IJIS: Vol.1, Issue 3, April 2025, Page: 10-31 ISSN 3049-3277

International Journal of Integrative Studies (IJIS)

Journal homepage:www.ijis.co.in

Antimicrobial Resistance: Mechanisms, Trends, and Future Directions

K Sumana Mounya[1], Sowmya Kumaravel[2], Amulya Arora[3], Sneha Khadse[4]

[1]Research Scholar, Department of Life Science, Gitam (Deemed to Be University)
[2]Assistant Professor, Department of Agricultural Microbiology, Bharath Institute of Higher Education and Research., Chennai, Tamil Nadu, India
[3]M.sc zoology final year student, Biosciences department, Chandigarh University, Mohali, Punjab

[4]Research Scholar, Department of Microbiology, Nirwan University, Jaipur, Rajasthan
Email.id -khadsesneha43@gmail.com

Abstract

Antimicrobial resistance (AMR) poses a worldwide health danger by rendering numerous antimicrobial treatments useless and leading to elevated healthcare costs and elevated mortality rates and increased morbidity standards as well as economic costs. The study explores antimicrobial resistance mechanisms by investigating enzymatic destruction alongside target alteration and cell pump activity and biofilm developmental capabilities of microorganisms for evading antimicrobial drug effects. This research investigates recent AMR developments by monitoring the increasing numbers of microbes that become resistant to multiple drugs known as MDR together with XDR strains and pan-drug-resistant bacteria. Resistive mechanisms have increased rapidly because of overuse of antibiotics in human medicine and its applications in animal farming as well as genetic exchange that allows microbes to travel among different regions. This paper outlines the importance of surveillance because it functions as an essential component fighting AMR alongside antimicrobial stewardship and infection control practices. Antimicrobial agents along with phage therapy options along with modern diagnostic methods make up the fundamental weapons against AMR. The proposed direction highlights the necessity for different organizations to collaborate because they should develop contemporary therapeutic approaches and strengthen antibiotic management systems worldwide.

Keywords: ***Antimicrobial resistance, antibiotic resistance mechanisms, multidrug resistance, efflux pumps, biofilm formation, antimicrobial stewardship, horizontal gene transfer, global health, surveillance, alternative therapies, phage therapy, tuberculosis, drug-resistant infections, molecular diagnostics, public health.***

Introduction

The growing antimicrobial resistance problem creates significant global healthcare difficulties because it threatens the effectiveness of current treatments for infectious illness (Nguyen, 2016). The development of resistance mechanisms has triggered higher medical death rates along with extended hospitalization periods and cost a large sum to global healthcare services (Niño-Vega et al., 2025). Human medicine along with animal husbandry and agricultural applications of antibiotics has challenged microorganisms through selective pressure because of unwarranted widespread antibiotic use (Gayathri et al., 2021). Resistant microbial strains spread quickly between territories because of three main factors which are globalization trade and straightforward international mobility along with process-connected food supply systems (Ruíz & Álvarez-Ordóñez, 2017). Bacteria evolve new resistance mechanisms at a speed even faster than scientists can develop new antimicrobial drugs thereby creating an expanding therapeutic void (Nguyen, 2016). The World Health Organization issued an alert to worldwide viewers about the "post-antibiotic era" because during this time basic infections will become dangerous again (Niño-Vega et al., 2025). We need urgent widespread antimicrobial resistance measures because bacteria now show powerful

multidrug resistance and extensive drug resistance with pan-drug resistance (Posada-Perlaza et al., 2019). Antimicrobial resistance demands worldwide collaboration for strengthening antimicrobial stewardship plans alongside enhanced infection control practices and prompt antimicrobial drug research with international surveillance of microorganism transmission (Nasiri et al., 2017).

Mechanisms of Antimicrobial Resistance

Microbes defeat antimicrobial agents by using enzymatic degradation combined with target structure modifications and transportation systems and surface layers from organisms (Nguyen 2016). Enzyme production renders antimicrobial drugs ineffective by chemically breaking down the antibiotics while modifying their chemical structure. Beta-lactamase produces by Microorganisms yields inactivation of penicillin beta-lactam rings and cephalosporin rings making this resistance mechanism common among Gram-negative bacterial species (Baho et al., 2018). Antibiotic mechanisms force bacteria to change their target structures or proteins to disable drug attachment and block their functional capacity. The development of mutations in ribosomal RNA combined with alterations in ribosomal proteins makes microorganisms immune to both aminoglycosides and macrolides.

Table 1: Summary of Common Antibiotic Resistance Mechanisms in Bacteria

Bacterial Species	**Resistance Mechanism**
Escherichia coli	Efflux pumps, beta-lactamases, target modification
Staphylococcus aureus	Beta-lactamases, alteration of target sites (penicillin-binding proteins)
Klebsiella pneumoniae	Carbapenemases, beta-lactamases, efflux pumps
Pseudomonas aeruginosa	Efflux pumps, beta-lactamases, aminoglycoside-modifying enzymes
Enterococcus faecalis	Vancomycin resistance, acquisition of resistance genes through plasmids
Mycobacterium tuberculosis	Mutations in RNA polymerase, efflux pumps, resistance to first-line drugs (isoniazid, rifampicin)

The transmembrane protein system known as efflux pumps transports antibiotics out of bacterial cells which lowers drug concentration under an inhibitory threshold (Nguyen, 2016). The antibiotic-efflux properties of many efflux pumps enable them to remove various antibiotic groups (Nguyen, 2016). The bacterial formation of biofilms through cellular aggregation which creates an extracellular matrix of polymeric substances shields bacteria against antibiotics in addition to immune system defenses. Some bacteria possess natural resistance to particular antimicrobial medications but antibiotic usage increases their likelihood to develop resistance. Different types of bacteria developed multidrug-resistant microorganisms through sharing their resistance genes (Hetta et al., 2023).

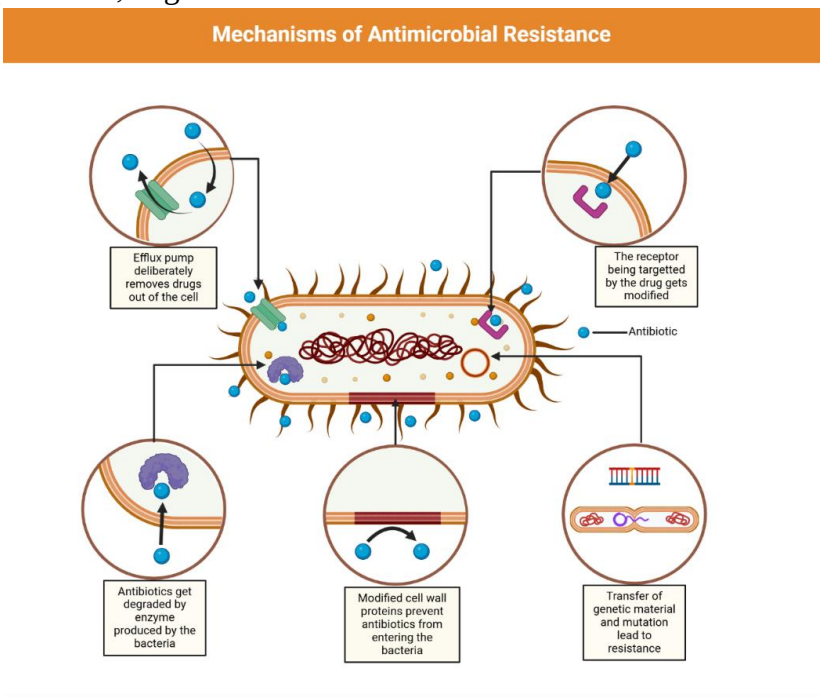


Figure 1: Mechanisms of Antimicrobial Resistance in Bacteria

(Available Sources :https://www.biorender.com/template/mechanisms-of-antimicrobial-resistance)

The resistance mechanisms work through decreased drug penetration into cells and antimicrobial agent enzymatic metabolism and modified antibiotic targets and antimicrobial target protection according to Varela et al. (2021) and Reygaert (2018). When different resistance mechanisms unite in the body they increase bacterial resistance until maximum levels are achieved (Duijkeren et al., 2018). External genes carried by mobile genetic elements generate antimicrobial resistance which covers full antimicrobial classifications (Dermott et al., 2003). Bacterial survival speed has increased due to natural antibiotic resistance development which allows bacteria to adopt resistance through protein gene mutations (Nguyen, 2016).

Trends in Antimicrobial Resistance

Medical safety throughout the world continues to deteriorate as antimicrobial resistance spreads toward numerous bacteria across different global populations at an overwhelming pace. Organisms with multi-drug resistance that spread across different communities create complex infection management issues which lead to increased illness severity along with death rates due to methicillin-resistant Staphylococcus aureus and both vancomycin-resistant Enterococci and carbapenem-resistant Enterobacteriaceae. Human medical practices together with agricultural operations using antibiotics have become the main culprits of bacterial resistance emergence through selective forces that act on bacterial communities. The quick transfer of bacterial genic resistance between different strains exists through horizontal gene transfer by mobile elements that include plasmids and transposons without regard to species boundaries (Sharma et al., 2019). Global antibiotic resistance expansion keeps surging due to how international transport leads to easy strain movement across countries making resistance containment more difficult because of decreasing geographical borders. Several factors have made treatable infections difficult to handle which forces medical professionals to use reserve antibiotics that create significant adverse effects while delivering small therapeutic benefits. Antibacterial resistance demonstrates an extreme threat to medicine treatments as well as cancer therapy and transplantation surgical operations and surgical interventions (Bharadwaj et al., 2022).

Medical costs rise during hospital stays become longer and killing more patients due to antibiotic resistance infections. Multiple bacterial strains that include Escherichia coli ST131 and Klebsiella pneumoniae ST258 as well as st11 together with methicillin-resistant Staphylococcus aureus USA 300

have become widespread across the globe (Wang et al., 2017). Antimicrobial resistance has intensified dramatically because of antibiotic misuse throughout the human-animal medical connection (Dadgostar, 2019). Mutations in M. tuberculosis chromosomes that result from antibiotic selection pressure constitute most of the bacterial resistance (Nguyen, 2016). PCR sequencing technology allows for fast biomarker recognition that provides critical bacterial drug resistance data assisting in better outcomes (Nihms514223.Pdf, n.d.). The government established new laws to control antibiotic applications as feeding additives in livestock through set limitations (Urban-Chmiel et al., 2022).

Future Directions

Several approaches are needed to combat antimicrobial resistance through enhanced monitoring systems along with proper antimicrobial use programs and infection prevention methods combined with new medical treatment developments. Surveillance systems require enduring strength to track resistance development together with emerging threats so healthcare professionals can make suitable public health strategies. The antimicrobial stewardship programs of healthcare organizations enable antibiotic administration which maximizes therapeutic outcomes and avoids unnecessary therapy (English & Gaur, 2009). Proper infection prevention measures between hand hygiene and isolation precautions and environmental disinfection determine how resistant organisms disperse within healthcare areas and community settings. Fresh antibiotic development requires urgent attention to create unique bacterial-fighting agents which will battle resistant bacterial threats in the current situation (El-Kafrawy et al., 2023).

Novel antimicrobial agents demand financial support that links with streamlined regulatory mechanisms and incentives driven by market demand. Research indicates alternative resistant infection prevention methods include combining phage therapy with immunotherapy and antimicrobial peptides. The examination of bacterial persistence and tolerance systems enables researchers to generate well-strategic therapeutic approaches (Singh & Chibale, 2021). Scientists can tackle bacterial resistance by thoroughly researching molecular pathways toward resistance development which involves fast efflux pump activation and faster creation of resistant mutants credited to bacterial stress responses and error-prone DNA repair mechanisms (Lange et al., 2019). Scientific investigations about host-directed therapies and efflux pump inhibitors attempt to achieve maximum treatment levels of resistant tuberculosis. Research on tuberculosis treatment adopts two main approaches that involve drug resistance targets alongside recycling previously used medications (Nguyen, 2016).

