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A One Health framework for global and local stewardship across the antimicrobial lifecycle

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Antimicrobial resistance (AMR) is a One Health challenge, affecting human and animal health, plants and the environment. It has significant impacts on population health, food security and economies of all countries. AMR is a complex problem that requires broad One Health stewardship from local to global levels, encompassing infection prevention together with stewardship across the six stages of the antimicrobial lifecycle, i.e., (1) research and development, (2) production, (3) registration evaluation and market authorization, (4) selection, procurement and supply, (5) appropriate and prudent use and (6) disposal, as outlined by the World Health Organization (WHO), the Food and Agriculture Organization (FAO), and the World Organization for Animal Health (WOAH). This requires the stewardship of innovation, access, use and disposal. Such end-to-end stewardship will individually and collectively help to maintain the efficacy of existing and new antimicrobials for the optimal management and prevention of infections in humans, animals, and plants while protecting the environment. This Perspective proposes a comprehensive One Health stewardship framework that spans the entire antimicrobial lifecycle—from innovation to disposal—across humans, animals, plants, and the environment as One Health sectors. By embedding stewardship principles at all levels, the framework aims to preserve antimicrobial efficacy, mitigate resistance, and safeguard global health, animal health food security, and ecosystems.

Curbing antimicrobial resistance is a global One Health priority

Antimicrobial resistance (AMR) occurs when microorganisms such as bacteria, viruses, fungi, and parasites evolve to resist the effects of antimicrobials, making infections harder or impossible to treat. Recognized by the World Health Organization as one of the top global public health and development threats, AMR jeopardizes the effectiveness of modern medicine and increases the costs and risks of disease spread, severe illness, and death. On September 26, 2024, the United Nations General Assembly (UNGA) reinforced AMR as a global public health priority when it passed the Political Declaration[1] of the High-level Meeting on AMR. The Declaration aims to mobilize governments to prevent, contain, and mitigate AMR by setting achievable commitments and recommending sustainable financing solutions to support the implementation of multi-sectoral National Action Plans on AMR. The 2024 Declaration further emphasizes the need to simultaneously monitor and address AMR within and across all One Health sectors globally, regionally, and locally, with a particular focus on low- and middle-income countries (LMICs) as they carry disproportionately high AMR burdens.

In 2021, resistant bacterial infections were linked to an estimated 4.71 million deaths worldwide, with the highest mortality rates in sub-Saharan Africa and South Asia, with projected mortality increases of ~70% by 2050[2]. Additionally, the global number of deaths due to fungal diseases is estimated to have doubled in the last decade to 3.8 million, with their management compromised by rising antifungal resistance in many settings[3,4]. The impact of AMR extends beyond lives lost. According to the World Bank[5], if left unchecked, AMR could lead to a decline in annual global gross domestic product (GDP) of an estimated 3.8% by 2050, pushing 28.3 million more people into extreme poverty, and increasing healthcare costs by over US$1

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trillion per year. More immediately, without concrete action, the treatment of resistant bacterial infections alone will impose a global economic burden of US$412 billion in healthcare costs and US$443 billion in lost productivity annually up to 2035[6].

There is increasing evidence of the economic impacts of AMR on animals, livestock, and fisheries, with estimates suggesting that output could decline by 11% by 2050, with the greatest losses in LMICs[5]. Additionally, there is a significant risk of AMR in animals spilling over to humans, directly to occupationally exposed workers, and indirectly via the food chain[7]. Predictive models using recent data on production and disease inputs indicate that antimicrobial use (AMU) and the associated AMR-disease burden are estimated to cause a cumulative GDP loss of US$575–US$953 billion by 2050, escalating to US$1.1–US$5.2 trillion, and not including the burdens associated with the potential for AMR spillover to humans[8]. Conversely, a global reduction in AMU of about 30% is estimated to increase global GDP by US$120 billion cumulatively by 2050[8]. What is less certain are the impacts of AMR in companion animals, although given evidence of bidirectional transmission of AMR between people and pets and the use of some medically important antimicrobials in companion animal medicine, it is important that this population is not excluded from a One Health approach to addressing AMR[9].

