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One Health Approach to Combat Antibiotic Resistance: Human, Animal, and Environmental Health Integration for Sustainability in Solving Global Health Issues

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ABSTRACT

One of the key health challenges in the twenty-first century is antimicrobial resistance (AMR). Considering that I have gained extensive experience in human medicine, veterinary medicine and environmental health, it becomes evident that the problem of AMR cannot be truly grasped and managed if this challenge is viewed in the prism of any one sphere of human activity. Pathogens which gain antimicrobial resistance irrespective of substances used for their elimination are not bounded by man-made barriers of hospital wards, farms or rivers. For example, a strain of E. coli bacteria becoming resistant to the antibiotics in the chicken houses may occur in the surface water surrounding the farm in few weeks, then in the microbiome of the farm workers and finally – in the body of the patient suffering from urinary tract infection in a distant hospital (Woolhouse et al., 2015; Founou et al., 2016). This chapter will show that having taken into account the experience accumulated in more than two decades

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of research in the area of AMR policy and management, the One Health approach is not only a new trend, but the necessity.

Introduction

One of the key health challenges in the twenty-first century is antimicrobial resistance (AMR). Considering that I have gained extensive experience in human medicine, veterinary medicine and environmental health, it becomes evident that the problem of AMR cannot be truly grasped and managed if this challenge is viewed in the prism of any one sphere of human activity. Pathogens which gain antimicrobial resistance irrespective of substances used for their elimination are not bounded by man-made barriers of hospital wards, farms or rivers. For example, a strain of E. coli bacteria becoming resistant to the antibiotics in the chicken houses may occur in the surface water surrounding the farm in few weeks, then in the microbiome of the farm workers and finally – in the body of the patient suffering from urinary tract infection in a distant hospital (Woolhouse et al., 2015; Founou et al., 2016). This chapter will show that having taken into account the experience accumulated in more than two decades of research in the area of AMR policy and management, the One Health approach is not only a new trend, but the necessity.

The goals of the current chapter can be defined in the following three sentences. First, it contextualizes the AMR problem by situating it in the context of its global epidemiology and economics, drawing on the recent burden of disease figures. Second, it justifies the concept of One Health approach by proving, through the analysis of the transmission pathway, the need to consider health of humans, animals, and the environment as an entity, not separately. Third, it illustrates how the implementation of One Health approach is carried out in each individual sector in the battle against AMR through case studies, tables and figures from both developed nations and LMICs.

Antimicrobial resistance develops as a result of the evolutionary nature of these microbes, and this process has been accelerated due to the intensive use of these medications in people, as well as animals used in livestock and aquaculture industries (Holmes et al., 2016; Aslam et al., 2018; Shamim et al. 2025). Although there were other health issues that had remained constant challenges for some particular populations or geographic areas, AMR is a worldwide threat that is self-sustained in the way that every unnecessary use of these medications, every suboptimal use of these drugs on animals to support their growth, as well as the release of these medicines into the river from pharmaceutical plants brings humans closer to contributing new resistance genes to the global gene pool (Berendonk et al., 2015; Larsson & Flach, 2022). This is why it is absolutely impossible to solve this issue in an ad hoc manner since the concept of One Health as an efficient strategy to address the issue of AMR has gained considerable popularity in recent years (World Health Organization [WHO], 2015; Food and Agriculture Organization [FAO], World Organisation for Animal Health [WOAH], & WHO, 2019).

Global Impact of AMR

The magnitude of the issue of AMR has been illustrated over the last five years due to the studies conducted in the framework of cooperation between the Institute for

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Health Metrics and Evaluation and the University of Oxford within the Global Research on Antimicrobial Resistance (GRAM) project. According to the groundbreaking findings obtained by the Antimicrobial Resistance Collaborators in 2022, the global number of fatalities due to bacterial AMR was 1.27 million in 2019, while AMR was a contributing cause to 4.95 million additional deaths (Antimicrobial Resistance Collaborators, 2022; Murray et al., 2022). To provide more perspective, the number of AMR fatalities in 2019 exceeded those related to HIV/AIDS infection (680,000 deaths) and malaria (627,000 deaths) (Antimicrobial Resistance Collaborators, 2022). The projected number of AMR-related fatalities up to 2050 based on the available data in 2024 shows that the number of AMR deaths will be 1.91 million and 8.22 million fatalities associated with AMR in 2050.

The distribution of this burden is very uneven. In a case study, for example, resistance caused 27.3 deaths of all ages per 100,000 individuals in western sub-Saharan Africa compared to 6.5 deaths of all ages per 100,000 individuals in Australasia (Murray et al., 2022). The reason for that is the inefficient infrastructure to manage infections coupled with poor quality control of antimicrobial drugs, prevalence of counterfeit medicine and inability to perform tests in LMICs (Iskandar et al., 2021; Gandra et al., 2020). Six pathogens caused the majority of the burden of resistance. They are E. coli, S. aureus, K. pneumoniae, S. pneumoniae, A. baumannii, and P. aeruginosa.

