP, Laguio-Vila M. The Slow-Motion Catastrophe of Antimicrobial Resistance and Practical Interventions for All Prescribers. *Mayo Clin Proc* 2019; **94**: 1040–7.
50. Mossialos E, Renwick M, Mossialos E. *Fostering R&D of novel antibiotics and other technologies to prevent and treat infection*. Available at: https://academic.oup.com/eurpub/article/30/Supplement_5/ckaa165.1203/5913902.
51. Kaur I. Novel Strategies to Combat Antimicrobial Resistance. *Journal of Infectious Diseases & Therapy* 2016; **4**.
52. Kpokiri EE, Budak JZ, Chang CC, *et al.* Innovative strategies to fight antimicrobial resistance: crowdsourcing to expand medical training. *F1000Res* 2020; **9**.
53. Langelier C, Graves M, Kalantar K, *et al.* Article Summary Line: Metagenomic study of enteric microbiota collected longitudinally from international travelers revealed an increase in

antimicrobial resistance genes and changes in discrete microbial populations following travel. Running Title: Microbiome and Resistome Dynamics in Travelers Title: Microbiome and Antimicrobial Resistance Gene Dynamics in International Travelers. Available at: <https://doi.org/10.1101/506394>.

54. Sridhar S, Turbett SE, Harris JB, Larocque RC. Antimicrobial-resistant bacteria in international travelers. *Curr Opin Infect Dis* 2021; **34**: 423–31.
55. Bokhary H, Pangesti KNA, Rashid H, Abd El Ghany M, Hill-Cawthorne GA. Travel-related antimicrobial resistance: a systematic review. *Trop Med Infect Dis* 2021; **6**.
56. Rogers BA, Aminzadeh Z, Hayashi Y, Paterson DL. Country-to-country transfer of patients and the risk of multi-resistant bacterial infection. *Clinical Infectious Diseases* 2011; **53**: 49–56.
57. Frost I, Van Boeckel TP, Pires J, Craig J, Laxminarayan R. Global geographic trends in antimicrobial resistance: The role of international travel. *J Travel Med* 2019; **26**.
58. Skandalis N, Maeusli M, Papafotis D, *et al*. Environmental spread of antibiotic resistance. *Antibiotics* 2021; **10**.
59. Molton JS, Tambyah PA, Ang BSP, Ling ML, Fisher DA. The global spread of healthcare-associated multidrug-resistant bacteria: A perspective from Asia. *Clinical Infectious Diseases* 2013; **56**: 1310–8.
60. Godman B, Egwuenu A, Haque M, *et al*. Strategies to improve antimicrobial utilization with a special focus on developing countries. *Life* 2021; **11**.
61. Singer RS, Williams-Nguyen J. Human health impacts of antibiotic use in agriculture: A push for improved causal inference. *Curr Opin Microbiol* 2014; **19**: 1–8.
62. Chattopadhyay MK. Use of antibiotics as feed additives: A burning question. *Front Microbiol* 2014; **5**.
63. Cantón R, Morosini MI. Emergence and spread of antibiotic resistance following exposure to antibiotics. *FEMS Microbiol Rev* 2011; **35**: 977–91.
64. Aarestrup FM. *Antimicrobial resistance in bacteria of animal origin*. ASM Press; 2006.
65. Tollefson L. *Impact of Antimicrobial Use in Animals and Regulatory Response*.
66. Addis M. A Review on Antibiotic Resistant and Implication on Food Chain. 2015; **42**. Available at: www.iiste.org.
67. Ishii S. Ecology of pathogens and antibiotic-resistant bacteria in environments: Challenges and opportunities. *Microbes Environ* 2019; **34**: 1–4.
68. Wallinga D. Today's food system: How healthy is it? *J Hunger Environ Nutr* 2009; **4**: 251–81.
69. Wilson ML. Infectious diseases and pathology: Opportunities and challenges. *Am J Clin Pathol* 2006; **125**: 654–5.

70. Mitsakakis K, D'Acremont V, Hin S, von Stetten F, Zengerle R. Diagnostic tools for tackling febrile illness and enhancing patient management. *Microelectron Eng* 2018; **201**: 26–59.
