Pakistan Veterinary Journal

ISSN: 0253-8318 (PRINT), 2074-7764 (ONLINE)
DOI: 10.29261/pakvetj/2025.327

REVIEW ARTICLE

Tackling Antimicrobial Resistance Using One Health Approach: A Review of Mechanisms, Current Therapies and Policies

Khalil Mohamed[1]*

[1]Department of Epidemiology and Medical Statistics, Faculty of Public Health and Health Informatics, Umm Al-Qura University, Saudi Arabia
*Corresponding author: khali72@gmail.com; kmismail@uqu.edu.sa

ARTICLE HISTORY (25-773)

Received: August 04, 2025
Revised: December 22, 2025
Accepted: December 24, 2025
Published online: December 26, 2025

Key words:

A B S T R A C T

Antimicrobial resistance poses a global threat to economic stability, public health, and food security, contributing to the deaths of an estimated 5 million people annually associated with resistant infections. This review examines the current knowledge of antimicrobial resistance (AMR) by analyzing the complex, multi-sectoral transformation dynamics of resistant pathogens among human, animal and environmental reservoirs using One Health principles. Novel antibiotics, bacteriophage therapy, CRISPR-Cas systems, and antimicrobial peptides are innovative therapies with promising results but face significant challenges including high costs, stability, and scalability limitations. Surveillance, policy enforcement, and public awareness are key strategies for addressing the AMR through One Health approach, which provides an integrated framework linking human, animal, and environmental health. Practical examples from Sweden and Jordan demonstrate the potential of regulations and multi-sectoral collaboration. The significant hurdles arise because of the global gap in coordination, funding and behavioral resistance. This review underscores the need for advanced diagnostics, sustained research, and equitable access to interventions for combating AMR. Addressing this global crisis requires coordinated efforts encompassing scientific innovation, community engagement, and effective policymaking to protect future generations.

To Cite This Article: Mohamed K, 2025. Tackling antimicrobial resistance using One Health approach: a review of mechanisms, current therapies and policies. Pak Vet J, 45(4): 1503-1513. http://dx.doi.org/10.29261/pakvetj/2025.327

INTRODUCTION

Microbes develop resistance to antimicrobial agents, a process defined as antimicrobial resistance (AMR) (Tang *et al.*, 2023). This resistance affects all classes of microbes, including viruses, bacteria, parasites, and fungi (Hazards *et al.*, 2021; Tang *et al.*, 2023). Antimicrobial resistance (AMR) enables bacteria to resist antibiotic treatment and complicates the management of infection (Mancuso *et al.*, 2021; Tarin-Pello *et al.*, 2022; Tang *et al.*, 2023). When a disease-causing bacterium or microbe faces challenges like antibiotics, they adapt and becomes stronger by developing resistance against those antibiotics. This selective pressure drives the emergence of resistance (Gan *et al.*, 2024). Rapid bacterial evolution driven by selective pressure from antibiotic use is the primary driver of antimicrobial resistance. Resistance development is accelerated through spontaneous mutation, horizontal gene transfer, and an increase in selective pressure from antibiotic overuse (Normark and Normark, 2002; Andersson *et al.*, 2020). Infections caused by antimicrobial-resistant microbes require more expensive alternative therapies and are difficult to treat (Pinheiro *et al.*, 2020; Tarin-Pello *et al.*, 2022). The spread of antimicrobial resistance can be slowed by narrow-spectrum antibiotics use and improved hygienic practices (Kollef and Micek, 2005; Harbarth *et al.*, 2015). These antimicrobial resistant microbes pose a dual threat to both animal and human health, while risking the global environmental integrity, which demands comprehensive One Health approach (Aslam *et al.*, 2021).

Bacterial infections have historically caused diseases in both humans and animals (Pearce-Duvet, 2006; Breitschwerdt *et al.*, 2010). While antibiotics effectively manage microbial infections, their continued use and misuse paradoxically drive the development of antimicrobial resistance (Fraise, 2002; Deresinski, 2007). If no measures are taken to reduce the present emergence and spread of AMR, it is estimated to cause a financial loss of 100 trillion dollars and deaths of 100 million people by 2050 (Moyer *et al.*, 2017; Bastawrous and Suni, 2020). According to the World Health Organization (WHO), 5 million deaths are associated with antimicrobial-resistant

infections annually, making them top global public health threat (Habte-Gabr, 2008; Walsh *et al.*, 2023). Moreover, the WHO reports that AMR caused 1.27 million deaths in 2019 (Aslam *et al.*, 2024). AMR spread results from population growth, increased human-animal contact, intensive farming practices, pollution, climate change, and ecosystem degradation (Woolhouse *et al.*, 2015; Hazards *et al.*, 2021; Magnano San Lio *et al.*, 2023). These factors also drive the emergence of new pathogens, for which the development of new antimicrobial agents is required (Cassell and Mekalanos, 2001).

The shared ecosystem of animals and humans facilitates the spread of resistant bacteria and antimicrobial genes between species (Da Costa *et al.*, 2013; Baquero *et al.*, 2019). Because of the ecosystem and reliance on animals for various products and by-products, human health is directly linked to them. This environmental expansion of resistance genes can trigger pandemics at the regional or global level. Conventional therapies face limitations in controlling and preventing infectious diseases, for which One Health approach has emerged (Mackenzie *et al.*, 2013; Ellwanger *et al.*, 2021). As a transdisciplinary approach, One Health shifts the focus from disease control and treatment to surveillance and disease monitoring (Conrad *et al.*, 2009; Kelly *et al.*, 2017; Scarpa and Casu, 2024). The integrating research on resistant microbes through One Health approach enhances the ability to understand the complex epidemiology of antimicrobial resistance, which is revolving in animals, humans and the environment (Hernando-Amado *et al.*, 2019; Aslam *et al.*, 2021).

This review examines the latest findings, emergence and spread of AMR, and techniques to tackle the AMR through One Health approach. It provides a base reference for understanding future scientific inventions of this global health threat.

MATERIALS AND METHODS

This review utilizes Google Scholar (www.scholar.google.com) as primary search platform. Other secondary websites include the use of Scopus (www.scopus.com), PubMed (pubmed.ncbi.nlm.nih.gov), ResearchGate (www.researchgate.net) and ScienceDirect (www.sciencedirect.com). The keywords used across Google Scholar, ScienceDirect, PubMed, and ResearchGate were "Antimicrobial activity, AND, antimicrobial resistance, AND One Health approach," which showed results and used as the basis for making this review.

Mechanisms for developing antimicrobial resistance: Understanding the drivers and mechanisms of AMR is essential for mitigating its threats to human health and biosecurity. While microorganisms naturally develop antimicrobial resistance, its selection and amplification are primarily driven by exposure to antimicrobials in health care, agriculture, and environmental settings (Serwecińska, 2020; Hazards *et al.*, 2021; Irfan *et al.*, 2022). The standards of infection control, sanitation, access to clean water, travel, migration, availability of quality antimicrobials, and diagnostics can affect the transmission of AMR (Abd El Ghany *et al.*, 2020; Endale *et al.*, 2023). Microorganisms employ five primary mechanisms of resistance through molecular and genetic processes. These include enzymatic drug inactivation, target site modification, reduced drug accumulation, metabolic pathways bypass, and horizontal gene transfer (McManus, 1997; Kumar and Varela, 2013; Belay *et al.*, 2024).

Antimicrobial resistance (AMR) is not merely a set of bacterial defense mechanisms but rather product of active evolutionary processes driven by selective pressure from antimicrobial use. Two primary evolutionary mechanisms drive resistance development: (1) spontaneous mutations that generate genetic variation, and (2) horizontal gene transfer that rapidly spreads previously evolved resistance genes. These evolutionary adaptations are manifested in the following mechanisms described as enzymatic inactivation, target modification, efflux and metabolism bypass. This evolutionary perspective of AMR is important to understand, as it provides an explanation of the velocity, tenacity, and versatility of resistant pathogens at the interface of humans, animals, and the environment.

Enzymatic degradation is the most common AMR strategy by microorganisms through the production of enzymes that degrade or exhibit chemical modification of antimicrobial compounds, making them ineffective before they can act on their targets (Wright, 2005; Annunziato, 2019; Murugaiyan *et al.*, 2022). Aminoglycoside provides antimicrobial activity by binding to the bacterial ribosomes, resulting in inhibition of bacterial protein synthesis (Eustice and Wilhelm, 1984; Davis, 1987). Microorganisms resist these antimicrobial agents through acetyltransferase, phosphotransferase, or nucleotidyltransferases and chemically modify the drug, preventing it from binding to ribosomes (Wright, 2005; Van Duijkeren *et al.*, 2018; El-Khoury *et al.*, 2022). Bacteria resist chloramphenicol through enzyme inactivation via chloramphenicol acetyltransferases (CAT). This CAT-mediated inactivation blocks the chloramphenicol's interaction with the 50S ribosomal subunit (Schwarz *et al.*, 2004). The β-lactam antibiotics bind to the penicillin-binding proteins (PBPs) and inhibit bacterial cell wall synthesis. Bacteria resist β-lactam antibiotics by producing β-lactamases, enzymes that hydrolyze the β-lactam ring structure, inactivating cephalosporins and penicillins (Fernandes *et al.*, 2013; King *et al.*, 2017). Extended-spectrum β-lactamases (ESBLs) can inactivate the third generation of cephalosporin antibiotics.

