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REVIEW ARTICLE

One Health Perspectives on Anthelmintic Resistance: Mechanisms, Surveillance Gaps and Control Strategies

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ABSTRACT

Anthelmintic resistance (AR) is one of the most rapidly increasing issues in livestock and companion animals, with the threat to animal health, livestock and companion farm productivity, and sustainable parasite control. AR is no longer a purely pharmacogenetic issue, but a multifactorial process shaped by biological, ecological, and management forces. This review presents the existing knowledge on AR in veterinary parasitology with a specific focus on livestock and companion animal parasites. There are still limitations in diagnostics since the Fecal Egg Count Reduction Test is not sensitive for early-stage diagnosis. Quantitative and droplet digital PCR and targeted surveillance tools are some of the developments that are improving accuracy and facilitating more sustainable drug use. The combination of various control strategies and improved farm management practices can decrease the use of dewormers. In general, AR is a multifaceted veterinary and One Health problem and needs the coordination of stewardship, enhanced diagnostics, and diversified control strategies. Future progress will require bridging the gap between molecular parasitology, ecological management, and veterinary practice to develop a sustainable approach for protecting animal health and productivity.

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INTRODUCTION

Brief overview of helminth infections and their burden on animal and human health: Helminth infections are one of the most critical limitations to livestock production at a global level, with higher burdens especially being reported in Europe, South America, Australia, and some regions of Africa, resulting in the reduction of growth rates, milk yield, decreased fertility, and vulnerability to secondary infections (Charlier *et al.,* 2014; Sutherland and Leathwick, 2011). This loss of production has far-reaching economic impacts that tally in the billions of dollars annually in the production of ruminants alone (Kaplan, 2004). AR has now become a significant issue in veterinary medicine on a global scale with cases of treatment failure in livestock becoming more common, which compromises the productivity of farms and the welfare of animals (Vineer *et al.,* 2020; Nielsen, 2022). Although helminth infections in humans are a global health challenge (with more than a billion infected), they are included in this review primarily to emphasize the One Health aspect of AR in which resistant parasites and drug-use behaviors in animals may have broader consequences of zoonotic spillover and human health (Kołodziej-Sobocińska *et al.,* 2020).

Definition and classical understanding of anthelmintic resistance: Despite the continuous attempts to ameliorate hygienic conditions, pasture practices, and vaccination, the use of anthelmintic drugs has been the main approach to the control of helminths. The effectiveness of anthelmintics has, however, been disrupted by a much more widespread and recently increasing phenomenon of anthelmintic resistance (AR). The classical definition of anthelminthic resistance is the inherited capacity of a helminthic parasite to survive exposure to the drugs that are effective when used at recommended doses (Taylor *et al.,* 2009). Such resistance is especially dominant in gastrointestinal nematodes of small ruminants, where the resistance to all major categories of drugs, including benzimidazoles, macrocyclic lactones, and imidazothiazoles, has already been reported and distributed around the world. The most common way to identify the AR is the fecal egg count reduction tests (FECRT) and the larval development assays, but there is increasing importance directed towards the molecular aspect with the use of tools aimed at identifying the specific mutation usually associated with the β-tubulin gene polymorphism (Kotze and Prichard, 2016). The major classes of anthelmintics, their mechanisms of action and the current global resistance status across major helminth species are summarized in Table 1.

Limitations of current approaches and the need for a paradigm shift in AR research: Regardless of decades of study, we still perceive AR as a fight on the pharmacological and genetic level. The prevailing discourse still rests on drug resistance genes, inadequate dosing, and treatment frequencies as the most important determinants of resistance without considering the ecological, immunological, and evolutionary background within which resistance emerges (Laing *et al.,* 2017). This limited perspective has given rise to reactive strategies in terms of control, such as the use of the new classes of drugs that, subsequently, fall prey to resistance in several years. Furthermore, the existing approaches do not always take into consideration human, animal, and environmental health interconnectedness as the key concept of the One Health concept. Extensive ecological shifts are also transforming the patterns of parasite transmission and altering the patterns of resistance (Rose *et al.,* 2015; Vercruysse *et al.,* 2018).

Scope, novelty and contribution of this review: This review suggests a theoretical and practical change in the perception, study and management of AR. Rather than considering AR as a pharmacogenetic effect of drug abuse and target site mutations, we define it as a process occurring at the system level that is influenced by the biology of the parasite, host immune response,

Table 1: Classes of anthelmintics and reported resistance across major helminth species

Drug Class (Example)	Target Parasite Group (illustrative)	Mechanism of Action	Resistance Status worldwide (illustrative species)
Benzimidazoles (albendazole, fenbendazole, Oxfendazole)	Gastrointestinal nematodes of small ruminants (e.g., *Haemonchus, Teladorsagia, Trichostrongylus*), equine cyathostomins, cattle (*Cooperia*), canine hookworm (*Ancylostoma caninum*)	Bind β-tubulin → inhibit microtubule polymerization (Collins *et al.,* 2024; Pallotto *et al.,* 2022)	Widespread, high- prevalence resistance in small ruminants across Europe/Americas/Asia; increasing reports in cattle and companion animals (Vineer *et al.,* 2020; Ehnert *et al.,* 2025)
Macrocyclic lactones (ivermectin, moxidectin, doramectin, eprinomectin)	Broad nematodes incl. small-ruminant GIN, cattle (*Ostertagia, Cooperia*), equine (*Parascaris, cyathostomins*), canine filaria (*Dirofilaria immitis*)	Potentiate glutamate-gated Cl^- channels → Flaccid paralysis (Abongwa, 2017)	Resistance common in small ruminants; established in cattle (Cooperia); equine Parascaris & cyathostomins show reduced efficacy; ML-resistant heartworm strains confirmed in the USA and now reported in Europe (Vineer, 2020; De Seram, 2023; Nielsen, 2022; Hampton *et al.,* 2024)
Imidazothiazoles / Tetrahydropyrimidines (levamisole; pyrantel/morantel)	Nematodes of ruminants and horses (e.g., cyathostomins)	Nicotinic ACh receptor (L-type) agonists → spastic paralysis (Abongwa, 2017)	Resistance is frequent in small-ruminant GIN; pyrantel resistance is widely reported in equine cyathostomins; variable by region (Vineer *et al.,* 2020; Nielsen, 2022; Alm *et al.,* 2023)
Amino-acetonitrile derivatives (AADs) (monepantel)	Small-ruminant GIN (esp. *Haemonchus, Teladorsagia*)	Targets nematode- specific DEG-3/DES-2 nAChRs (incl. MPTL-1) (Rufener *et al.,* 2009; Abongwa, 2017)	Field resistance now reported in multiple countries and species (e.g., Teladorsagia in the UK; Haemonchus in Brazil) (Turnbull *et al.,* 2019; Nascimento *et al.,* 2021)
Spiroindoles (derquantel; usually in combo with abamectin)	Small-ruminant GIN	Nicotinic ACh receptor antagonist: combination exploits different targets (Abongwa, 2017)	Reduced efficacy reported on some farms; overall resistance is less widespread than BZ/ML, but vigilance needed (Abbas *et al.,* 2021; Nielsen, 2022).
Cyclooctadepsipeptides (emodepside)	Companion-animal nematodes (e.g., *Toxocara, Ancylostoma*); in development for human nematodes	Activates SLO-1 (BK) K^+ channels (± latrophilin pathway) → neuromuscular inhibition (Kulke *et al.,* 2014; Njeshi *et al.,* 2024)	No widely confirmed field resistance to date; active against multi-drug-resistant canine hookworm in reports (Castro *et al.,* 2020; Jackson *et al.,* 2025)
Salicylanilides / Halogenated phenols (closantel, rafoxanide, oxyclozanide, nitroxinil)	Fasciolids (flukes), some blood-feeding nematodes (e.g., *Haemonchus*)	Uncouple oxidative phosphorylation in parasite mitochondria (Kane *et al.,* 1980)	Closantel resistance documented but generally less prevalent than BZ/ML; efficacy varies by region and species; ongoing monitoring recommended (Arsenopoulos)
Isoquinoline-pyrazines (praziquantel)	Cestodes (tapeworms) & schistosomes	Promotes Ca^{2+} influx/targets TRP channel → spastic paralysis & tegumental disruption (Park *et al.,* 2019; Marchant, 2024)	Overall efficacy remains high; focal reports of reduced responses, no consistent, widespread field resistance; continued pharmacovigilance advised
BZ flukicide (triclabendazole)	*Fasciola hepatica* (juveniles & adults)	BZ-class microtubule inhibitor	Resistance confirmed on every continent; numerous farm-level failures and occasional human cases; substantial threat where fasciolosis is endemic (Morales *et al.,* 2021; Beesley *et al.,* 2023; Larroza *et al.,* 2023)