Table 1. Global Burden and Projected Trajectory of Bacterial Antimicrobial Resistance

Indicator	2019 Estimate	2021 Estimate	2050 Projection
Deaths attributable to AMR (annual)	1.27 million	1.14 million (approx.)	1.91 million
Deaths associated with AMR (annual)	4.95 million	4.71 million (approx.)	8.22 million
Highest-burden region (attributable rate)	Western sub-Saharan Africa (27.3/100,000)	South Asia rising	South Asia projected highest absolute toll
Lowest-burden region (attributable rate)	Australasia (6.5/100,000)	Australasia	High-income regions relatively stable
Leading pathogens	E. coli, S. aureus, K. pneumoniae, S. pneumoniae, A. baumannii, P. aeruginosa	Similar profile with rising carbapenem resistance	Gram-negative carbapenem-resistant organisms dominant

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Highlighting. Reconstructed from the findings of Antimicrobial Resistance Collaborators (2022, 2024) and Murray et al. (2022). The data for 2021 have been interpolated from the reference.

Besides mortality, there is a great burden of morbidity, disability-adjusted life years (DALYs), and economic consequences in the case of AMR. As it can be seen from the estimation made in GRAM study in 2022, in 2019, 47.9 million and 192 million DALYs related to bacterial AMR have been registered (Antimicrobial Resistance Collaborators, 2022). In accordance with the forecasts of the World Bank, the annual decline in the world GDP will reach 1.1% to 3.8% because of the maximal impact of AMR till 2050; however, developing countries will suffer more compared to the developed ones (Jonas et al., 2017). That is why according to the Report of the Review on Antimicrobial Resistance, commissioned by the UK government, the lack of measures for the fight against the AMR problem might result in 10 million deaths per year and the economic loss of 100 trillion US dollars (O'Neill, 2016).

AMR: Resistances Mechanisms and Contributing Factors

The development of resistances is associated with a number of biological mechanisms such as enzyme inactivation, target modification, reduction of drug uptake by cellular membranes, active efflux and horizontal transfer of genes associated with resistances carried by plasmids, transposons, and integrons (Holmes et al., 2016; Hernando-Amado et al., 2019). As regards the key contributing factors in terms of the One Health approach, the horizontal transfer of genes should be singled out since this mechanism allows for the dissemination of resistances not only among various strains of the same bacterial species but also between various bacterial species and even ecosystems, from the intestines of animals to environmental bacteria and then human pathogens (Bengtsson-Palme et al., 2018; Larsson & Flach, 2022).

There is a wide variety of underlying factors contributing to the development of AMR that reinforce each other. Speaking about human healthcare, the following factors can be regarded as primary underlying causes: over-the-counter availability of antibiotics, uncertainties in the diagnosis process that lead to empirical prescriptions, inadequate infection prevention and control practices in hospitals, and limited access to the point-of-care diagnostics (Charani et al., 2019; Laxminarayan et al., 2013). Referring to the animal healthcare sector, frequent use of antibiotics for growth promotion and prophylaxis in animals, including livestock, poultry, and aquaculture intensive farming has traditionally been considered as one of the major underlying causes of the problem, especially in those situations where the use of antibiotics has replaced adequate husbandry and biosecurity measures (Van Boeckel et al., 2015; Tang et al., 2017). With respect to agriculture, frequent use of antibiotic treatment of fruits, prevention of diseases, as well as biocides and heavy metals that select AMR genes adds an additional dimension (Manyi-Loh et al., 2018).

Environmental factors also worsen this problem. The release of antimicrobials into rivers, soil, and groundwaters via emissions from antibiotic production factories, hospital wastewater, untreated sewage, and agricultural runoffs leads not only to the presence of antimicrobial pollution but also to the development of resistant bacteria in rivers, soil, and groundwaters, thus providing a way for gene exchange and the dissemination of the resistant genes (Bengtsson-Palme et al., 2018; Singer et al.,

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2016). Global warming and globalization are factors that contribute to the rapid spreading of resistant strains geographically, thus turning a local issue of resistance into a global one (Frost et al., 2019; MacFadden et al., 2018). Environmental factors provide evidence as to why the AMR is the best example of a One Health issue because there is no way to address the threat in one sector only (Robinson et al., 2016; McEwen & Collignon, 2018).

One Health Concept: Its History and Reasons for Its Emergence

The history of the emergence of the concept of One Health relates to the period of the nineteenth century when, for instance, physicians such as Rudolf Virchow understood that there was no difference between human and animal medicine in terms of pathology. Furthermore, at the middle of the twentieth century the term of "one medicine" was introduced by the veterinary epidemiologist Calvin Schwabe (Zinsstag et al., 2011). However, the period of institutionalization of the concept of one health started after the emergence of Highly Pathogenic Avian Influenza (H5N1) at the beginning of the twenty-first century and the disastrous effects of separate consideration of human and animal health issues became evident (Mackenzie & Jeggo, 2019). Hence, as the result of this, such international organisations as FAO, WOAH (formerly OIE) and WHO created the Tripartite in 2010 (One health systems strengthening in countries, 2023).