Colistin (polymyxin E), a cationic lipopeptide antibiotic that is a derivative of *Paenibacillus polymyxa* and is used as a last-resort antibiotic against severe infections caused by multidrug-resistant Gram-negative bacteria. It interacts with lipid A of lipopolysaccharide (LPS), which destabilizes the outer membrane, resulting in bacterial death. Colistin resistance is an emerging AMR concern and is primarily caused by lipid A modification through either chromosomal mutations in PhoPQ and PmrAB regulatory systems or via plasmid-mediated *mcr* genes that rapidly spread among bacterial populations. In livestock and poultry production, particularly in pigs and chickens, therapeutic and prophylactic use of colistin creates high selection pressure. Consequently, resistant bacteria and *mcr* genes are spread in the environment, meat products, and food animals, and are transmitted further

along the food chain to humans, posing a significant One Health issue.

Bacteria achieve reduced drug accumulation by limiting intracellular drug concentration. Efflux pumps and decreased membrane permeability are the primary mechanisms mediating this resistance strategy (Pagès and Amaral, 2009; Masi *et al.*, 2017). Some microorganisms develop alternative metabolic pathways, allowing them to bypass the inhibitory effects of antimicrobial drugs and thus produce AMR (Annunziato, 2019; Moo *et al.*, 2020). Sulfonamides and trimethoprim inhibit the folate synthesis, which is essential for DNA synthesis. However, resistant bacterial strains possessing dihydrofolate reductase genes circumvent this inhibition by modifying their metabolic pathways (Capasso and Supuran, 2019).

Bacteria exchange genetic material through three primary mechanisms: conjugation (plasmid transfer), transduction (phage-mediated transfer), and transformation (environmental DNA uptake). In conjugation, bacteria transfer plasmids carrying resistance genes to other bacteria through direct contact (Leungtongkam *et al.*, 2018). In transduction, bacteriophages transfer resistance genes between two bacteria (Volkova *et al.*, 2014; Colavecchio *et al.*, 2017; Fillol-Salom *et al.*, 2019). Transformation occurs when bacteria incorporate exogenous genetic material from the environment into their chromosomes. *Streptococcus pneumoniae* exemplifies this process by acquiring and incorporating DNA from the commensal streptococci (Claverys *et al.*, 2000; Johnsborg and Håvarstein, 2009; Marks *et al.*, 2012). Bacteria modify antimicrobial target sites, reduce drug binding affinity and render the antimicrobials ineffective (Reinert *et al.*, 2003; Jalava *et al.*, 2004; Nye *et al.*, 2019). The fluoroquinolones are rendered ineffective against microorganisms because their mechanism of action involves targeting the DNA gyrase and topoisomerase IV enzymes, leading to the development of resistance. Resistance develops when these mutations alter enzyme structure, preventing drug binding.

Reservoirs of antimicrobial resistance: Reservoirs serve as evolutionary channels where resistant genes are maintained, recombined and selected. The reservoirs of AMR refer to a setting where microorganisms having antimicrobial resistant properties persist, survive, and spread in the environment, humans, and animals (Despotovic *et al.*, 2023). Ticks are the biological vectors for various pathogens like anaplasmosis, babesia, etc. which contribute to the livestock AMR through bacterial transmission, protozoal parasites can also contribute to the development of resistance (Nawaz *et al*., 2020). These bacteria spread from reservoirs at both the global and local levels (Fig. 1). These reservoirs can be natural or come from man-made environments. Understanding these reservoirs is essential for controlling the global threat of the antimicrobial resistance crisis.

Due to frequent and inappropriate antibiotic use, the human gut microbiome is a notable reservoir for AMR. Trillions of bacteria take up residence in the human gut, and studies have revealed that certain bacteria within this environment carry antibiotic resistant genes (ARG). These genes transfer between commensal bacteria and pathogens through horizontal gene transfer mechanisms. Healthy individuals harbor antibiotic-resistant strains of *Enterococcus, Escherichia coli, Klebsiella pneumoniae* in their intestines (Wang *et al.*, 2022; Ribeiro *et al.*, 2023). These commensal bacteria serve as a source of AMR through horizontal gene transfer. Hospitals are major hotspots for resistant pathogens transmission due to extensive antibiotic use, cross contamination through medical devices, health workers, and surfaces, and high prevalence of immunocompromised patients (Firesbhat *et al.*, 2021). Methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE), and Carbapenem-resistant *Enterobacteriaceae* (CRE) are common hospital-acquired resistant pathogens (Chen *et al.*, 2019).

Because of the extensive use of antibiotics, animals are also a major AMR reservoir. The livestock and poultry industries significantly contribute to AMR emergence through intensive antibiotic use for growth promotion, leading to shifts in microbial community composition and increased antibiotic-resistant gene prevalence (de Mesquita Souza Saraiva *et al.*, 2022). Because antibiotics are used for growth promotion, disease prevention, and treatment in livestock, prolonged exposure selects for resistant bacteria in animal production systems. Resistant bacteria spread to humans through contaminated meat and dairy products, agricultural manure, and direct animal contact (Ali and Alsayeqh *et al*., 2022). When resistant bacteria enter water systems, they can affect aquatic organisms and humans; additionally, aquaculture facilities routinely use antibiotics such as oxytetracycline and chloramphenicol (Hossain *et al.*, 2022). Resistance to these antibiotics produces AMR in aquatic animals and subsequently transfers to humans through food consumption. Animal-source foods harbor multiple AMR pathogens, including multidrug-resistant *Salmonella* from poultry, carbapenem-resistant *Escherichia coli* from pork, and cephalosporin-resistant *Escherichia coli* from veal calves (Silva *et al.*, 2019). Seafood products also contains a number of carbapenem-resistant bacteria, including *Stenotrophomonas, Pseudomonas, and Myroides* species (Ramírez-Castillo *et al.*, 2023).

These reservoirs sustain AMR through complex, interconnected transmission routes that facilitate the spread of resistant bacteria and genes. Environmental dissemination is the critical pathway whereby human and animal waste rich in antibiotics and resistant bacteria enters aquatic and terrestrial ecosystems via wastewater, agricultural runoff, and manure application, creating environmental resistomes. These compartments serve as hotspots for horizontal gene transfer and facilitate human exposure to contaminated irrigation water or recreational water. This dissemination is perpetuated through food animals via intensive selective pressure exerted by antimicrobials used for growth promotion and disease prevention.

Transmission between humans and animals is bidirectional, occurring through direct contact, food chain and waste, which are mainly exposed in poorly maintained environments. These transmission routes collectively enable community transmission into individuals beyond direct clinical transmission. The lack of sufficient infrastructure in terms of water, sanitation, and hygiene leads to overcrowded centers in many areas, where faceo-oral transmission of resistant organisms is enhanced and serves as evidence of the relationship between the built

environment and the healthcare sector and the wider ecological transmission systems. The environment serves as a long-term reservoir of resistant genes because of pollution and the waste of animals. There is an increase in the number of antibiotic-resistant bacteria in rivers, lakes, and groundwater around farms and hospitals. Bacteria such as *Pseudomonas aeruginosa* may persist in pipes bearing biofilm, potentially creating reservoirs for antibiotic resistance (Sib *et al.*, 2019). Agricultural practices also facilitate the infiltration of resistant bacteria into the soil using manure and wastewater application. Additionally, resistant microbes may be transported by plants, while heavy metals in soil may co-select resistance.

Epidemiology of AMR: The epidemiology of antimicrobial resistance (AMR) is characterized by multidirectional transmission of resistant bacteria and genes across human, animal, and environmental compartments. This interdependence flow is at the core of One Health approach, highlighting that the resistance developed in one area could be quickly transferred to other areas through various ecological and anthropogenic routes. Environmental pollution, food systems, direct contact, and zoonotic transmission are key pathways facilitating continued circulation of resistance determinants (Endale *et al.*, 2023).

The AMR spread in reservoirs is highly contributed by human activities. Within healthcare settings, the combination of frequent antibiotic usage and high population density provides fertile ground for the emergence and proliferation of multidrug-resistant organisms, like MRSA and CRE, and these organisms may then contaminate wastewater, posing a risk to the surrounding environment. Resistance is further spread in the community by self-medication, international traveling and consumption of contaminated food or water. At the same time, livestock and aquaculture antimicrobial use leads to the excessive release of antibiotics and antimicrobial-resistant bacteria into manure and effluent. On soil or released into water bodies, these contaminants form hotspots in the environment where horizontal gene transfer takes place, and molecular resistance has the potential to survive and be transmissible across environmental and clinically relevant bacteria.

