**Review Article**

**The fallout from Antimicrobial resistance in food animals and Mitigation strategies - A Comprehensive Review**

**ABSTRACT**

Antimicrobial resistance (AMR) is a growing public health problem causing an extensive threat to the veterinary, medical and planetary sectors. The widespread indiscriminate use of antimicrobials in human and veterinary medicine, with a continuous spill-over to the environment, has led to the emergence of antimicrobial resistant ‘superbugs’. This review is aimed to provide an update on the past, present and future global trends of AMR in food animals, the drivers contributing to the spread of antibiotic-resistant bacteria (ARBs), interactions between humans, animals, and the environment. The usage of antimicrobials in livestock with an updated classification of important veterinary antimicrobials and public health impact of AMR have been highlighted. With an understanding of the ongoing AMR challenges, potential mitigation strategies, such as prudent use of antimicrobials, modern farming practices, exploration of antimicrobial mimetics, digital data and tools, drug reprofiling, cross-sectoral ‘Planetary health’ approach in livestock have been emphasised. Ultimately, the review underscores the need for new classes of antimicrobials, suitable alternatives and vaccines, rapid diagnostics, veterinary antimicrobial stewardship programs, resourced surveillance systems through collaborative strategies for reducing the global AMR burden.

**Keywords:** *Antimicrobial resistance, livestock, antimicrobial use, mitigation, one health, planetary health*

**1. INTRODUCTION**

A paradigm shift in the modern-day world's livestock production systems have led to an intensive and industrialized pattern and a close association between mankind, animals, and the environment. A rising demand in animal protein for human consumption has also further necessitated the scale-up in livestock production. On the contrary, these production systems seemed to pave way for inter-species transmission of microbial pathogens, resulting in zoonoses and environmental contamination. Ever since the discovery of antibiotics, these so-called ‘miracle drugs’ have revolutionised the field of medicine in maintaining good health or the major secondary infections post surgeries or therapies, in both humans and animals (Neculai-Valeanu et al., 2024]. The antimicrobials have also been used as growth promoters and therapeutics to meet the growing demands for animal protein, although banned in the recent past.

This extensive use of antimicrobial agents in both animals and humans has accelerated the development of resistant bacterial strains, reducing the effectiveness of essential treatments (O'Neill, 2016). Excess and indiscriminate use of antibiotics has resulted in multidrug-resistant pathogens, referred to as “superbugs” (WHO, 2025) which can spread through food chains, environmental contamination, and human-animal interactions (Collignon, 2016). Although antimicrobial resistance (AMR) may be considered natural in the bacterial evolution driven by antibiotics, it has now become a threat, challenging human and animal health across the globe (Prestinaci et al., 2015).

This has created the need to produce new antibacterial molecules that can overcome this problem of AMR, which might be time-consuming and may not overcome the ongoing crisis. Further the current scenario of AMR might hamper the achievement of 2030 Sustainable Development Goals associated with alleviation of poverty, hunger and improvement of health and economic growth (SDG-1,2,3, 8 and 10), due to the illnesses caused by the antibiotic-resistant pathogens (FAO, 2024a).

Human medicine reports of the abuse of antibiotics as mostly due to inadequate dosing, self-prescribing behaviour, and poor medication compliance. This issue precipitates in countries like India, where the legal policies for the judicious use of antibiotics are unrestricted. In livestock production, antibiotics administered as growth promoters in sub-therapeutic doses for prolonged periods or disease prophylaxis contribute to the environmental pollution due to animal excretions. The agricultural practice of using animal excreta as manure for the cultivable soils increases the spread of AMR from animals to plants, and later to humans, and aquaculture through contaminated food and water.

In addition, zoonotic pathogens with AMR can be transferred to humans through the consumption of contaminated meat, dairy, and other animal-derived products, contributing to the growing burden of untreatable infections (Laxminarayan et al., 2013; Van-Boeckel et al., 2019]. The situation becomes catastrophic as animal practitioners prefer human antibiotics for their better quality and easy availability. With a natural existence of interactions between humans, animals and environment, it becomes decisive to adopt “One-Health” approach laid by International organisations to combat the global AMR burden (WHO, 2025).

The onset of a "post-antibiotic era" in the 21st century has been envisaged by the World Health Organization (WHO) (WHO, 2014) in a study, indicating the alarming rise in antimicrobial resistance worldwide. In veterinary medicine, it is essential to advocate the appropriate use of existing antimicrobial agents. In addition, strategies such as vaccination and immunomodulation for managing bacterial infections (Schwarz et al., 2001) may reduce the burden due to AMR. However, a comprehensive understanding of epidemiology and evolution of antibiotic resistance is required. An urgent need to develop policies for judicious use of antimicrobials in animals and assess resistance levels (Lienen et al., 2021; Coyne et al., 2019) periodically, including environmental monitoring, is therefore essential.

Therefore, this review is intended to provide an overview of the multi-faceted phenomenon of antimicrobial resistance in food-producing animals. The outline describes the current status of AMR in India and other countries initially, followed by the major driving factors, transmission dynamics, antimicrobial usage in livestock, public health implications, mitigation strategies and future milestones to combat AMR crisis.

**2. GLOBAL AND NATIONAL TRENDS IN AMR**

The WHO states that the growing issue of AMR is one of the ten biggest health risks in humans (WHO, 2023). A moderately higher percentage (40-60%) of human bacterial infections are linked to resistant bugs (17%) in most of the developed countries (OECD, 2018). Analysis of the global burden of AMR from 204 countries and territories revealed 1.27 million deaths attributable to resistance, a value almost equal to that associated with major infections (Antimicrobial Resistance Collaborators, 2022). Since the study involved raw data from mostly high-income countries, the true burden of AMR might be much greater (Laxminarayan and Chaudhury, 2016). The growing impact of AMR is expected to be on an increasing trend in LMICs compared to developed countries. Increased mortality, higher morbidity, and huge economic losses have been observed as the direct outcomes of AMR in LMICs (Ahmed et al., 2017).

The global antimicrobial use quantity (AMUQ) is expected to reach ~143,481 tons by 2040, representing a 29.5% increase from 2019 figures, based on Livestock biomass (LBIO) and antimicrobial use intensity (AMUI). Asia has been projected to be the largest contributor of AMUQ, accounting for ~64.6% of the global total. A steep increase is anticipated in the total livestock AMUQ, reaching ~120,138 tons by 2040 mostly due to growth in LBIO [Acosta et al.,2025). By 2050, a catastrophic effect is anticipated as an outcome of AMR in humans, with an expected 3.5% drop in world GDP (Antimicrobial Resistance Collaborators, 2022).

The largest impact of AMR has been studied in countries with tropical climates and airborne transmissions including tuberculosis, although other demographic variables like population density and age seemed to be less significant (McDonnell et al., 2024). The World Bank also reported an impact resulting in an approximate 7.5% reduction in the animal food production (FAO, 2024a). The United Nations General Assembly (UNGA) has so far addressed five health issues, including AMR as global threats. The resistance conditions seem to pose a significant challenge to reach the United Nations Sustainable Development Goals (SDGs), especially in developing countries, namely SDG1 – No Poverty, SDG2 – Zero hunger, SDG3 – Good health and well-being, SDG8 – Economic growth, and SDG10 – Economic inequality (OECD,2018).

Eight pathogens related to AMR were recognized by the World Health Organization (WHO), including five bacteria, namely, *Mycobacterium tuberculosis, Escherichia coli, Staphylococcus aureus, Neisseria gonorrhoeae, and Klebsiella pneumoniae* (WHO, 2023)*.* Among these, third-generation cephalosporin-resistant and carbapenem-resistant Enterobacteriaceae (CRE, such as *Escherichia coli* and *Klebsiella pneumoniae*) were found to be responsible for a maximum number of severe infections and bloodstream infections worldwide annually (Temkin et al., 2018), followed by third-generation cephalosporin-resistant and ESBL-producing *Enterobacteriaceae* and methicillin-resistant *Staphylococcus aureus* (MRSA) (Wozniak et al., 2019).

Such antimicrobial-resistant pathogens in animals make treatments ineffective, allowing disease progression, reduced production, causing huge economic losses. While human antibiotics consumption of antibiotics is under monitoring through antibiotic sales databases, however, less attention has been given to the antibiotics consumption in livestock. Research findings have observed that although animals consumed more antibiotics than humans worldwide (Tiseo et al., 2020), more than fifty percent went unabsorbed into the excretions. Since data about antimicrobial consumption in livestock, regulations and policies to optimize the use of antibiotics in animals are not well targeted, the relation between antimicrobial consumption and resistance patterns are also poorly defined (Van Boeckel et al., 2019).

Resistance maps along with antimicrobial consumption data in livestock will enable an approximation of baseline estimate of the global AMR scenario. Ever since 2010, China and India have been listed as the largest antimicrobial consumers, owing to the high prevalence of bacterial diseases and limited regulatory provisions for antimicrobial usage. Further survey of common indicator pathogens (*E. coli, Campylobacter* spp., non-typhoidal *Salmonella*, *Staphylococcus aureus*) in LMICs reporting AMR in animals, identified northeastern China, northeastern India, northern Pakistan, Iran, eastern Turkey, the south coast of Brazil, Egypt, the Red River delta in Vietnam, and the areas surrounding Mexico City and Johannesburg as largest hotspots of resistance. New hotspots arising in Kenya, Morocco, Uruguay, southern Brazil, central India, and southern China have also been reported. The highest resistance rates were observed in tetracyclines, sulfonamides, and penicillins – the most commonly used antibiotics in animal production (Van Boeckel et al., 2019).

According to a meta-analysis study carried out in India at ICAR-NIVEDI, the prevalence of livestock-associated MRSA (LA-MRSA) in food-producing animals is approximately 10%, ranging from 7% in healthy animals to 12% in animals with clinical conditions. Various studies conducted in the eastern regions of the ICAR institutes have reported biofilm-producing multi-drug resistant ESBL and AmpC type-lactamase producers in a variety of livestock species, including chicken, ducks and backyard poultry. The food and companion animals have also been reported as major reservoirs of diseases, resistant to last-resort medications like carbapenem, which are infrequently utilized in animal husbandry. However, the resistance to cephalosporins resistance has increased in frequency among food animals due to the recent surge in the usage of higher-generation cephalosporins to treat bovine mastitis and bacterial pneumonia in food animals, (FAO, 2024a).

**3. DRIVERS OF AMR IN LIVESTOCK**

**3.1 Evolution of Bacterial resistance against Antimicrobials**

Antimicrobial resistance is a natural phenomenon, which happens when a commensal or pathogenic bacteria susceptible to an antibiotic, upon exposure to that antibiotic, turns resistant. The presence of broadly-specific antimicrobial efflux pumps, also called as drug extrusion is the major cause of the inherent resistance property of bacteria to antibiotics (Fernandes et al., 2003). This low grade of resistance, upon mutations or acquisition of new resistance genes through genetic exchange, later transform the bacteria as antimicrobial -resistant forms (Blakely, 2024). The rapid spread of antimicrobial resistance in bacteria is determined by the presence of resistance determinants, their vertical or horizontal transmission and a selection pressure eventually (Schwarz and Chaslus-Dancla, 2001).

**3.2 COMMON DRIVERS OF AMR**

Understanding the key drivers of AMR is essential for devising potential mitigation strategies. The major driving forces of AMR in livestock are - antimicrobials themselves, antibiotic resistance genes of the microbes, and environmental factors. The other factors include poor sanitation, release of non-metabolized antibiotics into the environment through host excretions, development of biofilms, use of antibiotics as growth promoters in poultry and livestock for a prolonged period, inappropriate usage, poor biosecurity measures and lack of awareness (Tilloston and Zinner, 2017).

**3.2.1 Abuse of Antimicrobial agents**

Among the well-defined categories of resistance-inducing drivers that contribute to antimicrobial resistance (AMR), extensive research data has demonstrated the importance of misuse of antibiotics for growth promotion and long-term disease prophylaxis, which has led to selection pressure favouring antimicrobial-resistant bacterial strains (ARBs) (WHO, 2017; Caneschi et al.,2023; Neculai-Valeanu et al., 2024).Thisis especially in countries where livestock, especially poultry and swine, are reared intensively (Prescott ,2017). In some countries, sub-therapeutic doses of tetracyclines are still administered in swine feed for prolonged periods to promote animal growth and prevent diseases (Ghimpețeanu et al., 2021).

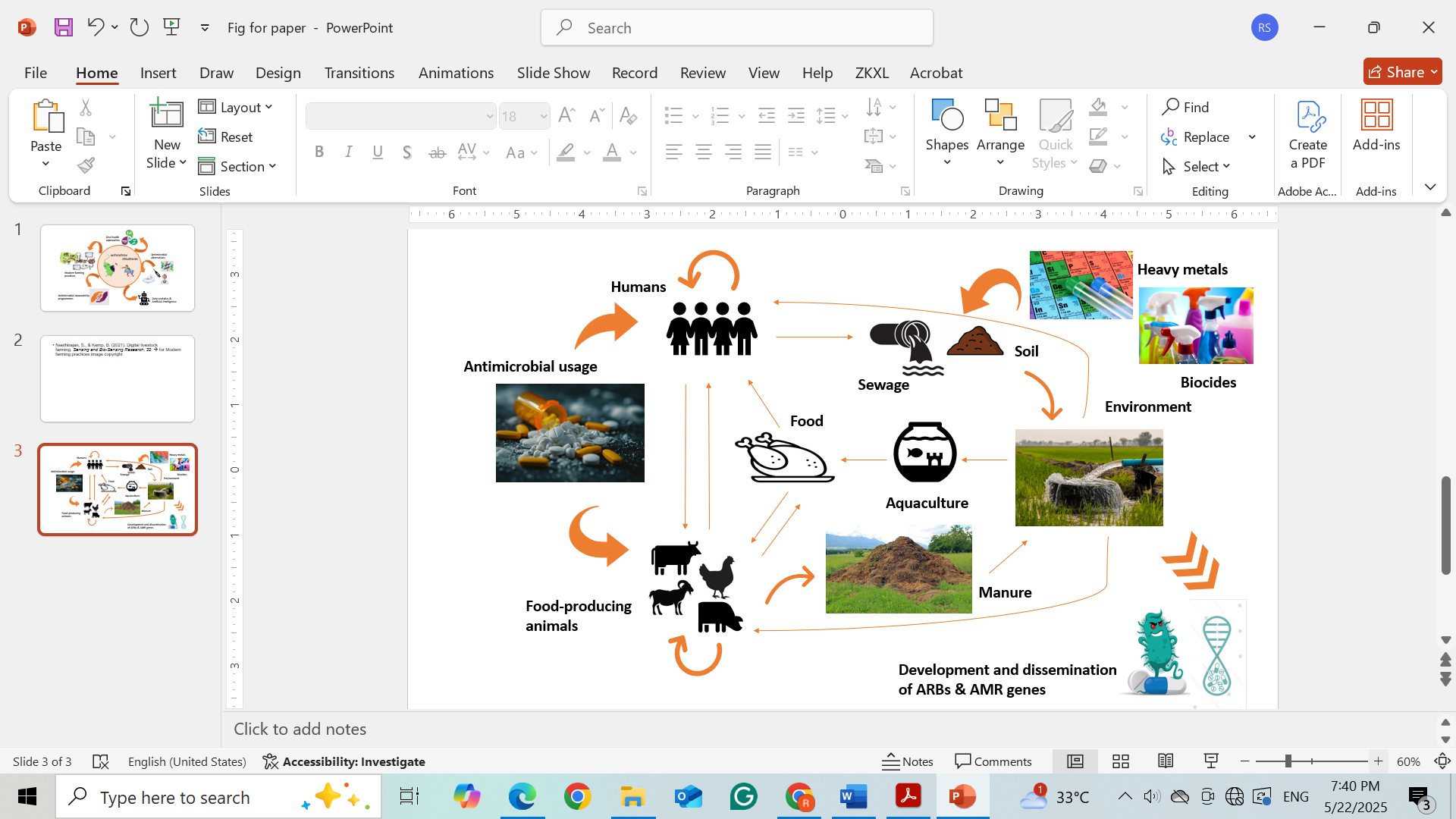
Currently, most of the antibiotic classes as well as the antimicrobial -resistant genes (ARGs) and ARBs are shared between humans and animals (Tulloch et al., 2021). In addition, the antimicrobials are also used in the large herds where the apparently healthy and clinically infected animals at risk are unable to be separated. The practice of AMU in such cases is usually done in order to curtail any spread of infection within the herd (Bandyopadhyay and Samanta, 2020).