microbiomes, environmental forces, agricultural systems and sociocultural actions as a part of the One Health system. This review goes beyond the traditional mechanisms of resistance to accommodate neglected and emerging drivers of AR in an array of biological and ecological contexts. One of the contributions of this review is that it provides a clear connection between diagnostic innovation and field-level decision-making. We describe recent progress in molecular diagnostics (qPCR, droplet digital PCR), in metabolomics, artificial intelligence-aided surveillance, and precision livestock farming and outline how these technologies can advance in transforming the status of resistance management.

Unlike earlier reviews, which predominantly tabulate resistance mutations or even classes of drugs, this paper has incorporated molecular parasitology, evolutionary ecology, environmental science, veterinary practice, and social science in a single system of analysis. This way, it transforms the concept of AR into a One Health issue that demands the application of coordinated cross-sector responsiveness, diversified control approaches and policy-aligned stewardship instead of chemical intervention.

Methodology: The review was carried out as a narrative synthesis. The search was done using databases of PubMed, Scopus, Web of Science, and Google Scholar to reach related researches that were published until July 2025. Grey literature such as reports made by the World Health Organization (WHO), the World Organisation for Animal Health (WOAH) and the Food and Agriculture Organization (FAO) were also reviewed.

The search strategy integrated free-text and controlled vocabulary searching AR and its multidimensional drivers. Keywords were AR, drug resistance in helminths, benzimidazole resistance, macrolactone resistance, molecular mechanisms, efflux transporters, epigenetics, microbiome-parasite interaction, fecal egg count reduction test, qPCR, diagnostics, climate change, environmental drivers, wildlife reservoirs, targeted selective treatment, and One Health.

Literature that was included in the search had to discuss AR in livestock, wildlife, companion animals or in humans and had to provide information on molecular, ecological, diagnostic, environmental or behavioral determinants of resistance. Articles focusing on management strategies, combined control initiatives or policy frameworks were also included. The inclusion criteria used to select only purely in vitro pharmacology assays without clinical or ecological background, non-English articles, duplications, and commentaries lacked substantive data. Information on the studies sampled was coded and integrated based on overarching themes. These were the evolutionary ecology of the resistance to helminths, unknown molecular and microbiome-based processes, diagnostic advances and gaps, environmental and agricultural dynamics, sociocultural and behavioral factors, combined parasite control measures, and policy systems.

The evolutionary ecology of resistance

Natural history and evolution of resistance before synthetic anthelmintics: The evolutionary history of helminths indicates that parasites have been under the influence of selection pressure long before the development of synthetic anthelmintics. Variations in host immunity, changing climatic conditions, and dietary intake of bioactive plant secondary metabolites (including tannins, alkaloids, and saponins) provided a multi-faceted ecological challenge in which the helminths evolved effective survival mechanisms. These involved the generalized detoxification pathways, and stress-response pathways, which subsequently turned out to be applicable to drug resistance (Chiumiento and Bruschi, 2009; Lespine *et al.,* 2012).

Cross-resistance due to natural plant compounds or historical treatments (e.g., arsenicals, nicotine): Historical ethno-veterinary measures such as nicotine and arsenical drenches may have imposed a pharmacological selection pressure to select parasite resilience prior to the synthetic drug era (Nouri *et al.,* 2016). Laboratory studies have often shown that tannin-containing forages can decrease parasite fecundity and induce detoxification enzymes in support of the hypothesis that natural products could alter instinctual resistance pathways (Butter *et al.,* 2001; Hoste *et al.,* 2015). In contrast, large-scale field trials tend to record minimal or transient effects, and this raises the possibility that concentrations of metabolites and diversity of host diet in real grazing systems are insufficient to establish committed resistance (Krueger *et al.,* 2010). Such pre-anthelmintic exposures created a resistance cooker of metabolism with efflux pumps, detoxifying enzymes, and modification in drug targets as a result. This long-standing evolutionary arms race challenges the notion that resistance is exclusively drug-driven and emphasizes the importance of understanding the natural history of helminth adaptation to environmental stressors. In this regard, modern AR must be regarded as a magnification of the past adaptive mechanisms, aggravated by the high rates and homogeneity of current anthelmintic use patterns (Laing *et al.,* 2017). Such ecological exposures demonstrate that the resistance characteristics can be developed as a result of the existing adaptive capacity, but not necessarily due to contemporary drug selection.

Role of refugia and microevolution in shaping resistance gene pools: Phenotypic neurogenetic plasticity (pre-adaptation) of helminth populations is one of the under-explored areas. Resistance traits, rather than being simply manifested by novel mutations, can be developed due to the already present genetic diversity, which can lead parasites to survive any stressor, such as chemical exposure, temperature changes, or immune challenge. Numerous helminths possess a ready-made detoxification pathway or stress-response inducible genes that can be co-opted when under drug pressure to speed the process of becoming drug-resistant (Gilleard and Beech, 2007; Kotze and Prichard, 2016). This plasticity may also be utilized to allow helminths to be highly tolerant of ecological fluctuations, which increases the resilience and tenacity of the resistant populations.

The key evolutionary trend in the history of AR is the concept of refugia populations of the parasites that do not experience drug pressure and hence act as reservoirs of drug-sensitive forms. Keeping refugia is essential in delaying the dissemination of resistance since this dilutes resistant genotypes in the parasite population when breeding cycles start to occur (Van Wyk, 2001). However, treatment strategies do not guide alone the size and resilience of refugia, which is also present in ecological conditions (pasture management, host density, and environmental variability). The refugial populations operate under the same micro-evolutionary environment and influence the resistance gene pools (Charlier *et al.,* 2014).

How climate-driven parasite migration affects resistance gene flow: Climate change is altering the parasite geographical distribution, which can contribute to the transfer of resistance alleles during the migration of hosts and pathogens. The changes in temperature, humidity, and precipitation widen the habitat of previously restricted helminths to enable the resistant genotypes to occupy new habitats (Morgan and Wall, 2009; Bouzid *et al.,* 2014). For example, *Haemonchus contortus*, previously having a tropical and subtropical distribution, has been reported in temperate Northern Europe and Canada, and in most cases is exhibiting signs of drug resistance (Bouzid *et al.,* 2014). Ecological re-distribution is also fueled by the human-controlled movements of animals, modifications in land use, and overlapping wild and livestock habitats. With changing communities of parasites, genetically variant resistance alleles reassemble with local populations, enhancing helminth plasticity and evolution of controlled and natural systems (Vercruysse *et al.,* 2018).

Evolutionary ecology showed that AR is a product of a complex interplay between adaptive characteristics retained through ancestors and current anthropogenic pressures. These ecological and evolutionary dimensions can be crucial in developing resistance-management strategies that extend beyond drug replacement.

Hidden and understudied molecular mechanisms

Molecular mechanisms of resistance: The resistance has several molecular mechanisms:

β -Tubulin mutations: The most frequently known resistance mechanisms involve mutations in the β-tubulin gene, especially those linked to benzimidazoles group of drugs. Benzimidazole targets this protein which plays a crucial role in parasites cell division. The effects of mutation in the β-tubulin gene may contribute to the alteration in the structure of the protein, which makes the drug binding potential lower and hence prevents the toxic effects of that drug (Tenorio *et al.,* 2024). The mutation has been reported in several helminth species such as *Haemonchus contortus* and *Teladorsagia circumcincta* (Martínez-Valladares *et al.,* 2020; do Prado *et al.,* 2024).