The underestimated contribution of companion animals is also important in the epidemiology of AMR. The frequent physical contact with human beings, coexistence, and clinical care practices put their lives in bilateral routes of transmitting the zoonotic pathogens. Recent surveillance information of the United States (2019-2021) indicates strong resistance in companion animals, such as high non-susceptibility rates of urinary *E. coli* to amoxicillin (33.0%) (Maeda *et al.*, 2025), as well as, of dermal *Staphylococcus pseudintermedius* to first-line cephalosporins (41.9%) (Feuer *et al.*, 2024). The geographical trends, including the high resistance in southeastern states, indicate the regional drivers, which should be investigated more closely. These reservoirs are further linked via environmental pathways such as wastewater discharge, agricultural runoff, and unconventional vectors like aerosols and wildlife, which allow these resistance genes to circulate across through food, water and direct exposure to human and animal populations.

This integrated transmission cycle is highly complex and makes it essential to consider a One Health surveillance strategy. Clinical, veterinary, or environmental samples used in isolation are not enough to provide the dynamics of AMR in all its manifestations. Rather, there is a need for integrated systems that simultaneously measure the trends of resistance in all sectors to map the routes of transmission, the high-risk interfaces, and put specific interventions in place. Due to the interconnected nature of AMR, stakeholders can produce more efficient approaches to reducing the spread of resistance and protecting human, animal, and environmental health.

One Health approach to AMR: One Health provides the most effective ways for dealing with AMR as it recognizes the interconnection between animals, humans, and environmental health. This method is important as the resistant genes and pathogens circulate freely between humans, livestock and their ecosystems through various routes of transmission (Endale *et al.*, 2023), as described in the Fig. 2. The continuous use of antibiotics in livestock production creates a reservoir of resistant bacteria in animals, while the overuse of antibiotics in humans drives resistance in communities. The environment acts as an amplifier and the receipt of resistance through soil, food systems and contaminated water.

Integrated surveillance is a key factor in the health approach as it monitors all the sectors for the presence of resistance patterns simultaneously. The surveillance of wastewater can identify an early warning of spread of resistance. International programs like WHO's GLASS (Global Antimicrobial Resistance and Use of Surveillance System and CDC's NARMS (National Antimicrobial Resistance Monitoring System) trace the newly existing resistance (Karp *et al.*, 2017). The control of AMR requires coordinated work from both human medicine and animal reproduction to decrease the unnecessary use of antibiotics (Kasimanickam *et al.*, 2021). One Health approach is important, as it targets the interconnected environments that facilitate the evolution and dissemination of resistance. Thus, healthcare facilities, such as farms and food industries, must adopt infection prevention practices to break the transmission chain. Moreover, improved treatment of waste and handling of manure are environment managemental strategies which can compensate for the spread of resistance.

The effectiveness of One Health approach can be demonstrated by successful implementation done by various nations. The ban of antibiotics in Denmark on the use of growth promoters in livestock sector reduced the resistance and maintained the productivity (Jensen and Hayes, 2014). The "Search and Destroy" program of Netherland for the combined screening of MRSA at both the hospital and farm levels reduced the infection rates (Wertheim *et al.*, 2004). Sweden became the global leader in restraining AMR because it adopted One Health early (Eriksen *et al.*, 2021). Still, the enormous challenges remain unchallenged like funding gaps, negligence of government, and behavioral use of antibiotics. To overcome these challenges, there is a need for international cooperation, alternative treatment expenses, and innovative technologies for predicting antimicrobial resistance. Thus, the AMR control depends upon the ability to retain the

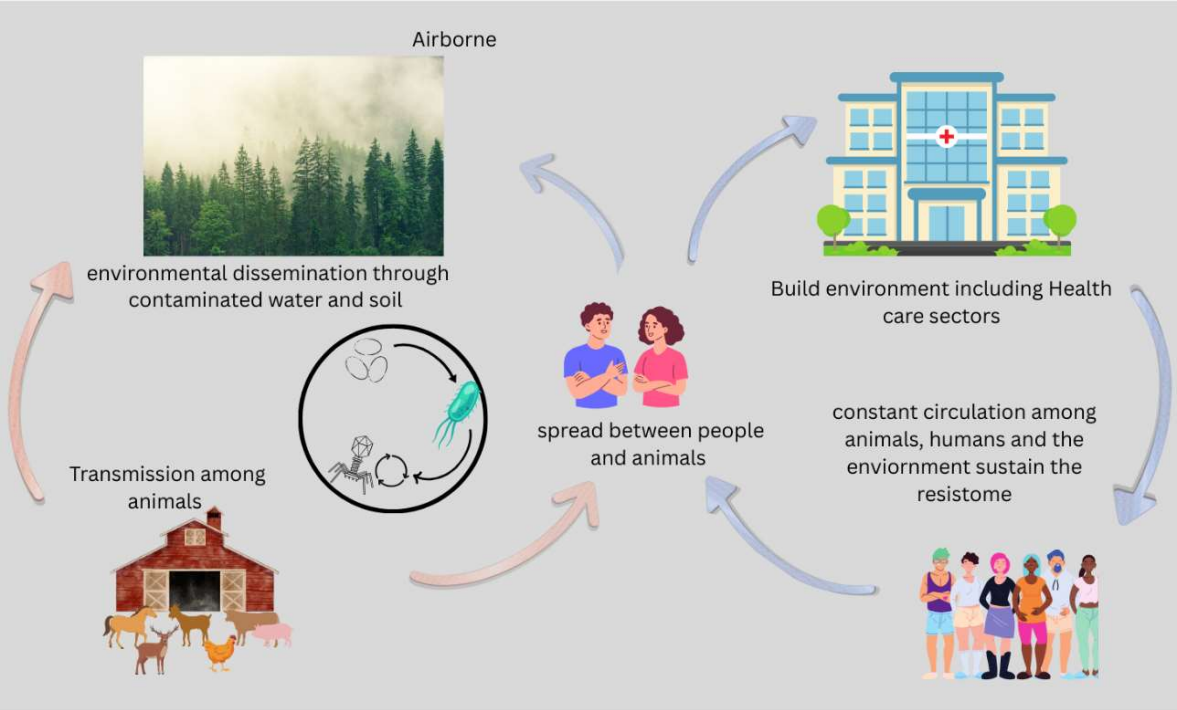

Fig. 1: Reservoirs of AMR and its interconnection between public, animals, and environmental health.

integrated system having multi-sector approach through research management.

The effectiveness of One Health approach can be demonstrated by successful implementation done by various nations. The ban of antibiotics in Denmark on the use of growth promoters in livestock sector reduced the resistance and maintained the productivity (Jensen and Hayes, 2014). The "Search and Destroy" program of Netherland for the combined screening of MRSA at both the hospital and farm levels reduced the infection rates (Wertheim *et al.*, 2004). Sweden became the global leader in restraining AMR because it adopted One Health early (Eriksen *et al.*, 2021). Still, the enormous challenges remain unchallenged like funding gaps, negligence of government, and behavioral use of antibiotics. To overcome these challenges, there is a need for international cooperation, alternative treatment expenses, and innovative technologies for predicting antimicrobial resistance. Thus, the AMR control depends upon the ability to retain the integrated system having multi-sector approach through research management.

Traditional strategies for the control of AMR: AMR is a silent global threat to the health, food security and economy of a state, with potential for pandemic-scale impacts. This all proceeds because of overuse and misuse of antibiotics in human medicine, agriculture and livestock production accelerating the emergence of drug-resistant pathogens, causing the treatment against microbes ineffective (Rahman *et al.*, 2022). The strategies used for combating AMR include the development of novel antibiotics, antimicrobial peptides, combination therapies, CRISPR-CAS systems, immune modulation, drug repurposing, nanotechnology, bacteriophage therapy, probiotics, and antibody therapies.

The continuous occurrence of resistant bacteria prioritizes the invention and development of new antibiotics that target the previously unnoticed mechanisms of bacteria. Texiobactin, Cefiderocol, and Lefamulin are recently developed novel antibiotics that have properties of targeting the unexplored mechanisms of bacteria (Cattoir and Felden, 2019; Taheri *et al.*, 2021; Muteeb *et al.*, 2023). Tiexobactin targets the cell wall precursors and is effective against Gram-positive pathogens (Homma *et al.*, 2016; Chiorean *et al.*, 2020), Cefiderocol disrupts the cell wall synthesis by exploiting the iron uptake system of bacteria and is effective against carbapenem-resistant Gram-negative bacteria (Syed, 2021; Yousefi *et al.*, 2024), and Lefamulin inhibits the protein synthesis of bacteria by binding to 50S ribosomal subunit and is effective against resistant strains like MRSA (Veve and Wagner, 2018; Wu *et al.*, 2020; Goudarzi *et al.*, 2021). But this strategy is expensive and requires more time because of lengthy development. Antimicrobial peptides are a broad spectrum of naturally occurring molecules effective against bacteria, viruses and fungi (Erdem Büyükkiraz and Kesmen, 2022). They work through the disruption of cell membrane and immune system modulation. LL-37, defensins, and polymyxins are some examples of antimicrobial peptides that have lower risks of resistance because of their multiple target potentials and fast killing. Polymyxin B shows higher efficacy in reducing the antimicrobial activity and against Carbapenem-resistant gram-negative bacterial infections (Zhuang *et al.*, 2025). But there is a need for the optimization of high cost, toxicity, and stability.