71. Trevas D, Caliendo AM, Hanson K, Levy J, Ginocchio CC. Diagnostic Tests Can Stem the Threat of Antimicrobial Resistance: Infectious Disease Professionals Can Help. *Clinical Infectious Diseases* 2021; **72**: E893–900.
72. Paharik AE, Schreiber HL, Spaulding CN, Dodson KW, Hultgren SJ. Narrowing the spectrum: The new frontier of precision antimicrobials. *Genome Med* 2017; **9**.
73. Yang B, Fang D, Lv Q, Wang Z, Liu Y. Targeted Therapeutic Strategies in the Battle Against Pathogenic Bacteria. *Front Pharmacol* 2021; **12**.
74. Anon. *Rapid Detection of Pathogens*.
75. Brink AJ, van Wyk J, Moodley VM, *et al*. The role of appropriate diagnostic testing in acute respiratory tract infections: An antibiotic stewardship strategy to minimise diagnostic uncertainty in primary care. *South African Medical Journal* 2016; **106**: 554–61.
76. Kozel TR, Burnham-Marusich AR. *Point-of-Care Testing for Infectious Diseases: Past, Present, and Future*. 2017. Available at: <https://journals.asm.org/journal/jcm>.
77. Lisby JG, Schneider UV. Point of care testing for infectious disease: Ownership and quality. *Journal of Antimicrobial Chemotherapy* 2021; **76**: III28–32.
78. Shami AY. Antimicrobial resistance strategies: Are we approaching the end? *J Pure Appl Microbiol* 2020; **14**: 93–102.
79. Bbosa GS, Mwebaza N, Odda J, Kyegombe DB, Ntale M. Antibiotics/antibacterial drug use, their marketing and promotion during the post-antibiotic golden age and their role in emergence of bacterial resistance. *Health N Hav* 2014; **06**: 410–25.
80. Thomas MG. *New Zealand Medical Journal 'Just say no'-reducing the use of antibiotics for colds, bronchitis and sinusitis*. 2000.
81. McCullough AR, Parekh S, Rathbone J, Del Mar CB, Hoffmann TC. A systematic review of the public's knowledge and beliefs about antibiotic resistance. *Journal of Antimicrobial Chemotherapy* 2016; **71**: 27–33.
82. Davey P, Pagliari C, Hayes A. The patient's role in the spread and control of bacterial resistance to antibiotics. *Clinical Microbiology and Infection* 2002; **8**: 43–68.
83. De Sá F, Fiol D, Barberato-Filho S, Lopes C, Inês De Toledo M. *Level of patient information on antibiotic use*. 2010.
84. Wise R, Blaser M, Carrs O, *et al*. The urgent need for new antibacterial agents. *Journal of Antimicrobial Chemotherapy* 2011; **66**: 1939–40.

85. Cave R, Cole J, Mkrtchyan H V. Surveillance and prevalence of antimicrobial resistant bacteria from public settings within urban built environments: Challenges and opportunities for hygiene and infection control. *Environ Int* 2021; **157**.
86. Ancillotti M, Eriksson S, Veldwijk J, Nihlén Fahlquist J, Andersson DI, Godsken T. Public awareness and individual responsibility needed for judicious use of antibiotics: A qualitative study of public beliefs and perceptions. *BMC Public Health* 2018; **18**.
87. Mathew P, Sivaraman S, Chandy S. Communication strategies for improving public awareness on appropriate antibiotic use: Bridging a vital gap for action on antibiotic resistance. *J Family Med Prim Care* 2019; **8**: 1867.
88. Vaz C P, MM A, AG R. Current and Novel Methods in Clinical Microbiology: Advantages and Pitfalls when Facing the Menace of Antimicrobial Resistance. *J Med Microbiol Diagn* 2018; **07**.