Efflux transporters and detoxification mechanisms: In resistance, overexpression of efflux transporters, including P-glycoproteins, is a key contributor. These transporters force anthelmintic drugs out of the parasite cells, reducing the intracellular drug concentration and causing the parasites to survive. Such mechanisms and the increase in the activity of the detoxification enzymes such as cytochrome P450, counteract the activities of anthelmintic drugs. Efflux pumps particularly have importance as resistance against macrocyclic lactones and imidazothiazoles (Fissiha *et al.,* 2021).

Transcriptional plasticity and non-target site resistance: Transcriptional plasticity has an important role in resistance. The helminths can reprogram transcriptomes, upregulate transporters (e.g., P-glycoproteins), or downregulate drug targets in response to sub-lethal concentrations of a drug (Godoy *et al.,* 2016). This plasticity makes the diagnosis of resistance difficult because once the pressure is removed, there is no longer a stable genetic signature as gene expression signatures may revert back to the original state (Ingham *et al.,* 2008).

The non-target site mechanisms of resistance are becoming a factor in the case of macrocyclic lactones and imidazothiazoles. These are changes in target drug uptake or efflux, a change in neurotransmission pathways, and the conversion of the target drug into inactive forms. For example, a study conducted on *Cooperia oncophora* indicated suppressed expression of the ligand-gated ion channels that are not the major target but influence the response to the drug (Junco *et al.,* 2021).

The role of small RNAs and epigenetic modifications in resistance: The more recent subject of interest is small RNAs-mediated regulation, whereby the most prominent have been microRNAs (miRNA) and small interfering RNAs (siRNA), which are known to be involved in a network of regulatory processes during stress, such as exposure to medications. Parasitic nematodes like *Haemonchus contortus* have been discovered to have small RNAs to regulate detoxification enzymes and transporters that neutralize/pump out anthelmintic compounds (Britton *et al.,* 2020). The post-transcriptional regulators can be induced quickly, and therefore they present a dynamic and reversible way of drug resistance without the conferment of mutation.

The evidence on the role of small RNAs in AR has been, to date, mostly based on laboratory and model-organism experiments, and there is a dearth of field-based experiments in livestock helminths.

Another branch of resistance control difficulties is epigenetic alterations that receive inadequate attention. DNA methylation, histone acetylation, and chromatin remodeling are emerging in such helminths as *Schistosoma mansoni* and *Ascaris spp.* as potential reasons to respond to environmental and pharmacological stress (Geyer *et al.,* 2011; Roquis *et al.,* 2015).

Support of epigenetic role in AR is still mostly experimental and field based longitudinal studies are few.

The Microbiome as a modulator of anthelmintic resistance

Microbiome-Drug interactions: Studies have demonstrated that the microbiome can be used to regulate the bioavailability of anthelmintic drugs (Zimmermann *et al.,* 2019). Moreover, microbiome-mediated alteration of host drug-metabolizing pathways, such as cytochrome P450 systems, can indirectly affect the outcome of treatment. Some microbes contain enzymes that can alter or inactivate anthelmintic compounds like ivermectin and albendazole, which can be an indirect cause of decreased drug activity and resistance (Wilson and Nicholson, 2017).

Immune modulation and treatment outcomes: Microbiomes have effects on host immune response, which is also involved in influencing drug efficacy. A healthy microbiota maintains immunity against parasitic infections and influences the result of the treatment (Belkaid and Hand, 2014). Misalignment of microbiome immune responses may decrease anthelmintic efficacy and preserve resistant strains of parasites (Nobel *et al.,* 2015).

Dysbiosis and indirect resistance: Regular deworming can alter microbiota of the gut, causing dysbiosis and decreased host resistance to parasites and other pathogens (Peachey *et al.,* 2017; Correa *et al.,* 2020; Weese and Rousseau, 2005). Some gut microbes have enzymes that are able to break down or alter anthelmintics before reaching the target parasites (Belo *et al.,* 2025; Kusada *et al.,* 2022). The data on possible microbiome drug interactions highlights the necessity of an all-encompassing strategy of managing parasites that combines targeted drug use with maintenance of gut microbial health, integrating One Health considerations into AR control (Sharpton *et al.,* 2020).

All these non-classical and hidden mechanisms broaden the concept of AR beyond single-gene mutations.

Molecular plasticity and interactions between the microbiome could be included in surveillance structures to enhance the identification and forecasting of resistance patterns. The hidden molecular mechanisms promoting the anthelmintic resistance are summarized in Table 2.

The interaction between molecular and ecological drivers contributing to AR is illustrated in Fig. 1.

Diagnostics and surveillance gaps

Limitations of traditional Fecal Egg Count Reduction Tests (FECRT): Fecal Egg Count Reduction Tests (FECRT) have been the gold standard tests used to estimate the efficacy of anthelmintic agents and in the diagnosis of AR in veterinary practice as well as in humans. However, FECRT also possesses a diversity of drawbacks and, therefore, it can hardly be called reliable regarding the ability to deal with the detection of AR, including its detection in the initial stages of development of resistance (Levecke et al., 2012). The main drawback of FECRT is that it depends considerably on host excretion of eggs that can vary widely between individuals and species. Also, the test requires many animals to achieve statistically relevant results, and thus it is barely applicable in large-scale agriculture and regular animal monitoring solutions (Levecke et al., 2012; Leathwick et al., 2025).

Table 2: Hidden molecular mechanisms of AR in helminths

Mechanism Category	Description	Potential Implications	References
Small RNAs	Regulate Gene expression related to detoxification and drug target modulation	May enable rapid adaptation and complicate resistance detection	Britton *et al.,* 2020
Epigenetic Modifications	DNA methylation and histone modifications alter gene expression without changing the DNA sequence	Can persist across generations and affect long-term resistance traits	Roquis *et al.,* 2015
Microbiome-Mediated Drug Degradation	Helminth-associated bacteria produce enzymes that degrade or inactivate anthelmintic drugs	Can lead to indirect resistance via symbiotic relationships	Williams *et al.,* 2021
Transcriptional Plasticity	Rapid Changes in gene expression in response to drug exposure without genetic mutations	Adds complexity to resistance profiling and prediction	Junco *et al.,* 2021
Non-Target Site Resistance	Alterations in cellular transporters, metabolic pathways, or membrane permeability reduce drug efficacy	Undermines classical target-specific resistance assays	Junco *et al.,* 2021
Oxidative Stress Response Pathways	Increased antioxidant enzyme activity helps the worm withstand oxidative damage induced by drugs	Offers new biomarkers or drug targets for monitoring and intervention	Perbandt *et al.,* 2014