The organisational triad involved in One-health namely - World Health Organization (WHO), Food and Agricultural Organization (FAO), and World Organization for Animal Health (WOAH) considered the use of medically-important antimicrobials (MIA) in animals for growth enhancement, prevention of diseases, and even metaphylaxis, as inappropriate antimicrobial usage (IAMU). A ban a ban on the usage of MIA for prophylaxis and growth promotion in healthy animals was recommended (WHO, 2017).

A short-term mass medication with therapeutic antimicrobial concentrations is sometimes administered immediately before a disease outbreak, or immediately at the onset of disease population, especially in beef feedlot and swine (Apley and Coetzee, 2013). A thorough scrutiny is underway of these practices, banned and replaced by disease-targeted therapy only.

**3.2.2 AMR Transmission pathways**

Several pathogenic bacteria are present in humans, domestic and wild animals/ avians and the environment. There also exists a close association between AMR in humans, farm and companion animals, and their surrounding environment (Woolhouse et al., 2015). Thereby, resistance can be cross-transmitted across these populations and similar resistance genes have been demonstrated in the pathogens, commensals of the host and the environmental bacteria (**Figure 1**).



**Figure 1: AMR transmission pathways**

The active transfer of ARGs, either by vertical or horizontal means, has been well-studied. Horizontal transmission occurs through the mechanisms of transformation, conjugation, and transduction (Liu et al., 2020). This paves way for the less problematic bacterial strains transforming to more dangerous bacterial species, with potentially disastrous results.

Mobile genetic elements, such as plasmids and transposons, frequently carry genes that encode various resistance mechanisms, facilitating their transmission between bacteria, both within and between species or genera (Von Wintersdorff et al.,2016; Liu et al., 2020). Extended-spectrum cephalosporin resistance in *E. coli* was transmitted by epidemic plasmids from varied bacterial species, hosts and countries (Zamudio et al., 2024). Additionally, certain transposons may have specialised regions called integrons among different bacterial species, especially between Gram-negative bacteria that can contain multiple resistant genes, making a bacterial species resistant to several antibiotics (Gillings, 2014). Interspecies and intraspecies transfer of antibiotic resistance determinants and virulence factors have also been identified in major hotspots like hospital effluents (Bruno and Mackay, 2012). New genes have been associated with drug resistance in food animals, including the mobile colistin resistance gene (mcr-1) in pigs, the plasmid-mediated tigecycline resistance gene (tet(X)) in chickens and pigs, and the β-lactam resistance gene (blaCTX–M–8) in chickens (Liu et al., 2016; He et al., 2019; Nesporova et al., 2021).

Chromosomal mutations within bacterial species normally spread by vertical transmission. However, they are later corrected by cellular mechanisms, which make them uncommon theraafter. Bacteria may become resistant to certain antibiotics or a class of antibiotics as a result of *de novo* mutations that arise from target-site gene alterations for that antibiotic (Bava et al., 2024). Such ARG transfers, both vertical and horizontal, have been widely documented in earlier studies. Regardless of previous antibiotic exposure, the natural biodiversity of the intestinal microbiome of humans and food-producing animals acts as reservoirs for the ARGs. The gut acts as a favourable habitat for the bacteria to exchange genetic materials containing ARGs between humans and animals (Toutain et al., 2016).

Recent research identified that cigarette smoke and its waste, facilitated the growth of ARB in the environment and on the cigarette filters. These contaminated butts spread dangerous ARBs to waterbodies. Smoking in humans also increased the spread of resistant germs in the lungs, reducing antibiotic effectiveness against future infections (Griebe, 2025).

Other factors contributing to the rise of AMR include food trade, environmental contamination, and social aspects such as international and intercontinental travel (Littmann and Viens, 2015).

**3.2.3 Environmental Bioaccumulation of Antimicrobials**

The WOAH classified certain antimicrobials as 'critically important' for livestock, which include representatives from all major classes of antimicrobials used in human medicine (WOAH, 2025). The antimicrobials administered in the animal farms are only partially absorbed in the animals, while a considerable proportion is not entirely metabolised and excreted in an active form (Sukul et al., 2009). These residual antimicrobials in the environment interact with the bacteria (like *Escherichia coli* from farm waste water, free-living *Vibrio cholerae*), activating biological processes, thereby promoting bacterial resistance. Thus, animal farms and livestock operations have invariably become the major sources of antibiotic-resistant bacteria. These bacteria can infect other susceptible animals and farm workers; contaminating raw milk, meat, and other dairy products, thereby posing a potential threat to human health through foodborne (Masse et al., 2021; Baker et al., 2022; Baghdadi et al., 2023; Robinson et al., 2016) route.

In many countries, animal faeces are used as fertilizers, which potentiates the spread of resistance genes through food and groundwater. Fresh fruits and vegetables, when taken raw, may still contain live, viable bacteria at the time of consumption. Cross-contamination of food with ARGs can also happen through faecal contamination during animal slaughter (Florez-Cuadrado et al., 2018) or when handled by consumers, or exposure to environment, or after processing (Robinson et al., 2016). Industrial and municipal wastewater, sewage sludge and animal manure applied to agricultural fields and aquaculture systems also act as major environmental transmission pathways for these resistance determinants (Samreen et al., 2021).

Dairy cattle populations reared intensively in many countries, contributing to the rural livelihood, nutrition, and country’s economy, are reviewed in this section, which serves as one of the potential sources of AMR in livestock. Inappropriate waste management practices have led to the proliferation of ARGs in the soil from the dairy farm manure, waste and (Kim et al., 2021; Baghdadi et al., 2023), wastewater treatment facilities (Todman et al., 2024), primary dairy slurry waste (Baker et al., 2022). On the contrary, a greater number of ARGs have been found in the animal faeces that have not been given antibiotics also, including those belonging to the critically important antimicrobial (CIAs) groups (such as carbapenems and quinolones) (VandenMeersche et al., 2020). ARGs are also commonly detected in the agricultural environment following antibiotic treatments to the animals (Johnsen et al., 2009).

In addition to antibiotics, the increasing usage of disinfecting products containing biocidal agents and the release of toxic wastes thereafter contribute to the development of drug- and solvent-resistant bacterial strains. In addition, the presence of co-selective agents, such as heavy metals (like lead, mercury, arsenic, chromium, cadmium, and nickel) from the environment and microplastics, acts as synergistic drivers of AMR (Balta et al., 2025). They have been studied to exert pressure on microbial communities, facilitating resistance and creating genetic exchange hotspots due to biofilm formation. Exposure to natural plant-derived compounds and organic solvents like toluene, octanol and hexane have also predisposed the selection of ARGs (Friedman, 2015). Co-selection has been found to occur through co-resistance, where the selection of one gene promotes the selection of another gene (Spellberg et al., 2016) and cross-resistance (Hall et al., 2018).

Soil and water ecosystems have also been identified as reservoirs for ARGs originating from anthropogenic activities (Balta et al., 2025). A metagenomics study discovered resistance genes in soil that were completely identical to those present in clinical isolates, across all major classes of antibiotics, demonstrating a horizontal gene transfer between soil bacteria and pathogens. For instance, the presence of resistance genes for synthetic quinolones (qnr genes) in soil suggested that the transfer likely occurred from the clinic to the soil rather than the other way around (Forsberg et al., 2012).

**3.2.4 Climate change and AMR**

In addition to the bioaccumulation of antimicrobials in the environment, the climate crisis has been studied as another driving force. Climate changes seemed to increase the spread of many infectious diseases, including vector-borne diseases, across the world. This has further contributed to the rise in AMU, and in turn, AMR in the respective sectors (Mackenzie and Jeggo, 2019). Fluctuating ecosystems and altered disease vectors have been reported to lead to the emergence of new antimicrobial-resistant infections or the spread of existing ones to new areas. Temperature and/or precipitation, human migrations, diverse vectors, agriculture and hydrology have also affected the development or transfer of AMR in bacteria (Knapp et al., 2021). Also, the effects of climate change on human lifestyle and other social determinants of infectious disease risks, pave way for increased AMU upon onset of diseases and the AMR scenario thereafter (Gillingham et al., 2023).

The links between two global challenges, namely AMR and climate change, have been demonstrated only in the recent past by a few authors, generating data of shared processes intensifying both threats. The planetary health approach has been reported to improve the One-health framework by identifying the broader environmental, social and economic factors responsible for the development and spread of AMR (Horvat and Kovačević, 2025).

**4. ANTIMICROBIALS USE (AMU) IN LIVESTOCK**

Diseases in food-producing animals directly impact availability of animal products for human consumption and nutritional security in humans. The prevalence of livestock-associated ARBs in humans and animals has been demonstrated to be directly related to the levels of AMU in humans and animals (Vieria et al., 2011).

In the recent past, bacterial diseases like Anthrax, Clostridial infections, Brucellosis, Haemorrhagic septicaemia, Leptospirosis, Foot-rot and Contagious bovine/caprine pleuropneumonia have been reported among animals in India and many other countries. This scenario henceforth is expected to escalate the sales of veterinary antimicrobials across the globe by 11.5%, with a parallel increase of 15% for AMU in humans by 2030. The greater extent of AMU in animals than humans (Tiseo et al., 2020), has established itself as the major driver for AMR. Also, extensive AMU in livestock, poultry and humans in developed countries and LMICs has resulted in the emergence of antimicrobial-resistant bacteria (ARBs) through natural selection, altering the ecosystem and food chain.

Based on importance in the treatment of serious animal diseases and availability of suitable alternatives, the WOAH list of Veterinary antimicrobials have been classified into three categories: Veterinary Critically Important Antimicrobial Agents (VCIA), Veterinary Highly Important Antimicrobial Agents (VHIA), Veterinary Important Antimicrobial Agents (VIA). Some of the antimicrobial agents listed by WOAH, namely – Fluoroquinolones, third and fourth generation Cephalosporins, Colistin (Polymyxin E), and Phosphonic acid derivatives have been classified as Highest Priority Critically Important (HPCIA) by WHO. On the contrary, WHO has classified the Medically Important Antimicrobials (MIA) based on selected criteria and their medical importance for treating critical illnesses in humans and probable transmission of AMR from bacteria to humans while using these antimicrobials in non-human sectors (WOAH, 2025).

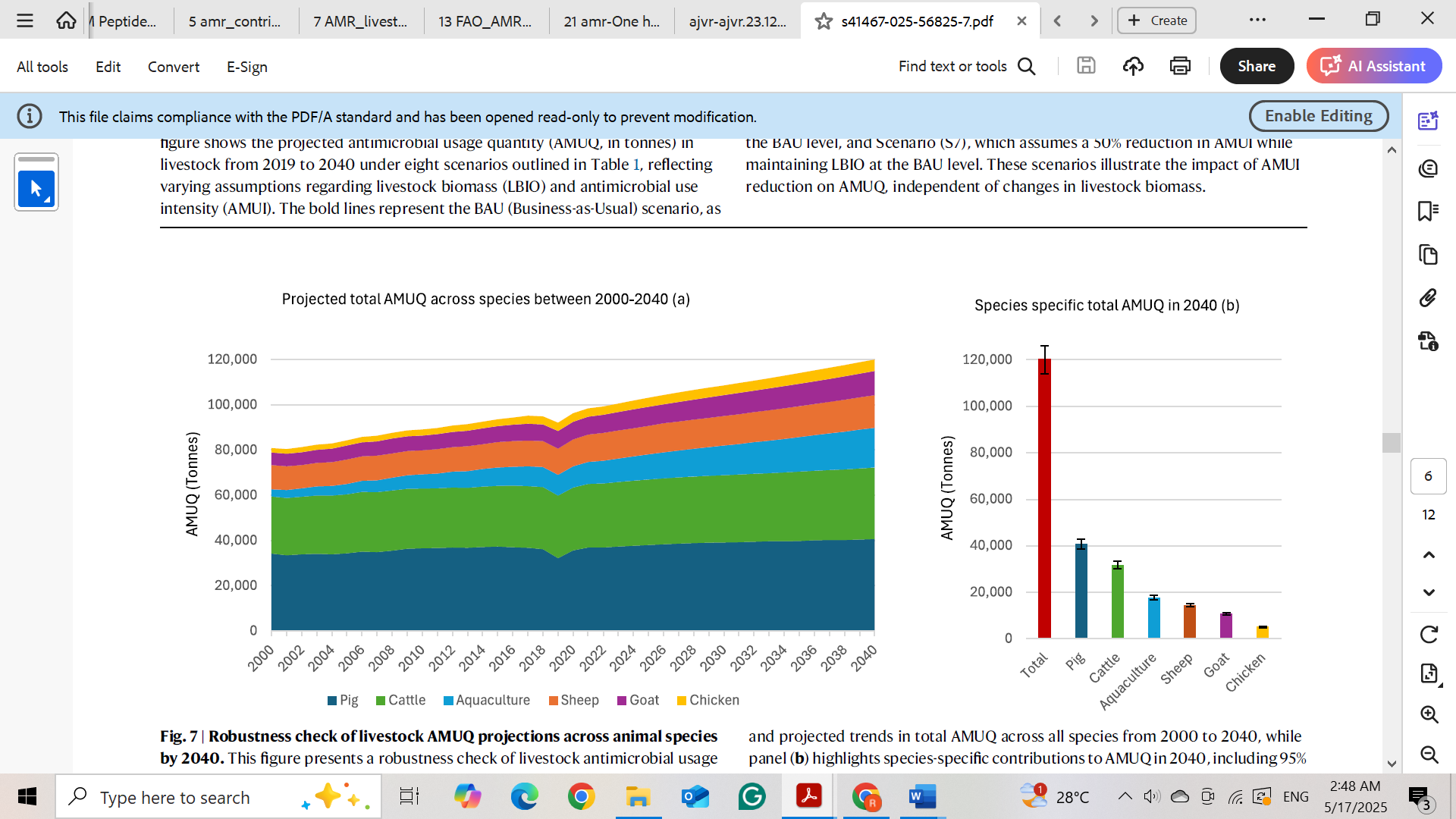
The important veterinary antimicrobials, their resistance mechanisms, WHO /WOAH classification and clinical indications as provided in the recent guidelines of WHO (2024b) and WOAH (2025) have been summarised in **Table 1.**