Combined therapies can be a way of dealing with AMR as combining antibiotics enhances efficacy and reduces the development of resistance because of different mechanisms of action. Trimethoprim-sulfamethoxazole and ceftazidime-avibactam combined therapies provide effective dealing with MRSA and multidrug resistant

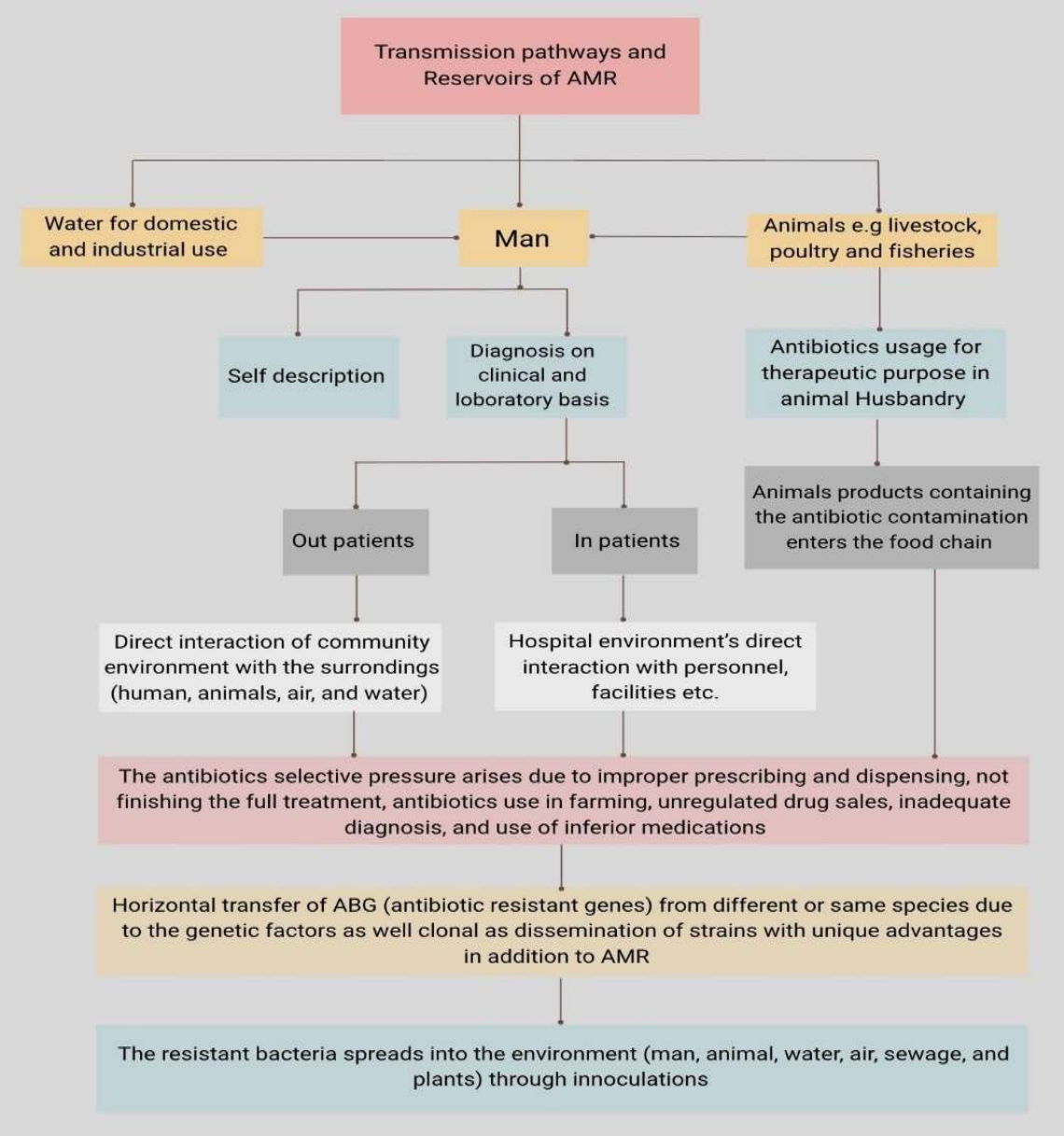

Fig. 2: Routes of transmission of antimicrobial resistance and its reservoirs in humans, animals, and the environment.

Gram-negative infections, respectively. But there is a risk of drug interactions with this strategy. CRISPR-Cas systems are gene editing tools that target and eliminate the selective antimicrobial resistance genes or virulence factors of bacteria. Phage therapy and nano-based therapy are applications of this system, which involves the modified bacteriophages CRISPR-Cas delivery for the disruption of resistance genes in the pathogen's structure and nano-sized CRISPR molecules for targeting the *mecA* gene, respectively.

Noncarriers, because of their efficient delivery and antimicrobial properties, are known therapies for dealing with AMR. Metal-organic frameworks (MOFs), silver nanoparticles (AgNPs), and constructed DNA nano platforms are examples of nanoparticles used for combating AMR. DNA multifunctional nano platform works as a versatile carrier for the delivery of bacteria specific antibiotics such as ciprofloxacin etc. (Wu *et al.*, 2023). They are characterized by the improved drug solubility and resistance provided by biofilm, but this therapy faces toxicity and production issues on a larger scale. Enhancing the immune system of an individual provides reduce reliance on antibiotics and reduces the risks of AMR and modulates the IgE-mediated Pathways which offers a more effective approach for combating resistant bacteria (Zhou *et al.*, 2022). Such immune modulation can be done through the strategies of vaccination, immunostimulant, and Granulocyte-Colony-Stimulating Factor (G-CSF). Another strategy for combating AMR is bacteriophage therapy, in which the phage viruses infect and lyse the specific bacteria (Muteeb *et al.*, 2023). Pyobacteriophages and lysins are applications of bacteriophage therapy, which is highly specific and safe for the ecosystem, but they have narrow ranges, and stability has to be maintained at specific values (Guo *et al.*, 2024; Patil *et al.*, 2025).

Table 1: Various antibacterial therapies / prophylaxis, their mechanisms, level of toxicity, risks of AMR and their clinical uses

Therapy	Microbial activity	Stability	Mechanism	Toxicity	AMR risk	Clinical use	References
Antibody-antibiotic conjugate	Eradicates intracellular pathogens, high specificity but ineffective against microbes lacking surface antigens	Has good stability because of its extended serum half-life	It works by minimizing the systemic exposure of the pathogen by delivering the antibiotic payload directly to the infected cells	Have minimal toxic effects because of localized release.	Low risk of AMR as it targets intracellular niches	Phase II trials for methicillin-resistant *Staphylococcus aureus*	(Lehar *et al.*, 2015; Zheng *et al.*, 2017)
Antimicrobial peptides	High bactericidal activity is because of broad spectrum action against both Gram positive and Gram-negative bacteria and fungi.	Good water solubility and maintain activity at pH 3-9 but degrades through proteases because of short half-life and stability in circulation	Works through the disruption of microbial membranes through electrostatic interactions and poor formation	Have the potential to cause cytotoxicity and hemolytic activity.	Low risk of AMR and require lipid membrane modifications for the development of resistance.	Used as topical pexiganan for diabetic ulcers, phase III.	(Hancock and Sahl, 2006; Mookherjee *et al.*, 2020)
Bacteriophages	Species-specific lysis, high specificity, minimal disruptions to host but narrow spectrum and have no access to intracellular pathogens	The lyophilized formulation can stabilize for years at lower temperatures and sensitive to UV light	Works through the activation of lytic enzymes like endolysins, degrading the peptidoglycan, cause the osmotic lysis of the cell.	Safe, but anaphylaxis is seen in phage component cases.	Moderate risk of AMR as bacteria can develop receptor mutations	Used for multi-drug-resistant *Pseudomonas aeruginosa* against wound infections	(Bull *et al.*, 2019; Jault *et al.*, 2019)
CRISPR-CAS9 antimicrobial	Gets antimicrobial property by targeting the antimicrobial genes with single precision.	Good stability in lipid nanoparticles or phage delivery, requires for the protection of gRNA	Works by the cleavage of DNA, which induces the break of resistant strain's lethal double-strand	Have the potential to activate the immune system as it is an off target editing in host microbiota	Higher risk of AMR if bacteria mutate the Proto-spacer-Adjacent motifs (PAMs)	Used pre-clinically against Carbapenem-Resistant *Enterobacteriaceae* ((El-Mowafy *et al.*, 2021))	(Bikard *et al.*, 2014a; Bikard *et al.*, 2014b; El-Mowafy *et al.*, 2021)
Silver nanoparticles (AgNPs)	Provides antimicrobial activity through the disruption of biofilm, broad spectrum actions	Have good stability and shelf life for 5 years but aggregates in saline	Works by releasing silver ions, which stimulates the generation of reactive oxygen species (ROS) and causes disruption of thiol groups	Has the potential to develop cytotoxic effects to the mammalian cells	Low risk of AMR because of its multi-target action	Clinically used in the catheter coating	(Rai *et al.*, 2009; Lansdown, 2010; Rai *et al.*, 2014)
Probiotics	Competitive elimination of pathogens	The stability of probiotics depends on gastric acid and drying-freezing protection	Works through the production of bacteriocin, which kills bacteria, pH modulation and immune stimulation	Even though it is normally considered safe, bacteremia can occur in immune-compromised patients, albeit rarely.	Possesses a non-lethal mode of action, so has a negligible risk of AMR	Clinically used for C. difficile, approved by FDA	(Ouwehand *et al.*, 2002; Suez *et al.*, 2018)
mRNA Vaccines	Prophylactic actions microbes by preventing the infection rather than to treat.	Since it is a vaccine, so the cold chain has to be maintained, for which ultra-cold storage.	Works by priming the adaptive immunity through spike protein expression	Can cause local reactions, rare cases have shown myocarditis	There is no risk of AMR as it prevents the infection	Pfizer/ BioNTech COVID-19 vaccine	(Pardi *et al.*, 2018; Verbeke *et al.*, 2019)
Photodynamic therapy	Localized antimicrobial activity for the biofilm of dentation	Has good stability under the influence of light as the name indicates	Works through the production of singlet oxygen, which damages the cellular components	Safe but mild photosensitivity appears in patients.	Low risk of AMR	Clinically used to treat periodontitis	(Bekmukhametova *et al.*, 2020; Mathur *et al.*, 2023)
Enzybiotics	Provides antibiotic activity against specific gram-positive bacteria	Showing good stability at room temperature for 2 years	Works through the hydrolysis of peptidoglycan through glycosidic bond cleavage.	No signs of toxicity in mammals	Shows a very low risk of AMR	Used in phase III (Exobases)	(Fischetti, 2016; Francis *et al.*, 2026)