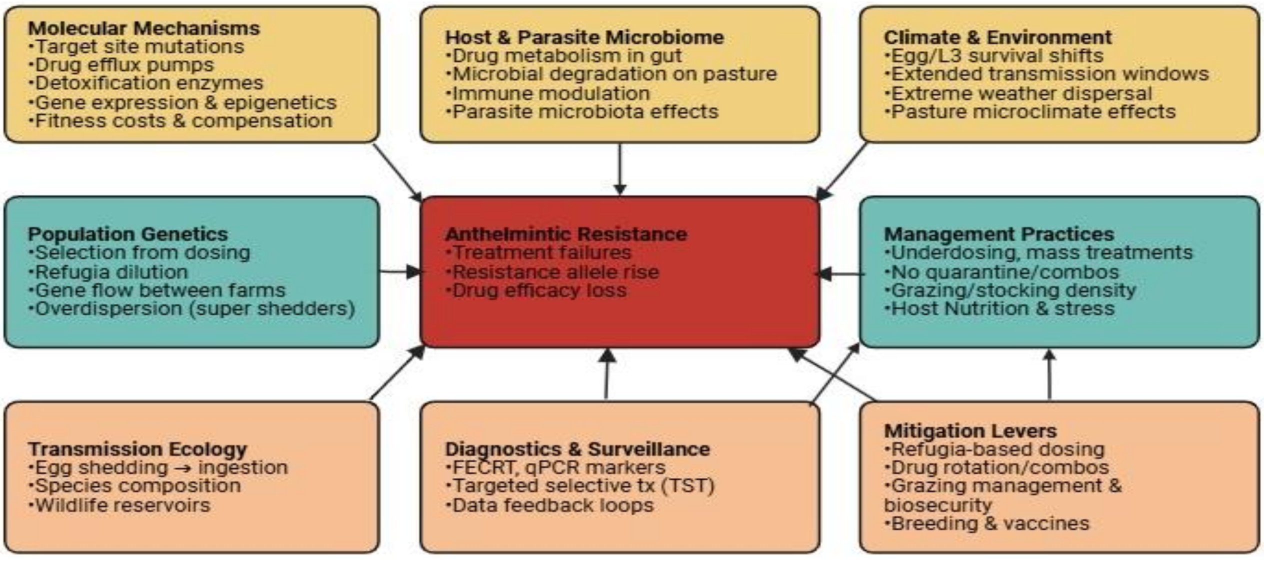


Fig. 1: Molecular and ecological interplay driving AR.

qPCR, ddPCR, metabolomics, and machine learning: Recent developments in molecular diagnostics have considerably enhanced the process of detection of AR beyond the constraints of FECRT. Quantitative PCR (qPCR) and droplet digital PCR (ddPCR) are more sensitive and specific as they directly measure the quantity of parasite DNA and detect genetic markers of resistance that enable measurement of parasite burden without using the number of eggs (Baltrušis and Höglund, 2023). qPCR has been extensively used in the detection of resistance-associated mutations and the changes of gene expression especially to the benzimidazoles and macrocyclic lactones and ddPCR provides a better sensitivity to detect low-frequency resistance mutations that can go undiagnosed with traditional methods (Hinney *et al.,* 2023).

In addition to genomics, metabolomics has also arisen as a complementary field, by detecting metabolic indicators capable of distinguishing between susceptible and resistant strains of helminths that facilitate the recognition of resistance at the earliest stages in advance before the failure in phenotype response is evident (Shaver and Andersen, 2024). Simultaneously, machine-learning techniques are also starting to be applied to combine molecular, metabolic and management data to improve pattern recognition and prediction ability, though scale validation has not yet been applied on a large scale in the field (Niciura and Sanches, 2024).

All these tools together make it possible to detect the resistance earlier, track its tendencies in real time, and make more informed treatment choices, which is a greatly needed improvement over traditional methods of diagnostics. A comparison between various diagnostic methods currently used for the detection of AR is presented in Table 3.

Absence of standardized surveillance in wildlife and peri-domestic animals: Despite the advancement in diagnostic tools, one of the most significant gaps in the management of AR is the absence of surveillance which is standardized, especially in wildlife and peri-domestic animals. Most existing AR surveillance systems pay little attention to animals inhabiting the peri-domestic landscape or in the periphery of human settlements, although they may act as reservoirs of resistant parasites, which can be spilled over to wildlife, livestock and human populations (Van Wyk, 2001; Vezeau and Kahn, 2024).

Table 3: Diagnostic methods for anthelmintic resistance

Diagnostic Method	Description	Advantages	Limitations	Sensitivity /LOD (typical)	Typical use-cases
Fecal Egg Count Reduction Test (FECRT)	Identifies the efficacy of anthelmintic treatment based on egg count reduction in feces	Gold-standard field screen; inexpensive; species-agnostic; standardized protocols available (Kaplan *et al.,* 2023)	Low sensitivity to early/low-frequency resistance; affected by aggregation, sample size, counting method, and timing; not species-resolved without larval ID; not validated against slaughter gold-standard in cattle (Vidyashankar *et al.,* 2012; Love *et al.,* 2017; Kaplan *et al.,* 2023)	Detects resistance reliably when resistant genotype ≳20-25% of worm population; power strongly depends on eggs per gram, n, and method (Vidyashankar *et al.,* 2012; Kaplan *et al.,* 2023)	Routine farm surveillance; first-line detection; benchmarking efficacy across drug classes (Kaplan *et al.,* 2023)
Quantitative PCR (qPCR)	Detects parasite DNA to identify resistance markers	Faster and cheaper than sequencing; scalable; quantifies allele frequencies; can be multiplexed; detects resistance before clinical failure (Alvarez-Sanchez *et al.,* 2005; von Samson-Himmelstjerna *et al.,* 2009)	Targets only known SNPs; mixed-species sample complicate interception; calibration/ standards required; dynamic range narrower than ddPCR (Alvarez-Sanchez *et al.,* 2005; von Samson-Himmelstjerna *et al.,* 2009)	Minor allele detection typically ~5-10% with careful assay design; linear over ~2-3 logs of template (Alvarez-Sanchez *et al.,* 2005; von Samson-Himmelstjerna *et al.,* 2009)	Early detection of BZ resistance; monitoring allele trajectories under refugia-based control
Droplet Digital PCR (ddPCR)	Absolute quantification of resistance alleles (same targets as qPCR)	Very high precision at low copy; absolute counts without standard curve; robust to inhibitors; excellent for low-frequency alleles and mixed templates (Baltrušis *et al.,* 2018; Hinney *et al.,* 2023)	Higher cost/instrumentation; still limited to known markers; assay design/ validation required (Baltrušis *et al.,* 2018)	Minor-allele LOD ~0.5-1% (and sometimes below) with sufficient DNA and droplets; 3-color assays enable multi-SNP calls in one reaction (Baltrušis *et al.,* 2018; Hinney *et al.,* 2023)	Sentinel surveillance and confirmatory testing where FECRT is borderline, detecting emerging resistance before efficacy loss
Metabolomics	Studies of metabolic profiles of helminths to identify early resistance markers	Hypothesis-free discovery of novel biomarkers & mechanisms (including non-target resistance) can differentiate resistant vs susceptible strains; complement genomics (Tuersong *et al.,* 2023; Shaver and Andersen, 2024)	Expensive, requires biobanking, standardization, and advanced analytics. May not identify all forms of resistance (Shaver and Andersen, 2024)	LOD depends on platform; untargeted LC-MS detects low-abundance metabolites (nM-pM), but diagnostic sensitivity/specificity are cohort-dependent; external validation needed (Tuersong *et al.,* 2023; Shaver and Andersen, 2024)	Biomarker discovery; mechanism-of-resistance studies; candidate diagnostic panels to be validated for point-of-care use
Machine Learning	Analyses large data sets to identify resistance patterns	Can predict multidrug resistance risk from farm management + FECRT; automates egg detection/ quantification from digital microscopy; scalable decision support (Sukas *et al.,* 2019; Niciura *et al.,* 2024; Xu *et al.,* 2024)	Needs large data sets and may require integration with other diagnostic methods, models may be opaque; does not directly measure genotype (Niciura *et al.,* 2024; Xu *et al.,* 2024)	Image-AI systems achieve high detection accuracy on benchmark sets; predictive MML models reported high cross-validated accuracy for flock-level resistance classification, but need wider validation (Niciura *et al.,* 2024; Xu *et al.,* 2024)	Risk stratification of flocks/herds; automating egg counts (field microscopy); integrating heterogeneous data to flag likely resistance hot spots

Abbreviations: BZ= benzimidazole; HRM=High resolution melt; LOD=limit of detection.