89. Gilbert P, Collier PJ, Brown2 MRW. *MINIREVIEW Influence of Growth Rate on Susceptibility to Antimicrobial Agents: Biofilms, Cell Cycle, Dormancy, and Stringent Response*. 1990.
90. Yao H, Liu J, Jiang X, Chen F, Lu X, Zhang J. Analysis of the clinical effect of combined drug susceptibility to guide medication for carbapenem-resistant klebsiella pneumoniae patients based on the Kirby–Bauer disk diffusion method. *Infect Drug Resist* 2021; **14**: 79–87.
91. Khan ZA, Siddiqui MF, Park S. Current and emerging methods of antibiotic susceptibility testing. *Diagnostics* 2019; **9**.
92. Jorgensen JH, Ferraro MJ. Antimicrobial Susceptibility Testing: A Review of General Principles and Contemporary Practices. *Clinical Infectious Diseases* 2009; **49**: 1749–55.
93. Tan R, Yu A, Liu Z, *et al*. Prediction of Minimal Inhibitory Concentration of Meropenem Against Klebsiella pneumoniae Using Metagenomic Data. *Front Microbiol* 2021; **12**.
94. Witebsky FG, Maclowry JD, French SS. *Broth Dilution Minimum Inhibitory Concentrations: Rationale for Use of Selected Antimicrobial Concentrations*. 1979. Available at: <https://journals.asm.org/journal/jcm>.
95. Dannaoui E, Espinel-Ingroff A. Antifungal susceptibility testing by concentration gradient strip etest method for fungal isolates: A review. *Journal of Fungi* 2019; **5**.
96. Conceição N, Rodrigues WF, De Oliveira KLP, *et al*. Beta-lactams susceptibility testing of penicillin-resistant, ampicillin-susceptible Enterococcus faecalis isolates: A comparative assessment of Etest and disk diffusion methods against broth dilution. *Ann Clin Microbiol Antimicrob* 2020; **19**.
97. Yee R, Bard JD, Simner PJ. The genotype-to-phenotype dilemma: How should laboratories approach discordant susceptibility results? *J Clin Microbiol* 2021; **59**.

98. Park S, Rana A, Sung W, Munir M. Competitiveness of Quantitative Polymerase Chain Reaction (qPCR) and Droplet Digital Polymerase Chain Reaction (ddPCR) Technologies, with a Particular Focus on Detection of Antibiotic Resistance Genes (ARGs). *Appl Microbiol* 2021; **1**: 426–44.
99. Taguchi T, Ishikawa M, Ichikawa M, *et al.* Amplification-free detection of bacterial genes using a signaling probe-based DNA microarray. *Biosens Bioelectron* 2021; **194**.
100. Frye JG, Jesse T, Long F, *et al.* DNA microarray detection of antimicrobial resistance genes in diverse bacteria. *Int J Antimicrob Agents* 2006; **27**: 138–51.
101. Besser J, Carleton HA, Gerner-Smidt P, Lindsey RL, Trees E. Next-generation sequencing technologies and their application to the study and control of bacterial infections. *Clinical Microbiology and Infection* 2018; **24**: 335–41.
102. Petrillo M, Fabbri M, Kagkli DM, *et al.* A roadmap for the generation of benchmarking resources for antimicrobial resistance detection using next generation sequencing. *F1000Res* 2021; **10**: 80.
103. Li Y, Yang X, Zhao W. Emerging Microtechnologies and Automated Systems for Rapid Bacterial Identification and Antibiotic Susceptibility Testing. *SLAS Technol* 2017; **22**: 585–608.
104. Arena F, Viaggi B, Galli L, Rossolini GM. Antibiotic susceptibility testing: Present and future. *Pediatric Infectious Disease Journal* 2015; **34**: 1128–30.