Probiotics are commensal bacteria which out-competes the pathogens and allow the body to regrow or restore the normal microbiota (Norton *et al.*, 2024). Lactobacilli and bifidobacteria inhibit *E. coli* and *S. aureus,* respectively, reduces the use of antibiotics but are strain specific in nature (El Far *et al.*, 2024). Drugs repurpose is a strategy in which an already existing drug with secondary antimicrobial actions provides a faster solution. Statins and chlorpromazine are applications of drug repurpose having safe profiles for faster clinic adoption, but suffer because of limited applicability and dose (Lago and Bahn, 2018). Antibody therapies are also a solution for controlling AMR as the monoclonal antibodies target a specific component of bacteria. Salvecin and bezlotoxumab are monoclonal antibodies having a lower risk of resistance and long-lasting effects but suffer from complex development and enormous cost for production (Adedokun *et al.*, 2025).

Strategies for tackling AMR through One Health approach: For addressing AMR, there is a need for a holistic One Health approach, which recognizes the interconnections of animals, humans, and environmental health. Traditional therapies and efforts focus on clinical setting but neglect the focus on the spread of resistant bacteria through contaminated water, food, and ecosystems (Serwecińska, 2020). This focus requires cross-sector collaboration to stop the spread of resistant bacteria. A single stage of the food chain contributes to the global threat of AMR crisis, from the farm-level antibiotics overuse to the environmental contamination and exposure of consumers (Founou *et al.*, 2016; Hazards *et al.*, 2021). Various strategies have been proposed for tackling antimicrobial resistance through One Health approach as summarized in Table 1.

The basic way of tackling AMR is through strengthening the governance and policy frameworks of nation, having proposed actions of developing and enforcing the AMR nation plans in collaboration with whom global actions (World Health, 2021), banning the use of antibiotics in the livestock sector as a growth promoter or any other non-therapeutic use, establishing a committee for steering AMR at multi-sectoral coordination from agriculture, health and environmental agencies, and links the AMR abidance for private companies to get licensing. The evidence can be seen from the work of Jordan's National Action Plan (NAP) on AMR involving One Health strategies and the Sweden's success ratio in reducing the risk of AMR by applying strict rules and regulations on use of antibiotics in livestock sector (Wierup *et al.*, 2021; Nashwan *et al.*, 2024; Ala'a *et al.*, 2025).

Another way of tackling AMR through One Health approach is through integrated surveillance and monitoring having actions of AMR real-time surveillance networks covering hospitals, lab and ecosystem, using genomic sequencing for tracking the resistant genes, monitoring the food products, water and soil for the antimicrobial residues, and launching a dashboard at a national level for sharing data (Fitzpatrick *et al.*, 2021; Struelens *et al.*, 2024). Evidence can be seen in the expansion of Jordan's AMR surveillance from 8 to 42 sites. Through integrated surveillance monitoring, Jordan highlights the multi-sector transmission risks and detects MDR *E. coli*, *Salmonella*, and MRSA in poultry farms, dairy farms, and irrigation water.

The proposed actions of Antimicrobial Stewardship (AMS) across the food chain for tackling the antimicrobial resistance includes enforced veterinary observations for control of antibiotics prescriptions in livestock sector, promotion of alternatives of antibiotics such as vaccines, probiotics, and phage therapy, and training farmers to reduce the infections by biosecurity measures. Public awareness and behavioral changes should be followed to guide the public to tackle the AMR (Gilham *et al.*, 2024). Launching national campaigns for the awareness of AMR in farmers, food keepers, food handlers, consumers and introducing the education of antimicrobial resistance into the curriculum of schools for inducing the long-term behavioral changes in the upcoming generations are the ideal actions through public awareness (Lambrou *et al.*, 2021). Raising awareness among farmers, shop handlers and consumers will reduce the misuse of antibiotics in livestock, maintain the hygienic practices to prevent contamination, and safe food handling, respectively. The importance of public awareness and behavioral changes on One health approach can be estimated by the success rate of Sweden in reducing the risk of AMR through public educational campaigns.

Through environmental management, One Health approach can help in tackling AMR through regulating antibiotic disposal, surveillance and monitoring the water sources, and promoting sustainable farming practices. These actions will help in preventing the environment from contamination, search for resistant pathogens in water, and treatment of manure before using it as a fertilizer. The treatment plants in Jordan found antibiotic residues, which indicates the need for management. Research and innovation are key factors for tackling AMR with One Health perspectives. Research and innovation can help in establishing an AMR Research fund at an international level for studying transmission pathways and alternative treatments of antibiotics, and pilot-test precision diagnostic facilities for inhibiting the misuse of antibiotics in the livestock sector. HPLC-MS/MS based quantification of antimicrobial agents in human plasma is a precision diagnostic for monitoring the concentration of antibiotics (Lou *et al.*, 2024). The research and innovation projects of Jordan and Sweden have international collaborations with WHO, FHO for the support in AMR research efforts.

For the effective tackling of AMR in the food chain, a well combined and coordinated One Health strategy is important. Policies and governance help in strengthening the regulations across multi-sectors. Surveillance provides the AMR monitoring integration in human, animals and environment, stewardship inhibits the misuse of antibiotics through alternatives and veterinary observations, awareness helps in educating the farmers and handlers regarding AMR risks, research helps in investing innovative solutions while environment helps in prevention of contamination of water and soil. The expanded AMR surveillance and policy framework of Jordan provides a model for other low-income countries. However, there is a need to sustain funding, enforcement and international collaboration for long-term success in tackling antimicrobial resistance with One Health perspectives.

Limitations: The review provides the important challenges in tackling the AMR, including the prolonged development

of novel antibiotics and high costs, which inhibits timely solutions. The use of combined therapies faces a risk of drug interactions, while the alternative therapies face specificity, stability, and scalability issues. Complications occur because of lack of global coordination in surveillance gaps and behavioral resistance. Shortages in funding, inconsistency in enforcement of policies, and multi-sectoral combination limit the world impact of One Health approach. These hurdles highlight the need for equitable, integrated and innovative strategies for combating AMR effectively.

Conclusions: Resistance is a critical global threat to food security, economic stability, and antimicrobial public health, requiring urgent and coordinated actions. This review provides an overview of the AMR complexity driven by the adaptability of microbes, overuse of the antibiotics, and contamination of environment. Since innovative therapies like CRISPR-Cas, bacteriophage therapy, novel antibiotics are good at rendering antimicrobial resistance, the use of One Health approach offers promising results for control of AMR but requires more attention and coordination from all the sectors. The effectiveness of alternative therapies is limited because of high costs, stability issues, requires more time because of lengthy development, and scalability. The gaps in global monitoring, behavioral resistance, and lack of policy enforcement to stewardship complicate the efforts for combating AMR. One Health approach interconnecting human, animal and environmental health arises as a vital framework for controlling AMR. The countries like Sweden and Jordan sets the examples of combating AMR through multi-sector collaboration, public awareness campaigns, and regulation potentials. But still, the existing barriers like sustained funding, international cooperation, and equitable access to the solutions are important to overcome. The key factors for addressing AMR are to prioritize research, advance diagnostic facilities, and foster innovations. The fight against AMR requires a united global effort combining scientific advancement, community engagement, and policymaking to safeguard future generations from this alleviating crisis.