A significant number of parasitic species with the potential to develop AR can be found in wildlife species, such as wild ruminants and rodents. They are commonly found in regions with limited access to veterinary care and limited exposure to deworming interventions that offer a possible source of resistance genes that can be transferred to domestic animals or human beings (Barone *et al.,* 2020). On the same note, peri-domestic animals that are occasionally in contact with wild and domestic hosts can promote the spread of resistant parasites (Thompson, 2013). There is no standardized surveillance in these populations, which restricts knowledge on AR dynamics and its possibility of being a zoonotic disease. Incorporation of wildlife and peri-domestic animal surveillance in larger One Health systems would help provide more comprehensive tracking of cross-species surveillance and policy advice on resistance control based on evidence (Ng'etich *et al.,* 2024). Cost-effective strategies (non-invasive fecal DNA sampling or environmental sampling) need to be adopted in standardization activities to identify resistant parasites in under-investigated populations (Schilling *et al.,* 2022). These strategies would enhance the knowledge about the AR dynamics and contribute to more sustainable interventions to control parasites.

Environmental and agricultural drivers: Drug resistance is largely caused by the residues of anthelmintic drugs in nature. They get deposited in animal feces, water, and soil following deworming, which is associated with selective pressure on the parasites and other organisms therefore, resistance develops more quickly (Vokral *et al.,* 2023). Animals that experience low but non-lethal doses of the drugs will develop resistance that may be transferred to other species ecologically (Goodenough *et al.,* 2019). Individual resistance is aggravated by misuse or overuse of anthelmintics, such as under-dose and frequent dosages (Khalifa *et al.,* 2024).

Impact of intensive grazing systems and co-grazing practices: Intensive grazing systems are generally used in large-scale livestock production, where they ultimately result in the development of resistance to anthelmintic treatments. Such systems typically involve the regular use of deworming drugs. The greater concentration of animals in these systems allows the resistant parasites to spread rapidly among the infected group and thus, the possibility of cross-infection increases (Bricarello *et al.,* 2023; Niciura and Sanches, 2024). Co-grazing, the practice that enables various livestock to graze simultaneously, is still among the transmission sources of resistant parasites. Hence, the scenario is complicated since resistant parasites can move from one host to another making the control of infection more complex and resulting in further resistance development (Ramos *et al.,* 2020). Besides, it is important to mention that intensive grazing systems normally lack any rotational grazing practices that might lead to a lower parasite load in the pasture as the pastures are given a break and the parasite's life cycle is terminated (Beaumelle *et al.,* 2024). Various strategies for reducing environmental contamination with anthelmintics are illustrated in Fig. 2.

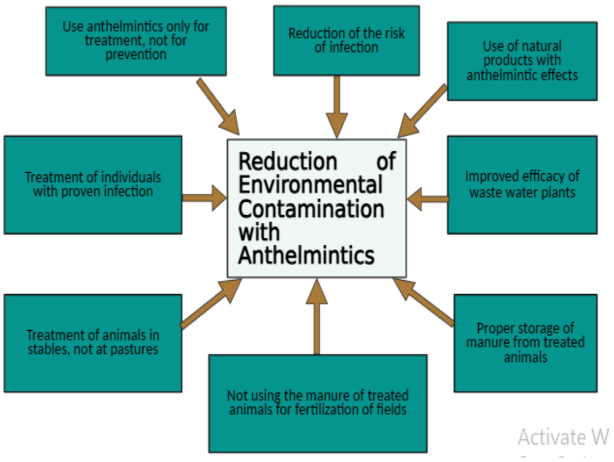


Fig. 2: Reduction of environmental contamination with anthelmintics

Resistance selection in non-target invertebrates in the ecosystem: The majority of AR studies have concentrated on helminths and their resistance to anthelmintics; however, a significant concern has been raised about the effect of drug residues on non-target invertebrates in the ecosystem. The organisms such as dung beetles, earthworms and soil arthropods that live in the environment are the major elements of the ecosystem, since they participate in nutrient cycling, soil aeration and waste decomposition (Lumaret and Errouissi, 2002). Nevertheless, the presence of residual drugs in their bodies can affect their propagation, survival, and the process of decomposition (Martínez *et al.,* 2017). Anthelmintic residues in the soil are the main contributor of harm to earthworms and other organisms living in the soil. Their growth and survival can be hindered as well as soil microbial communities changed and soil health maintained (Goodenough *et al.,* 2019). A summary of major ecological and agricultural drivers promoting AR is given in Table 4.

One Health Perspective on AR

Interconnectedness of Livestock, Wildlife, and Human Helminths: A One Health perspective acknowledges that human, animal, and environmental health are closely linked, particularly in disease transmission and drug resistance. The simplicity of helminth transmission among hosts creates complex transmission pathways that make AR difficult to manage (Ng'etich *et al.,* 2024). Zoonotic helminths (e.g., *Echinococcus*) have the ability to transmit between wildlife, domestic animals and humans either directly or indirectly by sharing a habitat (e.g., grazing areas, water sources). Wildlife that carries resistant parasites can infect domestic animals and infected human beings can continue the resistance cycles. The common environment of the wildlife, livestock and human populations thus suggests mutually linked health outcomes, requiring coordinated systems of cross-species monitoring and treatment where any resistance acquired in one species can be transferred between ecosystems (Kołodziej-Sobocińska *et al.,* 2020). One Health framework linking human beings, livestock populations and environmental drivers of resistance is illustrated in Fig. 3.

Table 4: Ecological and agricultural drivers of AR

Driver	Mechanism that influences AR	Notes / Examples	References
Grazing intensity /stocking rate	High stocking rates → heavier pasture contamination with infective L3 → higher parasite burdens → more (and more frequent) treatments → stronger directional selection for resistance; short residual swards increase L3 intake; set-stocking can maintain high challenge compared with well-designed leader-follower or mixed grazing.	Farm-level risk syntheses repeatedly identify management/treatment frequency links to AR; rotational systems don't automatically reduce parasites unless interval matches larval ecology.	Marley *et al.*, 2006; Wheeler, 2011; Sutherland and Leathwick, 2011; Saidu *et al.*, 2025
Drug persistence & residues in the environment	Long-acting MLs maintain sub-lethal but selective concentrations in treated hosts → prolonged suppression of susceptible worms and marked reduction of refugia, accelerating AR; excreted residues in dung/soil expose free-living stages and strongly impact dung fauna, altering dung degradation and potentially pasture contamination dynamics.	Macrocyclic lactones persist in dung at biologically active levels; environmental reviews document measurable residues and broad non-target effects; management guidance stresses avoiding sustained-release use where AR risk is high.	Boxall *et al.*, 2003; Liebig *et al.*, 2010; Sutherland and Leathwick, 2011; Lumaret *et al.*, 2012
Co-grazing / mixed grazing	Mixed species (e.g., cattle + sheep) can dilute host-specific nematodes (most GIN are host-preferred), reducing treatment need and slowing AR; however, shared species (e.g., *Trichostrongylus axei*) enable cross-transmission, and poorly planned co-grazing can maintain challenge. Leader-follower (cattle then sheep) often lowers lamb FECs.	Meta-analysis/field trials show lower lamb FECs and sometimes better growth under planned mixed or sequential systems; benefits depend on local species mix and timing.	Marley *et al.*, 2006; Wheeler, 2011; d'Alexis *et al.*, 2014; Charlier *et al.*, 2014
Climate change (warming & altered rainfall)	Warmer temps/humidity expand/translocate transmission windows, increase L3 development/survival and extend grazing seasons → more anthelmintic use and selection events; milder winters improve overwinter survival of some species; extreme events alter pasture contamination pulses.	Modelling and reviews predict earlier spring peaks and poleward/altitudinal shifts in GIN risk, raising cumulative selection pressure.	Morgan and Wall, 2009; Bautista-Garfias *et al.*, 2022
Wildlife reservoirs	Wild ruminants share generalist GIN with livestock; bidirectional spillover can introduce resistant alleles to farms; conversely, wildlife can serve as refugia for susceptible genotypes depending on contact structure and treatment intensity in livestock.	Recent metabarcoding shows benzimidazole-resistance markers present in both sheep and Alpine ibex before seasonal mixing; conceptual work frames wildlife as either sources or buffers of AR.	Brown *et al.*, 2022; Beaumelle *et al.*, 2024