105. Shin DJ, Andini N, Hsieh K, Yang S, Wang T-H. Emerging Analytical Techniques for Rapid Pathogen Identification and Susceptibility Testing. *Annual Review of Analytical Chemistry* **11**: 47. Available at: <https://doi.org/10.1146/annurev-anchem-061318->.
106. Chen J, Tomasek M, Cruz A, *et al.* Feasibility and potential significance of rapid in vitro qualitative phenotypic antimicrobial susceptibility testing of gram-negative bacilli with the ProMax system. *PLoS One* 2021; **16**.
107. Matic N, Willey B, Gascon B, *et al.* Clinical Impact of Rapid Identification (ID) and Phenotypic Antimicrobial Susceptibility Testing (AST) by Accelerate PhenoTM System (AXDX) for Gram-negative (GNB) Bloodstream Infections. *Open Forum Infect Dis* 2017; **4**: S595–S595.
108. Hwang JH, Lee SY, Choi J. Microscopic analysis of bacterial inoculum effect using micropatterned biochip. *Antibiotics* 2021; **10**.
109. Syal K, Mo M, Yu H, *et al.* Current and emerging techniques for antibiotic susceptibility tests. *Theranostics* 2017; **7**: 1795–805.
110. Liu T, Lu Y, Gau V, Liao JC, Wong PK. Rapid Antimicrobial Susceptibility Testing with Electrokinetics Enhanced Biosensors for Diagnosis of Acute Bacterial Infections. *Ann Biomed Eng* 2014; **42**: 2314–21.

111. Khaledi A, Weimann A, Schniederjans M, *et al.* Predicting antimicrobial resistance in *Pseudomonas aeruginosa* with machine learning-enabled molecular diagnostics. *EMBO Mol Med* 2020; **12**.
112. Li Y, Yang Q, Ding J. Metagenomic Next-generation Sequencing: Application in Infectious Diseases. *Explor Res Hypothesis Med* 2022; **7**: 19–24.
113. Ruppé E, Charretier Y, Lazarevic V, Schrenzel J. Integrating metagenomics in the routine lab. In: *Application and Integration of Omics-powered Diagnostics in Clinical and Public Health Microbiology*. Springer International Publishing, 2021; 133–52.
114. Queyrel M, Prifti E, Templier A, Zucker J-D. *Towards End-To-End Disease Prediction from Raw Metagenomic Data*.
115. McCall C, Xagorarakis I. Comparative study of sequence aligners for detecting antibiotic resistance in bacterial metagenomes. *Lett Appl Microbiol* 2018; **66**: 162–8.
116. Berglund F, Böhm ME, Martinsson A, *et al.* Comprehensive screening of genomic and metagenomic data reveals a large diversity of tetracycline resistance genes. *Microb Genom* 2020; **6**: 1–14.
117. Van Camp PJ, Haslam DB, Porollo A. Bioinformatics approaches to the understanding of molecular mechanisms in antimicrobial resistance. *Int J Mol Sci* 2020; **21**.
118. Peng Z, Mao Y, Zhang N, Zhang L, Wang Z, Han M. Utilizing Metagenomic Data and Bioinformatic Tools for Elucidating Antibiotic Resistance Genes in Environment. *Front Environ Sci* 2021; **9**.
119. Hocking L, Ali GC, D'Angelo C, *et al.* A rapid evidence assessment exploring whether antimicrobial resistance complicates non-infectious health conditions and healthcare services, 2010-20. *JAC Antimicrob Resist* 2021; **3**.
120. Antonelli G, Cappelli L, Cinelli P, *et al.* Strategies to tackle antimicrobial resistance: the example of *Escherichia coli* and *Pseudomonas aeruginosa*. *Int J Mol Sci* 2021; **22**.
121. Payne DJ, Miller LF, Findlay D, Anderson J, Marks L. Time for a change: Addressing R&D and commercialization challenges for antibacterials. *Philosophical Transactions of the Royal Society B: Biological Sciences* 2015; **370**.
122. Miethke M, Pieroni M, Weber T, *et al.* Towards the sustainable discovery and development of new antibiotics. *Nat Rev Chem* 2021; **5**: 726–49.