Acknowledgements: The authors extend their appreciation to Umm Al-Qura University, Saudi Arabia for funding this research work through grant number: 26UQU4330050GSSR01.

Funding statement: This research work was funded by Umm Al-Qura University, Saudi Arabia under grant number: 26UQU4330050GSSR01.

REFERENCES

Abd El Ghany M, Fouz N and Hill-Cawthorne GA, 2020. Human movement and transmission of antimicrobial-resistant bacteria, Antibiotic resistance in the environment: A worldwide overview. Springer: 311-344.

Adedokun AI, Adigun OA, Ibrahim AM, *et al.*, 2025. Exploring immunotherapeutic strategies for bacterial and viral diseases. Explor Immun 5: 1003202.

Ala'a B, Kanaan Da, Omar A, *et al.*, 2025. Tackling antimicrobial resistance in Jordan: bridging science, research, and policy for a healthier future. Jordan J App Sci-Nat Sci Series 19(si2).

Ali S, and Alsayeqh AF, 2022. Review of major meat-borne zoonotic bacterial pathogens. Front Pub Health 10: 1045599.

Andersson DI, Balaban NQ, Baquero F, *et al.*, 2020. Antibiotic resistance: turning evolutionary principles into clinical reality. FEMS Microb Rev 44(2): 171-188.

Annunziato G, 2019. Strategies to overcome antimicrobial resistance (AMR) making use of non-essential target inhibitors: A review. Int J Mol Sci 20(23): 5844.

Aslam B, Asghar R, Muzammil S, *et al.*, 2024. AMR and Sustainable Development Goals: at a crossroads. Globaliz Health 20(1):73.

Aslam B, Khurshid M, Arshad MI *et al.*, 2021. Antibiotic resistance: one health one world outlook. Front Cellular Infection Microb 11:771510.

Baquero F, Coque TM, Martínez JL, *et al.*, 2019. Gene transmission in the one health microbiosphere and the channels of antimicrobial resistance. Front Microb 10: 2892.

Bastawrous A and Suni AV, 2020. Thirty year projected magnitude (to 2050) of near and distance vision impairment and the economic impact if existing solutions are implemented globally. Ophth Epidem 27(2): 115-120.

Bekmukhametova A, Ruprai H, Hook JM *et al.*, 2020. Photodynamic therapy with nanoparticles to combat microbial infection and resistance. Nanoscale 12(41): 21034-21059.

Belay WY, Getachew M, Tegegne BA, *et al.*, 2024. Mechanism of antibacterial resistance, strategies and next-generation antimicrobials to contain antimicrobial resistance: a review. Front Pharm 15: 1444781.

Bikard D, Euler C, Jiang W *et al.*, 2014a. Development of sequence-specific antimicrobials based on programmable CRISPR-Cas nucleases. Nat Biotech 32(11):1146.

Bikard D, Euler CW, Jiang W, *et al.*, 2014b. Exploiting CRISPR-Cas nucleases to produce sequence-specific antimicrobials. Nat Biotech 32(11): 1146-1150.

Breitschwerdt EB, Maggi RG, Chomel BB, *et al.*, 2010. Bartonellosis: an emerging infectious disease of zoonotic importance to animals and human beings. J Vet Emerg Crit Care 20(1): 8-30.

Bull JJ, Levin BR and Molineux IJ, 2019. Promises and pitfalls of *in vivo* evolution to improve phage therapy. Viruses 11(12): 1083.

Capasso C and Supuran CT, 2019. Dihydropteroate synthase (sulfonamides) and dihydrofolate reductase inhibitors. Book Editor(s): Boyan B. Bonev, Nicholas M. Brown. Bacterial resistance to antibiotics–From molecules to man:163-172 .

Cassell GH and Mekalanos J, 2001. Development of antimicrobial agents in the era of new and reemerging infectious diseases and increasing antibiotic resistance. Jama 285(5): 601-605.

Cattoir V and Felden B, 2019. Future antibacterial strategies: from basic concepts to clinical challenges. J Infect Dis 220(3):350-360.

Chen YP, Liang CC, Chang R *et al.*, 2019. Detection and colonization of multidrug resistant organisms in a regional teaching hospital of Taiwan. Inter J Env Res Pub Health 16(7): 1104.

Chiorean S, Antwi I, Carney DW *et al.*, 2020. Dissecting the binding interactions of teixobactin with the bacterial cell-wall precursor lipid II. ChemBioChem 21(6):789-792.

Claverys JP, Prudhomme M, Mortier-Barrière I *et al.*, 2000. Adaptation to the environment: *Streptococcus pneumoniae*, a paradigm for recombination-mediated genetic plasticity? Mol Microb 35(2):251-259.

Colavecchio A, Cadieux B, Lo A *et al.*, 2017. Bacteriophages contribute to the spread of antibiotic resistance genes among foodborne pathogens of the *Enterobacteriaceae* family–a review. Front in Microb 8: 1108.

Conrad PA, Mazet JA, Clifford D *et al.*, 2009. Evolution of a transdisciplinary "One Medicine–One Health" approach to global health education at the University of California, Davis. Prev Vet Med 92(4):268-274.

Da Costa PM, Loureiro L and Matos AJF, 2013. Transfer of multidrug-resistant bacteria between intermingled ecological niches: the interface between humans, animals and the environment. Inter J Env Res Pub health 10(1): 278-294.

Davis BD, 1987. Mechanism of bactericidal action of aminoglycosides. Microbiological reviews 51(3): 341-350.

de Mesquita Souza Saraiva M, Lim K, do Monte DFM *et al.*, 2022. Antimicrobial resistance in the globalized food chain: A One Health perspective applied to the poultry industry. Braz J Microb 53(1): 465-486.

Deresinski S, 2007. Principles of antibiotic therapy in severe infections: optimizing the therapeutic approach by use of laboratory and clinical data. Clin Infect Dis 45(Supplement_3): S177-S183.

Despotovic M, de Nies L, Busi SB, *et al*., 2023. Reservoirs of antimicrobial resistance in the context of One Health. Curr Opin Microb 73: 102291.

El-Khoury C, Mansour E, Yuliandra Y, *et al*., 2022. The role of adjuvants in overcoming antibacterial resistance due to enzymatic drug modification. RSC Med Chem 13(11): 1276-1299.

El-Mowafy M, Elgaml A, El-Mesery M, *et al*., 2021. Changes of gut-microbiota-liver axis in hepatitis C virus infection. Biology 10(1): 55.

El Far MS, Zakaria AS, Kassem MA, *et al*., 2024. Characterization of probiotics isolated from dietary supplements and evaluation of metabiotic-antibiotic combinations as promising therapeutic options against antibiotic-resistant pathogens using time-kill assay. BMC Compl Med Ther 24(1):303.

Ellwanger JH, Veiga ABGd, Kaminski VdL, *et al*., 2021. Control and prevention of infectious diseases from a One Health perspective. Gen Mol Biol 44(1 Suppl 1): e20200256.

Endale H, Mathewos M and Abdeta D, 2023. Potential causes of spread of antimicrobial resistance and preventive measures in one health perspective-a review. Infec Drug Resis: 7515-7545.

Erdem Büyükkiraz M and Kesmen Z, 2022. Antimicrobial peptides (AMPs): A promising class of antimicrobial compounds. J App Microb 132(3): 1573-1596.

Eriksen J, Björkman I, Röing M, *et al*., 2021. Exploring the one health perspective in Sweden's policies for containing antibiotic resistance. Antibiotics 10(5):526.

Eustice DC and Wilhelm JM, 1984. Mechanisms of action of aminoglycoside antibiotics in eucaryotic protein synthesis. Antimic Agents Chemo 26(1): 53-60.

Fernandes R, Amador P and Prudêncio C, 2013. β-Lactams: chemical structure, mode of action and mechanisms of resistance. Rev Res Med Microb 24(1): 7-17.

Feuer L, Frenzer SK, Merle R, *et al*., 2024. Comparative analysis of Methicillin-Resistant *Staphylococcus pseudintermedius* prevalence and resistance patterns in Canine and Feline Clinical samples: insights from a three-year study in Germany. Antibiotics 13(7): 660.

Fillol-Salom A, Alsaadi A, Sousa JAMd, *et al*., 2019. Bacteriophages benefit from generalized transduction. PLoS Pathogens 15(7): e1007888.

Firesbhat A, Tigabu A, Tegene B, *et al*., 2021. Bacterial profile of high-touch surfaces, leftover drugs and antiseptics together with their antimicrobial susceptibility patterns at University of Gondar Comprehensive Specialized Hospital, Northwest Ethiopia. BMC Microbiology 21(1): 309.

Fischetti VA, 2016. Lysin therapy for Staphylococcus aureus and other bacterial pathogens, *Staphylococcus aureus*: Microbiology, Pathology, Immunology, Therapy and Prophylaxis. Springer: 529-540

Fitzpatrick KJ, Rohlf HJ, Sutherland TD, *et al*., 2021. Progressing antimicrobial resistance sensing technologies across human, animal, and environmental health domains. ACS Sensors 6(12): 4283-4296.