The development of quick detection methods for antibiotic resistance genes and resistant phenotypes stands as a top priority to supply correct antibiotic treatment paths. Further research on bacterial-host immunity links offers the possibility to find brand-new therapeutic solutions. The WHO Global Action Plan on Antimicrobial Resistance via Arip et al. (2022) asserts that diagnostic technologies and new treatment medicines and vaccines need simultaneous funding development. The implementation of additional strategies together with increased funding is needed according to Lange et al. (2019) to decrease reported tuberculosis incidence. Several scientific disciplines like microbiology and pharmacology and genomics and engineering must work together because their combined efforts become vital for creating anti-antibiotic resistance innovations. The care team comprising of healthcare providers and patients and community members needs educational campaigns for learning how to use antibiotics responsibly and prevent infections (Gupta & Sharma, 2022).

The fight against antimicrobial resistance needs better antibiotic regulation laws plus advanced research on novel antimicrobial drugs according to Sifri et al. (2019). Worldwide cooperation is essential to fight antimicrobial resistance because it enables organizations to match their actions while sharing effective techniques while delivering global access to working treatments. The creation of innovative pharmaceutical discovery methods depends on total microbiome understanding of the environment to achieve faster antibiotic development (Davies & Davies, 2010). Suspicious curves of resistance require tracking through joint worldwide programs that also facilitate information exchange and evidence-driven treatment implementations (Collignon & McEwen, 2019). Governments should join forces with

pharmaceutical industries and research facilities to establish group approaches which speed up the innovation process of antimicrobial drugs (Ahmed et al., 2024).

Literature Review

Antimicrobial resistance exists as an intricate system containing multiple root causes through which antibiotic excessive use intersects with horizontal gene transfer during natural selection processes (Elshobary et al., 2025). The development of antimicrobial resistance results from three distinct elements which include antibiotic misuse as a direct factor and poor sanitation as an indirect factor together with intrinsic bacterial characteristics as the third category (Bassetti & Garau, 2021). Antimicrobial resistance continues to grow because of multiple converging components which now expose it as a top health challenge worldwide. Antimicrobial resistance expands between epidemiological areas since it appears in all locations and establishes fluid resistance patterns (Oliveira et al., 2024). The outcomes of antimicrobial resistance stretch beyond what we observe to produce elevated morbidity as well as mortality rates and enhanced healthcare costs leading to financial losses. Antimicrobial resistance's clinical outcomes impact patients who undergo two groups of health risks comprised of elderly people and individuals with weak immune systems and patients with chronic illnesses.

Studies of antimicrobial resistance require knowledge from microbiology alongside infectious diseases and pharmacology and public health disciplines. Medical professionals share consensus on antibiotic resistance along with its dispersion mechanisms and its clinical impact as well as its resistance origin basics (Sabtu et al., 2015). Antimicrobial resistance poses a substantial public health risk for the world because antibiotics have become widely overused while resistance genes spread throughout populations (Hoellein et al., 2022). Current tuberculosis control shows increasing strain from continuing development of multidrug-resistant strains of *Mycobacterium tuberculosis* (Nguyen, 2016). The development of *M. tuberculosis* strain resistance from drug-sensitive to extensively drug-resistant types threatens worldwide efforts to manage tuberculosis (Nguyen, 2016). Various medical groups devote extensive efforts to establish new drug treatment protocols for fighting drug-resistant tuberculosis.

Multiple strategies employed by the medical field include natural antimicrobial research and innovative treatment approaches to fight antimicrobial resistance. Multiple new resistance mechanisms discovered together with rapid bacterial gene transfers result in a significantly harder resistance issue. Antimicrobial resistance growth weakens antibiotic potency which forces hospitals to extend patient stays at higher costs and elevates both mortality risks and patient expenses (Levy & Marshall, 2004). Multidrug-resistant pathogens represent the primary public health Issue in current settings as they spread between hospital and community environments (Chiș et al., 2022). The development of antibiotic-resistant pathogens has urged medical workers to request both antibiotic containment measures and structured antibiotic prescription methods (Ahmed et al., 2021).

The complete solution for antimicrobial resistance management involves consistent elements to stop transmission and identify patients and their treatment needs in addition to tracking resistant bacteria evolution. Modern medicine underwent a significant development thanks to antibiotic discoveries but resistance weakened their effectiveness according to Angelini 2024 and Nguyen 2016. Bacterial resistance continues to grow because doctors use antibiotics incorrectly for both animal and human medical care (Bharadwaj et al., 2022). Antibiotic resistance spreads across the entire world throughout all geographical areas and social classes. Antimicrobial resistance presents a hard challenge since healthcare professionals must work with limited treatment choices for resistant infections because antibiotics develop too slowly.

Methodology

Data Collection and Analysis:

This research depends on a thorough literature review method which combines scientific articles and international organization reports with related policy documents. Publicly available databases including World Health Organization Global Antimicrobial Resistance and Use Surveillance System and European

Antimicrobial Resistance Surveillance Network will provide data about antimicrobial resistance rates together with antibiotic consumption patterns and specific resistance mechanism distribution. Statistical procedures will analyze the collected data which allows experts to detect antimicrobial resistance developments throughout different geographic areas as well as healthcare environments.

Search Strategy:

This research employed an extensive search method using PubMed along with Scopus and Web of Science databases through which the search terms included "antimicrobial resistance" "antibiotic resistance mechanisms" "antimicrobial stewardship" and "drug-resistant infections". The research utilized Scopus Web of Science and PubMed databases to search for specific terms relating to antimicrobial stewardship alongside antibiotic resistance mechanisms and antimicrobial resistance and drug-resistant infections. This research will include a review of gray literature where reports and policy documents from organizations like World Health Organization, Centers for Disease Control and Prevention, along with European Centre for Disease Prevention and Control aim to present an extensive view of antimicrobial resistance trends.

Inclusion and Exclusion Criteria:

The research of antimicrobial resistance examined work published in peer-reviewed journals in the time period of 2015 to 2019 (Bulteel et al., 2020). The research included studies which provided original findings concerning antimicrobial resistance rates together with antibiotic consumption patterns plus antimicrobial stewardship intervention results. Research focusing on individual infections like respiratory or urinary tract infections was removed during the analysis. The exclusion criteria applied to studies published in any language other than English together with researches lacking details of their study protocols (Nieto Ramirez et al., 2020).

Epidemiological Surveillance:

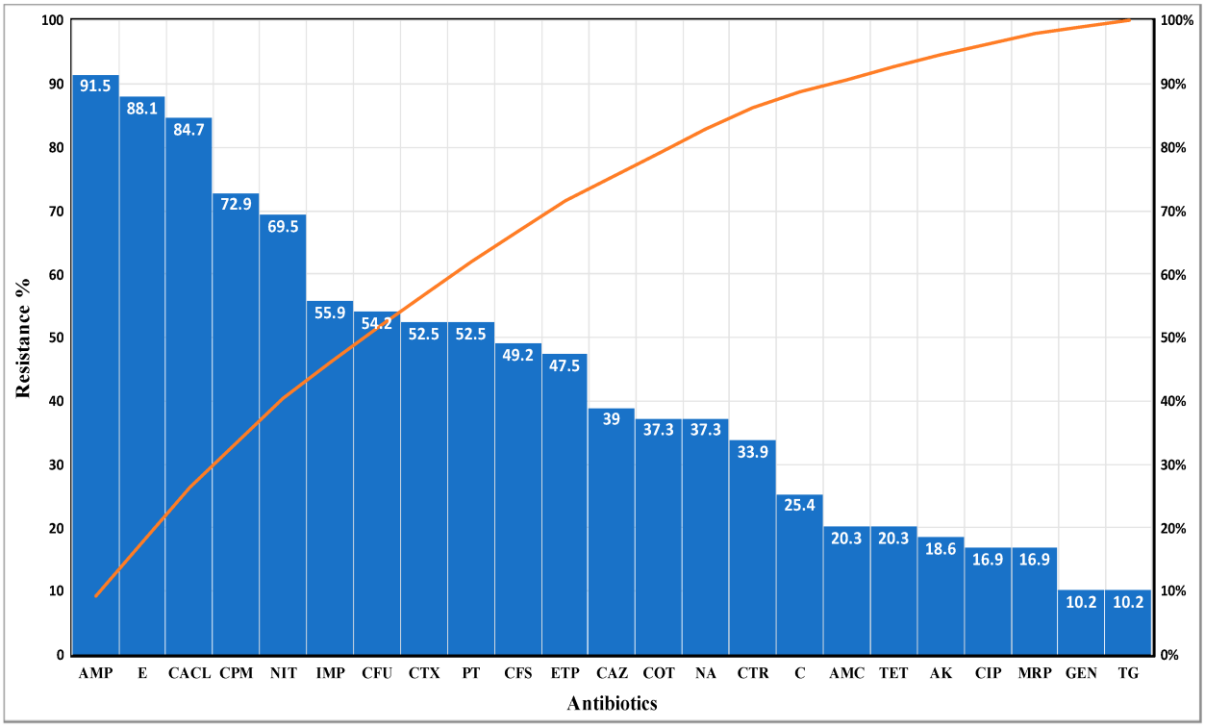
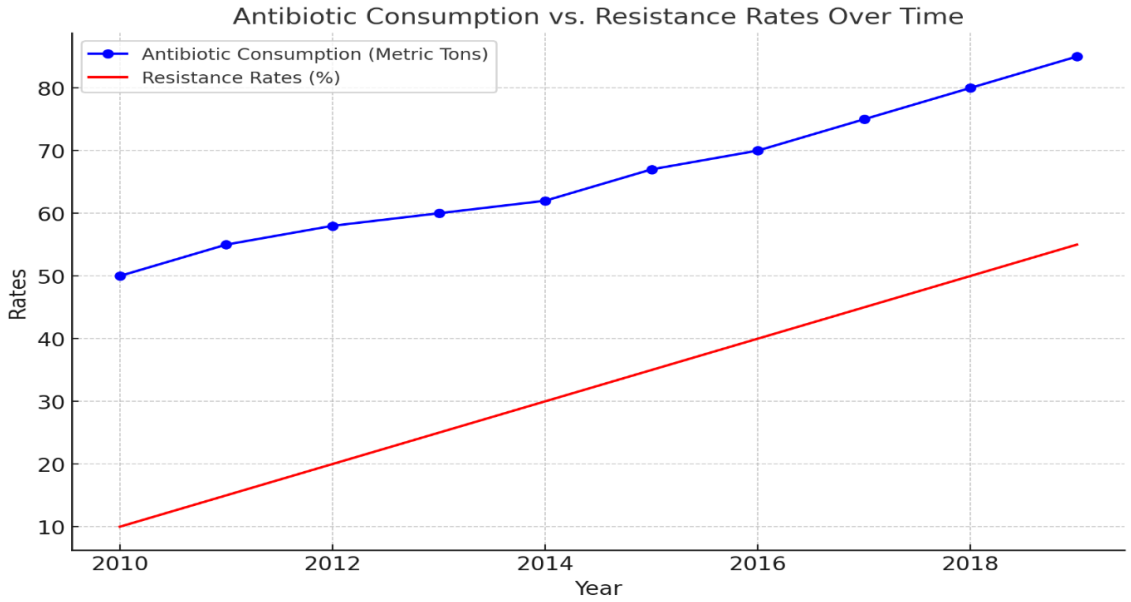


Figure 2: Global Prevalence of Antimicrobial Resistance (AMR)

Bacterial resistance surveillance practices serve as an effective tool to study antimicrobial sensitivity patterns which helps create regional containment methods while improving antibiotic usage (Martínez et al., 2014). A surveillance program functions to create a data system for measuring resistant infection occurrences and patterns which monitors resistant strain movements along with evaluating the outcomes of measures that reduce resistance.