**Table 1: Antimicrobial agents of Veterinary importance** (WHO, 2024b; WOAH, 2025)

| **Antimicrobials** | **Classification** | | **Resistance mechanism** | **Clinical indications** | |
| --- | --- | --- | --- | --- | --- |
| **WOAH** | **WHO** | **Animals** | **Humans** |
| Sulfonamides and  Potentiated Sulfonamides | VCIA | HIA | Changes in target enzymes and efflux pumps | Gastrointestinal, respiratory, skin (including pododermatitis), soft tissue, infections; sepsis; mastitis (topical), UTI infections, septicaemia, coccidia infections, cardiovascular, central nervous systems, systemic infections. | Acute bacterial meningitis, systemic nontyphoidal *Salmonella* spp. infections and other infections |
| Penicillins | VCIA | HIA | Synthesis of enzymes such as β-lactamases, which hydrolyse β-lactam rings that disrupt penicillins or cephalosporins, or by altering the penicillin-binding proteins (PBP2a) when bacteria have a decreased affinity for β-lactam drugs. | Arthritis; gastrointestinal, ophthalmic, respiratory, skin, urogenital infections, mastitis (topical use), peritonitis; pododermatitis, septicaemia; tetanus, omphalophlebitis, joint-ill infections in calves, botulism in poultry, cardiovascular, and systemic infections.  Infections caused by *Aeromonas* spp., *Photobacterium* spp., and *Streptococcus* spp. | *Listeria* and *Enterococcus* spp., Staphylococcal infections (*S. aureus*), Streptococcal infections, MDR *Shigella* spp., Leptospirosis, Yaws and Syphilis. |
| Cephalosporins | VHIA (1st and 2nd generation)  VCIA (3rd and 4th generation) | HIA (1st and 2nd generation)  HPCIA (3rd and 4th generation) | Early-generation cephalosporins: neutralized by β-lactamases;  3rd and 4th generations of cephalosporins: rendered inactive by extended-spectrum β-lactamases produced by some strains of gram-negative bacteria | First and second generation cephalosporins are used in mastitis (topical use), skin, respiratory, urinary tract infections, and systemic infections  Third and fourth-generation cephalosporins are used to treat metritis, respiratory infections, septicaemia in calves; mastitis (topical use), gastrointestinal, respiratory infections, skin, soft tissue, and urinary infections | Effective against infections caused by *Enterobacteriaceae*, gram-positive bacteria except *Enterococcus*, and anaerobic infections |
| Tetracyclines | VCIA | HIA | Energy-dependent drug efflux and alterations to the tetracycline binding sites at the 30S ribosomal units | Arthritis, navel ill (calves), ophthalmic, gastrointestinal, respiratory, genital infections, pododermatitis, septicaemia, ophthalmic infections, traumatic or surgical wounds (topical use), tick-borne diseases; superficial skin and ophthalmic infections (topical use), bacterial and coccidial infections, and systemic infections | Effective against *Rickettsia* spp., *Brucella* spp. and *Chlamydia* spp. |
| Aminoglycosides | VCIA | CIA | Degradation of the enzymes, modifications to the drug attachment sites (30S ribosomes), and changes in the cell surface receptor | Gastrointestinal infections, mastitis (topical use), systemic infections caused by Gram-negative bacteria, ophthalmic infections, otitis (topical use) and Histomoniasis.  Infections caused by *Aeromonas* spp., *Edwardsiella* spp., and *Vibrio* spp. | Enterococcal endocarditis, MDR tuberculosis, and MDR *Enterobacteriales*. |
| Amphenicol | VCIA | HIA | Efflux pumps, inhibition of intercellular drug transport, and enzymatic alterations by rRNA transferases | Ophthalmic infections, otitis (topical use), hoof, respiratory and skin infections | To treat against acute bacterial meningitis, typhoid and non-typhoid fever, and respiratory infections. |
| Macrolides | VCIA | CIA | Alterations to the drug binding sites at the 50S ribosomes (erm genes), drug inactivating enzymes, and efflux pumps encoded by mef gene | Ophthalmic, respiratory infections, necrobacillosis in calves, mastitis (topical use), arthritis, and gangrenous dermatitis  Infections caused by *Streptococcus* spp., *Lactococcus* spp., *Renibacterium* *salmoninarum* and *Francisella* spp. | *Legionella*, *Campylobacter*, and MDR *Salmonella* spp. and *Shigella* infections. |
| Lincosamides | VHIA | HIA | 23S rRNA methylation encoded by the erm gene, drug efflux pumps, and enzymatic modifications | Pyelonephritis, enterotoxaemia, tetanus, mastitis, bone, dental and skin infections, infections caused by anaerobic bacteria, infections of the central nervous system, colibacillosis, and fowl cholera | *Staphylococcus aureus,* including MRSA, *Enterococcu*s spp. |
| Quinolones | VHIA (1st generation)  VCIA (2nd generation) | CIA | Plasmid-mediated resistance, mutations in the quinolone resistance-determining region (QRDR) encoded genes of GyrA and ParC, reduced drug accumulation, increased efflux, target enzyme mutations (DNA Gyrase and Topoisomerase IV) | First generation used to treat gastrointestinal, skin, respiratory, urinary tract infections, colibacillosis, and fowl cholera.  Second generation used in arthritis, gastrointestinal, respiratory, urogenital system infections, septicaemia, mastitis (topical), otitis (topical), and systemic infections. | *Campylobacte*r spp., invasive disease due to *Salmonella* spp., and MDR *Shigella* spp. infections |
| Polypeptides | VHIA | IA | Altering cell surface charge, polysaccharide entrapment, and resistance to Bacitracin is rare | Gastrointestinal infections and Necrotic enteritis in poultry | Effective against gram-positive infections, superficial skin infections caused by *Staphylococcus aureus* |
| Polymyxins | VHIA | HPCIA | Lipid A modifications, intrinsic resistance, and colistin-resistance mediated by the mcr gene, that affect overall charges of LPS of bacterial cell membrane | Gastrointestinal infections, ophthalmic, skin infections, otitis (topical use), and colibacillosis | MDR *Enterobacteriales* (e.g., *Klebsiella* spp., *E. coli*, *Acinetobacter*, *Pseudomonas* spp.) |
| Aminocyclitol | VCIA | IA | Enzymatic inactivation by aminoglycoside-modifying enzymes (AMEs), ribosome target modification, reduced uptake and increased efflux pumps | Respiratory, gastrointestinal, urinary, skin, and systemic infections | Effective against *Neisseria gonorrhoeae* and *E. coli* infections |
| Ansamycin | VHIA | CIA | Mutations within the RNA polymerase target protein (RNAP), cell permeability changes, and modification through ADP-ribosylation | Mastitis (topical use), skin conditions (topical use), and *Rhodococcus* *equi* infections in foals | Treatment of mycobacterial diseases, including tuberculosis and MDR *S. aureus* |
| Fusidane | VIA | HIA | Mutations in the elongation factor G (EF-G), acquire resistance genes, namely, fusB and fusc, and altered drug permeability | Ophthalmic and skin infections (topical use) | Infections with MRSA |
| Phosphonic acid derivatives | VHIA | HPCIA | Enzymatic hydrolysis, modifications of the P-C bond, and overexpression of target genes | Gastrointestinal, central nervous system, respiratory and systemic infections | UTI infections, *E. coli* infections, and life-threatening carbapenem-resistant Enterobacteriales (CRE) infections |
| Streptogramins | VIA | HIA | Active efflux, mutations in the ribosomal RNA (rRNA), Expression of genes like vat(A), vat(B) or vat(C) code for acetyltransferases, and enzymatic inactivation | Liver abscess, necrotic enteritis | *Enterococcus* spp. and MRSA |
| Ionophores | VHIA | - | By shedding the cell membrane or enclosing in a glycoprotein armor (glycocalyx) | Coccidiosis, necrotic enteritis | **Not authorized for human use**  **Not authorized for human use** |
| Aminocoumarin | VIA | - | Mutation in target-gyrB | Mastitis (topical use), Staphylococcal infections |
| Avilamycin | VIA | - | Alterations in the 23S ribosomal (rRNA) | Necrotic enteritis in poultry, gangrenous dermatitis and colibacillosis |
| Pleuromutilins | VHIA | - | Plasmid-mediated (vga and cfr genes) and chromosomal (mutations in the 23S rRNA and rplC genes) | Gastrointestinal, central nervous system, systemic infections and enteric infections in poultry |
| Quinoxalines | VIA | - | Mutations in DNA gyrase and topoisomerase IV, Qnr proteins and multidrug efflux pumps | Gastrointestinal infections in swine |
| Arsenicals | VIA | - | Energy-dependent efflux of arsenite (AsIII), detoxification of organic arsenicals mediated by ArsL, ArsM and ArsH, and horizontal gene transfer, | Coccidiosis and gastrointestinal infections in swine |

VCIA: Veterinary Critically Important Antimicrobial Agents; VHIA: Veterinary Highly Important Antimicrobial Agents; VIA: Veterinary Important Antimicrobial Agents; HIA: Highly Important Antimicrobials; CIA: Critically Important Antimicrobials; HPCIA- Highest Priority Critically Important Antimicrobials; IA- Important Antimicrobials

The 2040- projected AMUQ among livestock species is expected to be; swine > cattle> sheep/goat > poultry (**Figure 2**). Swine are expected to remain as the predominant consumers of antimicrobials, while the lower AMUQ in poultry despite their smaller biomass is likely due to highly intensive rearing systems compared to other species (Acosta et al., 2025). Poultry slaughtered at an early age had the least antimicrobial usage, compared to other food animals. Animal species reared under intensive systems were exposed to far more antibiotics than the other animals (Ritchie and Fion Spooner, 2024).

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**Figure 2. Livestock AMUQ projections across animal species by 2040** (Acosta et al., 2025)

In general, veterinary antimicrobials are indicated for the treatment of diseases, predominantly, in addition to prevention and metaphylaxis of diseases and growth promotion in livestock and poultry (Bandyopadhyay and Samanta, 2020). They have also been used to save the lives of animals and reduce pathogen shedding and methane emission in the environment (Odongo et al., 2007). Mostly, antibiotics used for livestock were the same as those used in human medicine, which led to AMR and the spread of ARBs in farms (poultry and pigs) among humans, animals, and the environment (Reardon, 2017).

Although statistical data of species-level consumption in LMICs are limited, systematic investigations showed that tetracyclines were the most commonly used antibiotics, followed by aminoglycosides, beta-lactams, macrolides, arsenicals, fluoroquinolones, ionophores, penicillins, polymyxins, polypeptides, and sulfonamides (Lam et al., 2019). In a global data analysis, tetracycline and penicillin was accounted for a higher 47% and 12% of the total sold MIA for animal production on a weight basis in Japan, followed by 29% and 25% in Europe, 51% and 8% in Canada, 32% and 6% in USA, and 9% and 9.8% in Australia, respectively. (Innes et al., 2020).

In food-producing animals, the common antibiotics like tetracyclines and penicillins were used to treat bacterial skin diseases, including MRSA infections, prevent and treat bovine pneumonia, calf scours, foot rot, metritis, and Pasteurellosis. Other antimicrobials like macrolides, aminoglycosides, and fluoroquinolones have been used to treat bacterial skin diseases in bovines (Neculai-Valeanu et al., 2024). Ampicillin and tetracycline, have been reported to have low bioavailability (10% and 5-15% respectively) when administered orally in swine (Bibbal et al., 2007). The unabsorbed antibiotics altered the intestinal microbiota (Hansen et al., 2002) and continued to be pharmacologically active in the excreta, affecting microorganisms in the environment. The chances of resistance spread in the environment potentiated by the presence of β-lactam resistant *E. coli* have been reported in a piggery (Fournier et al., 2021).

Restricted usage of Critically Important Antimicrobials (CIAs) like higher generation cephalosporins, fluoroquinolones, and macrolides in specific infections, has been the major recommendation for more than two decades (Bager et al., 2001)*.* Nevertheless, there has been an increase in the use of higher generation cephalosporins recently, in the management of bovine mastitis, bacterial pneumonia in food animals, resulting in ‘Cephalosporin-resistance’. Shedding of extended spectrum β-lactamase (ESBL)-producing *E. coli* was found in the animal faeces, mainly due to the spread of a clonal lineage within the farm. Resistance of β-lactamase-producing Avian pathogenic *E. coli* (APEC) to third and fourth generation Cephalosporins have been demonstrated by the presence of *bla*CTX−M−15, *bla*TEM−1, and class 1 integron genes (Kang et al.,2022). Multi-drug resistant ESBL and AmpC type β-lactamase producers with biofilm production have also been reported in a wide range of animal species like cattle, swine, commercial and backyard poultry (FAO, 2024a).

Colistin (Polymyxin E), an effective antibiotic, was generally used as a last resort against Gram-negative bacterial infections. Misuse of this drug has led to resistant bacteria due to chromosomal mutations and acquisition of plasmid-mediated *mcr* (mobile colistin resistance) genes. Colistin-resistant *E. coli* with mcr-1 gene emerged in China, in humans, poultry, and pigs (Liu et al., 2016). Additional variants of *mcr* genes ranging from *mcr*-1 to *mcr*-10, mainly in *Enterobacteriaceae* have been reported recently across countries, in both humans and animals (Mondal et al., 2024). These findings made China, India, and many other countries to ban the use of colistin as a growth promoter in food-producing animals (Walsh and Wu, 2016). Isolation of Colistin-resistant *E. coli* from farm animals and farm workers substantiated the fact that animal farms may act as zoonotic reservoirs for ARBs (Vines et al., 2021). However, the gradual reintroduction of the drug recently, to treat infections caused by multi-drug resistant (MDR) Gram-negative bacteria, could ultimately lead to pan-resistance, creating an alarming situation (Mondal et al., 2024).

Oral administration of low, sub-therapeutic doses of antibiotics was supplemented in feed or water in the food animal production units sometime back, to improve growth and production. Tylosin and tetracyclines were frequently used antibiotics as feed additives in 88% of the growing pigs in the United States (Landers et al., 2012). Some of the non-MIAs, such as carbadox, bambermycins, and bacitracin, have also been used for growth promotion (Bandyopadhyay and Samanta, 2020), although these drugs have been put under scrutiny currently in many countries. But meta-analysis data indicated that the antibiotic-resistant bacteria were reduced in animals and humans, who had close contact with the animals, when antibiotics were restricted as growth promoters. However, the analysis was unable to determine the impact on the community (Tang et al., 2017).