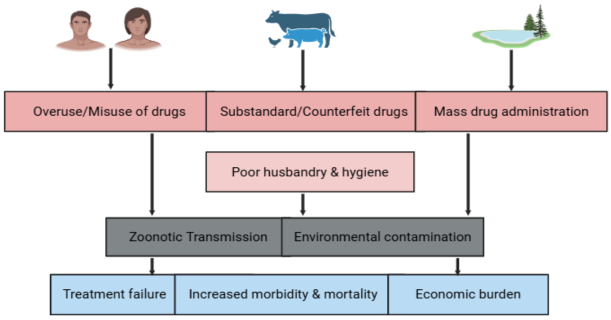


Fig. 3: One Health framework for AR

Urban and peri-urban helminth transmission and drug misuse: The urban and peri-urban areas, where there is a high population of people, animals, and livestock, are difficult to handle in regard to helminth infection and AR. Poor cleanliness and the lack of proper disposal of wastewater and animal wastes are other factors that contribute to the sustained occurrence of helminths in these environments. Due to the proximity between humans and animals, along with the fact that animals and their waste often contaminate communal areas, the risk of zoonotic infection and AR transmission is increased (Mackenstedt *et al.,* 2015; Ng'etich *et al.,* 2024). Uncontrolled anthelmintics and improper dosage in animals encourage parasite resistance by enhancing the selection pressure on the parasite populations (Saliya *et al.,* 2025). In the same manner, animals and livestock have also suffered from the resistance of parasites resulting from the unregulated usage of anthelmintics and wrong dosages (Alkadir and Ayana, 2024). High rates of helminth infections in the urban slums also indicate the role of poor hygiene and untreated populations in enabling the transmission of the parasites.

Anthelmintic use in pets and its overlooked contribution to community-level resistance: Another source of AR is the usage of anthelmintics in pets, which is relatively underestimated. Pet owners regularly treat their domesticated pets (especially in urban and peri-urban settings) against helminth infections, although uncontrolled use of drugs by pet owners is the primary source of resistance (Ng'etich *et al.,* 2024). Close contacts of pets with farm animals can contribute to further spread of resistant parasites across species, which increases AR and emphasizes the necessity of specific awareness among the urban and peri-urban owners of pets (Giannelli *et al.,* 2024).

Role of neglected helminths in zoonotic spillover and resistance amplification: Zoonotic helminths are mostly neglected in the context of AR even though they have significant implications on zoonotic spillover and resistance amplification. *Echinococcus* causes infection in humans and animals and are widespread in areas lacking sufficient veterinary coverage and a high potential of drug abuse. The spread of resistance in such neglected parasites can increase the impact on human health, especially in areas with limited resources with an already large burden of neglected tropical diseases (NTDs) (Thompson, 2015). The zoonotic helminths have not been adequately incorporated in the resistance-monitoring systems despite their capacity to harbor and transmit resistance genes among wildlife and domestic animals as well as humans (Thompson, 2023). This natural process of expansion in rural and urban habitats, coupled with a prolonged use of anthelmintics, provides an appropriate environment in which resistant strains develop and expand. To fill this gap, surveillance and combined control measures are required not only of human populations but also of animal populations in high-prevalence zones (Saelenset and Gabriël, 2020).

In combination, environmental pollution, companion-animal activities and abandoned zoonotic helminths demonstrate resistance goes beyond farms level dynamics. Interdependence in these reservoirs highlights the necessity of the interplay between wildlife, pets and human health in AR containment measures.

Sociocultural and behavioral Dimensions

Farmer knowledge, veterinary advice, and informal drug markets: The knowledge and behavior of the farmers, the veterinarians and the informal drug markets play a major role in the control of AR in livestock. The understanding of parasitic diseases, treatment methods and resistance by farmers is important in the dynamics of AR. Consequently, they usually depend on community-based knowledge that is passed from one generation to another or on unstructured networks for the purpose of livestock health management (Sazmand *et al.,* 2020).

Informal drug markets take up an important position as a source of anthelmintic drugs when there is no reliable veterinary advice. The resistance grows at a faster pace due to the combination of the use of low-quality or counterfeit drugs and the administration of the wrong dose of drugs. Sometimes, farmers might take matters into their own hands and buy anthelmintic drugs (Fissiha and Kinde, 2021). In remote areas where raising livestock is an important source of income, the unavailability of veterinary services is a major problem. In addition to market access and veterinary supervision, the traditional knowledge systems also influence treatment practices and drug resistance.

Influence of ethnoveterinary practices and self-medication: The practice of ethno-veterinary based on local and traditional knowledge systems affects the dynamics of AR especially in rural and indigenous populations. As previously reported for some viral diseases, such practices usually entail medicinal plants, agricultural methods, and locally based treatments (Shakir et al. 2025; Usmani et al. 2024). Their use, though cultural in origins and longstanding use, is not always scientifically effective in controlling parasitic infection and AR (Githiori *et al.,* 2005). In some cases, farmers use ethno-veterinary products together with modern anthelmintics without being fully aware of the possible outcomes. The effects of such combinations may change the pharmacokinetics of drugs, lower the effectiveness of the therapeutic effect, development of resistance (Abo-EL-Sooud, 2018).

Self-medication is another critical behavioral determinant of AR especially in rural or remote locations whereby farmers or pet owners give deworming medication without consulting the veterinarian because of the cost or time or inaccessible services. The practice leads to the risk of improper choice of drug, inappropriate dosage, and overuse of certain classes of anthelmintics, which accelerates the development of resistance (Sazmand *et al.,* 2020). Altogether, ethnoveterinary and self-medication demonstrate the complicated relationship between cultural traditions and contemporary veterinary medicine, and their influence on AR can be negative in the absence of scientific guidance and principles of disease management.

Gendered decision-making in animal health and its impact on AR dynamics: Another aspect of animal health management that has a significant, frequently neglected impact on AR is gendered decision-making. In most societies, livestock management and treatment decisions are often taken by men, whereas women engage more with day-to-day tasks like feeding, cleaning, milking, and simple health care (Arshad *et al.,* 2010; Ndwandwe *et al.,* 2025). Such a gendered division of roles leads to men and women assuming different roles but related roles in livestock health management. These divisions may have a direct influence on the selection, application, and management of anthelmintic treatments, and on the perceptions of AR. In some settings, women have the duty of dealing mainly with small ruminants or poultry, but matters related to drug choice and drug use are still under male authority (Njiru *et al.,* 2024). This disparity may create uneven knowledge and poor utilization of anthelmintics in the homes, which increases the chances of ineffective AR management (Ndwandwe *et al.,* 2025).

Access to education and knowledge of AR is also affected by gender-biased decision-making. Women also lack access to training and professional contacts to veterinary services, which limits their knowledge in preventing and controlling resistance. AR management activities, since the women are often left with day-to-day animal care and they are not involved in the broader decision-making, may be undermined. Gender-specific roles in livestock health should thus be identified in order to create inclusive, culturally relevant, and capable measures to counter AR (Gehano *et al.,* 2025).

Altogether, sociocultural practices, informal drug availability and decision-making arrangements greatly determine the rate and trend of resistance development. It is thus important to use these human dimensions as it is to comprehend molecular or ecological drivers of AR. An overview of the sociocultural and behavioral aspects that affect the use and resistance to anthelmintics is summarized in Table 5.