Antimicrobial Resistance: Trends and Patterns

Antimicrobial resistance continues to evolve as a worldwide health emergency requiring complete knowledge about its evolution and how organisms develop resistance. IUO refers to microorganisms retaining their ability to survive against antimicrobial drugs even if these drugs worked in the past (Dadgostar, 2019). The analysis will use both descriptive statistics to present antibacterial resistance rates alongside antibiotic consumption patterns and regression analysis to determine antimicrobial resistance influencing variables. The surveillance programs which track antimicrobial resistance prevalence patterns enable comprehensive understanding for this complex issue (Bulteel et al., 2020). Public health policies receive guidance from these data which also assist in the development of interventions against resistance (PIIS1473309916301906.Pdf, n.d.). The development of drug resistance in bacteria depends on various elements which comprise both patient demographics and previous treatment reactions as well as rifampicin resistance capability (PIIS1473309916301906.Pdf, n.d.). Whole understanding of transmission patterns requires distinguishing between first-time infections versus infections previously treated with antibiotics according to CHIANG et al. (2010).



Graph 1: Antibiotic Consumption vs. Resistance Rates Over Time

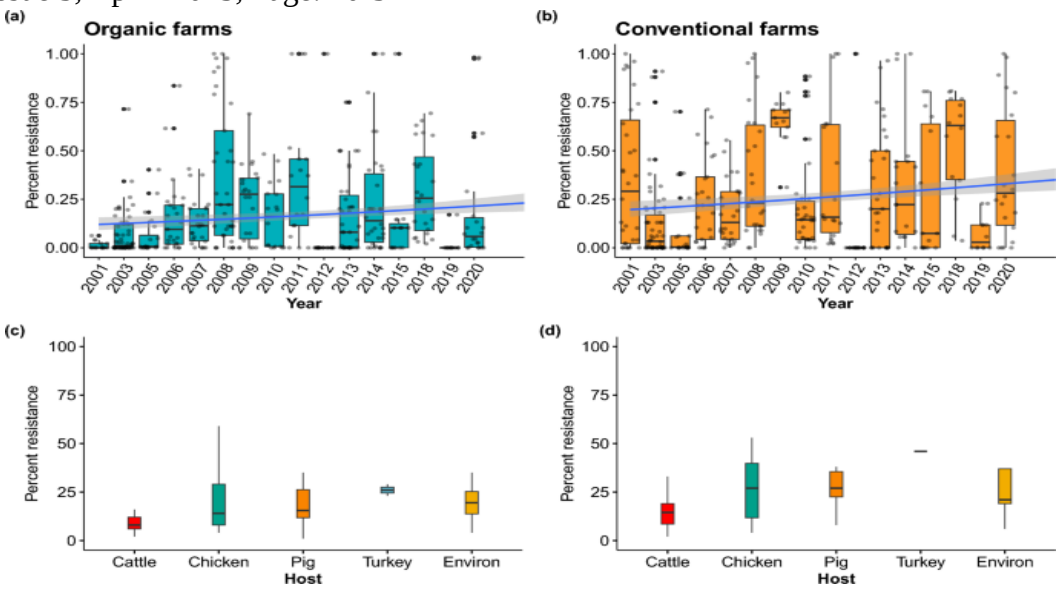


Figure 3: Trends in Antibiotic Resistance Over the Last Decade

New cases presenting antimuscular resistance signal transmission routes whereas resistance reported in treated patients could icome from treatment-resistant organism changes or reinfection with the drug-resistant agent or unobserved resistance mechanisms (CHIANG et al., 2010). During the 2002 to 2007 period CHIANG et al. (2010) retrieved full data about extensively drug-resistant tuberculosis from only 37 countries/territories. The development of operational surveillance systems stands essential for antimicrobial resistance management since these systems maintain continuous production of trustworthy exact data about resistance patterns. Laboratory protocols must be standardized and data management systems need to operate efficiently to obtain the success of surveillance which is based on accurate susceptibility data reporting systems (Saeed et al., 2017). The accessibility of local and institutional data proves essential for clinical patient care even though national and worldwide data shows drug resistance levels (Halstead et al., 2004).

Table 2: Regional Distribution of Key Drug-Resistant Pathogens

Pathogen	Region 1 (North America)	Region 2 (Europe)	Region 3 (Asia)	Region 4 (Africa)
Staphylococcus aureus	35% resistance to methicillin	30% resistance	40% resistance	50% resistance
Klebsiella pneumoniae	28% resistance to carbapenems	35% resistance	45% resistance	60% resistance
Pseudomonas aeruginosa	40% resistance to aminoglycosides	38% resistance	50% resistance	55% resistance
Escherichia coli	20% resistance to fluoroquinolones	18% resistance	25% resistance	40% resistance
Enterococcus faecalis	15% vancomycin resistance	12% vancomycin resistance	18% vancomycin resistance	25% vancomycin resistance

Twenty years back scientists easily recognized bacterial antimicrobial resistance through laboratory tests by checking higher drug concentrations than those needed for regular bacteria (Tenover, 2001). The development of resistance needs stable quality procedures for verifying antimicrobial susceptibility testing

data (Var et al., 2015). The administration of suitable initial antimicrobial medications leads to decreased patient mortality rates particularly for bloodstream infection cases (Shortridge et al., 2018). Drug surveillance systems that perform routine drug sensitivity tests on *Mycobacterium tuberculosis* isolates now operate across an expanding network of countries to check at least rifampicin resistance while covering at least 80% of pulmonary tuberculosis bacteriologically confirmed patients (Dean et al., 2022). Surveys sometimes limit their assessment to public healthcare institutions which neglects private sector patients or concentrate on specific regions rather than covering all national territory leading to possible biased results (Gandhi et al., 2010).

Drug Resistance Detection Methods

The nature of drug resistance in *M. tuberculosis* demonstrates both heterogeneity and consists of different levels including low-, moderate- and high-level drug resistance (Böttger, 2011). The conventional critical concentration detection methods used in clinical laboratories as standard procedure lack effectiveness for detecting the different levels of drug-resistant strains (Böttger, 2011). Laboratory diagnosis serves as the main method to detect drug resistance because conventional drug-susceptibility testing enables *M.tb* growth within specific anti-tuberculosis drugs (Calligaro et al., 2014). Drug susceptibility testing serves as an important phenotypic method to verify resistance while testing new medicines (Parsa et al., 2020).

Table 3: Comparison of Conventional vs. Molecular Methods for Detecting AMR

Method	**Time to Result**	**Cost**	**Efficiency**	**Description**
Conventional Methods	Several days (3-7)	Low to moderate	Moderate	Culture-based methods (e.g., disk diffusion, broth dilution)
Molecular Methods (e.g., PCR)	Several hours (1-6)	Moderate to high	High	Detects resistance mutations directly from clinical samples
Sequencing (Whole Genome or Targeted)	1-2 days	High	Very high	High sensitivity and specificity; detects multiple resistances
Automated Systems (e.g., VITEK)	Few hours	High	High	Provides fast identification and resistance profiling

Detecting Mycobacterium tuberculosis through traditional methods takes an extended period and costs a lot yet results in improper treatment planning that worsens patient distress (Xiong et al., 2024). Molecular methods detect resistance-conferring mutations quickly with accuracy and they function successfully according to Nguyen et al. (2019). Direct specimen testing enables these methods to detect resistance mutations swiftly since they perform better than conventional culture-based diagnostic procedures (Seifert et al., 2015). The patterns of Isoniazid resistance mutations change between different regions which requires consistent monitoring of diagnostic techniques for optimal performance (Seifert et al., 2015).

Identifying drug resistance early becomes essential because such methods cut down treatment initiation times thereby achieving better clinical outcomes while minimizing the spread of resistant strains across the population (Mugenyi et al., 2024). Scientific studies determine major drug resistance mutations by applying molecular genomic DNA sequencing analysis (Dom´ınguez et al., 2016). DNA sequencing works together with numerous detection methods which include solid-phase hybridization and microarrays

combined with real-time PCR and microscopic drug susceptibility assay and slide DST and phage-based assays as well as colorimetric and nitrate reductase analytical techniques to identify anti-TB drug resistance. (CHIANG et al., 2010). The GenoType Mycobacterium TB drug resistance second-line assay enables the detection of XDR *M. tuberculosis* strains within a time span of one to two days according to CHIANG et al. (2010).

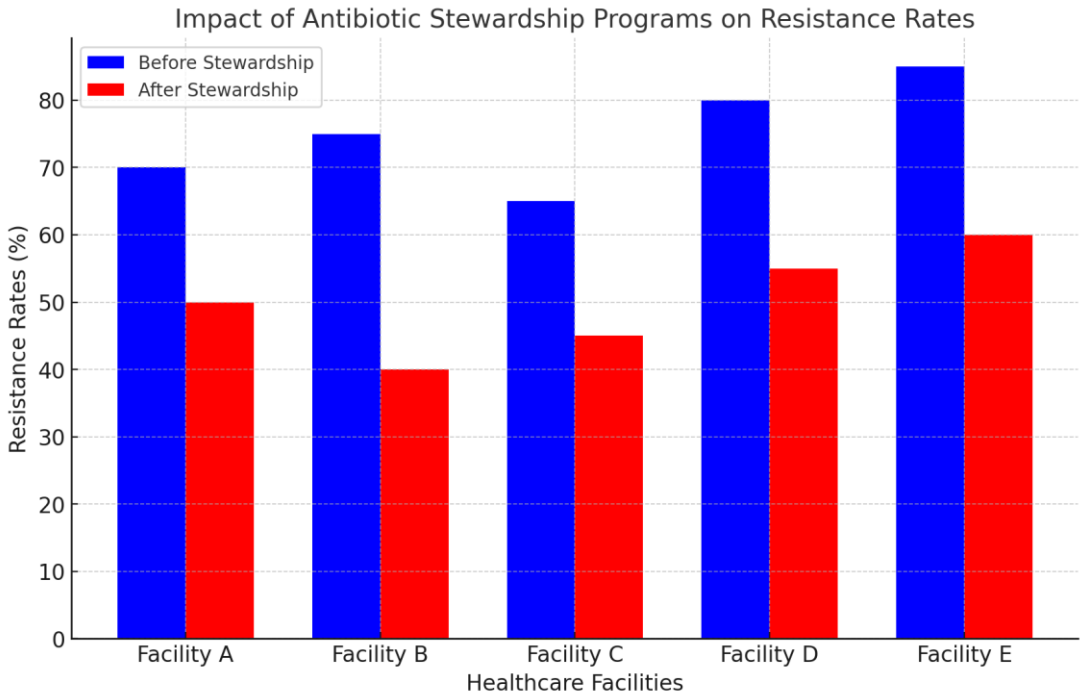
The MTBDRsl test functions as a molecular screening instrument which detects every major resistant mutation occurring against fluoroquinolones, aminoglycosides/cyclic peptides and ethambutol (Brossier et al., 2010). The medical field still needs rapid molecular diagnostic solutions for linezolid and bedaquiline and clofazimine treatments alongside nitroimidazoles and pyrazinamide (Georghiou et al., 2023). The identification of rifampicin and isoniazid resistance in *rpoB* and *katG* genes depends on scientific researchers who perform PCR technology combined with DNA strip assays for reverse hybridization-based examinations (Brossier et al., 2010). Analyzing pyrazinamide resistance requires whole gene sequence assessment and studying the promoter area while distinguishing drug resistance mutations from background sequence variation according to Georghiou et al. (2023). Regular culture techniques miss drug resistance mutations that molecular tests uncover to produce resistant drug properties (Seung et al., 2015).