This Perspective outlines a comprehensive One Health stewardship framework that spans the entire antimicrobial lifecycle—from research and development to disposal—across humans, animals, plants, and the environment as One Health sectors. It explores the key drivers of AMR, the economic and health impacts across different regions, and the urgent need for coordinated global and local action. The article also highlights sector-specific stewardship strategies and emphasizes the importance of embedding stewardship principles at all levels of governance. Ultimately, it advocates for a unified, cross-sectoral approach to preserve antimicrobial efficacy and mitigate the growing threat of AMR.

AMR drivers

It is important to understand the key drivers that lead to AMR increase. The drivers can be stratified as AMR-specific or AMR-sensitive. AMR-specific drivers directly relate to the use and misuse of antimicrobials in humans, animals, and plants that create pressure for the selection, development, dissemination and persistence of drug resistance in bacteria[10]. Bacteria may acquire multiple mechanisms of resistance, rendering many of the antimicrobials available to treat infections ineffective. The pipeline of new antimicrobials, active against multidrug-resistant bacteria, is nearly non-existent because of a significant lack of private investment and the exodus of scientific, clinical and regulatory experts to other areas[11,12]. Additionally, there is inadequate access to and utilization of rapid, effective diagnostics that enable confident decisions on the appropriate antibiotic to prescribe. Furthermore, it is estimated that at least 30–50% of all antibiotic prescriptions are inappropriately prescribed in human health[13,14].

However, concerns about AMU and AMR are not limited to humans. Antimicrobials are used extensively in livestock for prophylaxis, metaphylaxis, and therapeutic purposes[7,11,15,16]. Antimicrobials are also authorized for growth promotion in some countries, despite international calls to eliminate this practice. Additionally, farmers frequently apply medically important antimicrobials (MIAs) to plants for prophylaxis, with nearly 10% of rice crops receiving an MIA in some countries[17]. This is in addition to many other plant protection products that accelerate the development and spread of AMR[18]. Therefore, AMR selection and development occur in all One Health sectors.

AMR-sensitive drivers relate to the spread of drug-resistant microbes and are especially problematic in places with sub-optimal water, sanitation, and hygiene (WASH) provision in communities and/or inadequate infection prevention and control (IPC) programs in health facilities. On the global scale, only 60% of raw wastewater released from communities is subjected to effective waste treatment[19], with some countries having as low as 25% waste treatment coverage. This results in substantial quantities of drug-resistant microbes from human and animal waste entering the environment and being carried downstream. Such AMR contamination carried back to humans, animals, and crops, recirculates and amplifies the spread of AMR across all One Health sectors[20].

AMR spread is compounded by low vaccination rates to prevent infections and limited use of diagnostics to confirm the need for, and inform the choice of, antimicrobials. Factors such as these that increase baseline disease rates, especially when associated with diagnostic uncertainty, foster high levels of both necessary and unnecessary AMU.

Suboptimal IPC programs, often associated with poor biosecurity, animal husbandry and waste management practices in food animals, lead to increased AMR emergence and spread from such sites. For example, cattle feedlots with inadequate biosecurity showed that any antimicrobial use at a facility, even for therapeutic use only, can result in 1000 times higher levels of resistant microbes released into the environment in waste drains[21]. Given that wastewater management in animal and crop operations is often less stringent than in human systems and that animals generate about four times the mass of waste compared with humans at a global scale[22], inadequate biosecurity, animal husbandry, and farm waste management can consequently increase drug-resistant microbes entering the wider environment. This, in turn, contributes to the emergence, transmission and spread of AMR at massive scales.