In March 2022, the UNEP was included in the partnership, making the Tripartite partnership for One Health the Quadripartite partnership for One Health (WOAH, n.d.). The OHHLEP is an independent scientific advisory committee of experts created by the four organizations; in March 2022, OHHLEP defined One Health as the following:

"One Health is an integrated, multi-sectoral, and trans-disciplinary approach that seeks to achieve optimal health outcomes through the actions of various sectors, disciplines and partners, from the local to the global level. One Health recognizes the inter-related nature of human health, animal health and ecosystem health, and the role of the environment in health" (as cited in WOAH, n.d. & UNEP, n.d.).

In this respect, the definition is centered around interdependence rather than coexistence, as the beneficial effects achieved in one aspect are expected to have positive impact on the other two. Speaking of the problem of AMR, it becomes obvious that all attempts to establish the strictest health stewardship policies based on the human health concerns alone will prove to be ineffective in case of any abuse of antimicrobial agents in the field of animal health, as well as continuous environmental exposure of resistant microorganisms (Collignon & McEwen, 2019; Queenan et al., 2016). This is illustrated in Figure 1 below. All three aspects of the classic One Health approach face one single problem – AMR.

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Figure 1. The One Health Triad and Antimicrobial Resistance

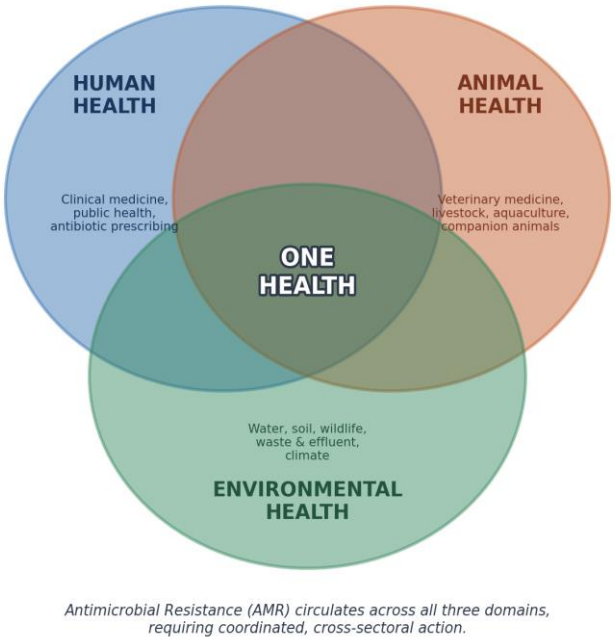


Figure 1. One Health Triad. Interactions between human, animal, and environmental health sectors influence the appearance of antimicrobial resistance. Based on the operational definition of OHHLEP (WOAH, n.d.; Destoumieux-Garzón et al., 2018).

Four principles outlined below may help to differentiate the real One Health approach to the issue of AMR from the multi-sectoral one: (a) equality of the sectors, when interests of the human health sector cannot dominate over the interests of the animals and environment; (b) socio-political and multicultural balance, meaning that all measures are to be taken jointly with those who are affected by the problem – small-scale farmers and their communities; (c) socio-ecological balance, meaning that any actions aimed at solving the problem of AMR should be ecologically sustainable in terms of the carrying capacity of ecosystems but not environmental pollution; and (d) trans-disciplinary cooperation of medical professionals, veterinarians, environmentalists, agronomists, economists, and social scientists (Mackenzie & Jeggo, 2019; Destoumieux-Garzón et al., 2018).

Pathways of Transmission of AMR Between Sectors

For the successful implementation of the one health approach to tackling AMR, it is imperative to have proper understanding of the pathways through which resistant bacteria and AMR genes are transmitted between different sectors. There are three major kinds of pathways that have consistently been noted in literature as pathways of transmission of resistance. One is food chain pathway, where the resistant bacteria found in food animals are transferred to the meat, milk, eggs, and fresh vegetables through irrigation water and fertilization using manure (Founou et al., 2016; Marshall & Levy, 2011). Second is direct contact pathway, whereby those involved in farming

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activities, veterinarians, slaughterhouse workers, and owners of pets come in contact with the animals and are thus exposed to resistant pathogens. Third is the environmental transmission pathway that has recently attracted the attention of researchers. In this case, the antimicrobial drugs residues, resistant bacteria, and AMR genes are released into the environment from agriculture runoff, aquaculture wastewater, sewage and manure application (Berendonk et al., 2015; Bengtsson-Palme et al., 2018).

