**A Comprehensive Review on Antimicrobial resistance in food animals: Global trends, Impacts and Mitigation strategies**

**ABSTRACT**

Antimicrobial resistance (AMR) in animals affects human health, animal welfare, and environmental sustainability, making it an actual One Health concern. The article provides a thorough road map for the human, veterinary, ecosystem healthcare workers and policymakers by combining worldwide trends, underlying factors, and a variety of mitigation options from on-farm sanitation to advanced CRISPR techniques. A comprehensive review of bibliographic databases and organisational reports was conducted, identifying 172 scientific literature (2015- early 2025) for datasets and updates on the global veterinary antimicrobial usage especially in livestock, future projections of veterinary AMR, the drivers and their impact across the human-animal-environment interface. The informations from these studies have been integrated to provide an understanding of the AMR burden in livestock – the challenges in addressing the issue, potential mitigation strategies that can be explored, research gaps to be filled in the animal sector and implementation of a cross-sectoral ‘Planetary health’ approach to combat AMR. Eventually, the review underscores the need for prudent AMU, new classes of antimicrobials or alternatives, suitable vaccines, rapid diagnostics, antimicrobial and environmental 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.

The indiscriminate use of antimicrobial agents in both animals and humans has enhanced the development of multidrug resistant bacterial strains, reducing the effectiveness of essential treatments (O'Neill, 2016). These multidrug-resistant pathogens, referred to as “superbugs” by World Health Organization (WHO) (WHO, 2025) 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). 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).

Reports of indiscriminate use of antibiotics in humans, are 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, antimicrobials administered as growth promoters or prophylactics, contribute to the environmental pollution from the animal excretions. The agricultural practice of using animal excreta as manure for the cultivable soils, increases the spread of AMR from animals to plants, humans, and aquaculture through contaminated food and water.

In addition, zoonotic pathogens with AMR can be transferred to humans through the consumption of contaminated 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 WHO (2014) in a study, indicating the alarming rise in antimicrobial resistance worldwide, with an equal or higher impact in plant, animal and environmental sectors. However, a comprehensive understanding of epidemiology and an update on the evolution of AMR in livestock is required. Policies for judicious use of antimicrobials in animals and periodic assessment of resistance levels (Coyne et al., 2019, Lienen et al., 2021) including environmental monitoring need to be developed. 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 and mitigation strategies to combat AMR crisis.

**2. REVIEW METHODOLOGY**

**2.1 Review question and scope**

The research question for this review was, “What is the current status of AMR in livestock – its global trends, driving forces, transmission pathways, extent of antimicrobial usage, public health impact and mitigation measures, with future directions?”

**2.2 Search Strategy**

The original search for the specific informations and data related to the review question was initiated in July 2024, covering relevant research published since 2000 and updates till 31st March 2025. In accordance with PRISMA2020 criteria of methods, systematic search of eResources like Directory of Open Access Journals, Oxford Academic Journals, PubMed Central, SAGE Publication Journals, Scopus, Web of Science, Springer open, Taylor and Francis Online, Wiley Online library accessed through eLibrary@TANUVAS (Tamil Nadu Veterinary and Animal Sciences University). The search strategy consisted of a selective combination of terms used to describe the review question (Eg: antimicrobials), antibiotic classes or specific names (Eg: Cephalosporins or Cefotaxime), livestock (Eg: domestic animals or specific species), indicator pathogen (Eg: E.coli or Salmonella), sector (Eg: animal health or human health or environmental), geographical location (national or global), impacts (Eg: bacterial, animal or human diseases), contextual factor terms (Eg: value or cost).

Peer-reviewed research papers, narrative reviews, grey literature sources on the websites of government and research organisations involved in AMR, were included for the review. The formal government reports, animal health reports, journal news and updates from International organisations like European Centre for Disease Prevention and Control (ECDC), European Medicines Agency (EMA), Food and Agriculture Organization of the United Nations (FAO), Indian Council of Agricultural Research (ICAR), Organisation for Economic Co-operation and Development (OECD), WHO, World Organisation for Animal Health (WOAH), United Nations Environment Programme (UNEP), were used to summarise the current trends of the research question, understanding the research gap to devise future plan of action. The prevalence and projection data were limited to livestock in this review and specifically the common bacterial pathogens affecting livestock.

**2.3 Search results**

The literature covered 628 full –length articles and 25 health and assessment reports from National and International organisations in the primary screening. A majority of the articles from the high - income countries and the LMIC’s, narrating the AMR trends, impact and control measures for AMR in livestock species included dairy, beef, cattle and swine, with impacts on human and environmental health. The scope of this review was confined to the studies relevant to the review question. Any other contributory factors, other animal species or hosts were excluded in order to restrict the comprehensive review to livestock. Later, the research findings, guidelines, informations and the future directives based on a shortlisted decade old literature (2015 – March, 2025), comprising of 172 articles and reports were reviewed in this paper, with an intent to provide an update on the AMR burden in livestock, and control strategies.

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

The growing issue of AMR has been identified as 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 is expected to be much greater (Laxminarayan and Chaudhury, 2016) with an increasing trend in the impact of AMR in Low and Middle income countries (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). 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). Asia has been projected to be the largest contributor of AMUQ, accounting for ~64.6% of the global total. 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 expected impact of reduction in food production by 7.5% (FAO, 2024a). The United Nations General Assembly (UNGA) has therefore included AMR in the list of global threats which needs to be addressed. 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).