The World Health Organization accepts several evaluation methods to identify tuberculosis drug responsiveness instead of molecular DST testing. Molecular DST enables scientists to accurately identify second-line resistance to medications according to scientific evidence (Dom´ınguez et al., 2016). The WHO approves the combination of Xpert MTB/RIF assay with LPAs as commercial testing methods for drug resistance detection (Dom´ınguez et al., 2016). Medical facilities can use Xpert MTB/RIF tests to detect both tuberculosis infections and immediate rifampicin resistance mutations as confirmed by WHO (Diallo et al., 2022).

The diagnosis of anti-tuberculosis drug resistance happens through phenotypic drug susceptibility testing (pDST) yet molecular tests enable fast detection of drug-resistant tuberculosis (Shamsher, 2012). Drug susceptibility tests following programmatic guidelines demand resistance evaluation of combinations between isoniazid and rifampin in step 1 followed by testing of ethambutol and streptomycin and pyrazinamide in step 2 and amikacin and kanamycin and capreomycin and ofloxacin in step 3 (CHIANG et al., 2010). The Xpert MTB/RIF assay provides medical staff with rapid detection of *rpoB* gene mutations indicative of rifampin resistance (Tabriz et al., 2020). PCR-SSCP and PCR-RFLP molecular examinations revealed antibiotic-resistant strains because most AMK and CIP-resistant isolates did not possess suggested candidate gene mutations (Tahmasebi et al., 2012). Scientific studies have demonstrated that pncA gene sequence analysis provides useful information for identifying MDR-TB resistance to pyrazinamide medications but examining other gene mutations could maximize their diagnostic potential (Heym et al., 1996).

Future Directions in Combating Antimicrobial Resistance

Innovations in pharmaceutical medicine and therapeutic management need urgent development because antimicrobial resistance grows as a significant healthcare threat. Scientists need to create new resistance mechanism understanding approaches along with diagnostic methods and drug targets to manage this spreading health risk. To prevent antimicrobial resistance from escalating medical science requires both increasing numbers of new medications and therapeutic and prophylactic options (Heym et al., 1996). Scientists develop antimicrobial resistance fighting drugs because researchers see this approach as an effective strategy to combat antimicrobial resistance. Research should maintain its focus on both resistance mechanisms and new drug targets to develop diagnostic tools for handling this escalating threat according to Silva and Palomino (2011). Phage therapy serves as one solution to fight resistant infections when combined with antimicrobial peptides and CRISPR-Cas systems (Hameed et al., 2018; CHIANG et al., 2010).



Graph 2: Impact of Antibiotic Stewardship Programs on Resistance Rates

Alternative therapeutic research by scientists includes combining phage therapy with immunotherapy to approach resistant infections (Desjardins et al., 2016). Scientists use their knowledge of drug resistance molecular and genetic elements to develop strategies that combat drug resistance (Wong et al., 2011). Scientists combat DR-TB through combination solutions which include researching better pharmaceuticals and therapies because these methods decrease the necessity for drug-susceptibility tests according to Singh and Chibale (2021). Scientists must conduct research on resistant evolution and effective multidrug-resistant and extensively drug-resistant TB treatments to solve this issue according to Gillespie and Singh (2011). The development of new therapy approaches and medicinal products stands as an essential requirement because of resistant infectious pathogens (Nguyen, 2016). The current drug-resistant TB emergency needs new medications to reach the market urgently (Nguyen 2016). Both resistance-targeting investigations and the development of new anti-TB drug classes have progressed alongside each other according to Nguyen (2016).

Developing different treatment approaches involves two main strategies: modification of *M. tuberculosis* virulence while adjusting immune response patterns in MTB patients (Gries et al., 2020). Drug discovery methods increased in use during recent years along with high-throughput screening becoming the main research focus (Zuniga et al., 2015). Organizations need to develop new medications in combination with therapeutic approaches together with preventive management strategies for treating drug-resistant TB (Kendall et al. 2019). Scientists need to find new treatment targets along with developing novel diagnostic techniques to meet the escalating TB menace (Bule et al., 2017). The achievement of a 2050 goal for TB elimination is possible according to modeling analyses (Merchant et al., 2022) through integrating advanced tools for active infection detection and dormant infection treatment with available vaccines and drugs.

Any pharmaceutical substance is vulnerable to change which means resistance development will eventually take place. The fundamental basis for extending medication effectiveness in treating tuberculosis stems from system-level analyses and resistance mechanism comprehension (Nguyen, 2016). Modern tuberculosis treatments demand parallel usage of different therapeutic options during new medicine research (Singh & Chibale, 2021). Phage therapy combined with immunotherapy along with medicine repurposing make up the current treatment strategies against tuberculosis. The development

process of drug resistance and the procedures for treating multi-drug resistant and extensively drug-resistant TB should be well-understood by scientists (Singh & Chibale, 2021). A significant challenge exists in TB research because scientists lack understanding about how MTB disables both therapeutic drugs and immune responses (Bhunu et al., 2017).

Results

Drug development and target-based screening and alternative pathway induction serve as methods for fighting multi-drug resistant tuberculosis alongside one another (Singh & Chibale, 2021). Current pharmaceutical products serve as investigatory bases that scientists use to combat drug resistance based on Singh and Chibale (2021). Anti-TB drug research aims at essential Mtb proteins GuaB2 and WecA and Wag31 since these proteins regulate both inosine monophosphate dehydrogenase and arabinogalactan transferase activity and cell division (Nguyen, 2016). New pharmaceutical products possessing drug resistance-strengthening properties constitute the essential approach to manage antimicrobial resistance.

Per Hameed et al. (2018), tuberculosis leads to worldwide fatalities that exceed those recorded from HIV infections. After announcing tuberculosis as a global health emergency in 1993 because of HIV/TB co-infection the WHO prescribes treatment with a six-month drug combination of isoniazid and rifampicin combined with pyrazinamide and ethambutol for drug-susceptible TB. Modern technological advancements did not affect the central position of infectious diseases in health challenges faced by the contemporary world. Tuberculosis takes a place in the World Health Organization's list of top ten international death causes while the organization recognizes it as the leading fatal infectious agent (Dahanayake & Jayasundera, 2020). The global death toll from tuberculosis reached 1.5 million individuals whereas HIV contributed to 214 000 deaths in the year 2020. Worldwide tuberculosis remains among several fatal infectious diseases which take lives from people across all continents. Drug resistance evolution stands as a fundamental cause of mortality that affects human populations. People continue to perish due to the ongoing development of resistant medical conditions (Nadgir & Biswas, 2023). MDR-TB infections are responsible for extensive mortality rates because they necessitate intricate medication protocols (Iacobino et al., 2020).

The growing worldwide tuberculosis health emergency becomes worse because bacterial populations continue to develop drug-resistant traits. The irrational patterns of development related to *Mycobacterium tuberculosis* (*M. tuberculosis*) infection create dangerous tuberculosis outbreaks in regions which hold the pathogen within one-third of their population (Baptista et al., 2021). MDR-TB strains make TB treatment difficult because they lower drug response and extend treatment duration while resulting in negative patient recovery (Cohen et al., 2014). The progressive emergence of Mycobacterium tuberculosis strains which resist multiple and extended drug subsets creates a grave treatment barrier for tuberculosis that results in higher mortality statistics (Mabhula & Singh, 2019). Drugs and novel therapies are necessary for medical research because drug resistance continues without proper control (Black et al., 2014).

Each year the widespread tuberculosis disease acts as a global health concern because it impacts more than 10 million people across the world. The global community believed there were 630,000 MDR tuberculosis cases. Medical practitioners confront mounting dangers because of primary resistance transmission of health care-acquired agents (PIIS1473309913700306.Pdf, n.d.). Molla et al. (2022) rank tuberculosis among the serious infectious disease-related disorders which kill patients worldwide. Drug resistance evolution represents the primary factor responsible for mortality statistics according to Mekonen et al. (2018) and PIIS1473309913700306.Pdf (n.d.). There exists a significant hurdle for medical practitioners to handle drug-resistant TB because few medications remain available for treatment.

The development of improved medical research and advanced tools for diagnosis and disease senator development and vaccine delivery for active and latent disease patients makes the 2050 target achievable. According to Song et al., 2021, antibiotic resistance causes the United States to lose more than 35,000

people annually among the 2.8 million population who experience antibiotic resistance. The global health emergency of antimicrobial resistance exists because the resistance affects human health together with animal health and the health of natural ecosystems worldwide. Scientists have declared antimicrobial resistance to represent the biggest challenge to public health in this modern century (Espinal, 2003). The drug resistance phenomenon presents a severe complication because it blocks all efforts to fight diseases worldwide. Researchers need to understand completely all areas related to antimicrobial resistance transmission and its causal elements to create successful treatments.

Professional health workers track the escalating healthcare issue concerning MTB resistant strains that affect both developed and developing countries worldwide (Mathuria et al., 2013). Results from 2012 Who research indicate that multidrug-resistant tuberculosis strains globally exceeded 5.7% (Falzon et al., 2014). Medical studies indicate MDR-TB strains of the *Mycobacterium tuberculosis* bacteria show resistance to both isoniazid and rifampicin while these drugs form the key therapeutic component of standard anti-tuberculosis medication protocols according to Silva et al., 2011). Extremely drug-resistant tuberculosis belongs to the World Health Organization classification because it shows resistance to both capreomycin and fluoroquinolones and at least one of two injectable drugs like kanamycin or amikacin. Patients with MDR-TB need long-term exposure to second-line antibacterial drugs that yield worse results than first-line medications and produce severe adverse reactions (Seung et al., 2015).

Medical authorities have recently started working on developing antimicrobial drugs following the worldwide rise of antibiotic resistance according to Mancuso et al. (2023). The growth of resistant bacteria known as superbugs creates severe public health dangers since researchers have not developed new antibiotics because antibiotic resistance continues to rise. Bacterial viruses and fungi and parasitic changes to medicines produce antibiotic resistance which leads to difficult infections and fatal diseases from severe states and spreads infectious diseases. Endemic allergies lead to severe damages to patients who experience elevated death rates and need extended durations of hospitalization that results in increased healthcare expenses (Niño-Vega et al., 2025). People adopt inappropriate practices when using antibiotics to treat both viral infections in the upper respiratory tract and when they use antibiotics for animal growth promotion thus accelerating natural antimicrobial resistance patterns (Posada-Perlaza et al., 2019). The global health security system faces serious threats because bacteria transfer their resistant genes which results in the development of multidrug-resistant microorganisms according to Hetta et al. (2023). These microbes continue to resist all newly discovered antibiotics as microbiologists conduct constant antibiotic research (Monika et al., 2020). The global health emergency status of drug resistance emerges because it blocks effective infection protection approaches and disease treatment solutions for bacterial, fungal and parasitic sources (Parmanik et al., 2022).

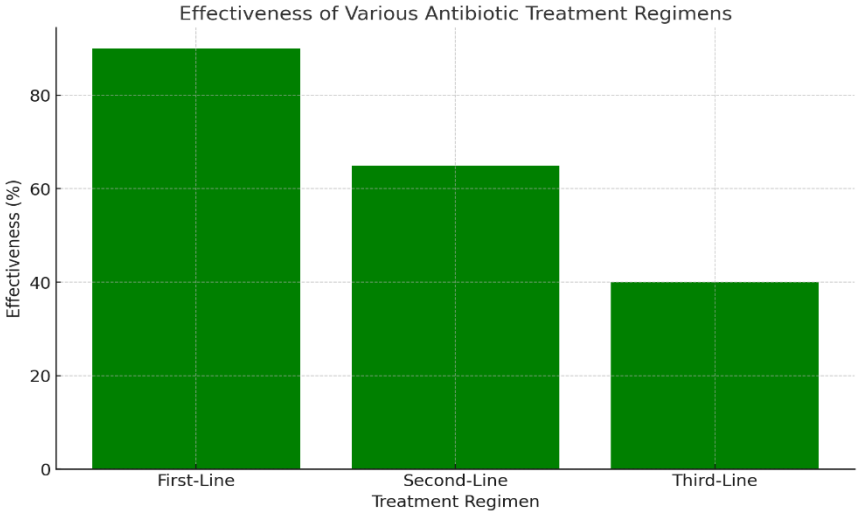
Antimicrobials are responsible for resistance development because of their improper and excessive human medicine applications combined with their animal medicine and agricultural uses (Parmanik et al., 2022). Human healthcare practices an incorrect use of antimicrobials through treating viral infections with antimicrobials along with using broad-spectrum drugs rather than specific narrow-spectrum medications (Tanwar et al., 2014). Antibiotics utilized in mass animal care create antibiotic-resistant microorganisms that humans encounter through food sources and direct contact. Antimicrobial selection pressure allows microorganisms to activate resistance genes that they can further transfer to other bacterial strains (McEwen & Collignon, 2018). Antimicrobial-resistant bacteria spread through the joint actions of international travel, trade and migration. Different factors that researchers have identified allow antimicrobial resistance to disseminate at high speed worldwide (Baho et al., 2018).