123. Mantravadi PK, Kalesh KA, Dobson RCJ, Hudson AO, Parthasarathy A. The quest for novel antimicrobial compounds: Emerging trends in research, development, and technologies. *Antibiotics* 2019; **8**.
124. Pagani L, Pieri A, Aschbacher R, *et al.* Country income is only one of the tiles: The global journey of antimicrobial resistance among humans, animals, and environment. *Antibiotics* 2020; **9**: 1–13.

125. Ma F, Xu S, Tang Z, Li Z, Zhang L. Use of antimicrobials in food animals and impact of transmission of antimicrobial resistance on humans. *Biosaf Health* 2021; **3**: 32–8.
126. Hotinger JA, Morris ST, May AE. The case against antibiotics and for anti-virulence therapeutics. *Microorganisms* 2021; **9**.
127. Mir S, Brett D, Adam de la B, Martha K. Antibiotics Overuse and Bacterial Resistance. *Annals of Microbiology and Research* 2019; **3**.
128. Mann A, Nehra K, Rana JS, Dahiya T. Antibiotic resistance in agriculture: Perspectives on upcoming strategies to overcome upsurge in resistance. *Curr Res Microb Sci* 2021; **2**.
129. Picchioni F, Aurino E, Aleksandrowicz L, *et al*. Roads to interdisciplinarity – working at the nexus among food systems, nutrition and health: 1st annual Agriculture, Nutrition and Health (ANH) Academy Week, Addis Ababa (Ethiopia), 20–24 June 2016. *Food Secur* 2017; **9**: 181–9.
130. Davies SC, Oxlade C. Innovate to secure the future: the future of modern medicine. *Future Healthc J* 2021; **8**: e251–6.
131. Meid AD, Ruff C, Wirbka L, *et al*. Using the causal inference framework to support individualized drug treatment decisions based on observational healthcare data. *Clin Epidemiol* 2020; **12**: 1223–34.
132. Keet R, Rip D. *Listeria monocytogenes* isolates from western cape, south africa exhibit resistance to multiple antibiotics and contradicts certain global resistance patterns. *AIMS Microbiol* 2021; **7**: 40–58.
133. Ashley EA, Shetty N, Patel J, *et al*. Harnessing alternative sources of antimicrobial resistance data to support surveillance in low-resource settings. *Journal of Antimicrobial Chemotherapy* 2019; **74**: 541–6.
134. Zhang M, Wang C, O AM. A Bayesian Latent Class Mixture Model With Censoring for Correlation Analysis in Antimicrobial Resistance Across Populations. 2020. Available at: <https://doi.org/10.21203/rs.3.rs-94417/v1>.
135. Acharya KP, Subramanya SH, Pitout JDD. Inclusion of next-generation leaders and cost-effective precision diagnostic techniques are vital in combatting antimicrobial resistance in low- And middle-income countries. *JAC Antimicrob Resist* 2020; **2**.
136. Rajesh A, Mohanan H, Thomas RP. A Review on Antimicrobial Stewardship Programs in Multiple Care Settings. *J Pharm Res Int* 2021: 264–70.
137. Yates TD, Davis ME, Taylor YJ, *et al*. Not a magic pill: A qualitative exploration of provider perspectives on antibiotic prescribing in the outpatient setting. *BMC Fam Pract* 2018; **19**.
138. Banamah OB, Alsamih MF, Alshehri HH, *et al*. Chances and prevention of antibiotic resistance in primary health care: literature review. *Int J Community Med Public Health* 2021; **8**: 875.

139. Palin V, Welfare W, Ashcroft DM, Van Staa TP. Shorter and Longer Courses of Antibiotics for Common Infections and the Association with Reductions of Infection-Related Complications including Hospital Admissions. *Clinical Infectious Diseases* 2021; **73**: 1805–12.