Pathogens related to AMR were recognized by the WHO, 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 Extended spectrum β lactmase (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 and huge economic losses. Monitoring of human antibiotics consumption is mostly done through antibiotic sales databases. However, less attention has been given to the antibiotics consumption in livestock. Research findings have observed that more than fifty percent of the antimicrobials consumed by animals, went unabsorbed into the excretions (Tiseo et al., 2020). Since the animal sector data about antimicrobial consumption in livestock, regulations and policies to optimize the use of antibiotics are not well targeted, the relation between antimicrobial consumption and resistance patterns are also poorly defined (Van Boeckel et al., 2019).

Resistance maps and antimicrobial consumption data enable an approximation of baseline estimate of the global AMR scenario. Overall antimicrobial consumption has been reported to be higher in humans than in food-producing animals in 19 of 29 European Union/European Economic Area (EU/EEA) countries. Ever since 2014, various effective measures taken at country-level has resulted in the substantial decrease in AMU in these animals. A good proportion of *E. coli* isolates have become susceptible to all tested antibiotics in 12 EU/EEA countries between 2014 and 2019. Eastern and southern Europe scored low, while the Northern parts had higher percentages for this indicator. The prevalence of ESBL-/AmpC-producing *E. coli* decreased in 14 countries between 2015-2019 (OECD, 2022). The overall sales of veterinary antimicrobials for all 29 EU/EEA countries, Switzerland and the United Kingdom, reporting data in 2021 represented a 4.9% decrease compared to 2020. These Member States have already (2018-2021) reached approximately one third of the 50% reduction target set for 2030 (EMA-ESVAC, 2022).

A phenomenal decrease in population-antibiotic consumption in the United Kingdom was recorded between 2014 and 2023, by 59% in animals and 18% in humans. The Highest-priority critically important antibiotic (HP-CIA) consumption in animals decreased by 84% resulting from veterinary antibiotic stewardship initiatives. Harmonised Monitoring Programme for AMR initially monitored AMR in non-typhoidal *Salmonella* spp., *Campylobacter* spp. and *Escherichia coli* in livestock and livestock products across Europe. Three new species of bacteria in pigs, namely *Campylobacter coli, Enterococcus faecalis* and *Enterococcus faecium* have been included recently (Veterinary Medicines Directorate, 2023).

Among the LMICs, China and India have been listed as the largest antimicrobial consumers ever since 2010, 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 was recorded approximately as 10%, ranging from 7% in healthy animals to 12% in animals with clinical conditions. The resistance to cephalosporins has reached a sudden height among food animals, due to the recent surge in the usage of higher-generation cephalosporins to treat bovine mastitis and bacterial pneumonia, 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 livestock and poultry (FAO, 2024a). An increasing prevalence of the ESBL-producing Enterobacteriaceae has been studied in livestock, even in animals raised without antibiotics, but associated with multiple environmental factors including wildlife (Lee et al., 2020).

However, the food animals, companion animals and wildlife have also been reported as major reservoirs of diseases that are resistant to the last-resort medications like carbapenems, which are infrequently utilized in animal husbandry (FAO, 2024a).

**4. DRIVERS OF AMR IN LIVESTOCK**

Understanding the key drivers of AMR is essential for devising potential mitigation strategies. The major driving forces of AMR in livestock are - antimicrobials themselves, antimicrobial resistance genes (ARGs) of the microbes, and environmental factors. The other factors include on-farm practices, evolutionary changes in microbes and lack of awareness (Tilloston and Zinner, 2017).

**4.1 Evolution of Bacterial resistance against Antimicrobials**

Antimicrobial resistance is an inherent resistance property of bacteria to antibiotics, due to the presence of broadly-specific antimicrobial efflux pumps (Fernandes et al., 2003) within the microbe. 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 AMR 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).