AMR drivers at One Health interfaces are particularly impactful as they present risks to more than one sector. MIAs are routinely used as growth promoters in livestock production in sub-therapeutic doses over long exposure periods, albeit in a minority of countries, creating optimal conditions for bacteria to entrench genes that confer resistance. These genes are subsequently transferred to human pathogens or commensals via occupationally exposed workers and farm families, potentially contaminating food or the environment. Antibiotics used in humans and animals are largely the same structural compounds or belong to the same drug classes, which facilitates the transmission of resistance between species. A growing body of evidence links antibiotic use in livestock and aquaculture to the emergence of antimicrobial resistance in clinical settings[23,24].

Bacteria that naturally reside in the environment can also serve as sources of resistance genes that can become incorporated into human and animal pathogens over time. This situation is exacerbated by the influx of resistance genes from livestock, fisheries, and human waste into the environment, and the entry of antibiotic residues from crop production, aquaculture, and pharmaceutical industries that create hotspots for AMR selection. Therefore, intensive livestock farms, aquaculture, and hospitals that do not have adequate biosecurity and waste management can consequently alter AMR levels in exposed microbial communities, increasing the probability of resistance selection, development, persistence, transmission and spread[25].

AMR in LMICs and Small Island Developing States (SIDS) is exacerbated by poor access to existing and new antimicrobials, fragile supply chains for essential antimicrobials and other products for WASH, and a lack of infection prevention and treatment in humans, animals, and plants. Additionally, limited surveillance and laboratory capacity, sub-optimal political and professional leadership in antimicrobial stewardship in one or more One Health sectors[26], and the proliferation of sub-standard and falsified antimicrobials contribute to the development and persistence of AMR[27]. Therefore, it is critical to understand the drivers of AMR within and across sectors and geographies in order to mitigate the problem using a One Health approach.

Finally, a growing body of evidence suggests that climate change will alter infectious disease epidemiology, and implicitly, AMR in various ways. For example, changes in coastal water temperatures, rising sea levels, extreme weather events, alterations in precipitation patterns, and the impact of flooding and drought on water infrastructure appear to be expanding geographic spread and incidence of food- and water-borne diseases caused