Founou LL, Founou RC and Essack SY, 2016. Antibiotic resistance in the food chain: a developing country-perspective. Front Microb 7: 1881.

Fraise AP, 2002. Biocide abuse and antimicrobial resistance—a cause for concern? J Antimic Chem 49(1): 11-12.

Francis D, Melvina C, George CR, *et al*., 2026. Enzybiotics: An Emerging Frontier in Antibacterial Therapy, Microbial Enzymes as Potential Biotherapeutics in Human Healthcare. CRC Press: 62-93

Gan Y, Huang H, Wu X, *et al*., 2024. What doesn't kill us makes us stronger: insights from neuroscience studies and molecular genetics. Curr Opin Beh Sci 59: 101431.

Gilham EL, Pearce-Smith N, Carter V, *et al*., 2024. Assessment of global antimicrobial resistance campaigns conducted to improve public awareness and antimicrobial use behaviours: a rapid systematic review. BMC Pub Health 24(1): 396.

Goudarzi M, Khoshbayan A and Taheri F, 2021. Retapamulin: current status and future perspectives. Structure 5(6): 11-14.

Guo Z, Yuan M and Chai J, 2024. Mini review advantages and limitations of lytic phages compared with chemical antibiotics to combat bacterial infections. Heliyon 10(14).

Habte-Gabr E, 2008. Antimicrobial resistance: a global public health threat. J Erit Med Assoc 3(1): 36-40.

Hancock REW and Sahl HG, 2006. Antimicrobial and host-defense peptides as new anti-infective therapeutic strategies. Nat Biotech 24(12): 1551-1557.

Harbarth S, Balkhy HH, Goossens H, *et al*., 2015. Antimicrobial resistance: one world, one fight! Antimic Resis Infec Cont 4(1): 49.

Hazards EPoB, Koutsoumanis K, Allende A, *et al*., 2021. Role played by the environment in the emergence and spread of antimicrobial resistance (AMR) through the food chain. EFSA J 19(6):e06651.

Hernando-Amado S, Coque TM, Baquero F, *et al*., 2019. Defining and combating antibiotic resistance from One Health and Global Health perspectives. Nat Microb 4(9): 1432-1442.

Homma T, Nuxoll A, Gandt AB, *et al*., 2016. Dual targeting of cell wall precursors by teixobactin leads to cell lysis. Antimic Agents Chemo 60(11): 6510-6517.

Hossain A, Habibullah-Al-Mamun M, Nagano I, *et al*., 2022. Antibiotics, antibiotic-resistant bacteria, and resistance genes in aquaculture: risks, current concern, and future thinking. Envir Sci Poll Res 29(8): 11054-11075.

Irfan M, Almotiri A and AlZeyadi ZA, 2022. Antimicrobial resistance and its drivers—a review. Antibiotics 11(10): 1362.

Jalava J, Vaara M and Huovinen P, 2004. Mutation at the position 2058 of the 23S rRNA as a cause of macrolide resistance in *Streptococcus pyogenes*. Ann Cl Microb Antimic 3(1): 5.

Jault P, Leclerc T, Jennes S, *et al*., 2019. Efficacy and tolerability of a cocktail of bacteriophages to treat burn wounds infected by *Pseudomonas aeruginosa* (PhagoBurn): a randomised, controlled, double-blind phase 1/2 trial. Lancet Infec Dis 19(1): 35-45.

Jensen HH and Hayes DJ, 2014. Impact of Denmark's ban on antimicrobials for growth promotion. Curr Op Microb 19: 30-36.

Johnsborg O and Håvarstein LS, 2009. Regulation of natural genetic transformation and acquisition of transforming DNA in *Streptococcus pneumoniae*. FEMS Microb Rev 33(3): 627-642.

Karp BE, Tate H, Plumblee JR, *et al*., 2017. National antimicrobial resistance monitoring system: two decades of advancing public health through integrated surveillance of antimicrobial resistance. Foodb Pathog Dis 14(10): 545-557.

Kasimanickam V, Kasimanickam M and Kasimanickam R, 2021. Antibiotics use in food animal production: escalation of antimicrobial resistance: where are we now in combating AMR? Med Sci 9(1): 14.

Kelly TR, Karesh WB, Johnson CK, *et al*., 2017. One Health proof of concept: Bringing a transdisciplinary approach to surveillance for zoonotic viruses at the human-wild animal interface. Prev Vet Med 137: 112-118.

King DT, Sobhanifar S and Strynadka NCJ, 2017. The mechanisms of resistance to β-lactam antibiotics, Handbook of antimicrobial resistance. Springer: 177-201

Kollef MH and Micek ST, 2005. Strategies to prevent antimicrobial resistance in the intensive care unit. Crit Care Med 33(8): 1845-1853.

Kumar S and Varela MF, 2013. Molecular mechanisms of bacterial resistance to antimicrobial agents. Chemotherapy 14(18): 522-534.

Lago SG and Bahn S, 2018. Clinical trials and therapeutic rationale for drug repurposing in schizophrenia. ACS Chem Neurosci 10(1): 58-78.

Lambrou AS, Innes GK, O'Sullivan L, *et al*., 2021. Policy implications for awareness gaps in antimicrobial resistance (AMR) and antimicrobial use among commercial Nepalese poultry producers. Glob Health Res Policy 6(1): 6.

Lansdown ABG, 2010. A pharmacological and toxicological profile of silver as an antimicrobial agent in medical devices. Adv Pharm Pharmaceut Sci 2010(1): 910686.

Lehar SM, Pillow T, Xu M, *et al*., 2015. Novel antibody–antibiotic conjugate eliminates intracellular *S. aureus*. Nature 527(7578): 323-328.

Leungtongkam U, Thummeepak R, Tasanapak K, *et al*., 2018. Acquisition and transfer of antibiotic resistance genes in association with conjugative plasmid or class 1 integrons of Acinetobacter baumannii. PLoS One 13(12): e0208468.

Lou Y, Cheng M, Cao Q, *et al*., 2024. Simultaneous quantification of mirabegron and vibegron in human plasma by HPLC-MS/MS and its application in the clinical determination in patients with tumors associated with overactive bladder. J Pharm Biomed Anal 240: 115937.

Mackenzie JS, Jeggo M, Daszak P, *et al*., 2013. One Health: The human-animal-environment interfaces in emerging infectious diseases. Springer.

Maeda A, Sato T, Toyting-Hiraishi J, *et al*., 2025. Prevalence, antimicrobial susceptibility, and virulence profiles of fluoroquinolone-resistant Escherichia coli isolated from companion animals in Sapporo, Japan. J Vet Med Sci 87(11): 1249-1258.

Magnano San Lio R, Favara G, Maugeri A, *et al*., 2023. How antimicrobial resistance is linked to climate change: an overview of two intertwined global challenges. Int J Env Res Pub Health 20(3): 1681.

Mancuso G, Midiri A, Gerace E, *et al*., 2021. Bacterial antibiotic resistance: the most critical pathogens. Pathogens 10(10): 1310.

Marks LR, Reddinger RM and Hakansson AP, 2012. High levels of genetic recombination during nasopharyngeal carriage and biofilm formation in *Streptococcus pneumoniae*. MBio 3(5):10-1128.

Masi M, Réfregiers M and Pos KM, 2017. Mechanisms of envelope permeability and antibiotic influx and efflux in Gram-negative bacteria. Nat Microb 2(3): 1-7.

Mathur A, Parihar AS, Modi S, *et al*., 2023. Photodynamic therapy for ESKAPE pathogens: an emerging approach to combat antimicrobial resistance (AMR). Microb Pathog 183: 106307.

McManus MC, 1997. Mechanisms of bacterial resistance to antimicrobial agents. Amer J Health-System Pharm 54(12): 1420-1433.

Moo CL, Yang SK, Yusoff K, *et al*., 2020. Mechanisms of antimicrobial resistance (AMR) and alternative approaches to overcome AMR. Curr Drug Disc Techn 17(4): 430-447.

Mookherjee N, Anderson MA, Haagsman HP, *et al*., 2020. Antimicrobial host defence peptides: functions and clinical potential. Nat Rev Drug Disc 19(5): 311-332.

Moyer JD, Eshbaugh M and Rettig J, 2017. Cost analysis of global road traffic death prevention: Forecasts to 2050. Dev Policy Rev35(6): 745-757.

Murugaiyan J, Kumar PA, Rao GS, *et al*., 2022. Progress in alternative strategies to combat antimicrobial resistance: focus on antibiotics. Antibiotics 11(2): 200.

Muteeb G, Rehman MT, Shahwan M,, *et al*., 2023. Origin of antibiotics and antibiotic resistance, and their impacts on drug development: A narrative review. Pharmaceuticals 16(11): 1615.

Nashwan AJ, Barakat M, Niaz F *et al*., 2024. Antimicrobial resistance: stewardship and one health in the Eastern Mediterranean region. Cureus 16(4).