**4.2 Antimicrobial misuse in livestock**

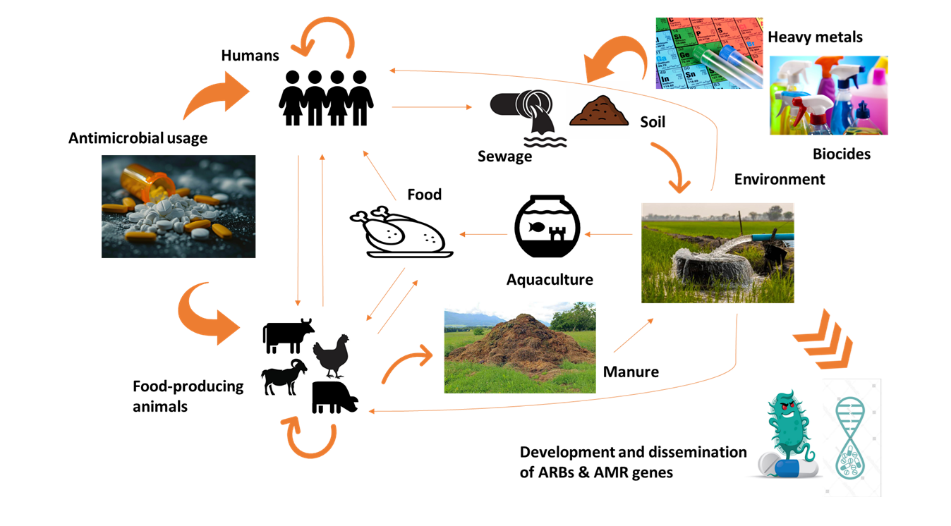
The misuse of antimicrobials in livestock, for a long-term disease prophylaxis or growth promotion is an important driver of AMR. This has led to a selection pressure favouring antimicrobial resistant bacteria (ARB) (WHO, 2017; Caneschi et al.,2023; Neculai-Valeanu et al., 2024).Thisis especially in countries where swine and poultry 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, ARB and their ARGs are shared between humans and animals over the years (Tulloch et al., 2021). In addition, the administration of a short-term mass medication with therapeutic antimicrobial concentrations was practised earlier, just before a disease outbreak, or soon after the onset of disease population, especially in beef feedlot and swine (Apley and Coetzee, 2013). The antimicrobials have also been used in the large herds where the apparently healthy and clinically infected animals at risk, were unable to be separated. The antimicrobial usage (AMU) in such cases was usually done in order to curtail any spread of infection within the herd (Bandyopadhyay and Samanta, 2020).

The then organisational triad involved in One-health namely - WHO, FAO and 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)”. Following a thorough scrutiny underway of these practices, a ban was imposed on the usage of MIA for prophylaxis and growth promotion in healthy animals and permitting only for disease-targeted therapy (WHO, 2017).

**4.3 AMR Transmission pathways**

Commensals and pathogenic bacteria have been reported to be a part of the normal and disease conditions respectively in humans, animals and environment. The impact of AMR becomes significant when there exists an interplay between these three components of ecosystem (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 by vertical or horizontal means across microbes, has been well-documented in earlier studies. Horizontal transmission commonly occurs through the mechanisms of transformation, conjugation, and transduction (Liu et al., 2020). This paves way for the less important bacterial strains transforming to more dangerous bacterial species, with disastrous results.

Mobile genetic elements, such as plasmids and transposons, frequently carry resistance genes and help in transfer (Von Wintersdorff et al., 2016; Liu et al., 2020). With a majority of ESBL-producing bacteria encoding the ESBL-genes on plasmids, spread of these genes occurred through horizontal gene transfer between bacteria. The recent findings have indicated the encoding of blaCTX-M genes in chromosomal DNA also (Teng et al. 2019). Extended-spectrum cephalosporin resistance in *E. coli* has been reported to be transmitted by epidemic plasmids from varied bacterial species, hosts and countries (Zamudio et al., 2024). Additionally, certain transposons having specialised regions called integrons were identified, especially among 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 demonstrated in major hotspots like hospital effluents (Bruno and Mackay, 2012). New genes associated with drug resistance have been identified in food animals namely the mobile colistin resistance gene (mcr-1) in pigs, the plasmid-mediated tetracyline 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. Bacteria may become resistant to certain antibiotics or a class of antibiotics as a result of such *de novo* mutations that arise from target-site gene alterations for that antibiotic (Bava et al., 2024). 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). Transmission of ARBs also occurs at the livestock-wildlife interface, with wildlife including wolves, seabreams, lynxes, wild boars, foxes, deer, bats, rodents and migratory birds acting as carriers in diverse habitats (Greig et al., 2015).

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. With respect to the host, smoking in humans 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).

**4.4 Environmental Pathways of Resistance**

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 ARBs can infect other susceptible animals and farm workers; contaminating raw milk, meat, and other livestock products, thereby posing a potential threat to human health through foodborne transmission (Robinson et al., 2016; Masse et al., 2021; Baker et al., 2022; Baghdadi et al., 2023).

In many countries, animal excreta are used as fertilizers, which potentiates the spread of resistance genes through food and groundwater. 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 serve as one of the potential sources of AMR in livestock. Inappropriate waste management practices have led to the proliferation of ARGs in the soil tested from the dairy farm manure, waste (Kim et al., 2021; Baghdadi et al., 2023) and 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 excreta that have not been given antibiotics (VandenMeersche et al., 2020) equally detected in the agricultural environment and, antimicrobial treated animals also (Johnsen et al., 2009).

In addition to antimicrobials, the increasing usage of disinfecting products containing biocidal agents and the resultant release of toxic wastes 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 seemed 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).

**4.5 Climate change and AMR**

In addition to the bioaccumulation of antimicrobials in the environment, the climate crisis has been studied as another driving force of AMR. 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 the onset of diseases and AMR eventually (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.

**5. 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 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 (Reardon, 2017). 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).