Some antimicrobials used for prophylaxis in the farm animals include Tylosin - used in calves to prevent hepatic abscesses, macrolides in cattle to prevent respiratory infections and β-lactams in dairy cows for prevention of mastitis (Neculai-Valeanu et al., 2024). The prophylactic use of antimicrobials is allowed in food-producing animals, including poultry, only for high-risk diseases, which do not have any alternatives, and especially the HPCIAs and CIAs are generally discouraged in groups of food animals (Weese et al., 2025).

**5. PUBLIC HEALTH IMPLICATIONS**

The impact of intensive and excess use of antimicrobial drugs on food-producing animals started two decades ago, with the emergence of multi-resistant food-borne pathogens posing a significant risk to public health (Catry et al., 2003) and still remains a challenge. This antimicrobial resistance hinders our therapeutic efforts to handle infectious diseases, to reduce the mortality and morbidity rates or prevent the secondary infections. Such a trend might increase the morbidity rate to about 10 million by 2050 (Mukherjee, 2024). Multidrug-resistant bacteria have emerged only after long-term, widespread use of antibiotics to treat infections and hence named as “Superbugs” (Salam et al., 2023). The recently updated WHO Bacterial Priority Pathogens List (BPPL)- 2024, categorised 15 families of antibiotic-resistant (ABR) pathogens, based on the importance for R&D and public health measures (WHO, 2024a).

Gram-negative bacteria resistant to last-resort antibiotics especially in LMICs, were classified as ‘Critical priority pathogens’ - namely, Carbapenem-resistant *Acinetobacter baumannii* (CRAB), leading to severe nosocomial infections, especially among intensive care patients; carbapenem-resistant *Enterobacteriales* (CRE) causing bloodstream, respiratory tract, intraabdominal and urinary tract infections; and third-generation cephalosporin-resistant *Enterobacteriales* (3GCRE) commonly resulting in neonatal sepsis, increased mortality and morbidity; and rifampicin-resistant (RR) *Mycobacterium tuberculosis.* ‘High priority pathogens’ included antibiotic-resistant *Pseudomonas aeruginosa* and *Staphylococcus aureus*, MDR- *Neisseria gonorrhoeae*, especially in health-care settings; antibiotic-resistant *Enterococcus faecium*, capable of transmitting resistance across animals, humans and the environment. Group A and B Streptococci, *Streptococcus pneumoniae* and *Haemophilus influenzae* were grouped in the ‘Medium-priority category’, causing public health impact. especially in resource-limited settings (WHO, 2024a).

Zoonotic pathogens have also been reported to cause public health hazards due to cross-species transfer of AMR in diseases like Anthrax (*Bacillus anthracis*), bovine Tuberculosis (*Mycobacterium tuberculosis*), Brucellosis (*Brucella abortus*), haemorrhagic colitis (*Escherichia coli*) (Rahman et al., 2020), Hendra virus and influenza A (Leifels et al., 2022), *Trypanosoma cruzi* and *Toxoplasma gondii* (Weiss, 2008). Mostly, antibiotic-resistant bacteria originated from livestock farms and infected humans as food-borne pathogens (Neculai-Valeanu et al., 2024). Zoonotic bacterial pathogens causing human illnesses by food-borne contamination commonly include; multidrug resistant strains of *S. aureus*, *Salmonella* sp., *Campylobacter* sp., *L. monocytogenes*, and *E. coli* (Abebe et al., 2020).

Bacteria and mobile genetic elements that confer resistance, have been demonstrated on animal skin and in faeces, spreading among themselves in various ways, and capable of infecting humans (Witte, 2000). In addition, treatment failure due to antibiotic resistance may occur if ARGs are horizontally transmitted into human pathogenic bacteria (Van den Bogaard and Stobberingh, 2000). The earlier reports of hospital-adapted lineage of 51 *Enterococcus faecium* strains was confirmed of their origin from a population mainly composed of animal strains (Lebreton et al., 2013). Different species of pathogenic bacteria carried resistance genes found in farm animals and livestock products (Gilbert et al., 2021).

Livestock-associated Methicillin-resistant *Staphylococcus aureus* (LA-MRSA), initially reported in animals, has recently emerged in human populations, resulting from inappropriate AMU. The zoonotic transmission from farm animals to farm workers has been reported as an occupational hazard in farm workers and veterinarians across many countries (Nadimpalli et al., 2018; Bandyopadhyay and Samanta, 2020), especially in piggery (Dong et al.,2021), dairy farms (Mithu et al.,2024), in low-income regions mostly due to factors such as delayed access to healthcare services (Zhou et al.,2024).

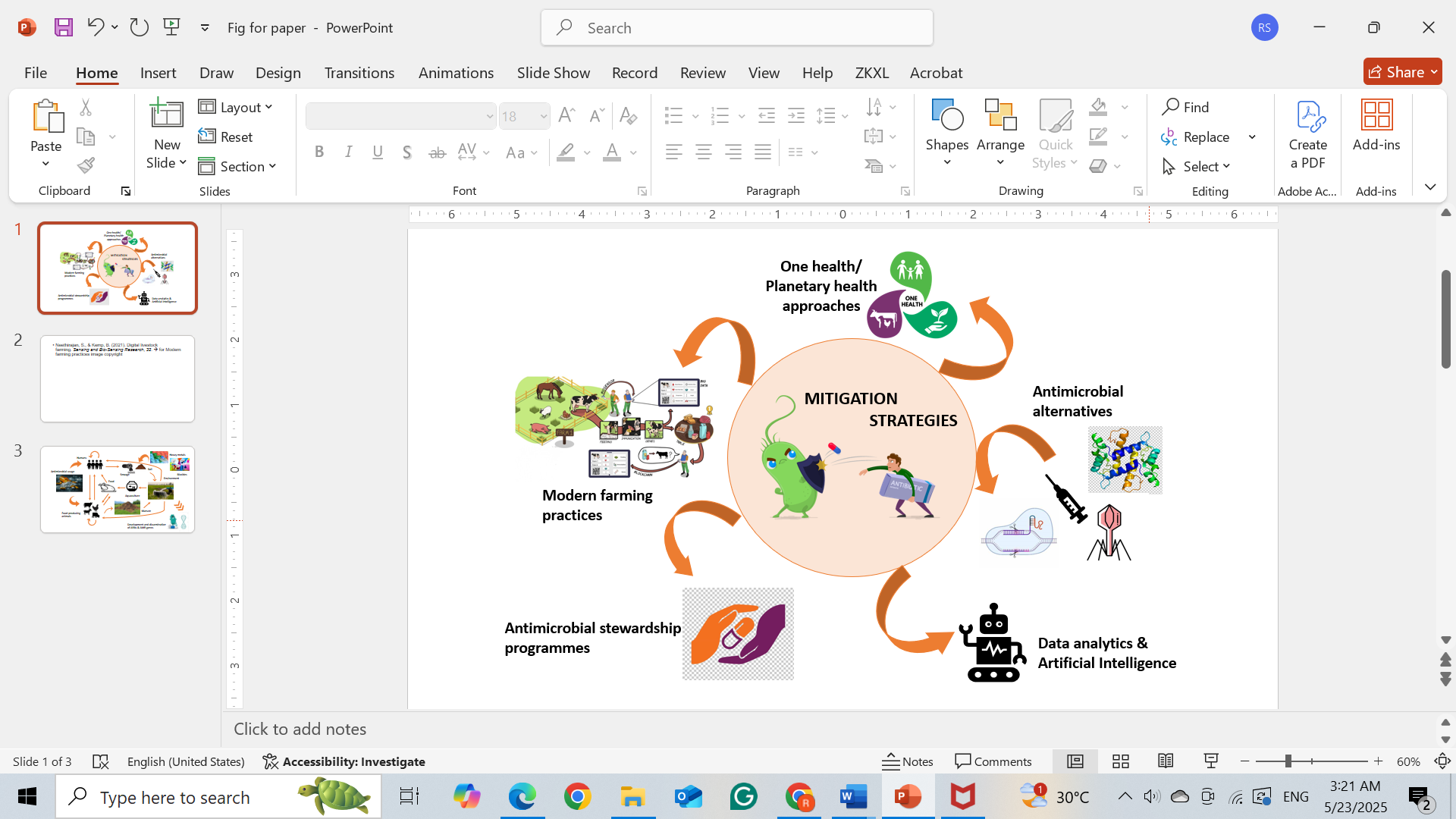
Foodborne diseases that impact human health have been reported to be caused by commensals in the livestock hosts (Bhutta et al., 2014). *Enterococcus faecium*, commonly inhabiting the gastrointestinal tract of both humans and animals, turned opportunistic, causing serious infections when immunocompromised. Although Vancomycin was a best therapeutic initially, significant healthcare challenges mounted when greater Vancomycin resistance was observed due to cross-species transmission dynamics. Later, research work in Denmark (Aarestrup et al. 2001) found that the ban of avoparcin, a glycopeptide antibiotic related to Vancomycin (earlier used as a growth promotion) reduced the glycopeptide-resistant *Enterococci* considerably, confirming that removal of selection pressure reduced the AMR.

The recent past has witnessed an increasing prevalence of fluoroquinolone-resistant (FQR) *Campylobacter jejuni* isolates as a major public health concern. The FQ-resistant (FQR) *C. jejuni* clones rapidly emerged after continuous exposure to the same drugs, and thereby got transmitted from animals to humans, exacerbating the AMR in humans (Park et al., 2022).

However, it is important to consider that the usage of antibiotics in veterinary medicine causes antimicrobial resistance in human medicine. Thus, it emphasizes the importance of a comprehensive approach within the framework of "One Health," which recognizes the collaborative effort of several disciplines operating at the local, national, and international levels to attain the optimal health for people, animals, and the environment (Baruah et al., 2024).

**6. MITIGATION STRATEGIES**

The development and spread of antibiotic resistance associated with livestock antibiotic usage presents several complex issues that have a wide range of effects on humans, animals and environment. Hence, mitigation strategies must also be multi-faceted, with a collaborative action from the medical, veterinary and environmental sectors (**Figure 3**).



**Figure 3. AMR Mitigation strategies**

The mitigation strategies that can help overcome the growing AMR burden are detailed below;

**6.1 Reduction of Antimicrobial Usage (AMU)**

The inappropriate use of antimicrobials is the major factor responsible for global AMR burden. Hence, all attempts taken to reduce the usage of antimicrobials in animals would be an effective primary mitigation strategy. However, the consequences of reduced AMU or substitution of antimicrobials may result in higher morbidity rates, further leading to production and economic losses. In such instances, regular health monitoring of the farm animals would enable early disease detection, with reduced morbidity and mortality (Woolhouse et al., 2015; Bandyopadhyay and Samanta, 2020). Also, suitable preventive measures with appropriate vaccinations pertaining to the animal species in relation to the disease endemicity in the respective locations would reduce the incidence of diseases to a greater extent. Improved clinical treatment of infectious diseases by improving the host immune system was also proposed to reduce AMU and in turn, AMR (Dance, 2024). Good biosecurity measures, balanced animal ration, good housing and husbandry practices with a judicious use of antimicrobials would be a comprehensive approach to reduce the AMU.

Herd-specific control measures to control mastitis in dairy farms, increasing the prices of antibiotics by taxation, were proposed by earlier researchers to reduce AMU (Bandyopadhyay and Samanta, 2020). A cocktail approach, involving molecules that help antimicrobials to work better, for example-interference with the biofilm formation, so that antimicrobials or immune cells can reach the pathogens easily and eliminate them, had been proposed recently (Gadar et al., 2023). Kaempferol, derived from strawberries, was discovered for its interference with the biofilms of *Acinetobacter baumannii*, one of the ESKAPE and nosocomial pathogens involved in AMR. This was intended as an alternative for the sublethal doses of Colistin usage.

The standards and guidelines for responsible and prudent use of antimicrobial agents in veterinary medicine have been updated by WOAH (2025) in addition to surveillance of AMU and AMR, as part of the AMR mitigation strategies.

**6.2 Antimicrobial Stewardship in Veterinary Medicine**

**6.2.1 Responsibility of Veterinarians**

While studying the relationship between AMU and AMR, many researchers have indicated the need for a management protocol to handle pathogens developing multidrug resistance (Ferroni et al., 2020) and the importance of optimizing antibiotics (Ferroni et al.,2022). One such was the application of antimicrobial stewardship for appropriate antimicrobial use by the veterinary clinicians.

By definition, ‘Antimicrobial stewardship’ referred to the practice of sustaining effective antimicrobial use, towards reducing the emergence of resistance for protection of animal, human, and environmental health systems. This involved a “5R” approach of **R**esponsibility, **R**eduction, **R**efinement, **R**eplacement, and **R**eview, under the Good Stewardship Practice (GSP) (Page et al., 2014).

Generally, antimicrobials must attain and maintain therapeutic concentrations at the infection site ("biophase") to ensure healing. On this basis, pharmacokinetics (PK), pharmacodynamics (PD) and PK/PD indices of any antimicrobial have enabled a rational optimization of the dosage regimens and clinical breakpoints. Since the Minimum Inhibitory Concentration (MIC) represented bacterial susceptibility to antibiotics, it has been commonly used as a PD parameter in all PK/PD indices. Other PK/PD indices such as percentage {%T>MIC; e.g., β-lactam antibiotics} and Area under the curve (AUC) {AUC/MIC; e.g., macrolides, fluoroquinolones, tetracyclines, aminoglycosides} have been used in veterinary medicine (Toutain et al., 2021) for clinical efficacy. However, several antibiotics (e.g., fluoroquinolones such as marbofloxacin, enrofloxacin, ciprofloxacin, and pradofloxacin) exhibited biophase concentrations higher than anticipated in certain species (pigs, calves, and dogs) (Messenger et al., 2012; Hauschild et al., 2013). Maintenance of a shorter residence time of the sub-optimal drug levels in the infected tissue helped to reduce the selection pressure and prevent AMR.

**6.2.2 Responsibility of Farmers**

Farmers owning food-producing animals play an important role in understanding the importance of AMR in animal and human welfare. Practising good animal husbandry, with an awareness of the impact of indiscriminate AMU in farm animals will be a key step to curb AMR at the farmers level (Gorton et al., 2023). However, this can be promising only if sufficient funding and insurance plans are provided to mitigate any potential losses due to disease outbreaks or investments on biosecurity and hygiene in livestock farming (Ferdous et al., 2019). Improving the awareness of farmers in LMICs especially, on prudent AMU, requires implementation of strict drug regulation, adequate veterinary healthcare facilities, or some perks to those rearing livestock with minimal or no use of antimicrobials. A need to assess the antibiotic residues in the animal products arose only when a small fraction of the farmers confessed about AMU in their farms; and measures to clear the misconceptions about AMU, including other alternative approaches (Neculai-Valeanu et al., 2024).