Figure 2. Cross-Sectoral Transmission Pathways of Antimicrobial Resistance

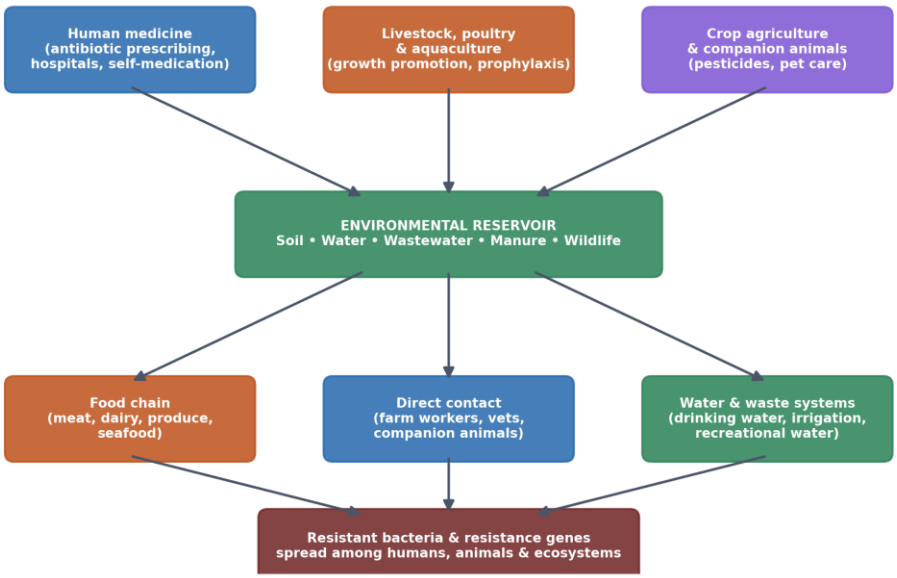


Fig. 2. The ways by which antimicrobial resistance is transferred between various sectors, in which the environment acts as a recipient and redistributor of the resistance genes from human medicine, animal husbandry, and agriculture. Adapted based on the ideas proposed by Berendonk et al. (2015), and Bengtsson-Palme et al. (2018).

The following two policy implications may be drawn from the above-mentioned pathway of transmission. First, because the environment acts as the recipient and redistributor of resistance genes from various sectors, it cannot be overestimated, and thus should be regarded as a necessary component of the resistance strategy implementation (Larsson & Flach, 2022; Singer et al., 2016). Second, since the process is cyclical and not linear, prohibition of some types of antibiotics in agriculture without implementing any changes in hospitals and sewage systems will produce no results at all (Aarestrup, 2015; Tang et al., 2017).

One Health Governance and Policy Making on the Global Scale

The realization of the significance of AMR in terms of the One Health governance approach has been greatly growing since 2015 globally. In May 2015, the World Health Assembly approved the Global Action Plan on Antimicrobial Resistance (GAP-AMR) that involved five main areas of focus, including awareness and knowledge, surveillance and research, infection control, optimization of use of antimicrobials, and economic rationale for investments in AMR (WHO, 2015). In

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addition, GAP-AMR has highlighted the need for the involvement of the Tripartite (Quadripartite now) in helping countries develop national plans to address AMR using the One Health approach (WHO, FAO & WOAH, 2019).

In September 2016, the United Nations General Assembly hosted a High-Level Meeting on AMR, the fourth such occasion when a public health issue was being addressed in this manner by the UN; therefore, the Political Declaration on AMR was endorsed, in which all member states committed themselves to the development of NAPs (Jasovský et al., 2016). Afterward, in 2019, the IACG of the UN released its report, "No Time to Wait," that recommended adopting the One Health approach, the whole-of-government and whole-of-society approach, as well as establishing an independent panel like the IPCC (Interagency Coordination Group on Antimicrobial Resistance [IACG], 2019). Table 2 gives a summary of the significant events in the history of global governance of One Health-AMR.

Table 2. Timeline of Major Global One Health and AMR Governance Milestones

Year	Milestone	Lead Actor(s)	Significance
2010	Tripartite Concept Note	FAO, WOAH, WHO	Formalised shared responsibility for zoonoses and human-animal-environment interface
2015	Global Action Plan on AMR (GAP-AMR)	WHO / World Health Assembly	Established five strategic objectives; required national multisectoral action plans
2016	UN High-Level Meeting on AMR	UN General Assembly	Elevated AMR to head-of-state level political commitment
2016	Review on Antimicrobial Resistance	UK Government (O'Neill)	Quantified economic and mortality projections to 2050
2017	WHO Priority Pathogens List	WHO	Guided R&D investment toward critical- and high-priority resistant organisms
2019	"No Time to Wait" report	UN IACG	Called for whole-of-society, One Health governance architecture
2021	OHHLEP established; One Health operational definition drafted	FAO, WHO, WOAH, UNEP	Provided unified conceptual and scientific basis for One Health

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Year	Milestone	Lead Actor(s)	Significance
2022	Quadripartite collaboration formalised	FAO, UNEP, WHO, WOAH	Integrated environment sector formally into global One Health governance
2022–2026	One Health Joint Plan of Action (OH JPA)	Quadripartite	Operational roadmap across six action tracks, including AMR
2024	Updated GRAM burden forecasts to 2050	GRAM / IHME / Oxford	Refined long-range mortality and resistance trend projections

Note. References from WHO (2015), IACG (2019), WOAH (n.d.), UNEP (n.d.), and Antimicrobial Resistance Collaborators (2024).