Based on importance in treatment of serious animal diseases and availability of suitable alternatives, the WOAH list of Veterinary antimicrobials has 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 and WHO /WOAH classification 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** |
| --- | --- | --- | --- |
| **WOAH** | **WHO** |
| Sulfonamides and  Potentiated Sulfonamides | VCIA | HIA | Changes in target enzymes and efflux pumps |
| 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. |
| 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 |
| Tetracyclines | VCIA | HIA | Energy-dependent drug efflux and alterations to the tetracycline binding sites at the 30S ribosomal units |
| Aminoglycosides | VCIA | CIA | Degradation of enzymes, modifications to the drug attachment sites (30S ribosomes), and changes in the cell surface receptor |
| 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 |
| Lincosamides | VHIA | HIA | 23S rRNA methylation encoded by *erm* gene, drug efflux pumps, and enzymatic modifications |
| 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) |
| Polypeptides | VHIA | IA | Altering cell surface charge, polysaccharide entrapment, and resistance to Bacitracin is rare |
| 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 |
| Ansamycin | VHIA | CIA | Mutations within the RNA polymerase target protein (RNAP), cell permeability changes, and modification through ADP-ribosylation |
| Fusidane | VIA | HIA | Mutations in the elongation factor G (EF-G), acquire resistance genes, namely, *fusB* and *fusC*, and altered drug permeability |
| Phosphonic acid derivatives | VHIA | HPCIA | Enzymatic hydrolysis, modifications of the P-C bond, overexpression of target genes |
| Ionophores \* | VHIA | - | By shedding the cell membrane or enclosing in a glycoprotein armor (glycocalyx) |
| Aminocoumarin \* | VIA | - | Mutation in target-*gyrB* |
| Avilamycin \* | VIA | - | Alterations in the 23S ribosomal (rRNA) |
| Pleuromutilins \* | VHIA | - | Plasmid-mediated (*vga*, *cfr* genes) and chromosomal (mutations in the 23S rRNA and *rplC* genes) |
| Quinoxalines \* | VIA | - | Mutations in DNA gyrase and topoisomerase IV, Qnr proteins and multidrug efflux pumps |
| Arsenicals \* | VIA | - | Energy-dependent efflux of arsenite (AsIII), detoxification of organic arsenicals mediated by ArsL, ArsM and ArsH, and horizontal gene transfer, |

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;

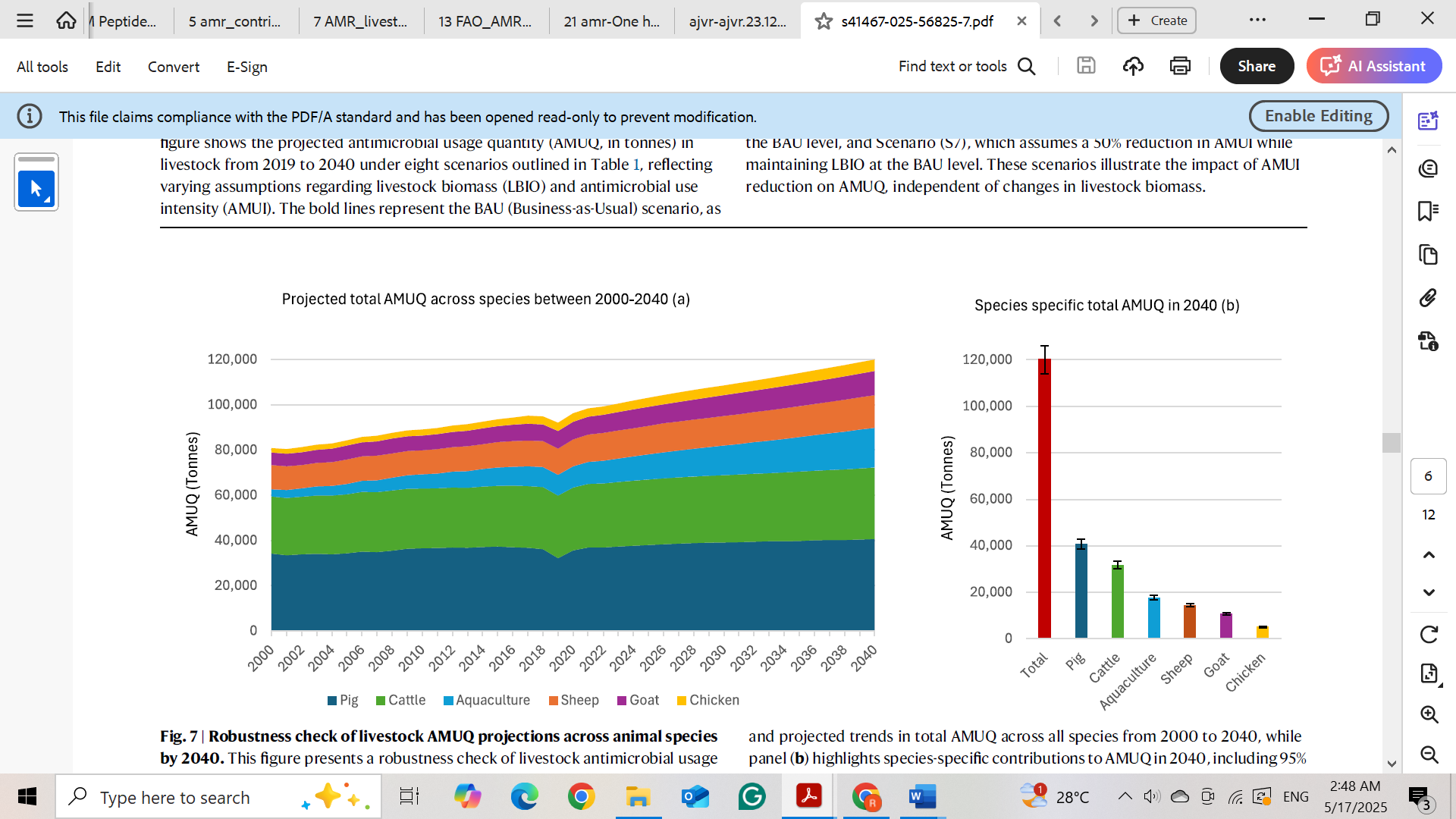
\* - Not authorised for human use.