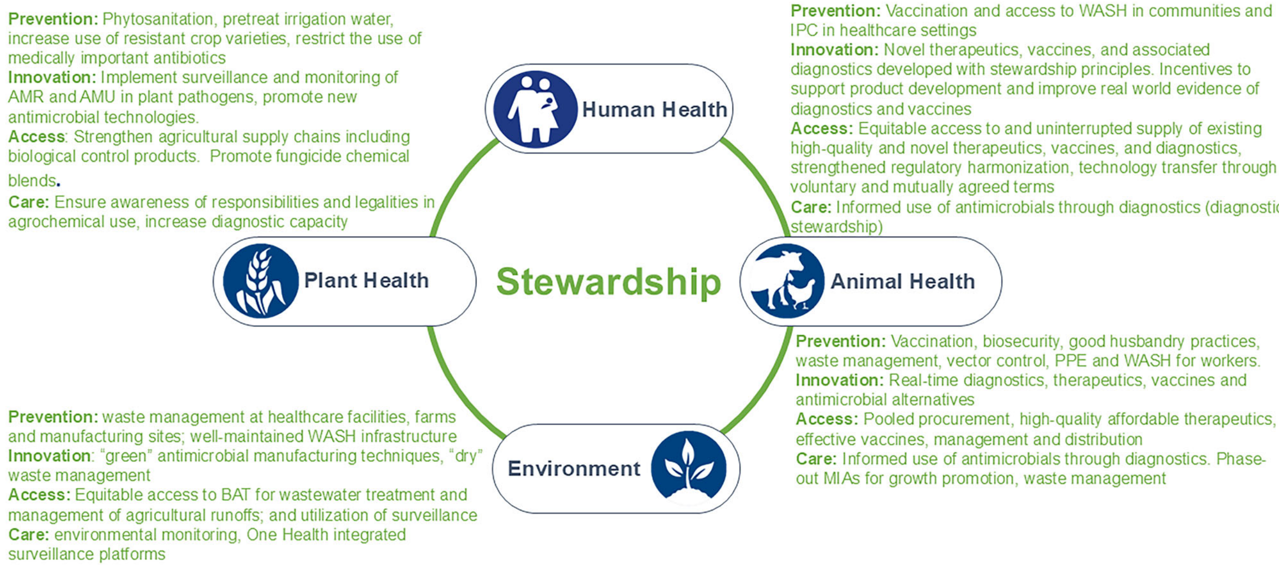

Fig. 1 | One Health framework for stewardship across the antimicrobial lifecycle. *WASH: water, sanitation and hygiene, IPC infection prevention control, AMR antimicrobial resistance, AMU antimicrobial use, MIA medically important antimicrobial.

Table 1 | One Health stewardship across the antimicrobial lifecycle: Prevention

Antimicrobial lifecycle	One Health element			
	Human health	Animal health	Plant health	Environment
Prevention	Enhance WASH, IPC and vaccination programs to reduce the incidence of infections while addressing broader governance, socio-economic and health system issues such as GDP/capita, health expenditure, education, infrastructure, etc.[33]. Ensure awareness and education among authorized prescribers, providers and users of antimicrobials.	Enhance biosecurity, including operational biosecurity to control the spread of infectious diseases both within and between farms, vaccination protocols, and good animal husbandry practices to reduce the incidence of infections and avoid the need for antimicrobials. Ensure awareness and education among veterinary professionals and farmers on prudent and responsible use of antimicrobials and on AMR.	Promote improved phytosanitation at all levels, including the use of pre-treated irrigation water. Encourage greater use of resistant crop varieties and undertake awareness campaigns on the importance of blending or alternating chemical use. Bolster extension services to provide timely and accurate advice. Phase out the use of MIAs in crop production and regulate the sale of related products.	Ensure contextually appropriate waste management infrastructure to prevent AMR from entering the environment as once AMR microbes, genes, and or chemicals that drive AMR enter the environment, control becomes exceedingly costly, if not impossible[25,34]. Improve waste containment and management from farms, healthcare facilities, manufacturing sites and other locations where there is potentially greater AMU.

This table summarizes key stewardship actions across the antimicrobial prevention lifecycle, tailored to each One Health sector.

by *Campylobacter*, *Escherichia coli*, *Cryptosporidium*, *Salmonella* and *Vibrio* species[28]. *Pseudomonas aeruginosa, Klebsiella pneumoniae* and *Staphylococcus aureus*, members of the ESKAPE pathogen group (Enterococcus, *S. aureus*, *K. pneumoniae*, *Acinetobacter baumannii*, *P. aeruginosa* and *Enterobacter* spp.) thrive at 32−36 °C and horizontal gene transfer also accelerates with temperature[29]. Climate change increases the incidence and prevalence of infections, resulting in greater AMU and the consequent selection pressure for the development/escalation of AMR. A warmer and more dynamic climate will thus alter infectious diseases and AMR in the future.

One Health stewardship

AMR is a complex problem that requires broader One Health stewardship across the antimicrobial value chain from local to global levels, encompassing infection prevention together with stewardship across the six stages of the antimicrobial lifecycle, i.e., (1) research and development, (2) production, (3) registration evaluation and market authorization, (4) selection, procurement and supply, (5) appropriate and prudent use, and (6) disposal[30]. Such end-to-end stewardship will individually and collectively help to maintain the efficacy of existing and new antimicrobials for the optimal management and prevention of infections in humans, animals, and plants while protecting the environment. Stewardship of shared classes of antimicrobials requires coordinated efforts to ensure their continued efficacy and equitable access in the relevant sectors while simultaneously reducing unintended transmission and spread in the environment.

The Merriam-Webster dictionary defines stewardship as "the careful and responsible management of something entrusted to one's care"[31]. Fig. 1 describes infection prevention, demand-driven innovation, uninterrupted and equitable access, and appropriate care (use and disposal) as central tenets of the proposed One Health stewardship framework. Tables 1–4 describe sector-specific stewardship considerations, including the more nebulous question of stewardship in the environment, which centers on prevention and integrated surveillance.