Efforts of different biochemical processes combined with genetic systems enable antimicrobial agents to develop complex resistance properties (Russo et al., 2022). The development of bacterial antibiotic resistance includes three primary mechanisms that include antibiotic breakdown by enzymes and modifications of target sites while drugs face reduced absorption and alternative metabolic pathways (Urban-Chmiel et al., 2022). Bacterial antibiotics show resistance through natural properties or acquire new resistant characteristics (Nguyen, 2016). Bacteria demonstrate two resistance mechanisms to treatment by using their natural intrinsic resistance and acquired resistance which develops through

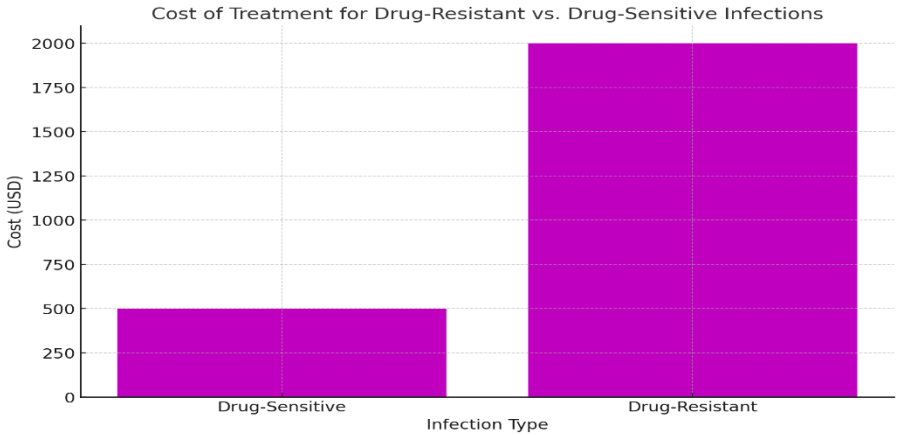
genetic changes and horizontal gene transfer mechanisms (Nguyen, 2016). Research indicates bacteria spread antimicrobial resistance via horizontal gene transfer mechanisms that work either through conjugation transduction and transformation (McCallum et al., 2009). Antimicrobial resistance spreads among environmental features and animal populations due to human activities which makes it a challenging multifaceted issue. The implementation of antibiotic resistance marker genes in genetically modified crops leads to antibiotic resistance emergence according to Capita & Alonso-Calleja (2012). Pollock & Meemelancas (2020) explain that antibiotic usage within human healthcare as well as within animal farming and agricultural settings has increased medical issues according to Verraes et al. (2013). Microorganism evolution naturally produces bacterial resistance yet accelerated development occurs because humans and animals misuse antibacterial medications (Wang et al., 2017).

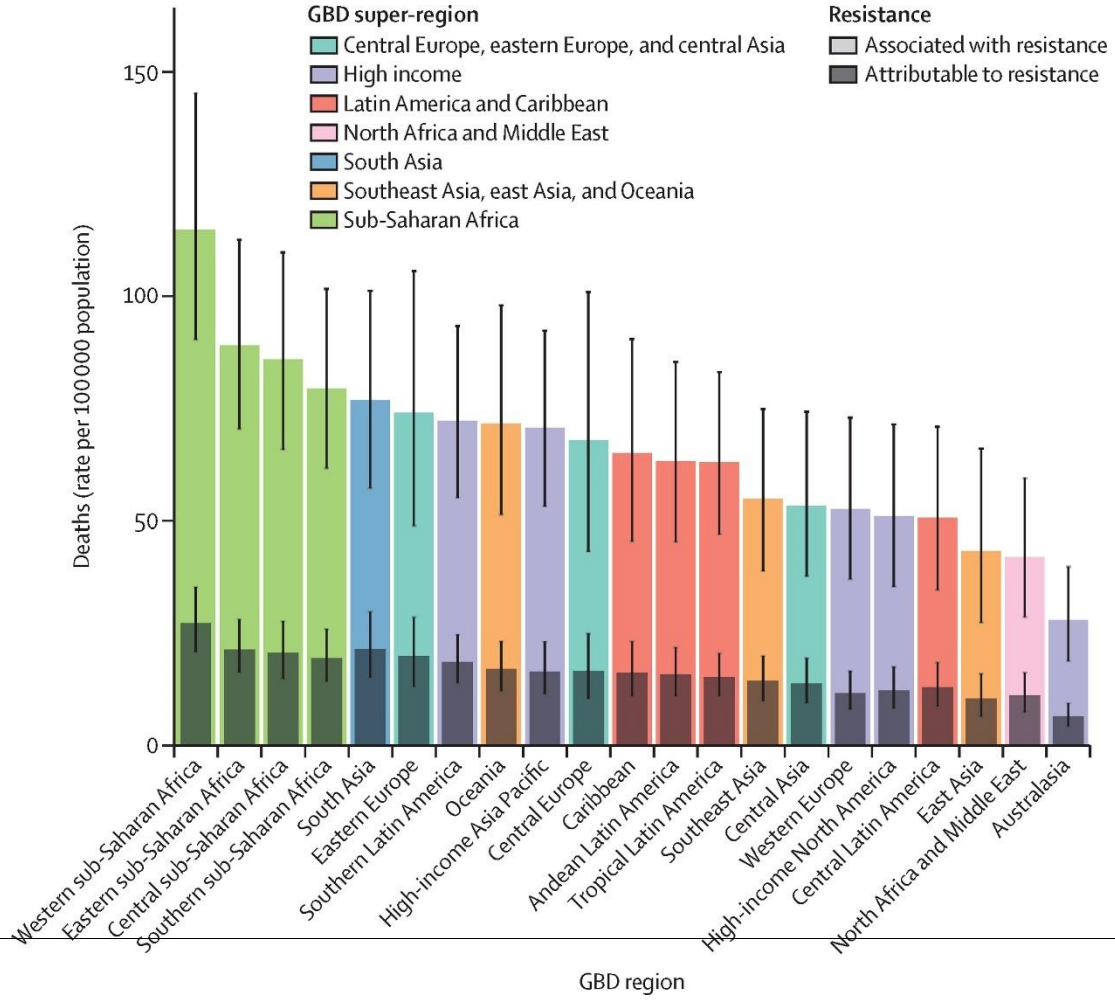
Bacteria create enzymes that weaken antibiotic elements into inactive forms as described by Bandara (2017). Drugs fail to work because antibiotic target sites change during drug binding prevention (Dermott et al., 2003). The bacterial cell membrane becomes permeable at a different rate during this process thus preventing antibiotics from reaching their intracellular targets. The mechanism of bacterial efflux pumps transports antibiotics outside of cells to decrease antibiotic drug levels in bacterial cells (Nguyen, 2016). The ability of bacteria to develop new metabolic pathways grants them resistance against antibiotics because they can survive antibiotic exposure (Duijkeren et al., 2018; Kapoor et al., 2017). The so-called efflux pumps, acting as transmembrane proteins, expel antibiotics from the cell. For this reason, the antibiotic properties are reduced. (Sharma et al., 2019). Different antibiotic export mechanisms become achievable because transport systems demonstrate broad substrate reach which leads to multidrug resistance (Costa et al., 2013). The bacterial cell of *E. coli* has AcrB as its broad-spectrum transporter (Nguyen, 2016). The drug resistance specialization requires regulatory proteins which control the expression patterns of transporters (Nguyen, 2016).

Discussion



Graph 3: Effectiveness of Various Antibiotic Treatment Regimens


Cost of Treatment for Drug-Resistant vs. Drug-Sensitive Infections
Cost (USD)
2000
1750
1500
1250
1000
750
500
250
0
Drug-Sensitive
Drug-Resistant
Infection Type


GBD super-region
Central Europe, eastern Europe, and central Asia
High income
Latin America and Caribbean
North Africa and Middle East
South Asia
Southeast Asia, east Asia, and Oceania
Sub-Saharan Africa
Resistance
Associated with resistance
Attributable to resistance
Deaths (rate per 100000 population)
150
100
50
0
Western sub-Saharan Africa
Eastern sub-Saharan Africa
Central sub-Saharan Africa
Southern sub-Saharan Africa
South Asia
Eastern Europe
Southern Latin America
Oceania
High-income Asia Pacific
Central Europe
Caribbean
Andean Latin America
Tropical Latin America
Southeast Asia
Central Asia
Western Europe
High-income North America
Central Latin America
East Asia
North Africa and Middle East
Australasia
GBD region

Graph 4: Cost of Treatment for Drug-Resistant vs. Drug-Sensitive Infections

Figure 4: Global Spread of Antimicrobial Resistance

Antimicrobial resistance exists as a complex multidimensional challenge that creates substantial health risks for human beings as well as animals and the natural environment. These converging elements result in fast antimicrobial resistance spread throughout the world (Mohammed et al., 2024). The solution to this challenge needs multiple stakeholders to work together including healthcare staff with policymakers and researchers and members of the general public according to Tenover (2006).

Conclusion

Protection against microbial resistance poses an increasing public health danger worldwide because people use antibiotics excessively and incorrectly across human medicine and veterinary care and agricultural settings.

Animal antibiotic use for production purposes worsens antimicrobial resistance through simultaneous drug and bacteria exposure of both humans and animals that happens when animals consume the products or release them into surrounding areas (Rossi et al., 2020). Public health faces a substantial danger from the quick rise of antibiotic resistance while new approaches to fight this problem become important immediately. The implementation of effective stewardship programs needs to occur at every healthcare level to achieve appropriate antimicrobial use. Healthcare providers should present diagnostic tools to help treatment plan selection while pursuing narrow-spectrum drugs and improving treatment schedules.