The usage of antimicrobials in both high-income countries and LMICs are mostly to treat animals and to maintain good farm hygiene. Fortunately, AMR in the high-income countries has been under a vigilant surveillance for more than a decade, unlike the LMICs, where similar monitoring systems are still nascent (Van Boeckel et al., 2019). Although statistical data of species-level consumption in LMICs are limited, systematic investigations showed that tetracyclines were the most commonly used, followed by aminoglycosides, beta-lactams, macrolides, arsenicals, fluoroquinolones, ionophores, penicillins, polymyxins, polypeptides and sulfonamides (Lam et al., 2019).

According to integrated surveillance reports, a comparable Quinolone resistance (upto 60%) was recorded between Europe and LMICs for *E. coli* and *Salmonella* spp., while the U.S. showed a lower resistance pattern of 2.4-4.6%. On the other hand, the degree of Gentamicin resistance was higher for the same pathogens in the U.S. and LMICs and (upto 40%), while Europe exhibited a lower resistance of 2.4-8.9%. However, the U.S. recorded a maximum resistance profile (100%) to tetracyclines across all animal species for *Campylobacter* spp., while all LMICs had an equivalent resistance profile as that of quinolones (~60%) (Van Boeckel et al., 2019).

In a global data analysis, 47% of tetracycline and 12% of penicillin was accounted for 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). Among *Salmonella* spp. recovered from carcass swabs of pigs and calves, the highest levels of resistance were observed for ampicillin, sulfamethoxazole and tetracycline. Signiﬁcantly decreasing temporal trends in resistance of *E. coli* isolates of calves and pigs to ampicillin, ciproﬂoxacin, cefotaxime, tetracycline and colistin were reported in several countries. Another signiﬁcant observation was the detection of linezolid-resistant LA-MRSA strains harbouring the *cfr* gene from pigs. Isolates of LA-MRSA in Europe predominantly belonged to clonal complex (CC) 398, although other livestock-associated clonal lineages have been reported (EFSA and ECDC, 2022).

In the recent past, the common 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. The 2040- projections of antimicrobial use quantity (AMUQ) among livestock species is expected to be; Swine > Cattle> Sheep/Goat > Poultry in a decreasing order of usage (**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 (Acosta et al., 2025). Poultry slaughtered at an early age had the least antimicrobial usage, compared to other food animals. Animal species reared intensively, were exposed to more antibiotics than the other animals (Ritchie and Fion Spooner, 2024).

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**Figure 2. Livestock AMUQ projections across a) Time period and**

**b) Animal species by 2040** (Acosta et al., 2025)

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, resulting in ‘Cephalosporin-resistance’. Multi-drug resistant ESBL and AmpC type β-lactamase producers with biofilm production have 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). 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). Additional *mcr* variants 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). 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).

Earlier reports of oral administration of low, sub-therapeutic doses of antibiotics supplemented in feed or water in the food animal production units had been documented to improve growth and production. Tylosin and tetracyclines were frequently used as feed additives in 88% of the growing pigs in the United States (Landers et al., 2012) and non-MIAs, such as carbadox, bambermycins, bacitracin, used for growth promotion (Bandyopadhyay and Samanta, 2020). 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 like Tylosin were also used for prophylaxis in calves to prevent hepatic abscesses. Macrolides were used in cattle to prevent respiratory infections and β-lactams used 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 were generally discouraged in groups of food animals (Weese et al., 2025).

**6. PUBLIC HEALTH IMPLICATIONS**

The excess use of antimicrobial drugs in food-producing animals since two decades has resulted in emergence of multi-resistant food-borne pathogens posing a significant risk to public health (Catry et al., 2003) and still remains a challenge. This AMR issue 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).

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. Later, research 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. Thus the impact of antibiotic restrictions on animal production likely varies due to simultaneous management changes aimed at improving animal health.

The high levels of AMR for several important bacterium - antibiotic combinations, namely, *Enterococcus faecium* to vancomycin, *Klebsiella pneumoniae* to carbapenems and third-generation cephalosporins, *Pseudomonas aeruginosa* and *Acinetobacter* sp.to carbapenems represented the status of the EU/EEA countries in 2020 (OECD, 2022).

The recently updated WHO Bacterial Priority Pathogens List (BPPL)- 2024, categorised 15 families of antibiotic-resistant pathogens, based on the importance for Research and Development 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, bovine Tuberculosis, Brucellosis, haemorrhagic colitis (Rahman et al., 2020), Hendra virus and influenza A (Leifels et al., 2022), *Trypanosoma cruzi* and *Toxoplasma gondii* (Weiss, 2008). Zoonotic bacterial pathogens causing human illnesses by food-borne contamination commonly included MDR strains of *S. aureus*, *Salmonella* sp., *Campylobacter* sp., *L. monocytogenes*, and *E. coli* (Abebe et al., 2020) and nearly one-third of WOAH-listed diseases are zoonoses. Most of the emerging diseases reported to WOAH were observed to impact human health by 57% (WOAH, 2022).