**6.3 Exploring Modern farming practices**

Precision Livestock Farming (PLF), one of the modern farming systems, uses technological improvements in milking, feeding systems, and other managements to increase the productivity of livestock. This farming practice aims to reduce the use of antibiotics and maintain good animal health and production. For example, any early signs of diseases or stress, or other parameters, can be automatically tracked and altered through dietary modifications and environmental factors (Sun et al., 2021; Hofstra et al., 2023). Similarly, detecting any changes in the composition and quality of the milk can be observed in the robotic milking systems, which can also detect mastitis and other udder infections, thereby preventing the frequent use of antibiotics (Bausewein et al., 2022).

Implementing digital health monitoring systems in the dairy industry could be useful in detecting various parameters such as activity patterns, body temperature, rumination activity, thereby identifying early symptoms and preventing diseases (Singh et al., 2022; Darwis et al., 2022). Therefore, smart health systems had enabled the assessment of t health conditions of the entire herd as well as individual animals (Alipio and Villena, 2023).

Both PLF and smart health systems can be combined to provide good herd health and effective management strategies that can reduce AMU. To facilitate the processing of antimicrobial administration data, electronic devices have been developed to calculate treatment frequencies and assist in tracking and reducing AMU (Seibt et al., 2022). Though PLF and digital health monitoring systems present many advantages in livestock farming, their implementation has been found to be hindered by challenges, like cost limitations (FAO, 2023; Dayoub et al., 2024), reluctance of farmers to adapt, technological restrictions and diversity in the practices (Kumar et al., 2021). Efforts can be made to accelerate these modern farming practices by encouraging partnerships among academics, industry stakeholders, policymakers, and financial supports from the Government to effectively mitigate AMR in livestock farms.

**6.4** **Antimicrobial Mimetics**

There has been an increasing trend in the exploration of suitable alternatives to antimicrobials and combination therapies in livestock disease management over the recent past. These non-antimicrobial approaches could thereby decrease the level of resistance by the microbes, as an effective way to mitigate AMR in animals. Some of the antimicrobial mimetics being explored include the following;

**6.4.1 Probiotics**

Prebiotics and probiotics as alternatives to antimicrobials, have been explored ever since a decade (Allen et al., 2013), sometimes also mixed together and called as ‘synbiotics’. Healthy microbiome of the animals was ensured by supplementation of probiotics such as *Sporidiobolus ruineniae* (against *Staphylococcus aureus)* (Kanpiengjai et al., 2020), lactic acid-utilizing yeasts to decrease ruminal lactic acid production (Moretti et al., 2023), or fecal transplantation, or improved nutrition (Aslam et al., 2021).

**6.4.2 Bacteriophages**

Bacteriophages or viruses that target specific bacteria, have been demonstrated for their suitability as alternatives to antibiotics, in addition to engineered phage proteins like endolysins and depolymerases, etc. (Aslam et al., 2021). The target specificity of the phages contributed significantly to their antibacterial function, thereby reducing the need for antibiotics and in turn the selection pressure for AMR. Their potential role has been explored in the management of bovine diseases and more specifically with a broad lytic spectrum targeting multiple genera, in the treatment of bovine mastitis (Neculai-Valeanu et al., 2024). Examples include phages whose efficacy was demonstrated against *Salmonella Typhimurium* in poultry and pigs, *Listeria monocytogenes* biofilms in food products, *E. coli* O157: H7 in aquaculture and food-producing animals (Aslam et al., 2021; Bava et al., 2024). However, the selection and delivery of phages and possibility of introducing virulence or ARG alleles into the bacteria still remain a challenge.

**6.4.3 Antimicrobial peptides**

Antimicrobial peptides (AMPs) are biomolecules, naturally synthesized by most of the organisms as a part of their innate immune response to pathogens. Unlike antimicrobials, AMPs act upon multiple sites of the pathogens, both extracellularly and intracellularly, with potent activity on even the drug-resistant microbes (Mwangi et al., 2019). The properties of broad-spectrum activity against pathogens, non-specific mechanism of action on the bacterial membranes, eco-friendly nature and ability to stimulate the host immune response to eliminate the pathogen, (Robles Ramirez et al., 2024) qualify the AMPs as promising antimicrobial mimetics, especially within the One-Health approach.

A series of AMPs have been tested in different livestock species against various pathogens with varied outcomes. The bacteriocins belong to a class of antimicrobial peptides with a diverse range of inhibiting action on the core metabolic activities of bacteria. Lactic acid bacteria (LAB) -especially *Lactobacillus curvatus*, *L. sakei,* and *Lactococcus lactis* targeted the biofilms of major food-borne pathogens (Gómez et al., 2016). Bacteriocins obtained from bacteria occurring as commensals in the equine gastrointestinal tract inhibited the growth of mastitis-causing bacteria in cattle (Godoy-Santos et al., 2019), while some derived from cow milk like beta-lactoglobulin, lactoferricin themselves possessed antimicrobial activity (Mohanty et al., 2016). Supplementation of the bacteriocins in bovine, goat, pigs, and poultry affected by gastrointestinal diseases altered the gut microbiome in the livestock species with increased concentration of *Enterococcaceae* and *Lactobacillaceae*, and reduced numbers of microbes of families *Enterobacteriaceae* and *Staphylococcaceae* (Robles Ramirez et al., 2024).

The other alternative strategies to tackle the AMR crisis included enzymes, quorum sensing quenchers, efflux pump inhibitors, clay, predatory bacteria, nano-material-based anti-infective particles, teat sealants, and antimicrobial photodynamic therapy, which need to be validated (Bandyopadhyay and Samanta, 2020). Studies showed that supplementation of essential oils were effective in treating mastitis in dairy cattle (Caneschi et al., 2023) while alcoholic extracts from plant sources like garlic, moringa, and oak barks could counteract pathogens causing endometritis (Mandhwani et al., 2017) and mastitis (Šukele et al., 2022) in bovines.

**6.5 Drug Reprofiling**

The present scenario of AMR can be overcome if a new set of antimicrobials are in the pipeline, but globally, identification of new antimicrobials is hindered by substantial investment requirements and time delays in proving the clinical efficacy. Hence, new therapeutic applications may be identified for the existing drugs, which are actually meant for specific indications- namely ‘Drug repurposing or reprofiling’ (Bandyopadhyay and Samanta, 2020). Therefore, the pharmaceutical industries have recently shifted to this cost cum-time-effective strategy.

However, only a few veterinary drugs have been explored for repurposing; for example, Fenbendazole has demonstrated efficacy against non-small cell lung cancer cells (Dogra et al., 2018) and isoxazoline in treating human vector-borne diseases. Several anthelmintic compounds including oxyclozanide, closantel, niclosamide, and rafoxanide, have exhibited antibacterial properties against a broad spectrum of pathogens, including methicillin-, linezolid-, daptomycin-, vancomycin-resistant *Staphylococcus aureus, Clostridium difficile, Klebsiella pneumoniae, Acinetobacter baumannii,* *Pseudomonas aeruginosa, and Helicobacter sp.* Further, Mebendazole has been reported to possess antifungal properties, while avermectins have been successfully tested against Mycobacterium and MRSA. Several NSAIDs (Celecoxib, aspirin, ibuprofen, and tacrolimus) have been tested against certain bacterial and fungal pathogens with promising results (Miró-Canturri et al., 2019). Various studies have explored the repurposing of anticancer drugs as antibacterials, with 5-fluorouracil and gallium nitrate proving effective against MDR *A. baumannii* and *Pseudomonas sp.* Moreover, Floxuridine, streptozotocin, and tamoxifen have demonstrated notable antibacterial activity against *Staphylococcus* isolates. However, the dosage of repurposed drugs is higher when used as antimicrobials, leading to abrupt changes in pharmacokinetic profiles, emphasizing clinical re-evaluation and toxicity testing.

Other appropriate options available as next-generation vaccines and gene editing, would be more ideal. Though vaccines are readily available against many viral diseases of livestock, there is currently limited routine use of vaccines that protect against bacterial infection. Since antibiotics are still accessible and more effective, the practice of vaccination or creating newer vaccines against bacterial diseases for farm animals is arguably not commercially motivated. Even when vaccines are available, farmers do not always employ them (Woolhouse et al., 2015). The best example was the administration of live oral Lawsonia in pigs. Although reduced oxytetracycline consumption by 80% and increased productivity was recorded (Bak and Rathkjen, 2009), the vaccine was not commonly used. Employing livestock that are genetically resistant to disease through the use of genetic modification technologies could serve as a sustainable approach to reduce the dependency on antibiotics in farm animals. (Lyall et al., 2011).

**6.6 ‘One Health’ and ‘Planetary health’ approaches**

Poor Water, Sanitation and Hygiene (WASH) and sub-optimal infection control, predispose infections warranting AMU, whilst improper waste disposal can spread resistance in the environment. The ‘One- Health’ approach therefore is an ideal solution to prevent and mitigate AMR. The global action plan on antimicrobial resistance (GAP) first laid down by WHO had identified the surveillance on AMU and drug-resistant pathogens as the major drivers to curb AMR (WHO, 2016). An evolving, multidisciplinary approach to a complex problem like AMR involving humans, animals and the environment was the ‘One Health’ strategy - by way of reducing AMU in both human and veterinary medicine, and in turn, the environment (Robinson et al., 2016). Since then, efforts have thus been undertaken to evaluate and regulate AMU (Lardé et al., 2021).

The Quadripartite Collaboration on ‘One- Health’, comprising of the WHO, the Food and Agriculture Organization of the United Nations (FAO), the World Organisation for Animal Health (WOAH) and the United Nations Environment Programme (UNEP), developed the One Health Joint Plan of Action (2022–2026), to integrate systems for better health management. With AMR focused under Action Track 5, the WOAH has recommended policy configuration in the veterinary sector (WOAH, 2024a).

Most of the developed and high-income countries have their National surveillance initiatives. The guidelines on AMU in animals have been customized based on their data. On the other hand, the LMICs have no proper surveillance systems to monitor AMU in animals, until some countries like India, which have adopted national action plans. The Indian government had organised the “National Programme on AMR Containment” programme in response to the AMR crisis in 2013, followed by the National AMR Surveillance Network (NARS-Net). Generation of quality data pertaining to AMR surveillance for the nine priority bacterial pathogens of public health importance—*Staphylococcus aureus, Enterococcus species, Klebsiella species, Escherichia coli, Pseudomonas aeruginosa, Acinetobacter baumannii/Acinetobacter calcoaceticus complex, Salmonella enterica* serotypes *Typhi* and *Paratyphi, Shigella species*, and *Vibrio cholerae* was the major objective.

The following table provides a list of important animal bacterial pathogens involved in resistance surveillance and monitoring programmes based on WOAH guidelines (WOAH, 2022);

**Table 2: Target animal species and animal bacterial pathogens included in resistance surveillance and monitoring programmes (WOAH, 2022)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Source** | **Respiratory pathogens** | **Enteric pathogens** | **Udder pathogens** | **Other pathogens** |
| CATTLE | *Pasteurella multocida* | *Escherichia coli* | *Staphylococcus aureus* |  |
| *Mannheimia haemolytica* | *Salmonella spp.* | *Streptococcus spp.* |  |
| SWINE | *Actinobacillus pleuropneumoniae* | *Escherichia coli* |  | *Streptococcus suis* |
| *Salmonella spp.* |
| POULTRY |  | *Salmonella spp.* |  | *Escherichia coli* |

The Indian Council of Agricultural Research, in collaboration with FAO, initiated the All India – ICAR-Indian Network for Fisheries and Animal Antibiotic Resistance (INFAAR) to fulfill the objectives laid down in India’s NAP on AMR. Financial constraints for the infrastructural support was the major challenge for the establishment and smooth functioning of a robust surveillance system on AMR/AMU in LMICs (FAO, 2024a).

Planetary health with a more ’anthropocentric’ focus, emphasizes the need for global cooperation to address both the ecological and health dimensions of AMR.  The importance of ecological sustainability, climate action, and environmental stewardship have to be targeted in reducing AMR (Horvat and Kovačević, 2025).

New approaches must be implemented to stop the spread of bacterial diseases and antibiotic resistance. Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR), protects prokaryotes from foreign DNA like plasmids and phages. By limiting horizontal gene transfer, the spread of antibiotic resistance is brought to a standstill. The CRISPR-Cas system has been used in identifying AMR genes especially through the FLASH (Finding Low Abundance Sequences by Hybridization) toolbox (Wang and Cui, 2020) and developing novel therapeutic approaches (Rafiq et al., 2024).

**6.7 Role of Data analytics and Artificial Intelligence (AI)**

The patterns and trends in AMU and AMR can be analysed through data analytics and AI in any livestock farms. By examining the AMU data, resistance profiles, treatment outcomes, one can determine how antibiotic prescriptions contribute to the genesis of antimicrobial resistance and derive solutions to prevent the further development of AMR (Malijan et al., 2022). For example, data analytics can help to identify the time or place where the antibiotics are often used and educate the farmers on the appropriate use of drugs (Rees et al., 2021; Vijay et al., 2023).

AI models have been used to identify animals at higher risk of developing antibiotic resistance and to screen for disease outbreaks. By applying these models, potential outcomes were predicted, and infections can be prevented without the use of antibiotics, and curtailing the spread of ARBs in the farms (Branda and Scarpa, 2024; Martin et al., 2024). Also, farmers can optimize farm management practices by using data analytics and Artificial Intelligence (AI) tools, for valuable insights on animal health, behaviour, and performance (Neculai-Valeanu et al., 2024).

Data from real-life experiments with antibiotics and pathogens have been used to train the algorithms to predict the molecule that can attack the bacteria. The compounds- Halocin and Abaucin were discovered by AI and found to target *A. baumannii* (Liu et al., 2023). Generative AI, which can develop new, potentially useful elements, has been explored recently and are under testing. Further inventions on newer antimicrobials, which will take time for resistance to develop, more than five years are also in the pipeline (Swanson et al., 2024).

**7. FUTURE DIRECTIONS**

Antimicrobial resistance has been a continuing global threat for a long time, affecting animal, human, and environmental health; hence, multifaceted approaches are required for its mitigation. The AMR crisis can henceforth be tackled by novel methods, which must be continuously explored beyond the usage of conventional antimicrobials.

One of the several approaches includes the development of new antibiotic classes with effective properties. Most of the existing antimicrobials have been isolated predominantly from the soil Actinomyces. Hence other ecological niches like the marine environment, antimicrobial peptides from animals and plants, microbial lipopeptide-mimetics, or completely synthetic drugs can be explored to cover the new antimicrobial diversity (Maddock et al.,2024).

The other potential alternative strategies, such as phage therapy, antimicrobial peptides, have shown significant potential to address AMR. Antibiotic-resistant breakers are also being subjected to trials, to restore the efficacy of existing antibiotics against bacteria that have developed resistance (Puri et al., 2024). A significant decrease in AMUQ could be achieved by targeting both ABUI and LBIO (antibiotic use intensity and Livestock biomass). The integrated approach of improved management practices, biosecurity, and technological change, with increasing productivity per animal rather than expanding herd sizes, is therefore essential, especially in LMICs (Acosta et al., 2025). Further, the CRISPR-Cas systems provide a versatile tool for creating a new therapy, targeting and eliminating antibiotic-resistant bacteria (Rafiq et al., 2024).