References

1. Ahmed, N. J., Haseeb, A., Hassali, A. A., & Khan, A. H. (2021). Antimicrobial Stewardship Interventions: Narrative Review. Journal of Pharmaceutical Research International, 62. https://doi.org/10.9734/jpri/2021/v33i23b31422
2. Ahmed, S. K., Hussein, S., Qurbani, K., Ibrahim, R. H., Fareeq, A., Mahmood, K. A., & Mohamed, M. G. (2024). Antimicrobial resistance: Impacts, challenges, and future prospects. Journal of Medicine Surgery and Public Health, 2, 100081. https://doi.org/10.1016/j.glmedi.2024.100081
3. Angelini, P. (2024). Plant-Derived Antimicrobials and Their Crucial Role in Combating Antimicrobial Resistance [Review of Plant-Derived Antimicrobials and Their Crucial Role in Combating Antimicrobial Resistance]. Antibiotics, 13(8), 746. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/antibiotics13080746
4. Arip, M., Selvaraja, M., Mogana, R., Tan, L. F., Leong, M. Y., Tan, P. L., Yap, V. L., Chinnapan, S., Ng, C. T., Abdullah, M., Dharmendra, K., & Jubair, N. (2022). Review on Plant-Based Management in Combating Antimicrobial Resistance - Mechanistic Perspective [Review of Review on Plant-Based Management in Combating Antimicrobial Resistance - Mechanistic Perspective]. Frontiers in Pharmacology, 13. Frontiers Media. https://doi.org/10.3389/fphar.2022.879495

5. Baho, S., Reid, R., & Samarasinghe, S. (2018). Adaptability to Various Growth Conditions of Biofilm Associated Extended-Spectrum-Beta-Lactamases Producing Bacteria. Journal of Infectious Diseases and Diagnosis, 3(1). https://doi.org/10.4172/2576-389x.1000121

6. Bandara, B. M. R. (2017). Medicinal plants to mitigate the problem of antibiotic resistance. Ceylon Journal of Science, 46(3), 1. https://doi.org/10.4038/cjs.v46i3.7437

7. Baptista, R., Bhowmick, S., Shen, J., & Mur, L. A. J. (2021). Molecular Docking Suggests the Targets of Anti-Mycobacterial Natural Products. Molecules, 26(2), 475. https://doi.org/10.3390/molecules26020475

8. Bassetti, M., & Garau, J. (2021). Current and future perspectives in the treatment of multidrug-resistant Gram-negative infections. Journal of Antimicrobial Chemotherapy, 76. https://doi.org/10.1093/jac/dkab352

9. Bharadwaj, A., Rastogi, A., Pandey, S., Gupta, S., & Sohal, J. S. (2022). Multidrug-Resistant Bacteria: Their Mechanism of Action and Prophylaxis [Review of Multidrug-Resistant Bacteria: Their Mechanism of Action and Prophylaxis]. BioMed Research International, 2022, 1. Hindawi Publishing Corporation. https://doi.org/10.1155/2022/5419874

10. Bhunu, B., Mautsa, R., & Mukanganyama, S. (2017). Inhibition of biofilm formation in Mycobacterium smegmatis by Parinari curatellifolia leaf extracts. BMC Complementary and Alternative Medicine, 17(1). https://doi.org/10.1186/s12906-017-1801-5

11. Black, P. A., Warren, R. M., Louw, G., Helden, P. D. van, Victor, T. C., & Kana, B. D. (2014). Energy Metabolism and Drug Efflux in Mycobacterium tuberculosis [Review of Energy Metabolism and Drug Efflux in Mycobacterium tuberculosis]. Antimicrobial Agents and Chemotherapy, 58(5), 2491. American Society for Microbiology. https://doi.org/10.1128/aac.02293-13

12. Böttger, E. C. (2011). The ins and outs of Mycobacterium tuberculosis drug susceptibility testing [Review of The ins and outs of Mycobacterium tuberculosis drug susceptibility testing]. Clinical Microbiology and Infection, 17(8), 1128. Elsevier BV. https://doi.org/10.1111/j.1469-0691.2011.03551.x

13. Brossier, F., Veziris, N., Aubry, A., Jarlier, V., & Sougakoff, W. (2010). Detection by GenoType MTBDRsl Test of Complex Mechanisms of Resistance to Second-Line Drugs and Ethambutol in Multidrug- Resistant Mycobacterium tuberculosis Complex Isolates.

14. Bule, M. H., Maqbool, F., Ahmed, I., Dhama, K., & Iqbal, H. M. N. (2017). Advances in the Treatment Options Towards Drug-Resistant Tuberculosis. International Journal of Pharmacology, 13(7), 746. https://doi.org/10.3923/ijp.2017.746.761

15. Bulteel, A. J. B., Larson, E., & Getahun, H. (2020). Identifying global research gaps to mitigate antimicrobial resistance: A scoping review [Review of Identifying global research gaps to mitigate antimicrobial resistance: A scoping review]. American Journal of Infection Control, 49(6), 818. Elsevier BV. https://doi.org/10.1016/j.ajic.2020.11.024

16. Calligaro, G., Moodley, L., Symons, G., & Dheda, K. (2014). The medical and surgical treatment of drug-resistant tuberculosis. [Review of The medical and surgical treatment of drug-resistant tuberculosis.]. PubMed, 6(3), 186. National Institutes of Health. https://doi.org/10.3978/j.issn.2072-1439.2013.11.11

17. Capita, R., & Alonso-Calleja, C. (2012). Antibiotic-Resistant Bacteria: A Challenge for the Food Industry [Review of Antibiotic-Resistant Bacteria: A Challenge for the Food Industry]. Critical Reviews in Food Science and Nutrition, 53(1), 11. Taylor & Francis. https://doi.org/10.1080/10408398.2010.519837

18. CHIANG, C., Centis, R., & Migliori, G. B. (2010). Drug-resistant tuberculosis: Past, present, future [Review of Drug-resistant tuberculosis: Past, present, future]. Respirology, 15(3), 413. Wiley. https://doi.org/10.1111/j.1440-1843.2010.01738.x

19. Chiș, A. A., Rus, L. L., Morgovan, C., Arseniu, A. M., Frum, A., Vonica-Țincu, A. L., Gligor, F. G., Mureșan, M. L., & Dobrea, C. M. (2022). Microbial Resistance to Antibiotics and Effective Antibiotherapy [Review of Microbial Resistance to Antibiotics and Effective Antibiotherapy]. Biomedicines, 10(5), 1121. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/biomedicines10051121

20. Cohen, K. A., Bishai, W. R., & Pym, A. S. (2014). Molecular Basis of Drug Resistance in Mycobacterium tuberculosis [Review of Molecular Basis of Drug Resistance in Mycobacterium tuberculosis]. Microbiology Spectrum, 2(3). American Society for Microbiology. https://doi.org/10.1128/microbiolspec.mgm2-0036-2013

21. Collignon, P., & McEwen, S. A. (2019). One Health—Its Importance in Helping to Better Control Antimicrobial Resistance [Review of One Health—Its Importance in Helping to Better Control Antimicrobial Resistance]. Tropical Medicine and Infectious Disease, 4(1), 22. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/tropicalmed4010022

22. Costa, S. S., Viveiros, M., Amaral, L., & Couto, I. (2013). Multidrug Efflux Pumps in Staphylococcus aureus: an Update. The Open Microbiology Journal, 7(1), 59. https://doi.org/10.2174/1874285801307010059

23. Dadgostar, P. (2019). Antimicrobial Resistance: Implications and Costs [Review of Antimicrobial Resistance: Implications and Costs]. Infection and Drug Resistance, 3903. Dove Medical Press. https://doi.org/10.2147/idr.s234610

24. Dahanayake, M. H., & Jayasundera, A. C. A. (2020). Nano-based drug delivery optimization for tuberculosis treatment: A review [Review of Nano-based drug delivery optimization for tuberculosis treatment: A review]. Journal of Microbiological Methods, 181, 106127. Elsevier BV. https://doi.org/10.1016/j.mimet.2020.106127

25. Davies, J., & Davies, D. (2010). Origins and Evolution of Antibiotic Resistance [Review of Origins and Evolution of Antibiotic Resistance]. Microbiology and Molecular Biology Reviews, 74(3), 417. American Society for Microbiology. https://doi.org/10.1128/mmbr.00016-10

26. Dean, A., Auguet, O. T., Glaziou, P., Zignol, M., Ismail, N., Kasaeva, T., & Floyd, K. (2022). 25 years of surveillance of drug-resistant tuberculosis: achievements, challenges, and way forward [Review of 25 years of surveillance of drug-resistant tuberculosis: achievements, challenges, and way forward]. The Lancet Infectious Diseases, 22(7). Elsevier BV. https://doi.org/10.1016/s1473-3099(21)00808-2

27. Dermott, P. F. M., Walker, R. D., & White, D. G. (2003). Antimicrobials: Modes of Action and Mechanisms of Resistance [Review of Antimicrobials: Modes of Action and Mechanisms of Resistance]. International Journal of Toxicology, 22(2), 135. SAGE Publishing. https://doi.org/10.1080/10915810305089

28. Desjardins, C. A., Cohen, K. A., Munsamy, V., Abeel, T., Maharaj, K., Walker, B. J., Shea, T., Almeida, D. V., Manson, A. L., Salazar, A., Padayatchi, N., O'Donnell, M. R., Mlisana, K., Wortman, J. R., Birren, S. J., Grosset, J., Earl, A. M., & Pym, A. S. (2016). Genomic and functional analyses of Mycobacterium tuberculosis strains implicate ald in D-cycloserine resistance. Nature Genetics, 48(5), 544. https://doi.org/10.1038/ng.3548

29. Diallo, K., Ansoumana, D., Shinga, W. B., Awa, C., Habibou, S., Ngone, C. M., Alassane, D., & Magloire, M. N. (2022). Performance of GeneXpert in the Diagnosis of Tuberculosis in a Decentralized Area: Example of Hopital De La Paix, in Ziguinchor, Southern Senegal from 2016 to 2018. International Journal of Tropical Diseases, 5(1). https://doi.org/10.23937/2643-461x/1710059

30. Dom´ınguez, J., Boettger, E. C., Cirillo, D., Cobelens, F., Eisenach, K. D., Gagneux, S., Hillemann, D., Horsburgh, R., Molina-Moya, B., Niemann, S., Tortoli, E., Whitelaw, A., Lange, C., & TBNET and RESIST-TB networks, for the. (2016). Clinical implications of molecular drug resistance testing for Mycobacterium tuberculosis: a TBNET/RESIST-TB consensus statement.

31. Duijkeren, E. van, Schink, A., Roberts, M. C., Wang, Y., & Schwarz, Š. (2018). Mechanisms of Bacterial Resistance to Antimicrobial Agents. Microbiology Spectrum, 6(2). https://doi.org/10.1128/microbiolspec.arba-0019-2017

32. El-Kafrawy, S. A., Abbas, A. T., Oelkrug, C., Tahoon, M., Ezzat, S., Zumla, A., & Azhar, E. I. (2023). IgY antibodies: The promising potential to overcome antibiotic resistance [Review of IgY antibodies: The promising potential to overcome antibiotic resistance]. Frontiers in Immunology, 14. Frontiers Media. https://doi.org/10.3389/fimmu.2023.1065353

33. Elshobary, M. E., Badawy, N. K., Kamel, Y. A., Zatioun, A. A., Masriya, H. H., Ammar, M., Mohamed, N. A., Mourad, S., & Assy, A. M. (2025). Combating Antibiotic Resistance: Mechanisms, Multidrug-Resistant Pathogens, and Novel Therapeutic Approaches: An Updated Review [Review of Combating Antibiotic Resistance: Mechanisms, Multidrug-Resistant Pathogens, and Novel Therapeutic Approaches: An Updated Review]. Pharmaceuticals, 18(3), 402. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/ph18030402

34. English, B. K., & Gaur, A. H. (2009). The Use and Abuse of Antibiotics and the Development of Antibiotic Resistance [Review of The Use and Abuse of Antibiotics and the Development of Antibiotic Resistance]. Advances in Experimental Medicine and Biology, 73. Springer Nature. https://doi.org/10.1007/978-1-4419-0981-7_6

35. Espinal, M. (2003). The global situation of MDR-TB [Review of The global situation of MDR-TB]. Tuberculosis, 83, 44. Elsevier BV. https://doi.org/10.1016/s1472-9792(02)00058-6

36. Falzon, D., Mirzayev, F., Wares, F., Baena, I. G., Zignol, M., Nguyen, L., Weyer, K., Jaramillo, E., Floyd, K., & Raviǵlione, M. (2014). Multidrug-resistant tuberculosis around the world: what progress has been made? European Respiratory Journal, 45(1), 150. https://doi.org/10.1183/09031936.00101814

37. Gandhi, N. R., Nunn, P., Dheda, K., Schaaf, H. S., Zignol, M., Soolingen, D. van, Jensen, P., & Bayona, J. (2010). Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. The Lancet, 375(9728), 1830. https://doi.org/10.1016/s0140-6736(10)60410-2