Table 5: Sociocultural and behavioral dimensions of anthelmintic use

Dimension	Mechanisms	Examples	References
Farmer Practices (knowledge, dosing, frequency)	Limited knowledge of parasitic biology and drug classes → routine prophylactic use, underdosing, or blanket treatments; limited adoption of refugia-based strategies; peer-to-peer advice and tradition often stronger than veterinary guidance.	Blanket drenching of all animals at fixed intervals regardless of need; underdosing due to weight underestimation; lack of fecal egg count (FEC)-guided dosing.	Morgan and Wall, 2009; Kotze and Prichard, 2016; Qamar and Alkheraije, 2023
Ethnoveterinary methods	Traditional plant-based remedies or cultural practices can reduce drug dependence (delaying AR), but variable efficacy and lack of standardization limit reliability; some communities integrate herbal remedies with modern drugs.	Use of tannin-rich forages (e.g., *Sericea lespedeza* in small ruminants); decoctions from neem, garlic, or local plants in South Asia and Africa.	Waller and Chandrawathani, 2005; Githiori *et al.,* 2006; Hoste *et al.,* 2015; Abubakar *et al.*, 2024; Haider *et al.* 2024; Štrbac *et al.*, 2024.
Informal drug markets & access pathways	Over the counter or black-market sales bypass veterinary oversight → poor-quality or counterfeit drugs, lack of prescription, unsupervised dosing; price-driven choices → preference for cheap generics regardless of efficacy.	Reported circulation of substandard or expired anthelmintics in East Africa and South Asia; farmers often purchase small-dose sachets without guidance.	Fissiha and Kinde, 2021; Vidhamaly *et al.,* 2022
Gendered decision-making in livestock care	Gender roles influence who manages livestock, decides on treatment, and controls resources; in many settings, women handle small ruminants but lack financial decision-making power for purchasing anthelmintics.	Women often primary caregivers of goats/poultry n African/Asian systems but male household heads make spending decisions; empowerment linked to improved animal health outcomes.	Kristjanson *et al.,* 2014; Taylor, 2024
Pet-owner behavior (companion animals)	Irregular deworming schedules, preference for OTC vs vet-prescribed product, online drug purchases; lack of awareness of zoonotic risks; “deworming fatigue” when owners perceive over-treatment; contributes to AR in parasites like *Toxocara* and hookworms.	High frequency of benzimidazole-resistant *Ancylostoma caninum* reported in dogs in USA and Australia; compliance depends on socioeconomic status and vet-owner communication.	Di Cesare *et al.,* 2014; Jimenez Castro *et al.,* 2019; von Samson-Himmelstjerna *et al.,* 2021

Integrated control strategies: From theory to implementation:

Combining drugs with vaccines, botanicals, or probiotics: The management of AR requires integrated strategies that help to manage the population of the parasites, as well as minimize drug-mediated selection pressure, as has been reported previously for immunomodulation of animals (Usmani *et al*., 2023; Hassan *et al*., 2023). Integrating traditional anthelmintic medications with alternative interventions like vaccines, botanicals, and probiotics is a prospective integration approach (Manjusa and Pradeep, 2022). The majority of helminth vaccines are still at their initial stages of development; however, they could potentially decrease the need for repeated courses of drugs. For example, a vaccine against *Haemonchus contortus* has been shown to have potential in reducing the occurrence of deworming and resistance rates when used together with conventional agents (Trujillo-Rodríguez *et al.,* 2025; Sajovitz-Grohmann *et al.,* 2025). Plant-based extracts especially botanicals have recently gained speculation as an alternative or supplement to chemical anthelmintics. Some of the compounds within plant species have anthelmintic properties against gastrointestinal nematodes and can be implemented as part of an integrated management approach to constrain resistance selection (Hoste *et al.,* 2022). Probiotics might also play a part in the regulation of microbiota in supporting host resilience to parasitic infections, which will decrease the load of parasites and decrease the necessity of chemical therapy (Grondin *et al.,* 2024). Combined, these combined strategies contribute to more sustainable and long-term management of AR.

Targeted Selective Treatment (TST) and Precision Livestock Farming (PLF): Targeted Selective Treatment (TST) focuses on treating only animals that require intervention, following appropriate parasite diagnosis rather than administering drugs to an entire herd or flock. TST requires the use of diagnostic methods like FECRT or molecular diagnostics to find those individuals in which the parasites have multiplied significantly, whereas the rest of the animals will not be treated. By this selective treatment, a decrease in drug resistance is achieved because fewer drugs are used (Bassetto *et al.,* 2024). Precision Livestock Farming (PLF) technologies can be listed as one of the significant factors of the TST success. With these systems, the health and behavior of each animal can be continuously checked using sensors that measure body temperature, feed intake, and movement patterns, allowing the farmers to decide the time and the place of the treatment with the anthelmintics (Tzanidakis *et al.,* 2023). By combining PLF and TST, there is a great possibility of cutting off the use of blanket deworming, which is largely responsible for AR, by only treating animals that have active infections and limiting the use of drugs and selective pressure on parasite populations, which is especially significant in large-scale farming systems (Šlapeta *et al.,* 2024).

Use of wearable biosensors and AI for parasite monitoring and targeted deworming: The use of wearable biosensors with the assistance of artificial intelligence (AI) to track the levels of parasite loads and deliver specific deworming is one of the most recent innovations in the sphere of parasite control. Biosensors may be implanted on animals to track vital information like temperature, pulse, and activity level and to check their behavior related to parasitic infestation (including reduced activity and altered feeding patterns). These sensors are able to collect data that can be analyzed using AI algorithms to predict parasite infections, so that farmers can only apply treatment when necessary (Yu *et al.,* 2024). Biosensors are capable of producing a large amount of data that must be processed and analyzed and advanced AI and machine learning algorithms can detect patterns applicable to parasite infections and aid in diagnostics. AI algorithms also treat according to the type of parasite, the severity of the infection, and the health of the animal, which will reduce the emergence of resistance and increase the sustainability of parasite control systems (Zhao *et al.,* 2025). Even though AI-based surveillance models demonstrate a promising predictive ability in pilot studies, the large-scale usage and filed testing of the systems are still in the process of development in a variety of production systems.

These integrated interventions reduce reliance on single-drug strategies and help distribute selection pressure across multiple control layers. Implementation success, however, depends on alignment with surveillance systems, farmer engagement and regulatory oversight.

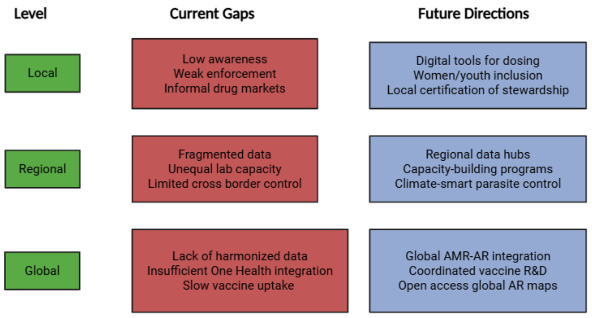
Policy, stewardship, and future directions:

Current policy gaps in anthelmintic regulation and veterinary oversight: The AR control has its loopholes in the existing policy frameworks, especially in the drug regulation and the role of veterinarians. Despite the awareness of drug resistance in veterinary and human medicine, the sale and supply of anthelmintic drugs is not properly regulated in many countries, and anthelmintic drugs are widely abused and overused (OIE, 2021; Kovaļčuka *et al.,* 2022). Lack of stringent rules particularly in rural and low-income regions permit farmers and people who own animals to purchase and utilize deworming medications on their own, which is exacerbated by the fact that there are minimal non-chemical therapies available and that people are still relying on the actual resistance-inducing medications (Salami *et al.,* 2023).

Moreover, veterinarians play a minor role in AR management in areas with poor or weak veterinary infrastructure where veterinarians might not be well trained and animal health services are unavailable. This forms a loop of improper drug use, lack of monitoring, and poor parasite control which aggravates AR (WHO, 2022). Enhancing veterinary surveillance and improving regulation of anthelmintic drugs are consequently important measures towards successful global AR management.