Operationalizing One Health stewardship through policy and governance

Ensuring impact will require action throughout the AMR ecosystem by all sectors at the global, regional, national, and institutional levels. Globally, multilateral organizations should embed stewardship

Table 2 | One Health stewardship across the antimicrobial lifecycle: Innovation

Antimicrobial Lifecycle	One Health element			
	Human health	Animal health	Plant health	Environment
Innovation	Support research to generate and strengthen real-world evidence on the burden of AMR, advance and/or refine the development of target product profiles for therapeutics, diagnostics and vaccines in response to the infectious disease and AMR burdens generally and specifically in LMICs so that R&D delivers the required products. Sustain existing funding mechanisms such as CARB-X and GARDP that support R&D ("push" incentives) and encourage nascent programs that reward successful R&D by ensuring future revenue that is not tied to volume ("pull" incentives).	Support research to generate and strengthen real-world evidence on the burden of AMR, aligning with initiatives like the Global Burden of Animal Diseases (GBADs)[a] to better quantify the economic and health impacts of AMR in animals. Increase development of real-time rapid diagnostics, therapeutics and vaccines, as well as antimicrobial alternatives and feed additives.	Advance the increased adoption of integrated pest management (IPM)[b] methods and innovative active ingredients which are related to the biochemistry of the pathogen, such as RNAi [c] technology. Implement surveillance and monitoring programs to track fungicide use, antibiotic use and resistance patterns in agricultural environments.	Integrate One Health principles into all stewardship frameworks, including prevention at source and surveillance across the One Health sector using harmonized methods, and gathering key metadata needed to contextualize intersectoral AMR and AMU. Greater innovation is also needed to prevent AMR from entering the environment, such as waste reduction and employing "green" antimicrobial manufacturing techniques that promote waste minimization and/or waste separation and reuse to reduce waste releases and make waste more treatable. Reduce the mobilization of human and other waste by using "dry" waste management, which does not mobilize AMR in water[35].

This table summarizes key stewardship actions across the antimicrobial innovation lifecycle, tailored to each One Health sector.

[a]https://animalhealthmetrics.org/.

[b]Integrated pest management is a sustainable approach to managing pests and diseases by combining biological, cultural, physical and chemical tools in a way that minimizes economic, health, and environmental risks.

[c]RNA interference technology enables sequence-specific DNA regions to be silenced, leading to a detrimental effect on the pathogen.

Table 3 | One Health stewardship across the antimicrobial lifecycle: Access

Antimicrobial lifecycle	One Health element			
	Human health	Animal health	Plant health	Environment
Access	Strengthen equitable access and continuous supply to quality-assured products and laboratory reagents through the development and diversification of local manufacturers; technology transfer through voluntary and mutually agreed terms; improved affordability of products and investment in health systems; strengthened regulatory harmonization and in-country registration facilitated by the World Health Organization's pre-qualification process in LMICs; and, pooled procurement, subscription or other models that support uninterrupted supply chains[36].	Ensure that high-quality medicines, vaccines, and diagnostics are accessible and affordable for animal health. Encourage pooled procurement and management to reduce costs and optimize distribution and use of these products, avoiding over-the-counter sales of antimicrobials as well as sub-standard and falsified medicines. Increase the veterinary workforce to ensure availability of affordable services especially in LMICs.	Strengthen agricultural supply chains and encourage professional bodies to promote good practice. Facilitate greater access to biological control products through local production and demand, promote fungicidal chemical blends along with phasing out single active ingredient products.	Facilitate equitable access to best available technology (BAT) for wastewater treatment and management of agricultural runoffs; and, utilization of surveillance

principles into their global action plans and global guidance documents, addressing the entire antimicrobial value chain—innovation, access, use, and disposal. National governments should integrate these principles into their National Action Plans through guidelines, regulations, and policies. At the organizational level, policies must encompass the four pillars of stewardship, i.e., prevention, innovation, access, and care.