140. Fleming-Dutra KE, Mangione-Smith R, Hicks LA. *How to Prescribe Fewer Unnecessary Antibiotics: Talking Points That Work with Patients and Their Families*. 2016. Available at: www.aafp.org/afp.
141. Harbarth S, Hackett J. Introduction: DRIVE-AB's definitions and indicators to monitor responsible antibiotic use. *Journal of Antimicrobial Chemotherapy* 2018; **73**: vi2.
142. Littmann J, Rid A, Buyx A. Tackling anti-microbial resistance: Ethical framework for rational antibiotic use. *Eur J Public Health* 2018; **28**: 359–63.
143. Lomazzi M, Moore M, Johnson A, Balasegaram M, Borisch B. Antimicrobial resistance - Moving forward? *BMC Public Health* 2019; **19**.
144. Joshi MP, Hafner T, Twesigye G, *et al*. Strengthening multisectoral coordination on antimicrobial resistance: a landscape analysis of efforts in 11 countries. *J Pharm Policy Pract* 2021; **14**.
145. Joshi MP, Chintu C, Mpundu M, *et al*. Multidisciplinary and multisectoral coalitions as catalysts for action against antimicrobial resistance: Implementation experiences at national and regional levels. *Glob Public Health* 2018; **13**: 1781–95.
146. Humboldt-Dachroeden S, Mantovani A. Assessing environmental factors within the one health approach. *Medicina (Lithuania)* 2021; **57**.
147. Ruckert A, Fafard P, Hindmarch S, *et al*. Governing antimicrobial resistance: a narrative review of global governance mechanisms. *J Public Health Policy* 2020; **41**: 515–28.
148. Cama J, Leszczynski R, Tang PK, *et al*. To Push or to Pull? in a Post-COVID World, Supporting and Incentivizing Antimicrobial Drug Development Must Become a Governmental Priority. *ACS Infect Dis* 2021; **7**: 2029–42.
149. Metsemakers WJ, Zalavras C, Schwarz EM, Chen AF, Trampuz A, Moriarty TF. Antimicrobial Resistance, the COVID-19 Pandemic, and Lessons for the Orthopaedic Community. *Journal of Bone and Joint Surgery* 2021; **103**: 4–9.
150. Sturm L, Flood M, Montoya A, Mody L, Cassone M. Updates on Infection Control in Alternative Health Care Settings. *Infect Dis Clin North Am* 2021; **35**: 803–25.
151. Cars O, Chandy SJ, Mpundu M, Peralta AQ, Zorzet A, So AD. Resetting the agenda for antibiotic resistance through a health systems perspective. *Lancet Glob Health* 2021; **9**: e1022–7.
152. Mancuso G, Midiri A, Gerace E, Biondo C. Bacterial antibiotic resistance: the most critical pathogens. *Pathogens* 2021; **10**.

153. Ruiz J. *Microbes, Infection and Chemotherapy IDEAS AND OPINIONS*. 2021. Available at: <https://orcid.org/0000-0002-4431-2036>.
154. Jung H, Yang J, Kim E, Lee J. The effect of mid-to-long-term hospitalization on the catastrophic health expenditure: Focusing on the mediating effect of earned income loss. *Healthcare (Switzerland)* 2021; **9**.
155. Rodríguez-Baño J, Rossolini GM, Schultsz C, *et al.* Antimicrobial resistance research in a post-pandemic world: Insights on antimicrobial resistance research in the COVID-19 pandemic. *J Glob Antimicrob Resist* 2021; **25**: 5–7.
156. Viegas C, Viegas S. Special issue “antimicrobial resistance: from the environment to human health”. *Microorganisms* 2021; **9**.
157. Wozniak TM, Smith-Vaughan H, Andrews R. Convergence of surveillance blind spots with antimicrobial resistance hotspots. *Aust N Z J Public Health* 2021; **45**: 541–2.
158. Littmann J, Viens AM, Silva DS. The Super-Wicked Problem of Antimicrobial Resistance. In: , 2020; 421–43.