At the regional and national levels, implementation of this framework is carried out through the six action tracks of the Quadripartite's One Health Joint Plan of Action (2022-2026) focused on decreasing the burden of AMR through improving surveillance, the prudent and responsible use of antimicrobials, and infection prevention and control (FAO et al., 2022, as cited in Geneva Environment Network, n.d.). Along with the described global framework, WOAH Terrestrial Animal Health Code and FAO Action Plan on Antimicrobial Resistance give additional recommendations for the veterinary and agricultural organizations, while the WHO list of Critically Important Antimicrobials for Human Medicine includes national restrictions on the use of some antimicrobial classes in human medicine (WHO, 2019; FAO, 2016).

Intervention Strategies by the Various Sectors

For the intervention approach under One Health approach to be realized, it is important to ensure coordinated and specific intervention by the various sectors while considering the cross-sectoral impact of the interventions. The following paragraphs highlight the major intervention strategies of each of the four sectors using two decades' experience gained from program evaluation.

Human Health Sector

Antimicrobial Stewardship Program (ASP) has been among the most important strategies for interventions in the human health sector. Prospective audit and feedback, restriction of use of reserve antibiotics, decision support system and de-escalation have been the strategies used in ASP in hospitals to ensure harmonization between use of antibiotics and diagnostics (Charani et al., 2019). Delays in prescriptions, point of care C-reactive protein testing and antibiotic awareness programs like World Antibiotics Awareness Week have greatly helped to reduce inappropriate antibiotic prescription for respiratory infections (Laxminarayan et al., 2013; Ventola, 2015). IPC which includes hand hygiene, isolation and safety of injections have greatly reduced infection cases (Holmes et al., 2016). Solutions such as the improvement of the ability of the state bodies to regulate access to prescription

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antibiotics, along with drug quality control measures reducing the prevalence of poor-quality and counterfeit products in the market, will address one of the most crucial issues underlying the problem in many LMICs (Hoffman et al., 2015).

Animal Health and Veterinary Sector

The first important action undertaken in the animal sector during the last twenty years is the ban on antibiotics that served as growth promoters. As shown by the ban on antibiotics in Denmark from 1998 through 2000 and subsequent research conducted in the frame of the DANMAP project, it was found out that it was possible to achieve a significant reduction of the total consumption of antibiotics without any drop in production efficiency provided that it was done with the application of biosecurity and husbandry practices (Aarestrup, 2015). Such practices have also been accepted in the European Union, where since 2006, the use of antibiotics as growth promoters is prohibited, as well as the latest Veterinary Medicinal Products Regulation introduced in 2022 (Tang et al., 2017; Shah et al. 2024).

The other noteworthy case is the one related to the Netherlands as there was an evident fast decline in the use of antibiotics among veterinarians against the rise of ESBL-producing strains in chickens. In order to address this issue, the government of the Netherlands adopted a new regulation that required all veterinarians who did not produce antimicrobial substances but prescribed them to reduce their use by 50% since 2009 on the basis of benchmarking at the farm level (Speksnijder et al., 2015). However, apart from the above-mentioned measures, other actions can be taken in this situation, which include vaccinations, improvements in biosecurity and stocking density, dry cow therapy instead of universal therapy (in terms of the dairy industry), and the prohibition of the use of highly prioritized antimicrobials (i.e., third and fourth generation cephalosporins and fluoroquinolones) (WHO, 2019; Van Boeckel et al., 2017).

Environmental Sector

Among various factors that are considered while implementing the One Health strategy to address AMR, the environmental factor can be identified as the most immature one; however, at the same time, it develops rapidly. First, the priorities here are improvement of wastewater treatment infrastructure with respect to facilities that are situated near hospitals, antibiotic-producing factories, and farms where intensive animal husbandry occurs in order to eliminate any traces of antibiotics and bacteria before discharging the wastewater; establishment of discharge standards for wastes from the production of antibiotics that is crucial since most active ingredients of antibiotics are produced in regions with insufficient regulations (Larsson & Flach, 2022); and implementation of techniques like composting and anaerobic digestion in order to minimize the risk of developing resistance before application of manure in the soils (Bengtsson-Palme et al., 2018). Resistance gene and residue monitoring in surface waters, sediments, and wildlife is already recognized as a part of the One Health strategy rather than something additional to it (Singer et al., 2016).