Bacteria and mobile genetic elements that confer resistance, have been demonstrated on animal skin and in excreta, spreading among animals, and capable of infecting humans too (Witte, 2000) through livestock products (Gilbert et al., 2021). 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 *Enterococcus faecium* strains were confirmed of their origin from a population mainly composed of animal strains (Lebreton et al., 2013).

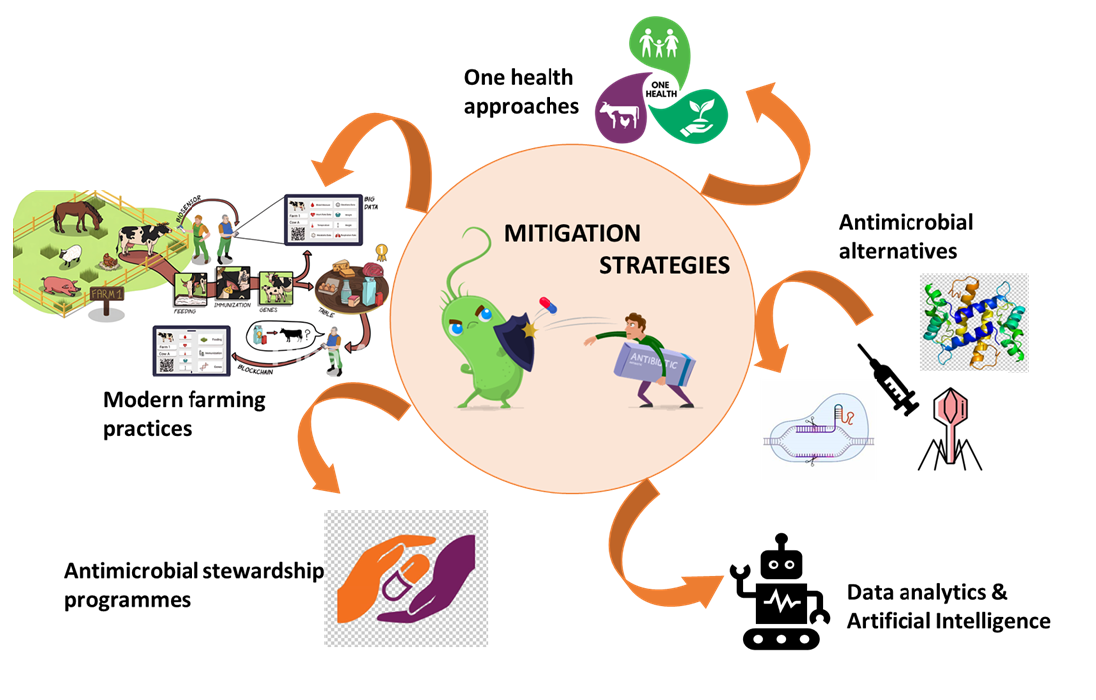
Livestock-associated Methicillin-resistant *Staphylococcus aureus* (LA-MRSA), initially reported in animals, has recently emerged in human populations, resulting from inappropriate AMU. The zoonotic transmission from farm animals to farm workers and veterinarians has been reported as an occupational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

The recent past has also 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 AMU in veterinary medicine causes AMR 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).

**7. 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. Multifaceted approaches to mitigate AMR in livestock**

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

**7.1 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, appropriate prophylactic vaccinations pertaining to the animal species in relation to the disease endemicity in the respective locations, would reduce the incidence of diseases, lowering AMU and preventing AMR (Maddock et al., 2024). Improved clinical treatment of infectious diseases by improving the host immune system was also proposed to reduce AMU and in turn, AMR (Dance, 2024).

A higher incidence of bacterial contamination in retail meats when antibiotic restrictions were applied has been reported earlier (Pol and Ruegg, 2007; Keelara et al., 2013). Conversely, many other studies found either no change in contamination rates or a decrease in contamination within the intervention group (Miranda et al., 2009; Zhang et al., 2010). AMR trends varied depending on increased production costs due to longer feeding times required to achieve target weight under restricted antibiotic use (Morley et al., 2011). Another study observed a reduction in veterinary costs with antibiotic restrictions, although the specific cost components and factors driving this reduction were not specified. These conflicts emphasize the need for surveillance, reporting, and interpretation of AMR data to guide effective policy and control measures.

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). 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.

**7.2 Antimicrobial Stewardship in Veterinary Medicine**

**7.2.1 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 more than expected in certain species like pigs, calves, and dogs (Messenger et al., 2012; Hauschild et al., 2013).

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 (Maddock et al., 2024). With incomplete pharmacokinetic and pharmocodynamic 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.

With this basis, Veterinary antimicrobial stewardship can be improved by defined effective treatment regimens by the clinicians. By allowing a shorter residence time of the sub-optimal drug levels in the infected tissue, selection pressure can be reduced, and preventing AMR. Targeted education of veterinarians and veterinary students on appropriate AMU is therefore, a critical need in veterinary antimicrobial prescriptions.