38. Gayathri, K. V., Aishwarya, S., Kumar, P. S., Rajendran, U. R., & Gunasekaran, K. (2021). Metabolic and molecular modelling of zebrafish gut biome to unravel antimicrobial peptides through metagenomics. Microbial Pathogenesis, 154, 104862. https://doi.org/10.1016/j.micpath.2021.104862

39. Georghiou, S. B., Vos, M. de, Velen, K., Miotto, P., Colman, R. E., Cirillo, D. M., Ismail, N., Rodwell, T. C., Suresh, A., & Rühwald, M. (2023). Designing molecular diagnostics for current tuberculosis drug regimens. Emerging Microbes & Infections, 12(1). https://doi.org/10.1080/22221751.2023.2178243

40. Gillespie, S. H., & Singh, K. P. (2011). XDR-TB, What is it; How is it Treated; and why is Therapeutic Failure so High? [Review of XDR-TB, What is it; How is it Treated; and why is Therapeutic Failure so High?]. Recent Patents on Anti-Infective Drug Discovery, 6(2), 77. Bentham Science Publishers. https://doi.org/10.2174/157489111796064641

41. Gries, R., Sala, C., & Rybniker, J. (2020). Host-Directed Therapies and Anti-Virulence Compounds to Address Anti-Microbial Resistant Tuberculosis Infection. Applied Sciences, 10(8), 2688. https://doi.org/10.3390/app10082688

42. Gupta, R., & Sharma, S. (2022). Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis [Review of Role of alternatives to antibiotics in mitigating the antimicrobial resistance crisis]. The Indian Journal of Medical Research, 156(3), 464. Medknow. https://doi.org/10.4103/ijmr.ijmr_3514_20

43. Halstead, D., Gomez, N., & McCarter, Y. S. (2004). Reality of Developing a Community-Wide Antibiogram [Review of Reality of Developing a Community-Wide Antibiogram]. Journal of Clinical Microbiology, 42(1), 1. American Society for Microbiology. https://doi.org/10.1128/jcm.42.1.1-6.2004

44. Hameed, H. M. A., Islam, Md. M., Chhotaray, C., Wang, C., Liu, Y., Tan, Y., Li, X., Tan, S., Delorme, V., Yew, W. W., Liu, J., & Zhang, T. (2018). Molecular Targets Related Drug Resistance Mechanisms in MDR-, XDR-, and TDR-Mycobacterium tuberculosis Strains [Review of Molecular Targets Related Drug Resistance Mechanisms in MDR-, XDR-, and TDR-Mycobacterium tuberculosis Strains]. Frontiers in Cellular and Infection Microbiology, 8. Frontiers Media. https://doi.org/10.3389/fcimb.2018.00114

45. Hetta, Helal F., Ramadan, Y. N., Al-Harbi, A. I., Ahmed, E. A., Battah, B., Ellah, N. H. A., Zanetti, S., & Donadu, M. G. (2023). Nanotechnology as a Promising Approach to Combat Multidrug Resistant Bacteria: A Comprehensive Review and Future Perspectives [Review of Nanotechnology as a Promising Approach to Combat Multidrug Resistant Bacteria: A Comprehensive Review and Future Perspectives]. Biomedicines, 11(2), 413. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/biomedicines11020413

46. Heym, B., Philipp, W., & Cole, S. T. (1996). Mechanisms of Drug Resistance in Mycobacterium tuberculosis [Review of Mechanisms of Drug Resistance in Mycobacterium tuberculosis]. Current Topics in Microbiology and Immunology, 49. Springer Science+Business Media. https://doi.org/10.1007/978-3-642-80166-2_3

47. Hoellein, L., Kaale, E., Mwalwisi, Y. H., Schulze, M. H., Vetye-Maler, C., & Holzgrabe, U. (2022). Emerging Antimicrobial Drug Resistance in Africa and Latin America: Search for Reasons [Review of Emerging Antimicrobial Drug Resistance in Africa and Latin America: Search for Reasons]. Risk Management and Healthcare Policy, 827. Dove Medical Press. https://doi.org/10.2147/rmhp.s205077

48. Iacobino, A., Fattorini, L., & Giannoni, F. (2020). Drug-Resistant Tuberculosis 2020: Where We Stand. Applied Sciences, 10(6), 2153. https://doi.org/10.3390/app10062153

49. Kapoor, G., Saigal, S., & Elongavan, A. (2017). Action and resistance mechanisms of antibiotics: A guide for clinicians [Review of Action and resistance mechanisms of antibiotics: A guide for clinicians]. Journal of Anaesthesiology Clinical Pharmacology, 33(3), 300. Medknow. https://doi.org/10.4103/joacp.joacp_349_15

50. Kendall, E. A., Sahu, S., Pai, M., Fox, G. J., Varaine, F., Cox, H., Cegielski, J. P., Mabote, L., Vassall, A., & Dowdy, D. W. (2019). What will it take to eliminate drug-resistant tuberculosis? The International Journal of Tuberculosis and Lung Disease, 23(5), 535. https://doi.org/10.5588/ijtld.18.0217

51. Lange, C., Dheda, K., Chesov, D., Mandalakas, A. M., Udwadia, Z., & Horsburgh, C. R. (2019). Management of drug-resistant tuberculosis [Review of Management of drug-resistant tuberculosis]. The Lancet, 394(10202), 953. Elsevier BV. https://doi.org/10.1016/s0140-6736(19)31882-3

52. Levy, S. B., & Marshall, B. (2004). Antibacterial resistance worldwide: causes, challenges and responses [Review of Antibacterial resistance worldwide: causes, challenges and responses]. Nature Medicine, 10. Nature Portfolio. https://doi.org/10.1038/nm1145

53. Mabhula, A., & Singh, V. (2019). Drug-resistance inMycobacterium tuberculosis: where we stand [Review of Drug-resistance inMycobacterium tuberculosis: where we stand]. MedChemComm, 10(8), 1342. Royal Society of Chemistry. https://doi.org/10.1039/c9md00057g

54. Mancuso, G., Midiri, A., Gaetano, S. D., Ponzo, E., & Biondo, C. (2023). Tackling Drug-Resistant Tuberculosis: New Challenges from the Old Pathogen Mycobacterium tuberculosis [Review of Tackling Drug-Resistant Tuberculosis: New Challenges from the Old Pathogen Mycobacterium tuberculosis]. Microorganisms, 11(9), 2277. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/microorganisms11092277

55. Martínez, E., Hernández, C., Pallares, C., Pacheco, R., Hurtado, K., & Recalde, M. (2014). Frecuencia de aislamientos microbiológicos y perfil de resistencia bacteriana en 13 clínicas y hospitales de alta complejidad en Santiago de Cali - Colombia. Infectio, 18(1), 3. https://doi.org/10.1016/s0123-9392(14)70734-9

56. Mathuria, J. P., Samaria, J. K., Srivastava, G. N., Mathuria, B. L., Ojha, S. K., & Anupurba, S. (2013). Primary and acquired drug resistance patterns of Mycobacterium tuberculosis isolates in India: A multicenter study. Journal of Infection and Public Health, 6(6), 456. https://doi.org/10.1016/j.jiph.2013.03.003

57. McCallum, N., Berger-Bächi, B., & Senn, M. M. (2009). Regulation of antibiotic resistance in Staphylococcus aureus [Review of Regulation of antibiotic resistance in Staphylococcus aureus]. International Journal of Medical Microbiology, 300, 118. Elsevier BV. https://doi.org/10.1016/j.ijmm.2009.08.015

58. McEwen, S. A., & Collignon, P. (2018). Antimicrobial Resistance: a One Health Perspective [Review of Antimicrobial Resistance: a One Health Perspective]. Microbiology Spectrum, 6(2). American Society for Microbiology. https://doi.org/10.1128/microbiolspec.arba-0009-2017

59. Mekonen, A., Ayele, Y., Berhan, Y., Woldeyohannes, D., Erku, W., & Sisay, S. (2018). Factors which contributed for low quality sputum smears for the detection of acid fast bacilli (AFB) at selected health centers in Ethiopia: A quality control perspective. PLoS ONE, 13(6). https://doi.org/10.1371/journal.pone.0198947

60. Merchant, S. A., Shaikh, M. J. S., & Nadkarni, P. M. (2022). Tuberculosis conundrum - current and future scenarios: A proposed comprehensive approach combining laboratory, imaging, and computing advances [Review of Tuberculosis conundrum - current and future scenarios: A proposed comprehensive approach combining laboratory, imaging, and computing advances]. World Journal of Radiology, 14(6), 114. Baishideng Publishing Group. https://doi.org/10.4329/wjr.v14.i6.114

61. Mohammed, A. M., Mohammed, M., Oleiwi, J. K., Osman, A. F., Adam, T., Betar, B. O., Gopinath, S. C. B., & Ihmedee, F. H. (2024). Enhancing Antimicrobial Resistance Strategies: Leveraging Artificial Intelligence for Improved Outcomes. South African Journal of Chemical Engineering. https://doi.org/10.1016/j.sajce.2024.12.005

62. Molla, K. A., Reta, M. A., & Yimam, Y. (2022). Prevalence of multidrug-resistant tuberculosis in East Africa: A systematic review and meta-analysis [Review of Prevalence of multidrug-resistant tuberculosis in East Africa: A systematic review and meta-analysis]. PLoS ONE, 17(6). Public Library of Science. https://doi.org/10.1371/journal.pone.0270272

63. Monika, Sharma, S., & Kumar, N. (2020). Use of plant derived antimicrobials as an alternative to antibiotics. Journal of Pharmacognosy and Phytochemistry, 9(2), 1524. https://doi.org/10.22271/phyto.2020.v9.i2y.11069

64. Mugenyi, N., Ssewante, N., Baluku, J. B., Bongomin, F., Irene, M. M., Andama, A., & Byakika-Kibwika, P. (2024). Innovative laboratory methods for improved tuberculosis diagnosis and drug-susceptibility testing. Frontiers in Tuberculosis, 1. https://doi.org/10.3389/ftubr.2023.1295979

65. Nadgir, C. A., & Biswas, D. (2023). Antibiotic Resistance and Its Impact on Disease Management [Review of Antibiotic Resistance and Its Impact on Disease Management]. Cureus. Cureus, Inc. https://doi.org/10.7759/cureus.38251

66. Nasiri, M. J., Haeili, M., Ghazi, M., Goudarzi, H., Pormohammad, A., Fooladi, A. A. I., & Feizabadi, M. M. (2017). New Insights in to the Intrinsic and Acquired Drug Resistance Mechanisms in Mycobacteria [Review of New Insights in to the Intrinsic and Acquired Drug Resistance Mechanisms in Mycobacteria]. Frontiers in Microbiology, 8. Frontiers Media. https://doi.org/10.3389/fmicb.2017.00681

67. Nguyen, L. (2016). Antibiotic resistance mechanisms in M. tuberculosis: an update [Review of Antibiotic resistance mechanisms in M. tuberculosis: an update]. Archives of Toxicology, 90(7), 1585. Springer Science+Business Media. https://doi.org/10.1007/s00204-016-1727-6

68. Nguyen, T. N. A., Berre, V. L., Bañuls, A., & Nguyen, T. V. A. (2019). Molecular Diagnosis of Drug-Resistant Tuberculosis; A Literature Review [Review of Molecular Diagnosis of Drug-Resistant Tuberculosis; A Literature Review]. Frontiers in Microbiology, 10. Frontiers Media. https://doi.org/10.3389/fmicb.2019.00794

69. Nieto Ramirez, L. M., Quintero Vargas, K., & Diaz, G. (2020). Review Whole Genome Sequencing for the Analysis of Drug Resistant Strains of Mycobacterium tuberculosis: A Systematic Review for Bedaquiline and Delamanid.

70. nihms514223.pdf. (n.d.).