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Agriculture and Food Systems

Other than animal husbandry, agriculture practices involving crops is one other area where there is antibiotic burden since antibiotics are used in the treatment of bacterial infections in crops through streptomycin and oxytetracycline and due to co-selection of resistant genes caused by the presence of metals and biocides in crops and animal farming (Manyi-Loh et al., 2018). Food safety agencies can help in tackling the problem of AMR by establishing maximum residue limits of antimicrobials in food products, traceability systems that help in recalling of contaminated batches of foods and advocating for integrated pest/disease management practices so as to reduce dependence on chemicals/antimicrobials (Founou et al., 2016).

Integrated One Health Surveillance Systems

For effective governance of the One Health approach, there should be capacity to monitor, detect and compare trends in resistance in human, animal and environment sectors using standardized techniques. The WHO GLASS surveillance system put in place in 2015 gathers data from member countries who use the system on human isolates and antimicrobial usage, while ANIMUSE and InFARM of WOAH and FAO respectively collect data on animal resistance and usage. These international surveillance systems have been highlighted in Table 3, which can prove useful for a One Health approach to AMR.

Table 3. Selected International One Health Surveillance Platforms for AMR

Platform	Custodian	Sector Focus	Core Function
GLASS	WHO	Human clinical & consumption data	Standardised reporting of resistance rates and antimicrobial consumption across member states
ANIMUSE / Annual Reports on Antimicrobial Agents	WOAH	Animal health	Global monitoring of veterinary antimicrobial use and stewardship progress
InFARM	FAO	Food and agriculture	Integrated surveillance of AMR in food and agriculture systems
DANMAP	Denmark (national)	Human, animal, food	Long-running integrated national programme; model for other countries
European Antimicrobial Resistance Surveillance Network	European CDC	Human clinical isolates	Regional benchmarking of resistance rates across the EU/EEA

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Platform	Custodian	Sector Focus	Core Function
(EARS-Net)			
Global Sewage Surveillance Project	Research consortia (e.g., DTU)	Environmental (wastewater)	Metagenomic tracking of resistance genes at population scale via sewage

Note. Compiled from WHO (2022), programme descriptions referenced in Aarestrup (2015), and Gandra et al. (2020).

Nevertheless, integration into the platforms remains far from being accomplished. The issue of the inadequacy of laboratory capacity, reliable microbiology, data management, infrastructure, training, etc. continues to hamper the ability of many LMICs to collect the data regarding national resistance (Iskandar et al., 2021; Gandra et al., 2020). Establishing laboratory networks, working on whole genome sequencing and creating the data sharing mechanisms within the organizations, working on human health, veterinary and environment sectors are seen as essential in surveillance (WHO, FAO, & WOAH, 2019).

National Action Plans and Policy Coherence

Since the implementation of the GAP-AMR plan in 2015, almost all WHO member states have worked out their National Action Plan on AMR but the diversity of approaches to integration of those plans into the process remains enormous (WHO, FAO, & WOAH, 2019). The fully-developed NAP must include the following components listed in Table 4.

Table 4. Core Components of an Effective One Health National Action Plan on AMR

Component	Description	Responsible Sector(s)
Multisectoral coordination mechanism	A standing committee or task force with representation from health, agriculture, environment, and finance ministries	Whole of government
Situation analysis and baseline surveillance	Assessment of existing resistance rates, antimicrobial consumption, and system capacity	Human, animal, environment
Awareness and education strategy	Public and professional communication campaigns on prudent antimicrobial use	Human, animal, food
Infection prevention and control standards	Hygiene, sanitation, biosecurity, and vaccination protocols	Human, animal
Regulatory and legislative reform	Prescription-only access, quality assurance, restriction of critically important	Human, animal, regulatory

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Component	Description	Responsible Sector(s)
	antimicrobials in animals	bodies
Research and innovation agenda	Support for diagnostics, alternatives to antimicrobials, and vaccine development	Academic and private sector
Financing and sustainability plan	Domestic and international resource mobilisation, cost-effectiveness analysis	Finance ministries, donors
Monitoring and evaluation framework	Indicators aligned with GLASS and WOAH/FAO reporting requirements	All sectors

Note. Synthesised from WHO (2015), WHO, FAO, and WOAH (2019), and IACG (2019).

Other implementation-related challenges that have been well researched in the field of health policies include insufficient funding from the ministries of agriculture and environment in comparison with health ministries with regard to allocation of budgets to AMR actions because they are supposed to solve the upstream causes of resistance (Hoffman et al., 2015; Roope et al., 2019). As per the results of the political economy analysis, the lack of coordination between a single ministry (typically the Ministry of Health) implementing the National Action Plans with no collaboration from the ministries of agriculture and environment means that there will be success in one sector and not in the other two (Queenan et al., 2016).