Veterinarians can utilize the categorization of antibiotics laid down by the Antimicrobial Advice Ad Hoc Expert Group (AMEG) of European Medicines Agency (EMA) based on public health issues of increased AMR when used in animals, and the need for their use in veterinary medicine as listed below in table 2

Table 2: Use of antibiotics in in veterinary medicine

|  |  |  |
| --- | --- | --- |
| **Category A** | **AVOID** | Antibiotics not authorized as veterinary medicines in food-producing animals |
| **Category B** | **RESTRICT** | Critically important antibiotics for humans, and use in animals restricted to mitigate risk to public health. |
| **Category C** | **CAUTION** | Antibiotics considered for use only when there are no antibiotics in Category D |
| **Category D** | **PRUDENCE** | Antibiotics used as first line treatments, with prudence and only when medically needed |

The major outcomes of an on-farm stewardship would be improved crop yields and livestock health, reduced input and production costs and a resilient agroecosystem. Socio-economic benefits in terms of an economic farm viability improving the rural livelihood, enhanced food security and competitive advantage in the market line would be the positive impacts.

**7.2.2 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).

Benchmarking AMU enabled the farm-level antimicrobial stewardship by evaluation of disease and continuous monitoring of AMU and therapeutic outcomes (Schrag et al., 2022). A series of updated initiatives implemented in antimicrobial stewardship since 2019, seemed to reduce the AMR burden in UK (Veterinary Medicines Directorate, 2023).

**7.3 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).

Moreover, contradictory findings also exist regarding animal health. Two studies observed an increased prevalence of intramammary infections and mastitis-causing pathogens associated with restricted antibiotic use due to organic farming practices (Pol and Ruegg, 2007; Park et al., 2012); while another study found no significant difference in mastitis occurrence between the groups (Roesch et al., 2006).

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 the health conditions of the entire herd as well as individual animals (Alipio and Villena, 2023).

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.

**7.4** **Antimicrobial Mimetics**

This refers to products such as vaccines, antibodies, pattern recognition receptors (PRRs), probiotics, bacteriophages, peptides, phytochemicals, metals and antimicrobial enzymes, used as alternatives for antimicrobial agents. 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;

**7.4.1 Probiotics**

Probiotics have been explored as alternatives to antimicrobials, 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).

**7.4.2 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 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.

**7.4.3 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).

**7.4.4 Other Alternatives**

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.

**7.5 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.

**7.6 New approaches**

**7.6.1 New antimicrobials**

The development of new antibiotic classes with effective properties and their clinical trials will take more time than the speed at which AMR is rising globally. 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 (Saxena et al.,2025). 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). Research gap of identifying and ensuring antimicrobials that can remain effective for a long period without resistance can be prioritized in veterinary medicine (Swanson et al., 2024).

**7.6.2 Novel vaccines**

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.

**7.6.3 Gene editing**

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, although ethical considerations must be balanced (Lyall et al., 2011).

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPRs) are a set of short palindromic repeat sequences with spacers derived from mobile genetic elements such as bacteriophages and plasmids in between them. Upon a second infection of the host by the same virus, the CRISPR defense system would cleave the incoming viral DNA sequence that matches the spacer sequence already present in the spacer, and protect the bacteria from the attacking virus. This can be repurposed to turn it against the pathogen itself making it a potential genome editing tool for creating antimicrobials. The CRISPR-Cas system will be able to inactivate genes responsible for biofilm formation, pathogenicity, and encoding of virulence factors in the host bacteria (Sen and Mukhopadhyay, 2025) and act as new therapeutics. By limiting horizontal gene transfer using the CRISPR-Cas system, the spread of AMR can also be controlled.

Sufficient data in support of the antimicrobial property and safety in natural microbial communities, the chances of inactivation of the CRISPR-Cas system by antiCRISPR proteins, the need of authorized guidelines for utilization of CRISPR based technologies are the challenges in the way ahead.

**7.7 ‘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 (GAP) on antimicrobial resistance (GAP) 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 human and veterinary medicine, and the environment (Robinson et al., 2016). Since then, efforts have thus been undertaken to evaluate and regulate AMU (Lardé et al., 2021) including the “Tricycle” model implemented in several countries by Global antimicrobial resistance and use surveillance system (GLASS) (WHO, 2022), ResAlert – the One Health approach to AMR risk management in UK (Veterinary Medicines Directorate, 2023), the Danish Integrated Antimicrobial Monitoring and Research Programme (DANMAP) - a gold standard example of One Health surveillance (WHO 2024c).

The Quadripartite Collaboration on ‘One- Health’, comprising of the WHO, FAO, WOAH and 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 aim has been to preserve antimicrobial efficacy and ensure sustainable and justified access to antimicrobials for prudent use (WOAH, 2024a).

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 with prudent use of antimicrobials

2) Resourced 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) and Global Antimicrobial Resistance and Use Surveillance System (GLASS).

3) Prevention of diseases by animal vaccination regimens implemented as per WOAH-listed priority diseases. This should be complemented with effective implementation of biosecurity, good animal husbandry practices and rapid, low-cost diagnostic tests for AMR.