Stewardship should be central to all actions taken by global stakeholders, national governments, and organizations as they work to increase investment and implement new policies in line with the 2024 UNGA Political Declaration of the High-Level Meeting on AMR. Achieving the commitments set out in the Declaration requires coordinated efforts from every sector and collective action across all stakeholder communities, including policymakers and the public. A holistic, One Health, whole-of-society approach is essential, breaking away from traditional siloed efforts and embracing interconnected strategies. Collaboration, cooperation, consultation, communication, education, and capacity-building must form the foundation of all stewardship initiatives[40]. These principles ensure that each sector contributes to a unified strategy, sharing knowledge, experiences, and resources to effectively mitigate AMR.

In summary, a robust, cross-sectoral stewardship framework, which recognizes the interconnectedness of human, animal, plant, and environmental health, is critical to safeguarding ecosystems and public health worldwide. The integrated approach of One Health stewardship will ultimately protect the efficacy of antimicrobials for future generations and mitigate the devastating impacts of AMR on global health, food security, and the environment.

Table 4 | One Health stewardship across the antimicrobial lifecycle: Care

Antimicrobial lifecycle	One Health element			
	Human health	Animal health	Plant health	Environment
Care (use and disposal)	Enable appropriate use through increased utilization of timely diagnostics to inform treatment decisions. Implement the 5 Ds of AMS where the right drug is given at the right dose in the right dosage form/route with timely de-escalation for the right duration[37]. Ensure minimal contamination of aquatic and soil environments by introducing emission limits for manufacturing plants[38,39], healthcare facilities and farms.	Promote prudent and responsible use of antimicrobials, aligned with the CODEX guidelines[32] for foodborne AMR and AMU along the food chain and the food production environment, and phase out the use of MIAs for growth promotion where applicable based on AMR risk analysis. Ensure the availability and increased utilization of diagnostics to reduce AMU while increasing profitability for food producers. Develop guidelines for AMU in different species and production systems. Ensure proper management of aquaculture and livestock farm waste management and discharges (such as treatment of manure or the use of digestate as organic fertilizers), slaughterhouse effluents and clinical waste from veterinary health facilities (including unused or expired antibiotics and other veterinary drugs) to prevent contamination of the surrounding crop fields, waterways and the broader environment.	Highlight the environmental responsibilities and legalities associated with the use of agrochemicals especially those associated with timing and proximity to water ways. Promote triple rinsing of chemical containers and establish local collection schemes for empty containers so as to prevent localized hotspots of concentrated chemicals leaching into groundwater.	Extend integrated surveillance as much as possible from existing local environmental surveillance activity to provide the greatest value on new data for the lowest cost. Conduct AMR surveillance alongside AMU surveillance using quantitative indicators of "health" in humans, animals and plants, and include surveillance of other pollution and conditions within local environments. Environmental surveillance data guides where stewardship interventions are most needed, as activity in the human, animal, and plant health sectors is evidenced in the environment[35].

This table summarizes key stewardship actions across the antimicrobial care and use lifecycle, tailored to each One Health sector.

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Author contributions

B.A. and S.E. developed the conceptual One Health stewardship framework and drafted the initial manuscript. L.O. and E.D. contributed to the human health sections. H.A. led the drafting of the animal health content. P.T. supported the development of the plant health content, and D.G. helped integrate the environment into the One Health Framework contributed to the environment content. All authors reviewed and approved the final manuscript.

Competing interests

Bruce M. Altevogt is an employee of bioMérieux and a shareholder in Pfizer stock. Sabiha Y. Essack is chairperson of the Global Respiratory Infection Partnership and a member of the Global Hygiene Council, sponsored by unrestricted educational grants from Reckitt (Pty.) Ltd, UK. Authors Philip Taylor, Holy Teneg Akwar, David W. Graham, Lesley A. Ogilvie, and Erin Duffy declare no competing interests.

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