71. Niño-Vega, G. A., Ortiz-Ramírez, J. A., & López-Romero, E. (2025). Novel Antibacterial Approaches and Therapeutic Strategies. Antibiotics, 14(4), 404. https://doi.org/10.3390/antibiotics14040404

72. Oliveira, M., Antunes, W., Mota, S., Madureira-Carvalho, Á., Dinis-Oliveira, R. J., & Silva, D. D. da. (2024). An Overview of the Recent Advances in Antimicrobial Resistance [Review of An Overview of the Recent Advances in Antimicrobial Resistance]. Microorganisms, 12(9), 1920. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/microorganisms12091920

73. Parmanik, A., Das, S., Kar, B., Bose, A., Dwivedi, G. R., & Pandey, M. M. (2022). Current Treatment Strategies Against Multidrug-Resistant Bacteria: A Review [Review of Current Treatment Strategies Against Multidrug-Resistant Bacteria: A Review]. Current Microbiology, 79(12). Springer Science+Business Media. https://doi.org/10.1007/s00284-022-03061-7

74. Parsa, S., Soleimanpour, S., Derakhshan, M., Nik, L. B., Mir, R., & Izadi, N. (2020). A Review of Phenotypic and Genotypic Methods for Detection of Drug Resistance in Mycobacterium tuberculosis [Review of A Review of Phenotypic and Genotypic Methods for Detection of Drug Resistance in Mycobacterium tuberculosis]. Iranian Journal of Medical Microbiology, 14(2), 108. Iranian Society of Microbiology. https://doi.org/10.30699/ijmm.14.2.108

75. PIIS1473309913700306.pdf. (n.d.).

76. PIIS1473309916301906.pdf. (n.d.).

77. Posada-Perlaza, C. E., Rojas, A. A. R., Porras, P., Adu-Oppong, B., Botero-Coy, A. M., Hernández, F., Anzola, J. M., Díaz, L., Dantas, G., Reyes, A., & Zambrano, M. M. (2019). Bogotá River anthropogenic contamination alters microbial communities and promotes spread of antibiotic resistance genes. Scientific Reports, 9(1). https://doi.org/10.1038/s41598-019-48200-6

78. Reygaert, W. (2018). An overview of the antimicrobial resistance mechanisms of bacteria [Review of An overview of the antimicrobial resistance mechanisms of bacteria]. AIMS Microbiology, 4(3), 482. AIMS Press. https://doi.org/10.3934/microbiol.2018.3.482

79. Rossi, C. C., Pereira, M. F., & Giambiagi-deMarval, M. (2020). Underrated Staphylococcus species and their role in antimicrobial resistance spreading. Genetics and Molecular Biology, 43. https://doi.org/10.1590/1678-4685-gmb-2019-0065

80. Ruíz, L., & Álvarez-Ordóñez, A. (2017). The Role of the Food Chain in the Spread of Antimicrobial Resistance (AMR). In Elsevier eBooks (p. 23). Elsevier BV. https://doi.org/10.1016/b978-0-323-41625-2.00002-8

81. Russo, T. P., Minichino, A., Gargiulo, A. R., Varriale, L., Borrelli, L., Pace, A., Santaniello, A., Pompameo, M., Fioretti, V., & Dipineto, L. (2022). Prevalence and Phenotypic Antimicrobial Resistance among ESKAPE Bacteria and Enterobacterales Strains in Wild Birds. Antibiotics, 11(12), 1825. https://doi.org/10.3390/antibiotics11121825

82. Sabtu, N., Enoch, D., & Brown, N. M. (2015). Antibiotic resistance: what, why, where, when and how? [Review of Antibiotic resistance: what, why, where, when and how?]. British Medical Bulletin. Oxford University Press. https://doi.org/10.1093/bmb/ldv041

83. Saeed, D. K., Hasan, R., Naim, M., Zafar, A., Khan, E., Jabeen, K., Irfan, S., Ahmed, I., Zeeshan, M., Wajidali, Z., Farooqi, J., Shakoor, S., Chagla, A. H., & Rao, J. (2017). Readiness for antimicrobial resistance (AMR) surveillance in Pakistan; a model for laboratory strengthening. Antimicrobial Resistance and Infection Control, 6(1). https://doi.org/10.1186/s13756-017-0260-6

84. Seifert, M., Catanzaro, D. G., Catanzaro, A., & Rodwell, T. C. (2015). Genetic Mutations Associated with Isoniazid Resistance in Mycobacterium tuberculosis: A Systematic Review [Review of Genetic Mutations Associated with Isoniazid Resistance in Mycobacterium tuberculosis: A Systematic Review]. PLoS ONE, 10(3). Public Library of Science. https://doi.org/10.1371/journal.pone.0119628

85. Seung, K. J., Keshavjee, S., & Rich, M. (2015). Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis [Review of Multidrug-Resistant Tuberculosis and Extensively Drug-Resistant Tuberculosis]. Cold Spring Harbor Perspectives in Medicine, 5(9). Cold Spring Harbor Laboratory Press. https://doi.org/10.1101/cshperspect.a017863

86. Shamsher, S. (2012). Diagnostic Methods for Mycobacterium tuberculosis and Challenges in Its Detection in India. In InTech eBooks. https://doi.org/10.5772/31714

87. Sharma, A., Gupta, V., & Pathania, R. (2019). Efflux pump inhibitors for bacterial pathogens: From bench to bedside [Review of Efflux pump inhibitors for bacterial pathogens: From bench to bedside]. The Indian Journal of Medical Research, 149(2), 129. Medknow. https://doi.org/10.4103/ijmr.ijmr_2079_17

88. Shortridge, D., Pfaller, M. A., Castanheira, M., & Flamm, R. K. (2018). Antimicrobial activity of ceftolozane-tazobactam tested against Enterobacteriaceae and Pseudomonas aeruginosa collected from patients with bloodstream infections isolated

in United States hospitals (2013–2015) as part of the Program to Assess Ceftolozane-Tazobactam Susceptibility (PACTS) surveillance program. Diagnostic Microbiology and Infectious Disease, 92(2), 158. https://doi.org/10.1016/j.diagmicrobio.2018.05.011

89. Sifri, Z. C., Chokshi, A., Cennimo, D., & Horng, H. (2019). Global contributors to antibiotic resistance. Journal of Global Infectious Diseases, 11(1), 36. https://doi.org/10.4103/jgid.jgid_110_18

90. Silva, P. E. A. da, & Palomino, J. C. (2011). Molecular basis and mechanisms of drug resistance in Mycobacterium tuberculosis: classical and new drugs [Review of Molecular basis and mechanisms of drug resistance in Mycobacterium tuberculosis: classical and new drugs]. Journal of Antimicrobial Chemotherapy, 66(7), 1417. Oxford University Press. https://doi.org/10.1093/jac/dkr173

91. Silva, P. E. A., Groll, A., Martin, A., & Palomino, J. C. (2011). E¥uxas a mechanism for drug resistance in Mycobacterium tuberculosis.

92. Singh, V., & Chibale, K. (2021). Strategies to Combat Multi-Drug Resistance in Tuberculosis [Review of Strategies to Combat Multi-Drug Resistance in Tuberculosis]. Accounts of Chemical Research, 54(10), 2361. American Chemical Society. https://doi.org/10.1021/acs.accounts.0c00878

93. Song, S., Gao, P., Sun, L., Kang, D., Kongsted, J., Poongavanam, V., Zhan, P., & Liu, X. (2021). Recent developments in the medicinal chemistry of single boron atom-containing compounds [Review of Recent developments in the medicinal chemistry of single boron atom-containing compounds]. Acta Pharmaceutica Sinica B, 11(10), 3035. Elsevier BV. https://doi.org/10.1016/j.apsb.2021.01.010

94. Tabriz, N., Skak, K., Kassayeva, L. T., Omarkulov, B., & Grigolashvili, M. (2020). Efficacy of the Xpert MTB/RIF Assay in Multidrug-Resistant Tuberculosis. Microbial Drug Resistance, 26(8), 997. https://doi.org/10.1089/mdr.2019.0326

95. Tahmasebi, P., Farnia, P., Sheikholslami, F., & Velayati, A. A. (2012). Rapid identification of extensively and extremely drug-resistant tuberculosis from multidrug resistant strains; using PCR-RFLP and PCR-SSCP. PubMed. https://pubmed.ncbi.nlm.nih.gov/23205246

96. Tanwar, J., Das, S., Fatima, Z., & Hameed, S. (2014). Multidrug Resistance: An Emerging Crisis [Review of Multidrug Resistance: An Emerging Crisis]. Interdisciplinary Perspectives on Infectious Diseases, 2014, 1. Hindawi Publishing Corporation. https://doi.org/10.1155/2014/541340

97. Tenover, F. C. (2001). Development and Spread of Bacterial Resistance to Antimicrobial Agents: An Overview [Review of Development and Spread of Bacterial Resistance to Antimicrobial Agents: An Overview]. Clinical Infectious Diseases, 33. Oxford University Press. https://doi.org/10.1086/321834

98. Tenover, F. C. (2006). Mechanisms of Antimicrobial Resistance in Bacteria [Review of Mechanisms of Antimicrobial Resistance in Bacteria]. The American Journal of Medicine, 119(6). Elsevier BV. https://doi.org/10.1016/j.amjmed.2006.03.011

99. Urban-Chmiel, R., Marek, A., Stępień–Pyśniak, D., Wieczorek, K., Dec, M., Nowaczek, A., & Osek, J. (2022). Antibiotic Resistance in Bacteria—A Review [Review of Antibiotic Resistance in Bacteria—A Review]. Antibiotics, 11(8), 1079. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/antibiotics11081079

100. Var, S. K., Hadi, R., & Khardori, N. M. (2015). Evaluation of regional antibiograms to monitor antimicrobial resistance in hampton roads, Virginia. Annals of Clinical Microbiology and Antimicrobials, 14(1). https://doi.org/10.1186/s12941-015-0080-6

101. Varela, M. F., Stephen, J., Lekshmi, M., Ojha, M., Wenzel, N., Sanford, L. M., Hernandez, A. J., Parvathi, A., & Kumar, S. (2021). Bacterial Resistance to Antimicrobial Agents [Review of Bacterial Resistance to Antimicrobial Agents]. Antibiotics, 10(5), 593. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/antibiotics10050593

102. Verraes, C., Boxstael, S. V., Meervenne, E. V., Coillie, E. V., Butaye, P., Catry, B., Schaetzen, M.-A. de, Huffel, X. V., Imberechts, H., Dierick, K., Daube, G., Saegerman, C., Block, J. D., Dewulf, J., & Herman, L. (2013). Antimicrobial Resistance in the Food Chain: A Review [Review of Antimicrobial Resistance in the Food Chain: A Review]. International Journal of Environmental Research and Public Health, 10(7), 2643. Multidisciplinary Digital Publishing Institute. https://doi.org/10.3390/ijerph10072643

103. Wong, S. Y., Lee, J. S., Kwak, H.-K., Via, L. E., Boshoff, H. I., & Barry, C. E. (2011). Mutations in gidB Confer Low-Level Streptomycin Resistance in Mycobacterium tuberculosis. Antimicrobial Agents and Chemotherapy, 55(6), 2515. https://doi.org/10.1128/aac.01814-10

104. Xiong, X., Zhang, X.-D., Yan, J., Huang, T.-T., Liu, Z., Li, Z., Wang, L., & Li, F. (2024). Identification of Mycobacterium tuberculosis Resistance to Common Antibiotics: An Overview of Current Methods and Techniques. Infection and Drug Resistance, 1491. https://doi.org/10.2147/idr.s457308

105. Zuniga, E. S., Early, J. V., & Parish, T. (2015). The Future for Early-Stage Tuberculosis Drug Discovery [Review of The Future for Early-Stage Tuberculosis Drug Discovery]. Future Microbiology, 10(2), 217. Future Medicine. https://doi.org/10.2217/fmb.14.125