Case Studies in One Health Implementation

Scandinavia: Sweden's STRAMA and Denmark's DANMAP

Strategic Programme for the Rational Use of Antimicrobial Agents (STRAMA) in Sweden, which was launched in the middle of the 1990s, is regarded as the first project of national antimicrobial stewardship. The program involves infectious diseases specialists, microbiologists, veterinarians, and public health representatives whose joint efforts allow tracking the dynamics of the trends in terms of the use and emergence of antibiotic resistance (Aarestrup, 2015). Monitoring system in Denmark called DANMAP, which unites three sectors including human, animal, and food and was developed back in 1995, served as the basis for proving the necessity of the Danish ban of the antimicrobial growth promoters, and it showed that veterinary antimicrobial use could be reduced by more than 50 percent within twenty years without any negative impact on animal production (Aarestrup, 2015). These projects exemplify the typical trait of the successful application of the One Health approach – the commitment to the data collection system for decades that enables the policymakers to monitor in real-time the effect of intervention in one sector on the pattern of resistance in another sector.

The Netherlands: Veterinary-Led Antimicrobial Reduction

The cause of Netherlands' success in reducing the usage of antibiotics in their animals by 50-70 percent within less than ten years can be seen in Section 7.2 since the

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successful implementation of a number of measures such as benchmarking of the usage of antibiotics which was mandatory, a separate prescription system of veterinarians, and negotiation of the reduction target in different sectors by the farmers' organizations can be seen (Speksnijder et al., 2015).

Implementation of the One Health Approach: Low- and Middle-Income Countries' Settings – India and Sub-Saharan Africa

India being one of the biggest consumers of antibiotics all over the world has chosen a special approach to implementing the One Health approach, namely, it has implemented the Red Line program implying the presence of a red line warning on prescription-only antibiotics' packaging, Chennai Declaration proposed by representatives of the medical field to introduce changes in the antibiotic policy and surveillance at the state level (Gandra et al., 2020). However, in sub-Saharan Africa, the implementation of the One Health approach is hindered by the fact that poor laboratory infrastructure and diagnostic capacities exist. Nevertheless, there are some examples of successful implementation of the One Health approach: AMR surveillance in the region with the support of Fleming Fund and community-based interventions in the regions involving human and veterinary medicine in pastoralist settings that pose high risks of transmission because of proximity of people and animals (Founou et al., 2016; Iskandar et al., 2021).

Economic Factors Related to AMR

There is certainly an economic rationale for focusing on the implementation of one health approaches to tackle AMR by comparing rather inexpensive preventive measures to the ever-growing expenses of inaction. As seen from the research carried out by the World Bank in 2017, in the high-impact case of antimicrobial resistance, there will be a reduction in the global GDP from 1.1% to 3.8% per year up to 2050, particularly in poor countries, where the adverse impact will result in numerous issues (Jonas et al., 2017). From the perspective of the health care industry, AMR definitely contributes to the increase in length of hospital stays, therapeutic failure, requirement for a secondary or even tertiary therapy, and mortality rates, which definitely implies additional expenses compared to treatment of susceptible infections (Dadgostar, 2019; Naylor et al., 2018).

Table 5. Illustrative Economic Impacts of Antimicrobial Resistance

Economic Dimension	Illustrative Estimate	Source
Global annual GDP loss by 2050 (high-impact scenario)	1.1%–3.8%	Jonas et al. (2017), World Bank
Cumulative global economic loss by 2050 (worst case)	Up to US$100 trillion	O'Neill (2016)
Additional healthcare cost per resistant infection (hospital setting)	Substantially higher than susceptible infection; magnitude varies by pathogen	Naylor et al. (2018); Dadgostar (2019)

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Economic Dimension	Illustrative Estimate	Source
	and country	
Annual global HIV/AIDS response funding (for comparison)	~US$50 billion	Cited in de Kraker et al. (2022) discussion, The Lancet
Projected annual AMR deaths by 2050	10 million (original 2016 projection)	O'Neill (2016)

Note. Figures are illustrative order-of-magnitude estimates drawn from the cited sources and should be interpreted with awareness of differing methodologies and underlying assumptions across studies.

The basis of the economic theory of AMR lies in the possibility of classifying the use of antimicrobials as common-pool resources because each prescription, both legal and illegal, reduces the total stock of the efficiency of these medicines and creates an externality, which is always underpriced in the unregulated market (Roope et al., 2019). Thus, the economic theory provides a strong argument for the regulation, which does not depend on the obligations of particular medical professionals and farmers but emphasizes the necessity of developing new financing mechanisms, including the 'Netflix' pricing approach for new antibiotics, which does not link the profits of manufacturers with their sales volumes (Roope et al., 2019).