Nawaz Z, Rasool MH, Siddique AB, *et al*., 2020. Frequency and molecular detection of *Giardia intestinalis* in children attending pediatrics of Punjab, Pakistan. Jundish J Microbiol 13(1): 1-6.

Normark BH and Normark S, 2002. Evolution and spread of antibiotic resistance. J Int Med 252(2): 91-106.

Norton P, Trus P, Wang F, *et al*., 2024. Understanding and treating diabetic foot ulcers: insights into the role of cutaneous microbiota and innovative therapies. Skin Health Dis 4(4): ski2-399.

Nye TM, Jacob KM, Holley EK, *et al*., 2019. DNA methylation from a Type I restriction modification system influences gene expression and virulence in *Streptococcus pyogenes*. PLoS Pathogens 15(6): e1007841.

Ouwehand AC, Salminen S and Isolauri E, 2002. Probiotics: an overview of beneficial effects. Ant V Leeuw 82(1): 279-289.

Pagès J-M and Amaral L, 2009. Mechanisms of drug efflux and strategies to combat them: challenging the efflux pump of Gram-negative bacteria. Bioch Bioph Acta (BBA)-Prot Proteom 1794(5): 826-833.

Pardi N, Hogan MJ, Porter FW, *et al*., 2018. mRNA vaccines—a new era in vaccinology. Nat Rev Drug Disc 17(4): 261-279.

Patil R, Arora S, Kumar D, *et al*., 2025. Multifunctional Nanocarriers in Bacteriophage Delivery: A Paradigm Shift in Treating Multidrug-Resistant Infections. Wiley Interdis Rev: Nanomed Nanobiotech 17(3): e70021.

Pearce-Duvet JMC, 2006. The origin of human pathogens: evaluating the role of agriculture and domestic animals in the evolution of human disease. Biolog Rev 81(3): 369-382.

Pinheiro REE, Chaves TP, Melo ES, *et al*., 2020. Modulatory-antibiotic activity of the essential oil from *Eucalyptus citriodora* against MDR bacterial strains. Cell Mol Biol, 66(4): 60-64.

Rahman MM, Alam Tumpa MA, Zehravi M, *et al*., 2022. An overview of antimicrobial stewardship optimization: the use of antibiotics in humans and animals to prevent resistance. Antibiotics 11(5): 667.

Rai M, Kon K, Ingle A, *et al*., 2014. Broad-spectrum bioactivities of silver nanoparticles: the emerging trends and future prospects. App Microb Biotech 98(5): 1951-1961.

Rai M, Yadav A and Gade A, 2009. Silver nanoparticles as a new generation of antimicrobials. Biotech Adv 27(1): 76-83.

Ramírez-Castillo FY, Guerrero-Barrera AL and Avelar-González FJ, 2023. An overview of carbapenem-resistant organisms from food-producing animals, seafood, aquaculture, companion animals, and wildlife. Front Vet Sci 10: 1158588.

Reinert RR, Lütticken R, Bryskier A, *et al*., 2003. Macrolide-resistant *Streptococcus pneumoniae* and *Streptococcus pyogenes* in the pediatric population in Germany during 2000-2001. Antimic Ag Chem 47(2): 489-493.

Ribeiro J, Silva V, Monteiro A, *et al*., 2023. Antibiotic resistance among gastrointestinal bacteria in broilers: A review focused on *Enterococcus* spp. and *Escherichia coli*. Animals 13(8): 1362.

Scarpa F and Casu M, 2024. Genomics and bioinformatics in one health: transdisciplinary approaches for health promotion and disease prevention. Int J Env Res Pub Health 21(10): 1337.

Schwarz S, Kehrenberg C, Doublet B *et al*., 2004. Molecular basis of bacterial resistance to chloramphenicol and florfenicol. FEMS Microb Rev 28(5): 519-542.

Serwecińska L, 2020. Antimicrobials and antibiotic-resistant bacteria: a risk to the environment and to public health. Water 12(12): 3313.

Sib E, Voigt AM, Wilbring G, *et al*., 2019. Antibiotic resistant bacteria and resistance genes in biofilms in clinical wastewater networks. Int J Hyg Env Health 222(4): 655-662.

Silva N, Carvalho I, Currie C, *et al*., 2019. Extended-Spectrum-β-Lactamase and Carbapenemase-Producing Enterobacteriaceae in Food-Producing Animals in Europe: An Impact on Public Health? Antib Drug Resis: 261-273.

Struelens MJ, Ludden C, Werner G, *et al*., 2024. Real-time genomic surveillance for enhanced control of infectious diseases and antimicrobial resistance. Front Sci 2: 1298248.

Suez J, Zmora N, Zilberman-Schapira G, *et al*., 2018. Post-antibiotic gut mucosal microbiome reconstitution is impaired by probiotics and improved by autologous FMT. Cell 174(6): 1406-1423.

Syed YY, 2021. Cefiderocol: a review in serious Gram-negative bacterial infections. Drugs 81(13): 1559-1571.

Taheri Y, Joković N, Vitorović J, *et al*., 2021. The burden of the serious and difficult-to-treat infections and a new antibiotic available: cefiderocol. Front Pharm 11: 578823.

Tang KWK, Millar BC and Moore JE, 2023. Antimicrobial resistance (AMR). British J Biomed Sci 80: 11387.

Tarin-Pello A, Suay-Garcia B and Perez-Gracia MT, 2022. Antibiotic resistant bacteria: current situation and treatment options to accelerate the development of a new antimicrobial arsenal. Exp Rev Anti-infective Therapy 20(8): 1095-1108.

Van Duijkeren E, Schink AK, Roberts MC, *et al*., 2018. Mechanisms of bacterial resistance to antimicrobial agents. Antimic Resis Bact Livest Comp Animals: 51-82.

Verbeke R, Lentacker I, De Smedt SC, *et al*., 2019. Three decades of messenger RNA vaccine development. Nano Today 28:100766.

Veve MP and Wagner JL, 2018. Lefamulin: review of a promising novel pleuromutilin antibiotic. Pharmac: J Human Pharm Drug Therapy 38(9): 935-946.

Volkova VV, Lu Z, Besser T, *et al*., 2014. Modeling the infection dynamics of bacteriophages in enteric *Escherichia coli*: estimating the contribution of transduction to antimicrobial gene spread. App Env Microb 80(14): 4350-4362.

Walsh TR, Gales AC, Laxminarayan R, *et al*., 2023. Antimicrobial resistance: addressing a global threat to humanity No. 20. e1004264. Public Library of Science San Francisco, CA USA.

Wang X, Zhang Y, Li C, *et al*., 2022. Antimicrobial resistance of *Escherichia coli*, Enterobacter spp., *Klebsiella pneumoniae* and *Enterococcus* spp. isolated from the feces of giant panda. BMC Microb 22(1): 102.

Wertheim HFL, Vos MC, Boelens HAM, *et al*., 2004. Low prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) at hospital admission in the Netherlands: the value of search and destroy and restrictive antibiotic use. J Hosp Infec 56(4): 321-325.

Wierup M, Wahlström H and Bengtsson B, 2021. Successful prevention of antimicrobial resistance in animals—a retrospective country case study of Sweden. Antibiotics 10(2): 129.

Woolhouse M, Ward M, Van Bunnik B, *et al*., 2015. Antimicrobial resistance in humans, livestock and the wider environment. Philos Trans Royal Society B: Biolog Sci 370(1670):20140083.

World Health O, 2021. Antimicrobial resistance and the United Nations sustainable development cooperation framework: Guidance for United Nations Country teams. World Health Organization.

Wright GD, 2005. Bacterial resistance to antibiotics: enzymatic degradation and modification. Adv Drug Deliv Rev 57: 1451-1470.

Wu S, Zheng Y, Guo Y, *et al*., 2020. In vitro activity of lefamulin against the common respiratory pathogens isolated from Mainland China during 2017–2019. Front Microb 11: 578824.

Wu T, Fu Y, Guo S, *et al*., 2023. Self-assembly multifunctional DNA tetrahedron for efficient elimination of antibiotic-resistant bacteria. Aggregate 5(1).

Yousefi B, Kashanipoor S, Mazaheri P, *et al*., 2024. Cefiderocol in combating Carbapenem-Resistant *Acinetobacter baumannii*: action and resistance. Biomedicines 12(11): 2532.

Zheng JH, Nguyen VH, Jiang SN, *et al*., 2017. Two-step enhanced cancer immunotherapy with engineered *Salmonella typhimurium* secreting heterologous flagellin. Sci Trans Med 9(376): eaak9537.

Zhou Y, Li L, Yu Z *et al*., 2022. *Dermatophagoides pteronyssinus* allergen Der p 22: Cloning, expression, IgE-binding in asthmatic children, and immunogenicity. Ped All Imm 33(8): e13835. doi: 10.1111/pai.13835.

Zhuang HH, Chen QH, Wang W, *et al*., 2025. The efficacy of polymyxin B in treating stroke-associated pneumonia with carbapenem-resistant Gram-negative bacteria infections: a multicenter real-world study using propensity score matching. Front Pharm 16: 1413563.