In addition to National policies and interventions at the farm level, innovative economic and financial mechanisms laid by the Government, like abatement markets, bonds, credits, and a global fund for reduction are required to address AMUQ as a global challenge. The establishment of an independent panel for action against AMR would serve to facilitate the generation and use of scientific evidence to tackle AMR effectively (Acosta et al., 2025), like FAO’s RENOFARM (Reduce the Need for Antimicrobials on Farms) program, which aims to reduce the farm – AMU (FAO, 2024b).

In a therapeutic setup, phenotypic antimicrobial susceptibility testing (AST) for identification of the ideal antimicrobials for therapy, and genotypic antimicrobial resistance testing (ART) indicating the inappropriate antimicrobials; are still vague in veterinary diagnostic medicine due to high cost associated with routine use and the lack of outcome studies. With incomplete PK-PD data for some antimicrobial drugs in various animal species, extrapolation of breakpoints is usually done with the available data from a few animal species or humans. Veterinary antimicrobial stewardship can be improved by defined effective treatment regimens for different types of infections. Also, targeted education of veterinarians and veterinary students on appropriate AMU is a critical need in veterinary antimicrobial prescriptions. Prophylactic vaccines, on the other hand, can help lower AMU, as a preventive measure, highly effective to prevent AMR. (Maddock et al.,2024).

Currently, Artificial Intelligence (AI) is an emerging tool in antibiotic and drug development, resistance pattern analysis, and the development of cost-effective and personalized treatment plans. Integrating AI with bioinformatics and whole-genome sequencing will provide valuable data in identifying new resistance genes and understanding microbial evolution (Dance, 2024).

With an existing interplay between the animals, humans, and the environment, the development of rapid diagnostics and the implementation of the ‘One Health’ and ‘Planetary health’ approaches will be the best solutions to address AMR across sectors. Rapid and sensitive diagnostics of diseases with molecular tools will enable an early diagnosis to prescribe the ideal antibiotic at the outset, and avoid multiple antibiotics or unnecessary use. Research gap of identifying and ensuring antimicrobials that can remain effective for a long period without resistance can be prioritized in veterinary medicine. Genotypic ART kits to detect multidrug-resistant organisms (MRDO) are required in veterinary medicine.

The following priorities laid down by WOAH for the animal health sector (WOAH, 2024b), would serve as key milestones in the efforts to curb AMR,;

1) Cross-sectoral coordination

Prudent use of antimicrobials and emphasis on the interrelation of human and veterinary medicine with broader environmental and social systems.

2) Resourced surveillance systems

Upgraded National surveillance systems on AMR and AMU are required, with data shared across sectors under the One Health approach, effectively utilising ANImal antiMicrobial USE (ANIMUSE), International FAO Antimicrobial Resistance Monitoring (InFARM), Global Antimicrobial Resistance and Use Surveillance System (GLASS).

3) Prevention

Animal vaccination regimens may be defined and implemented as per WOAH-listed priority diseases and thereby reduce AMU. This should be complemented with effective implementation of biosecurity, good animal husbandry practices and rapid, low-cost diagnostic tests for AMR.

4) Sustainable financing

Sustainable and predictable sources of funding need to be established at national and global levels to support the implementation of cost-effective interventions across sectors, based on surveillance data.

**Conclusion**

Antimicrobial resistance represents a growing public health concern across human, animal, and environmental sectors globally. Responsible and prudent use of antimicrobials, both in human and veterinary medicine, with an awareness of the PK/PD approaches that can optimize dosage regimens, will be a predominant solutions to prevent AMR. Quantification of AMU in various livestock species can help tp develop a benchmarking system to reduce AMU. Disease prevention through improved biosecurity and hygiene management in animal farms, timely access to vaccines and diagnostics, especially in LMICs, as recommended by WOAH will enable to close the gap in the animal health sector. Periodic genotypic AMR testing in livestock, poultry, and aquaculture ensures identification of reservoirs of ARBs, ARGs, environmental resistome and transmission dynamics of ARGs.

Addressing AMR requires a multifaceted approach involving antimicrobial and environmental stewardship programmes across human, animal and environmental sectors. Governments, international organizations, and researchers in all countries must collaborate by implementing National action plans in addition to periodic surveillance programmes including wildlife and companion animals. Investing in the research and development of thermostable combined vaccines for prevalent animal diseases, new antibiotics, long-term alternative therapies, advanced farm effluent treatment technologies, and rapid diagnostic tools to reduce the AMR-associated burden is equally important. By incorporating technological advancements, sustainable agricultural practices and management strategies, the animal sector can play a pivotal role in combating AMR.A multisectoral coordination, combining One-Health and planetary health in every country, synergistically addressing human and veterinary medicine, environmental hygiene in relation to the prevailing climate, will serve to reduce the global AMR crisis, ensuring a safe, healthy environment for future generations.

**DISCLAIMER (ARTIFICIAL INTELLIGENCE)**

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of this manuscript.

**REFERENCES**

Aarestrup, F. M., Seyfarth, A. M., Emborg, H. D., Pedersen, K., Hendriksen, R. S., and Bager, F. (2001). Effect of abolishment of the use of antimicrobial agents for growth promotion on occurrence of antimicrobial resistance in fecal enterococci from food animals in Denmark. *Antimicrobial Agents and Chemotherapy*, 45(7), 2054-2059.

Abebe, E., Gugsa, G., and Ahmed, M. (2020). Review on major food‐borne zoonotic bacterial pathogens. *Journal of Tropical Medicine*, 1, 4674235.

Acosta, A., Tirkaso, W., Nicolli, F., Van Boeckel, T. P., Cinardi, G., and Song, J. (2025). The future of antibiotic use in livestock. *Nature Communications*, 16(1), 2469.

Ahmed, S. A., Baris, E., Go, D. S., Lofgren, H., Osorio-Rodarte, I., and Thierfelder, K. (2017). Assessing the global economic and poverty effects of antimicrobial resistance. World Bank Policy Research Working Paper, 8133.

Alipio, M., and Villena, M. L. (2023). Intelligent wearable devices and biosensors for monitoring cattle health conditions: A review and classification. *Smart Health*, 27, 100369.

Allen, H. K., Levine, U. Y., Looft, T., Bandrick, M., and Casey, T. A. (2013). Treatment, promotion, commotion: antibiotic alternatives in food-producing animals. *Trends in Microbiology*, 21(3), 114-119.

Antimicrobial Resistance Collaborators.(2022). Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *Lancet*, 399(10325), 629-655.

Apley, M.D., and Coetzee, J.F. (2013). Antimicrobial drug use in cattle. In Giguère, S., Prescott, J.F., and Dowling, P.M (Eds.), Antimicrobial Therapy in Veterinary Medicine, (5th ed., p 495– 518). Wiley Blackwell, Ames, IA.

Aslam, B., Khurshid, M., Arshad, M. I., Muzammil, S., Rasool, M., Yasmeen, N., et al. (2021). Antibiotic resistance: one health one world outlook. *Frontiers in Cellular and Infection Microbiology*, 11, 771510.

Bager, F., Monnet, D.L., and Andersen, S. (2001). DANMAP 2000: Consumption of Antimicrobial Agents and Occurence of Antimicrobial Resistance in Bacteria from FoodAnimals, Foods and Humans in Denmark. ISSN 1600-2032 (Accessed on Decemver 20, 2024)

Baghdadi, M., Brassard, P., Godbout, S., Létourneau, V., Turgeon, N., Rossi, F., et al. (2023). Contribution of Manure-Spreading Operations to Bioaerosols and Antibiotic Resistance Genes’ Emission. *Microorganisms*, 11, 1797.

Bak, H., and Rathkjen, P. H. (2009). Reduced use of antimicrobials after vaccination of pigs against porcine proliferative enteropathy in a Danish SPF herd. *Acta Veterinaria Scandinavica*, 51(1), 1.

Baker, M., Williams, A.D., Hooton, S.P., Helliwell, R., King, E., Dodsworth, T., et al. (2022). Antimicrobial Resistance in Dairy Slurry Tanks: A Critical Point for Measurement and Control. *Environment International*, 169, 107516.

Balta, I., Lemon, J., Gadaj, A., Cretescu, I., Stef, D., Pet, I., et al. (2025). The interplay between antimicrobial resistance, heavy metal pollution, and the role of microplastics*. Frontiers of Microbiology*, 16, 1550587.

Bandyopadhyay, S., and Samanta, I. (2020). Antimicrobial resistance in agri-food chain and companion animals as a re-emerging menace in post-COVID epoch: low-and middle-income countries perspective and mitigation strategies. *Frontiers In Veterinary Science*, 7, 620.

Baruah, J., Shantikumar Singh, L., Salvia, T., and Sarma, J. (2024). Antimicrobial resistance a continued global threat to public health–A perspective and mitigation strategies*. Journal of Laboratory Physicians*, 16(4).

Bausewein, M., Mansfeld, R., Doherr, M. G., Harms, J., and Sorge, U. S. (2022). Sensitivity and specificity for the detection of clinical mastitis by automatic milking systems in Bavarian dairy herds. *Animals*, 12(16), 2131.

Bava, R., Castagna, F., Lupia, C., Poerio, G., Liguori, G., Lombardi, R., et al. (2024). Antimicrobial Resistance in Livestock: a serious threat to Public Health*. Antibiotics*, 13(6), 551.

Bhutta, Z. A., Sommerfeld, J., Lassi, Z. S., Salam, R. A., and Das, J. K. (2014). Global burden, distribution, and interventions for infectious diseases of poverty. *Infectious Diseases of Poverty*, 3, 1-7.

Bibbal, D., Dupouy, V., Ferré, J. P., Toutain, P. L., Fayet, O., Prere, M. F., and Bousquet-Mélou, A. (2007). Impact of three ampicillin dosage regimens on selection of ampicillin resistance in Enterobacteriaceae and excretion of bla TEM genes in swine feces. *Applied and Environmental Microbiology*, 73(15), 4785-4790.

Blakely, G. W. (2024). Mechanisms of horizontal gene transfer and DNA recombination. In Molecular Medical Microbiology, 309-324.

Branda, F., and Scarpa, F. (2024). Implications of artificial intelligence in addressing antimicrobial resistance: Innovations, global challenges, and healthcare’s future. *Antibiotics*, 13(6), 502.

Bruno, A. V., and Mackay, C. (2012). Antimicrobial resistance and the activities of the Codex Alimentarius Commission. *Revue Scientifique et Technique* (International Office of Epizootics*)*, 31(1), 317-323.

Caneschi, A., Bardhi, A., Barbarossa, A., and Zaghini, A. (2023) The Use of *Antibiotics* and Antimicrobial Resistance in Veterinary Medicine, a Complex Phenomenon: A Narrative Review. *Antibiotics*, 12, 487.

Catry, B., Laevens, H., Devriese, L. A., Opsomer, G., and De Kruif, A. (2003). Antimicrobial resistance in livestock. *Journal of Veterinary Pharmacology and Therapeutics*, 26(2), 81-93.

Collignon, P. (2016). World Health Organization and World Bank estimates of the global burden of antimicrobial resistance in 2016: A systematic review and modeling study. *The Lancet Infectious Diseases*, 19(1), 1-8.

Coyne, L., Arief, R., Benigno, C., Giang, V.N., Huong, L.Q., Jeamsripong, S., et al. (2019). Characterizing Antimicrobial Use in the Livestock Sector in Three South East Asian Countries (Indonesia, Thailand, and Vietnam). *Antibiotics*, 8, 33.

Dance, A. (2024). Five ways science is tackling the antibiotic resistance crisis. *Nature*, 632(8025), 494-496.

Darwis, D., Mehta, A. R., Wati, N. E., Samsugi, S., and Swaminarayan, P. R. (2022). Digital Smart Collar: Monitoring Cow Health Using Internet of Things. In 2022 International Symposium on Electronics and Smart Devices (ISESD), 1-5. IEEE.

Dayoub, M., Shnaigat, S., Tarawneh, R. A., Al-Yacoub, A. N., Al-Barakeh, F., and Al-Najjar, K. (2024). Enhancing animal production through smart agriculture: possibilities, hurdles, resolutions, and advantages. *Ruminants*, *4*(1), 22-46.

Dogra, N., Kumar, A., and Mukhopadhyay, T. (2018). Fenbendazole acts as a moderate microtubule destabilizing agent and causes cancer cell death by modulating multiple cellular pathways. *Scientific Reports*, 8(1), 11926.

Dong, Q., Liu, Y., Li, W., Liu, Y., and Ye, X. (2021). Cross-species transmission risk of livestock-associated MRSA: A systematic review and Bayesian meta-analysis of global data. *Preventive Veterinary Medicine*, 194, 105429.

Ferdous, J., Sachi, S., Al Noman, Z., Hussani, S. A. K., Sarker, Y. A., and Sikder, M. H. (2019). Assessing farmers’ perspective on antibiotic usage and management practices in small-scale layer farms of Mymensingh district, Bangladesh. *Veterinary World*, 12(9), 1441.

Fernandes, P., Ferreira, B. S., and Cabral, J. M. S. (2003). Solvent tolerance in bacteria: role of efflux pumps and cross-resistance with *Antibiotics. International Journal of Antimicrobial Agents*, 22(3), 211-216. doi: 10.1016/S0924- 8579(03)00209- 7.

Ferroni, L., Albini, E., Lovito, C., Blasi, F., Maresca, C., Massacci, F. R., et al. (2022). Antibiotic consumption is a major driver of antibiotic resistance in calves raised on Italian cow-calf beef farms. *Research in Veterinary Science*, 145, 71-81.

Ferroni, L., Lovito, C., Scoccia, E., Dalmonte, G., Sargenti, M., Pezzotti, G., et al. (2020). Antibiotic consumption on dairy and beef cattle farms of central Italy based on paper registers. *Antibiotics*, 9(5), 273.

Florez-Cuadrado, D., Moreno, M. A., Ugarte-Ruíz, M., and Domínguez, L. (2018). Antimicrobial resistance in the food chain in the European Union. *Advances in Food and Nutrition Research*, 86, 115-136.

Food and Agriculture Organization (FAO). (2023). FAO Investment Centre What Factors Shape Small-Scale Farmers’ and Firms’ Adoption of New Technologies? <https://www.fao.org/support-to-investment/news/detail/en/c/1652579/> (Accessed on Jan 9, 2025).

Food and Agricultural Organisation (FAO). (2024a). White paper: Antimicrobial resistance in the animal sector in India. New Delhi. <https://doi.org/10.4060/cc9535en>

Food and Agriculture Organization of the United Nations (2024b). Reduce the need for antimicrobials on farms for sustainable agri food systems transformation. <https://www.fao.org/antimicrobial-resistance/background/fao-role/renofarm/en/> (Accessed on Jan 17, 2025)

Forsberg, K. J., Reyes, A., Wang, B., Selleck, E. M., Sommer, M. O., and Dantas, G. (2012). The shared antibiotic resistome of soil bacteria and human pathogens. *Science*, 337(6098), 1107-1111.