Need for global and regional AR stewardship programs: Since resistance to anthelmintics is complex, global, and regional AR stewardship programs are urgently needed to provide clear and coherent strategies to tackle AR across different regions. These initiatives must also involve safe drug administration, drug rotation, drug-free parasite control methods, policies that facilitate the prudent use of anthelmintics, and the acknowledgement of AR as a One Health challenge which points to the veterinary and human health (WHO, 2024). International stewardship efforts need to be coordinated between international organizations like the World Health Organization (WHO), World Organization of Animal Health (OIE) and regional veterinary organizations to set standards regarding responsible anthelmintic use and to monitor the spread of resistance (Picot *et al.,* 2022). The regional programs can respond to the local AR challenges by making international policies fit the regional contexts and enhancing human resource development in the farmers, veterinarians, and other stakeholders to contribute to sustainable parasite control practices (FAO, 2016; WHO, 2017). Moreover, promotion of cost-efficient solutions, including vaccines, probiotics, and botanicals, can help decrease the use of chemical solutions, decelerate the emergence of resistance, and enhance the productivity of animals. The policy and stewardship measures that should be adopted to combat AR are illustrated in Fig. 4.

Call for interdisciplinary research platforms: AR is so complicated that it requires a combination of knowledge areas such as veterinary medicine, public health, ecology, and molecular biology. There should be interdisciplinary collaboration between scientists to learn more about the evolution of parasites, environmental selection of resistance and social and behavioral mechanisms affecting the control of parasites (Picot *et al.,* 2022). The interdisciplinary studies must center on the creation of new diagnostic techniques and treatment plans to track and control resistance. Further developments in genomics, metabolomics, and bioinformatics have the potential to aid resistance marker identification and the explanation of adaptive mechanisms, whereas social science and economic studies can be used to interpret the reasons behind inappropriate anthelmintic use and guide more effective interventions and policies (Ng'etich *et al.,* 2024). Forums by which scientists, policymakers, veterinarians, and farmers can work inter-disciplinarily are thus necessary in creating sustainable solutions to AR management. Key stewardship measures, existing gaps and future policy directions are summarized in Table 6.



Level	Current Gaps	Future Directions
Local	Low awareness Weak enforcement Informal drug markets	Digital tools for dosing Women/youth inclusion Local certification of stewardship
Regional	Fragmented data Unequal lab capacity Limited cross border control	Regional data hubs Capacity-building programs Climate-smart parasite control
Global	Lack of harmonized data Insufficient One Health integration Slow vaccine uptake	Global AMR-AR integration Coordinated vaccine R&D Open access global AR maps

Fig. 4: Policy and stewardship to combat AR

Table 6: Policy and stewardship to combat AR

Level	Stewardship measures	Current gaps	Future directions	References
Local / Farm	• Enforce diagnosis-led treatment (FEC, TST). • Promote correct dosing (weighing, calibrated equipment), refugia concepts and integrated parasite management (grazing, nutrition, resistant breeds). • Vet-led prescribing and farmer education on AR stewardship. • Local surveillance; routine FECRT, sentinel sampling and reporting to regional registry.	• Widespread reliance on calendar/blanket drenching and under-dosing (lack of FEC services). • Limited farmer awareness of AR biology/refugia. • Informal drug supply and poor access to veterinary advice in many settings. • Few farm-level incentives or metrics for stewardship.	• Subsidize community FEC services, mobile diagnostic clinics, and farmer field schools with measurable uptake targets (e.g., % farms using TST within 3 years). • Implement farmer incentive schemes (certificates) for "AR-responsible" practices. • Track on-farm indicators (treatments/month, % animals TST-selected).	WOAH, 2021; Kaplan *et al.,* 2023; Vineer *et al.,* 2020
Regional / National	• National guidelines for prudent anthelmintic use (prescription-only frameworks where feasible). • Post-market quality surveillance of veterinary anthelmintics regulation of informal markets. • National AR surveillance networks integrating diagnostic data (FECRT, molecular assays) + centralized database. • Extension and gender-sensitive programs to improve equitable access to diagnostics and stewardship.	• Weak regulatory enforcement (substandard/counterfeit products persist). • Fragmented or patchy surveillance (sampling bias, limited georeferenced data). • Limited cross-sector coordination (animal health, environment, agriculture). • Underinvestment in laboratory capacity for molecular/ddPCR surveillance.	• Adopt WOAH/FAO/WAAVP guidance into national action plans with timelines & KPIs (e.g., % farms in registry, % tested before treatment). • Strengthen veterinary medicines regulation and post-market surveillance (target reduction in counterfeit reports). • Invest in regional reference labs and trainings for qPCR/ddPCR; deploy sentinel networks. • Mandate routine reporting of treatment failures to national veterinary authorities.	Vineer *et al.,* 2020; WOAH, 2021; FAO/WOAH, 2021; Kaplan *et al.,* 2023
Regional (multinational coalitions / EU/ASEAN/AFRICAN	• Standardize surveillance protocols and data formats for cross-border comparability. • Shared AR maps and risk-prediction tools (climate + management + FEC data). • Regional procurement / quality assurance mechanisms for veterinary drugs; joint enforcement actions on transnational illegal trade. • Capacity building hubs (reference labs, training centers).	Heterogeneous policies across neighboring countries hinder harmonized control. • Lack of open, interoperable AR databases and standardized metrics. • Varied lab capacity and funding across member states.	• Create interoperable regional AR databases (shared API, standardized sampling). • Joint procurement mechanisms to ensure quality and lower costs. • Regional training hubs and "AR rapid response" teams to investigate outbreaks. • Regional KPIs (e.g., countries with AR surveillance functioning).	Vineer *et al.,* 2020; FAO/WOAH, 2021; OECD, 2023
Global	• Global standards & guidance (WOAH/OIE, FAO, WHO) adapted to anthelmintics: stewardship, surveillance, and One Health integration. • Global reporting and early-warning (an AR "watchlist") and open data repositories. • Support for low-income countries: technical assistance, funding for diagnostics and regulated drug supply. • Research agenda and funding for alternatives (vaccines, novel chemistries, biocontrol, selective breeding).	Most global AMR frameworks focus on antimicrobials (bacteria); anthelmintics-specific policy uptake is patchy. • Funding and political attention for helminth AR are lower than for bacterial AMR. • Gaps in harmonized molecular markers and validated diagnostics for many helminth species.	• Formalize AR within global AMR action plans (WHO/FAO/WOAH joint targets) with dedicated funding lines. • Global repository for AR genetic/molecular data + open-access dashboards. • Incentivize R&D via public-private partnerships for non-chemical interventions and new activities. • Global KPIs: % countries with national AR plan, % labs performing molecular diagnostics, decline in counterfeit drug incidence.	WHO, 2015; Vineer *et al.,* 2020; WHO, 2021; FAO, 2021; OECD, 2023

Conclusions: Anthelmintic resistance is a significant public health and veterinary health issue that affects sustainable animal production, food security and control of zoonotic diseases. For a long time, the issue of anthelmintic resistance was regarded solely pharmacogenetic. However, it is now seen as a multifactorial phenomenon. To counter these loopholes, several priority actions are required. Harmonized surveillance systems should build interconnected networks at the global and regional levels that combine data from livestock, wildlife, and humans, employing molecular and digital tools for early-stage resistance detection. AI-enhanced diagnostics and precision tools should expand the use of ddPCR/qPCR platforms, and machine-learning models to facilitate on-the-spot monitoring and direct targeted selective treatments. One health policy integration should implement harmonized rules that not only regulate the illegal sale of drugs but also minimize pharmaceutical residues in nature and synchronize veterinary, human medicine and environmental stewardship. Diversified control strategies should develop resources, to eliminate the use of chemical dewormers as the only source of treatment, hence reducing the selective pressure. Education and behavioral change should improve the training of farmers and pet owners on the use of the correct dose, management of refugia, and the responsible use of drugs, while dealing with the gendered decision-making in animal health. Future research has to be interdisciplinary, combining molecular parasitology, microbiome science, climate ecology, artificial intelligence and social science. Practicing such integrated and progressive strategies is the only way to keep AR under control, guaranteeing the maintenance of both animal welfare and human health in a time of global health interdependence.

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