4) Sustainable financing established at national and global levels to support the implementation of cost-effective interventions across sectors, based on surveillance data.

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. These countries often use the other data sources closer to actual consumption that provide more accurate information on antimicrobial consumption, but many LMICs lack the structures and processes to collect data at these levels and require support (WHO, 2022). 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 RENOFARM (Reduce the Need for Antimicrobials on Farms) program under the FAO, which aimed to reduce AMU in the farm (FAO, 2024b) is a good example of an on-farm stewardship, for efforts against AMR (Acosta et al., 2025).

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 and USFDA guidelines (WOAH, 2022; USFDA, 2025);

**Table 3: Target animal species and animal bacterial pathogens included in surveillance and monitoring programmes for AMR (WOAH, 2022; USFDA, 2025)**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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 National Action Plan 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 impact of AMR on livestock and aquaculture sectors are more, as climate stressors increase disease prevalence, leading to higher antibiotic usage and production losses (Gilbert et al., 2021). Environmental AMR mainly results from antimicrobial accumulations from pharmaceutical wastes, human waste, agricultural and aquacultural runoffs and hence transdisciplinary efforts are therefore required. Public health campaigns, policy reforms and increased global cooperation are essential to offer a planetary health approach for AMR mitigation. The importance of ecological sustainability, climate action, and environmental stewardship have to be targeted in reducing AMR (Horvat and Kovačević, 2025).

**7.7.1 Challenges in implementation of One health or Planetary health**

Implementing surveillance programmes and control policies in the fight against AMR, across countries including LMICs face several practical challenges (Van Boeckel et al., 2019; Arnold et al., 2024) as enlisted below;

a) Lack of systematic surveillance systems for AMR in animal sector, weaker legislations, fragmented governance, lesser awareness, need for financial resources and lack of stakeholder coordinations in LMICs.

b) Lack of evidence-based assessment, or established monitoring systems in some LMICs where the resistance levels may also be reduced by lesser meat consumption and inadequate access to veterinary antimicrobials in rural areas of LMICs.

c) Point prevalence surveys in LMICs offer a largely underutilized resource for mapping AMR trends and hence creating resistance maps from these surveys is difficult.

d) Varied diagnostic specificities and sensitivities of the diagnostic methods available to identify AMR. Careful evaluation and interpretation of the results of multiple tests is therefore required to arrive at discrete conclusions for AMR mitigation.

e) Sampling biases can occur due to differences from identifying appropriate data, funding for research focusing on specific hosts, environments, and geographies, which do not always coincide with high-risk hotspots and data confidentiality issues.

f) Need to access complex and large-scale data by knowledge mapping the data ecosystem, integrate and visualise diverse data sources, understand how to synthesise AMR data, data biases at every spatial and biological level, interpretation of data for business, policy makers, and decision makers.

g) Lack of prominence of the environment in global and national action plans on AMR control and prevention

h) Mapping wildlife and companion animals potentially involved in AMR dispersal

**7.8 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). Integrating AI with bioinformatics and whole-genome sequencing will provide valuable data in identifying new resistance genes and understanding microbial evolution (Dance, 2024).

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. AI-based stewardship augmenting traditional antimicrobial governance and precision medicine, contribute towards effective antibiotic usage. On the other hand, lack of sufficient transparency and reasoning of clinician’s logic for therapy, limited clinical datasets liable for inherent biases, data quality, and real-world implementation barriers still remain as challenges for this option (Ahmed et al., 2024).

**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 the predominant approach to prevent AMR. Quantification of AMU in various livestock species can help to 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, aquaculture and environment, will ensure identification of reservoirs of ARBs, ARGs and transmission dynamics of ARGs. Comprehensive strategies can be developed only with an understanding of the resistant bacteria and the environmental influences.

Addressing AMR, thus 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, and improving the research gaps across the involved sectors 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.

**Recommendations for future research in AMR**

Suitable research focussed on mitigation of AMR in livestock is one of the important approaches to reduce AMR. The research gaps to be targeted about AMR in the animal health sector include;

i) Robust surveillance systems to monitor AMU and AMR in livestock farms

ii) On-farm, environmental and veterinary antimicrobial stewardship programmes for responsible use of antimicrobial agents, governed by stringent regulations and disease biosecurity measures.

iii) Development of novel antimicrobials or alternative drugs for effective disease control in livestock

iv) Therapeutic regimens proven by suitable clinical trials

v) Development of rapid, low-cost diagnostics for disease diagnosis in livestock.

vi) Genotypic identification of the ARGs in sewage, farm and hospital effluents

vii) Research and development of efficacious next-generation vaccines to prevent bacterial diseases in livestock

viii) Phylodynamic studies to examine the transmission of resistance involved at the human-animal-environment interface

ix) Modelling approaches to understand AMR flow

x) Systems-based data-science approaches within a One Health framework to understand AMR evolution and dissemination in the environment

**Disclaimer (Artificial intelligence)**

Option 1:

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 the writing or editing of this manuscript.

Option 2:

Author(s) hereby declare that generative AI technologies such as Large Language Models, etc. have been used during the writing or editing of manuscripts. This explanation will include the name, version, model, and source of the generative AI technology and as well as all input prompts provided to the generative AI technology

Details of the AI usage are given below:

1.

2.

3.

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