Fournier, C., Nordmann, P., Pittet, O., and Poirel, L. (2021). Does an antibiotic stewardship applied in a pig farm lead to low ESBL prevalence*?. Antibiotics*, 10(5), 574.

Friedman, M. (2015). Antibiotic-resistant bacteria: prevalence in food and inactivation by food-compatible compounds and plant extracts. *Journal of Agricultural and Food Chemistry*, 63(15), 3805-3822. doi: 10.1021/acs.jafc.5b00778

Gadar, K., de Dios, R., Kadeřábková, N., Prescott, T. A., Mavridou, D. A., and McCarthy, R. R. (2023). Disrupting iron homeostasis can potentiate colistin activity and overcome colistin resistance mechanisms in Gram-Negative Bacteria. *Communications Biology*, 6(1), 937.

Ghimpețeanu, O. M., Pogurschi, E. N., Popa, D. C., Dragomir, N., Drăgotoiu, T., Mihai, O. D., et al. (2022). Antibiotic use in livestock and residues in food—A public health threat: A review. *Foods*, 11(10), 1430.

Gilbert, W., Thomas, L. F., Coyne, L., and Rushton, J. (2021). Mitigating the risks posed by intensification in livestock production: the examples of antimicrobial resistance and zoonoses. *Animal*, 15(2), 100123.

Gillingham, E.L., Lake, I., Iacono, G.L., Nichols, G. (2023). Health Effects of Climate Change (HECC) in the UK: 2023 Report. CPRE; London, UK. Effect of climate change on infectious diseases in the UK

Gillings, M. R. (2014). Integrons: past, present, and future. *Microbiology and Molecular Biology Reviews*, 78(2), 257-277.

Godoy-Santos, F., Pinto, M. S., Barbosa, A. A., Brito, M. A., and Mantovani, H. C. (2019). Efficacy of a ruminal bacteriocin against pure and mixed cultures of bovine mastitis pathogens. *Indian Journal of Microbiology*, 59, 304-312.

Gómez, N. C., Ramiro, J. M., Quecan, B. X., and de Melo Franco, B. D. (2016). Use of potential probiotic lactic acid bacteria (LAB) biofilms for the control of Listeria monocytogenes, Salmonella Typhimurium, and Escherichia coli O157: H7 biofilms formation. *Frontiers in Microbiology*, 7, 863.

Gorton, M., Yeh, C. H., Chatzopoulou, E., White, J., Tocco, B., Hubbard, C., and Hallam, F. (2023). Consumers' willingness to pay for an animal welfare food label. *Ecological Economics*, 209, 107852.

Griebe, B. (2025). Smoking and antibiotic resistance: How cigarette waste promotes the spread of resistant germs. *Environmental Health Perspectives*. <https://phys.org/news/2025-03-antibiotic-resistance-cigarette-resistant-germs.html>

Hall, L.M., Holtum, J. A. M., and Powles, S. B. (2018). Mechanisms responsible for cross resistance and multiple resistance, In *Herbicide resistance in plants* (pp. 243-262). CRC Press. doi: [10.1201/9781351073189-9](http://dx.doi.org/10.1201/9781351073189-9)

Hansen, L. H., Aarestrup, F., and Sørensen, S. J. (2002). Quantification of bioavailable chlortetracycline in pig feces using a bacterial whole-cell biosensor. *Veterinary Microbiology*, 87(1), 51-57.

Hauschild, G., Rohn, K., Engelhardt, E., Sager, M., Hardes, J., and Gosheger, G. (2013). Pharmacokinetic study on pradofloxacin in the dog–Comparison of serum analysis, ultrafiltration and tissue sampling after oral administration. *BMC Veterinary Research*, 9, 1-8.

He, T., Wang, R., Liu, D., Walsh, T. R., Zhang, R., Lv, Y., et al. (2019). Emergence of plasmid-mediated high-level tigecycline resistance genes in animals and humans. *Nature Microbiology,* 4(9), 1450-1456.

Hofstra, G., van Abeelen, H., Duindam, M., Houben, B., Kuijpers, J., Arendsen, T., et al. (2023). Automated monitoring and detection of disease using a generic facial feature scoring system–A case study on FMD infected cows. *Preventive Veterinary Medicine*, 213, 105880.

Horvat, O., and Kovačević, Z. (2025). Human and Veterinary Medicine Collaboration: Synergistic Approach to Address Antimicrobial Resistance Through the Lens of Planetary Health. *Antibiotics*, 14(1), 38.

Innes, G. K., Randad, P. R., Korinek, A., Davis, M. F., Price, L. B., So, A. D., et al. (2020). External societal costs of antimicrobial resistance in humans attributable to antimicrobial use in livestock. *Annual Review of Public Health*, 41(1), 141-157.

Jensen, L. B., Hammerum, A. M., Poulsen, R. L., and Westh, H. (1999). Vancomycin-resistant Enterococcus faecium strains with highly similar pulsed-field gel electrophoresis patterns containing similar Tn 1546-like elements isolated from a hospitalized patient and pigs in Denmark. *Antimicrobial Agents and Chemotherapy*, 43(3), 724-725.

Johnsen, P.J., Townsend, J.P., Bøhn, T., Simonsen, G.S., Sundsfjord, A., and Nielsen, K.M. (2009). Factors Affecting the Reversal of Antimicrobial-Drug Resistance. *Lancet Infect. Dis*., 9, 357–364.

Kang, H. J., Lim, S. K., and Lee, Y. J. (2022). Genetic characterization of third-or fourth-generation cephalosporin-resistant avian pathogenic Escherichia coli isolated from broilers. *Frontiers in Veterinary Science*, 9, 1055320.

Kanpiengjai, A., Khanongnuch, C., Lumyong, S., Kummasook, A., and Kittibunchakul, S. (2020). Characterization of Sporidiobolus ruineniae A45. 2 cultivated in tannin substrate for use as a potential multifunctional probiotic yeast in aquaculture. *Journal of Fungi*, 6(4), 378.

Kim, Y., Seo, K. H., Kim, B., Chon, J. W., Bae, D., Yim, J. H., et al. (2021). Distribution of Antibiotic-Resistant Bacteria in the Livestock Farm Environments. *Journal of Dairy Science and Biotechnology*, 39(1), 1-8.

Knapp C.W., Turner R., Salifu E., Khan S., Stillings M., and Tonner R.(2021).Microbiomes and the Global Climate Change. Springer; Singapore: 2021. Climate change: Any dangers from antimicrobial resistant bacteria,145–171.

Kumar, N., Sharma, G., Leahy, E., Shome, B. R., Bandyopadhyay, S., Deka, R. P., et al. (2021). Understanding antibiotic usage on small-scale dairy farms in the Indian states of Assam and Haryana using a mixed-methods approach—Outcomes and challenges. *Antibiotics*, 10(9), 1124.

Lam, Y., Fry, J. P., and Nachman, K. E. (2019). Applying an environmental public health lens to the industrialization of food animal production in ten low-and middle-income countries. *Globalization and Health*, 15, 1-20. doi: 10.1186/s12992-019-0479-5

Landers, T. F., Cohen, B., Wittum, T. E., and Larson, E. L. (2012). A review of antibiotic use in food animals: perspective, policy, and potential. *Public Health Reports*, 127(1), 4-22. doi: 10.1177/003335491212700103

Lardé, H., Dufour, S., Archambault, M., Massé, J., Roy, J. P., and Francoz, D. (2021). An observational cohort study on antimicrobial usage on dairy farms in Quebec, Canada*. Journal of Dairy Science*, 104(2), 1864-1880.

Laxminarayan, R, Chaudhury, R.R. (2016). Antibiotic Resistance in India: Drivers and Opportunities for Action. *PLoS Med*.,13(3).

Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A.K.M., Wertheim, H.F.L., and Sumpradit, N. (2013). Antibiotic resistance—the need for global solutions. *Lancet Infect Dis* , 13, 1057–98. doi: 10.1016/S1473- 3099(13)70318- 9

Lebreton, F., Van Schaik, W., and Manson, A. (2013). Global spread of vancomycin-resistant Enterococcus faecium from distinct nosocomial genetic complex. *MBio* 2013; 4: e00534–13.

Leifels, M., Khalilur Rahman, O., Sam, I.C., Cheng, D., Chua, F. J. D., Nainani, D., et al. (2022). The one health perspective to improve environmental surveillance of zoonotic viruses: lessons from COVID-19 and outlook beyond. *ISME Communications*, 2, 107.

Lienen, T., Schnitt, A., Hammerl, J.A., Maurischat, S. and Tenhagen, B.A.(2021). Genomic Distinctions of LA-MRSA ST398 on Dairy Farms From Different German Federal States with a Low Risk of Severe Human Infections. *Front. Microbiol*., 2021, 11, 575321.

Littmann, J., and Viens, A. M. (2015). The ethical significance of antimicrobial resistance. *Public Health Ethics*, 8(3), 209-224.

Liu, G., Catacutan, D. B., Rathod, K., Swanson, K., Jin, W., Mohammed, J. C., et al. (2023). Deep learning-guided discovery of an antibiotic targeting Acinetobacter baumannii. *Nature Chemical Biology*, 19(11), 1342-1350.

Liu, Y., Tong, Z., Shi, J., Jia, Y., Yang, K., and Wang, Z. (2020). Correlation between exogenous compounds and the horizontal transfer of plasmid-borne antibiotic resistance genes. *Microorganisms*, 8(8), 1211.

Liu, Y. Y., Wang, Y., Walsh, T. R., Yi, L. X., Zhang, R., Spencer, J., et al. (2016). Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. *The Lancet Infectious Diseases*, 16(2), 161-168.

Lyall, J., Irvine, R. M., Sherman, A., McKinley, T. J., Núñez, A., Purdie, A., ... and et al. (2011). Suppression of avian influenza transmission in genetically modified chickens. *Science*, 331(6014), 223-226.

Mackenzie, J. S., and Jeggo, M. (2019). The one health approach—why is it so important?. *Tropical Medicine and Infectious Disease*, 4(2), 88.

Maddock, K. J., Bowden, R., Cole, S. D., Diaz-Campos, D., Daniels, J. B., LeCuyer, T. E., et al. (2024). Current state and future directions for veterinary antimicrobial resistance research. *American Journal of Veterinary Research*, 85(3). <https://doi.org/10.2460/ajvr.23.12.0294>.

Malijan, G. M., Howteerakul, N., Ali, N., Siri, S., Kengganpanich, M., Nascimento, R., ... and OH-DART Study Group. (2022). A scoping review of antibiotic use practices and drivers of inappropriate antibiotic use in animal farms in WHO Southeast Asia region. *One Health*, 15, 100412.

Mandhwani, R., Bhardwaz, A., Kumar, S., Shivhare, M., and Aich, R. (2017). Insights into bovine endometritis with special reference to phytotherapy. *Veterinary World*, 10(12), 1529.

Martin, H., Gribben, L., Regan, Á., Manzanilla, E. G., McAloon, C. G., and Burrell, A. M. (2024). Recording antimicrobial use on Irish dairy farms: Barriers and facilitators to using technology and sharing data. *Journal of Dairy Science*, 107(7), 5001-5015.

Massé, J., Lardé, H., Fairbrother, J. M., Roy, J. P., Francoz, D., Dufour, S., et al. (2021). Prevalence of antimicrobial resistance and characteristics of Escherichia coli isolates from fecal and manure pit samples on dairy farms in the province of Québec, Canada*. Frontiers in Veterinary Science*, 8, 654125.

McDonnell, A., Countryman, A., Laurence, T., Gulliver, S., Drake, T., Edwards, S., et al. (2024). Forecasting the Fallout from AMR: Economic Impacts of Antimicrobial Resistance in Humans. World Organisation for Animal Health and World Bank: Paris, France.

Messenger, K. M., Papich, M. G., and Blikslager, A. T. (2012). Distribution of enrofloxacin and its active metabolite, using an in vivo ultrafiltration sampling technique after the injection of enrofloxacin to pigs. *Journal of Veterinary Pharmacology and Therapeutics*, 35(5), 452-459.

Miró-Canturri, A., Ayerbe-Algaba, R., and Smani, Y. (2019). Drug repurposing for the treatment of bacterial and fungal infections. *Frontiers in Microbiology*, 10, 41.

Mithu, C.R., Tonmoy, C., Muhammad, T.F., Md. Mahmudul, H., Eman, Z., Md. Masudur, R., et al. (2024). Zoonotic linkage and environmental contamination of Methicillin-resistant Staphylococcus aureus (MRSA) in dairy farms: A one health perspective, *One Health*, 18:100680

Mohanty, D., Jena, R., Choudhury, P. K., Pattnaik, R., Mohapatra, S., and Saini, M. R. (2016). Milk derived antimicrobial bioactive peptides: a review. *International Journal of Food Properties*, 19(4), 837-846.

Mondal, A. H., Khare, K., Saxena, P., Debnath, P., Mukhopadhyay, K., et al. (2024). A review on colistin resistance: an antibiotic of last resort. *Microorganisms,* 12(4), 772.

Moretti, A. F., Brizuela, N. S., Bravo-Ferrada, B. M., Tymczyszyn, E. E., and Golowczyc, M. A. (2023). Current applications and future trends of dehydrated lactic acid bacteria for incorporation in animal feed products. *Fermentation*, 9(8), 742.

Mukherjee, K. (2024). Antimicrobial Resistance and its Impact on Public Health. International *Journal of Medical Research and Review*, 12(3),72-83.

Mwangi, J., Hao, X., Lai, R., and Zhang, Z. Y. (2019). Antimicrobial peptides: new hope in the war against multidrug resistance. *Zoological Research*, 40(6), 488.

Nadimpalli, M. L., Stewart, J. R., Pierce, E., Pisanic, N., Love, D. C., Hall, D., et al. (2018). Face mask use and persistence of livestock-associated Staphylococcus aureus nasal carriage among industrial hog operation workers and household contacts, USA. *Environmental Health Perspectives*, 126(12), 127005.

Neculai-Valeanu, A. S., Ariton, A. M., Radu, C., Porosnicu, I., Sanduleanu, C., and Amariții, G. (2024). From herd health to public health: Digital tools for combating antibiotic resistance in dairy farms. *Antibiotics*, 13(7), 634.

Nesporova, K., Valcek, A., Papagiannitsis, C., Kutilova, I., Jamborova, I., Davidova-Gerzova, L., et al. (2021). Multi-drug resistant plasmids with ESBL/AmpC and mcr-5.1 in Paraguayan poultry farms: the linkage of antibiotic resistance and hatcheries. *Microorganisms*, 9(4), 866.

Odongo, N. E., Bagg, R., Vessie, G., Dick, P., Or-Rashid, M. M., Hook, S. E., et al. (2007). Long-term effects of feeding monensin on methane production in lactating dairy cows. *Journal of Dairy Science*, 90(4), 1781-1788. doi: 10.3168/jds.2006-708

O'Neill, J. (2016). Review on Antimicrobial Resistance. Tackling drug resistant drugs globally: Final report and recommendations. <https://amr-review.org>

Organisation for Economic Co-operation and Development (OECD). (2018). Stemming the Superbug Tide: Just a Few Dollars More. Paris: OECD publishing <https://doi.org/10.1787/9789264307599-en>

Page, S., Prescott, J., and Weese, S. (2014). The 5Rs approach to antimicrobial stewardship. *The Veterinary Record*, 175(8), 207. [http://dx.doi.org/10.1136/vr .g5327](http://dx.doi.org/10.1136/vr%20.g5327).

Park, M., Kim, J., Feinstein, J., Lang, K. S., Ryu, S., and Jeon, B. (2022). Development of fluoroquinolone resistance through antibiotic tolerance in Campylobacter jejuni. *Microbiology Spectrum*, 10(5), e01667-22.

Prescott, J.F. (2017). History and current use of antimicrobial drugs in veterinary medicine. *Microbiology Spectrum*, 5(6), ARBA-0002- 2017.

Prestinaci, F., Pezzotti, P., and Pantosti, A. (2015) Antimicrobial Resistance: A Global Multifaceted Phenomenon. *Pathog. Glob. Health*, 109, 309–318.

Puri, B., Vaishya, R., and Vaish, A. (2024). Antimicrobial resistance: Current challenges and future directions. *Medical Journal Armed Forces India*, 81(3), 247-258.

Rafiq, M. S., Shabbir, M. A., Raza, A., Irshad, S., Asghar, A., Maan, M. K., et al. (2024). CRISPR-Cas system: a new dawn to combat antibiotic resistance. *BioDrugs*, 38(3), 387-404.

Rahman, M. T., Sobur, M. A., Islam, M. S., Ievy, S., Hossain, M. J., El Zowalaty, M. E., et al. (2020). Zoonotic diseases: etiology, impact, and control. *Microorganisms*, 8(9), 1405.

Reardon, S. (2017). Resistance to last-ditch antibiotic has spread farther than anticipated. *Nature*, 10(10.1038).

Rees, G. M., Barrett, D. C., Sánchez-Vizcaíno, F., and Reyher, K. K. (2021). Measuring antimicrobial use on dairy farms: A method comparison cohort study. *Journal of Dairy Science*, 104(4), 4715-4726.

Ritchie, H., and Spooner, F. (2024). Large amounts of *Antibiotics* are used in livestock, but several countries have shown this doesn’t have to be the case. *Our World in Data*. https://ourworldindata.org/*Antibiotics*-livestock

Robinson, T. P., Bu, D. P., Carrique-Mas, J., Fèvre, E. M., Gilbert, M., Grace, D., et al. (2016). Antibiotic resistance is the quintessential One Health issue. *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 110(7), 377-380.

Robles Ramirez, O., Osuna, G., Plisson, F., and Barrientos-Salcedo, C. (2024). Antimicrobial peptides in livestock: a review with a one health approach. *Frontiers in Cellular and Infection Microbiology*, 14, 1339285.

Salam, M. A., Al-Amin, M. Y., Salam, M. T., Pawar, J. S., Akhter, N., Rabaan, A. A., et al. (2023). Antimicrobial Resistance: A Growing Serious Threat for Global Public Health. *Healthcare* (Basel, Switzerland), 11(13), 1946. <https://doi.org/10.3390/healthcare11131946>

Samreen Ahmad, I., Malak, H. A., and Abulreesh, H. H. (2021). Environmental antimicrobial resistance and its drivers: a potential threat to public health. *Journal of Global Antimicrobial Resistance*, 27, 101-111.

Schwarz, S., and Chaslus-Dancla, E. (2001). Use of antimicrobials in veterinary medicine and mechanisms of resistance. *Veterinary Research*, 32, 201–225.

Schwarz, S., Kehrenberg, C., and Walsh, T.R. (2001). Use of antimicrobial agents in veterinary medicine and food animal production. Int. J. *Antimicrob. Agents*, 17, 431–437.

Seibt, U., Klötzer, P., Rachidi, F., Truyen, U., Speck, S., Starke, A., ... and Honscha, W. (2022). Development of an electronic interface for transfer of antimicrobial administration data in dairy farms. *Plos one*, 17(12), e0278267.

Singh, D., Singh, R., Gehlot, A., Akram, S. V., Priyadarshi, N., and Twala, B. (2022). An imperative role of digitalization in monitoring cattle health for sustainability. *Electronics*, 11(17), 2702.

Spellberg. B., Hansen, G.R., Kar, A., Cordova, C.D., Price, L.B., and Johnson, J.R.(2016). Antibiotic resistance in humans and animals. *NAM Perspect*, 6. doi: 10.31478/201606d.

Šukele, R., Skadiņš, I., Koka, R., and Bandere, D. (2022). Antibacterial effects of oak bark (Quercus robur) and heather herb (Calluna vulgaris L.) extracts against the causative bacteria of bovine mastitis. *Veterinary World*, 15(9), 2315.

Sukul, P., Lamshöft, M., Kusari, S., Zühlke, S., and Spiteller, M. (2009). Metabolism and excretion kinetics of 14C-labeled and non-labeled difloxacin in pigs after oral administration, and antimicrobial activity of manure containing difloxacin and its metabolites. *Environmental Research*, 109(3), 225-231.

Sun, D., Webb, L., van der Tol, P. P. J., and van Reenen, K. (2021). A systematic review of automatic health monitoring in calves: glimpsing the future from current practice. *Frontiers in Veterinary Science*, 8, 761468.

Swanson, K., Liu, G., Catacutan, D. B., Arnold, A., Zou, J., and Stokes, J. M. (2024). Generative AI for designing and validating easily synthesizable and structurally novel Antibiotics. *Nature Machine Intelligence*, 6(3), 338-353.

Tang, K. L., Caffrey, N. P., Nóbrega, D. B., Cork, S. C., Ronksley, P. E., Barkema, H. W., et al. (2017). Restricting the use of *Antibiotics* in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis. *The Lancet Planetary Health*, 1(8), e316-e327. doi: 10.1016/S2542-5196(17)30141-9.

Temkin, E., Fallach, N., Almagor, J., Gladstone, B.P., Tacconelli, E., and Carmeli, Y. (2018). Estimating the number of infections caused by antibiotic-resistant Escherichia coli and Klebsiella pneumoniae in 2014: a modelling study. *Lancet Glob Health*., 6, e969–79. doi: 10.1016/S2214-109X(18)30278-X

Tillotson, G.S., and Zinner, S.H. (2017). Burden of antimicrobial resistance in an era of de- creasing susceptibility. *Expert Rev Anti Infect Ther*., 15, 663–76. doi: 10. 1080/14787210.2017.1337508.

Tiseo, K., Huber, L., Gilbert, M., Robinson, T. P., and Van Boeckel, T. P. (2020). Global trends in antimicrobial use in food animals from 2017 to 2030. *Antibiotics*, 9(12), 918.

Todman, H., Helliwell, R., King, L., Blanchard, A., Gray-Hammerton, C. J., Hooton, S. P., et al. (2024). Modelling the impact of wastewater flows and management practices on antimicrobial resistance in dairy farms. npj *Antimicrobials and Resistance*, 2(1), 13.

Toutain, P.L., Ferran, A.A., Bousquet-Melou, A., Pelligand, L., Lees, P. (2016). Veterinary Medicine Needs New Green Antimicrobial Drugs. *Frontiers in Microbiology*, 7, 1196.

Toutain, P. L., Pelligand, L., Lees, P., Bousquet‐Mélou, A., Ferran, A. A., and Turnidge, J. D. (2021). The pharmacokinetic/pharmacodynamic paradigm for antimicrobial drugs in veterinary medicine: Recent advances and critical appraisal. *Journal of veterinary Pharmacology and Therapeutics*, 44(2), 172-200.

Tulloch, J.S.P., Owczarczak-Garstecka, S.C., Fleming, K.M., Vivancos, R., and Westgarth, C. (2021) English hospital episode data analysis (1998–2018) reveal that the rise in dog bite hospital admissions is driven by adult cases. *Science Report*, 11, 1767.

Van Boeckel, T. P., Pires, J., Silvester, R., Zhao, C., Song, J., Criscuolo, N. G., ... and Laxminarayan, R. (2019). Global trends in antimicrobial resistance in animals in low-and middle-income countries. *Science*, 365(6459), eaaw1944.

Van den Bogaard, A. E., and Stobberingh, E. E. (2000). Epidemiology of resistance to *Antibiotics*: links between animals and humans. *International Journal of Antimicrobial Agents*, 14(4), 327-335.

VandenMeersche, T., Rasschaert, G., Vanden Nest, T., Haesebrouck, F., Herman, L., Van Coillie, E., et al. (2020). Longitudinal Screening of Antibiotic Residues, Antibiotic Resistance Genes and Zoonotic Bacteria in Soils Fertilized with Pig Manure. *Environmental Science and Pollution Research*, 27, 28016–28029.

Vieira, A. R., Collignon, P., Aarestrup, F. M., McEwen, S. A., Hendriksen, R. S., Hald, T., and Wegener, H. C. (2011). Association between antimicrobial resistance in Escherichia coli isolates from food animals and blood stream isolates from humans in Europe: an ecological study. *Foodborne Pathogens and Disease*, 8(12), 1295-1301.

Vijay, D., Bedi, J. S., Dhaka, P., Singh, R., Singh, J., Arora, A. K., and Gill, J. P. S. (2023). Monitoring of antimicrobial usage among adult bovines in dairy herds of Punjab, India: A quantitative analysis of pattern and frequency. *Frontiers in Veterinary Science*, 10, 1089307.

Viñes, J., Cuscó, A., Napp, S., Alvarez, J., Saez-Llorente, J. L., Rosàs-Rodoreda, M., et al. (2021). Transmission of similar mcr-1 carrying plasmids among different Escherichia coli lineages isolated from livestock and the farmer. *Antibiotics*, 10(3), 313.

Von Wintersdorff, C. J., Penders, J., Van Niekerk, J. M., Mills, N. D., Majumder, S., Van Alphen, L. B., et al. (2016). Dissemination of antimicrobial resistance in microbial ecosystems through horizontal gene transfer. *Frontiers in Microbiology*, 7, 173.

Walsh, T.R., and Wu, Y.(2016) China bans colistin as a feed additive for animals*. Lancet Infect Dis.*, 16(10),1102-1103. doi: 10.1016/S1473-3099(16)30329-2.

Wang, Z., and Cui, W. (2020). CRISPR‐Cas system for biomedical diagnostic platforms. *View*, *1*(3), 20200008.

Weese, S., Valsson,O., Mateus, A.L.P. (2025). Antimicrobial prophylaxis in animals. Rome, FAO. UNEP, WHO and WOAH. (Accessed on March 25, 2025).

Weiss, L. M. (2008). Zoonotic parasitic diseases: Emerging issues and problems. *International Journal for Parasitology*, 38(11), 1209.

Witte, W. (2000) Ecological impact of antibiotic use in animals on different complex microflora: environment. *International Journal of Antimicrobial Agents*, 14, 321–325.

Woolhouse, M., Ward, M., Van Bunnik, B., and Farrar, J. (2015). Antimicrobial resistance in humans, livestock and the wider environment. Philosophical Transactions of the Royal Society B, *Biological Sciences*, 370(1670), 20140083.

World Health Organization (WHO) (2014). Antimicrobial Resistance: Global Report on Surveillance; World Health Organization: Geneva, Switzerland, <https://www.who.int/publications/i/item/9789241564748> (Accessed on Jan10, 2025).

World Health Organization (WHO) (2016).Global Action plan on antimicrobial resistance.[*https://www.who.int/publications/i/item/9789241509763*](https://www.who.int/publications/i/item/9789241509763)(Accessed on Dec 23, 2024).

World Health Organization (WHO) (2017). WHO Guidelines on Use of Medically Important Antimicrobials in Food-Producing Animals, WHO: Geneva, Switzerland. <https://www.who.int/publications/i/item/9789241550130> (Accessed on Dec 23, 2024).

World Organisation for Animal Health (WOAH). (2022). Chapter 6.8. Harmonisation of National antimicrobial resistance surveillance and monitoring programmes – Terrestrial Animal Health Code, 2nd Edn., pp 4. <https://www.woah.org/fileadmin/Home/eng/Health_standards/tahc/current/chapitre_antibio_harmonisation.pdf> (Accessed on Apr 15, 2025).

World Health Organization (WHO) (2023). Antimicrobial Resistance. <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance> (Accessed on Apr20, 2025).

World Health Organization (WHO) (2024a). Bacterial Priority Pathogens List. Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance. Geneva: World Health Organization. <https://www.who.int/publications/i/item/9789240093461> (Accessed on Feb 12, 2025).

World Health Organization (WHO) (2024b). WHO's List of medically important antimicrobials: a risk management tool for mitigating antimicrobial resistance due to non-human use. Geneva: WHO. <https://cdn.who.int/media/docs/default-source/gcp/who-mia-list-2024-lv.pdf> (Accessed on  Jan 15, 2025).

World Organisation for Animal Health (WOAH) (2024a). Tackling Antimicrobial Resistance using the One Health approach-the animal health perspective: Policy brief. <https://www.woah.org/app/uploads/2024/06/tackling-amr-using-the-one-health-approach.pdf> (Accessed on Jan 12, 2025).

World Organisation for Animal Health (WOAH) (2024b). WOAH’s factsheet of the 2024 UN Political Declaration on AMR. <https://worldvet.org/news/woahs-factsheet-of-the-2024-un-political-declaration-on-amr> (Accessed on May 01, 2025).

World Organisation for Animal Health (WOAH) (2025). WOAH List of Antimicrobial Agents of Veterinary Importance. <https://www.woah.org/app/uploads/2021/06/202501-en-woah-trd-list.pdf> (Accessed on Feb15, 2025).

Wozniak, T.M., Barnsbee, L., Lee, X.J., and Pacella, R.E. (2019). Using the best available data to estimate the cost of antimicrobial resistance: a systematic review. *Antimicrob Resist Infect Contl*., 8,26. doi: 10.1186/s13756-019-0472-z

Zamudio, R., Boerlin, P., Mulvey, M. R., Haenni, M., Beyrouthy, R., Madec, J. Y., et al. (2024). Global transmission of extended-spectrum cephalosporin resistance in Escherichia coli driven by epidemic plasmids. *EBioMedicine*, 103.

Zhou, S., Hu, X., Wang, Y., Fei, W., Sheng, Y., and Que, H. (2024). The Global Prevalence of Methicillin-Resistant Staphylococcus Aureus in Patients with Diabetic Foot Ulcers: A Systematic Review and Meta-Analysis. *Diabetes, Metabolic Syndrome and Obesity*, 563-574.