Challenges and Barriers to One Health Implementation

Despite having over two decades of policy formulation, there are still some structural barriers that serve as barriers for the application of the One Health strategy to address the issue of AMR. There is a way in which ministries of health, agriculture and environment operate where each has a different budget, reporting and mandate. It is quite challenging to continue with the co-governance approach after funding the donor sponsored pilots (Hoffman et al., 2015; Queenan et al., 2016). Countries, particularly low- and middle-income countries, lack the infrastructure to join the dots regarding human, animal and environmental resistance (Iskandar et al., 2021; Gandra et al., 2020). The small-scale farmers see the cutting down of antimicrobials as a serious challenge for their livelihood without taking other preventive measures such as vaccination (Van Boeckel et al., 2017; Tiseo et al., 2020). Despite the presence of the legislation regulating the distribution of antibiotics without prescriptions and stating that the sales should be done under the prescription only by the veterinarian, it is not enforced due to the inability to control supply chains (Aslam et al., 2018). The environmental agencies have received the least amount of funding for AMR although there is an increasing body of evidence regarding the role of environment in AMR development; the reason for the low priority of the environmental approach is the novelty of the issue as compared to the microbiological one (Larsson & Flach, 2022; Singer et al., 2016). The development of the new antibiotics slowed down whereas the rates of resistance increased due to the conflict between the socially optimal use of the antibiotic and the monetary gain for pharmaceutical companies from the antibiotic sales (Roope et al., 2019; O'Neill, 2016).

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The overcoming of these challenges will require not only additional finances but also institutional design in the form of mandatory systems of inter-ministerial coordination, with budgetary and accountability regimes shared between them, to be included into the performance metrics of the industry concerned, along with the proper political will, ensuring that AMR is not perceived merely as a healthcare challenge but a development challenge of society as a whole (IACG, 2019; Mackenzie & Jeggo, 2019).

Innovations and Future Directions

In connection with all of this, there are particular trends which have to be noted as they have great potential concerning the implementation of the One Health approach as a way of combating AMR challenge in the next ten years. Apart from the existing antibiotics, bacteriophages, probiotics and prebiotics, antimicrobial peptides, and feed additives influencing immunity are developed as alternatives to the antibiotic classes of drugs which overlap between human and veterinary medicine (Hernando-Amado et al., 2019). Furthermore, vaccination is regarded as one of the most effective methods of preventing an infection as well: according to various researches, the vaccination for the existing vaccines against Streptococcus pneumoniae and development of vaccines against Klebsiella pneumoniae and extraintestinal pathogenic E. coli will save millions of lives from AMR and antibiotics (Kim et al., 2023, according to GRAM vaccine-attributable burden analysis).

Rapid and inexpensive diagnostic tests for pathogens and their resistance, such as lateral flow assays, mobile PCR, and CRISPR diagnostics, will contribute to the reduction in empiric treatment in medicine and veterinary due to immediate identification of bacteria and their resistance in situ (Holmes et al., 2016). The whole genome sequencing and metagenomics of sewage streams obtained via the Global Sewage Surveillance Project will serve as a cost-effective and efficient tool to monitor resistance gene spread in the population, especially in those areas where there is no sampling from the clinical setting (Aarestrup, 2015; Berendonk et al., 2015).

There is some research on the application of artificial intelligence and machine learning to screen chemical libraries for new antibiotics and develop antibiograms and clinical decision-making tools in hospitals and to predict transmission dynamics at the human/animal/environment interface based on surveillance data (Hernando-Amado et al., 2019). Finally, alternative financial incentives, like market entry reward system and subscription models, irrespective of the number of units sold, are discussed as means to stimulate the development of new antibiotics and their rational use (Roope et al., 2019).

Conclusion

In light of the last twelve years of experience in AMR in various sectors of medicine, policy and surveillance, it is now quite clear that AMR is a disease that cannot be dealt with on a single-discipline or single-ministry level basis since it is a problem of the system, and it requires a systemic approach from the human, animal and environmental health systems. It may be stated that the One Health approach that was developed by such international organizations as FAO, UNEP, WHO, and WOAH (Quadrripartite) in their joint efforts, as well as in the OHHLEP definition of One

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Health, may be regarded as the only existing approach to dealing with this problem. It is impossible to remain complacent towards the number of deaths that are caused by AMR as it is one million a year and is expected to reach two millions by mid-century (Antimicrobial Resistance Collaborators, 2022, 2024).

From examples of interventions in Denmark, the Netherlands, Sweden, and the steadily growing number of LMIC interventions, it becomes clear that a significant decrease in the use of antimicrobials and resistance levels is possible when there is adequate collaboration between the different elements of surveillance, regulation, professional responsibility, and cross-sector governance. However, the fragmented institutional environment, lack of surveillance, weak enforcement mechanisms, and lack of funding of the environmental sector remain important obstacles for many regions around the globe. To fully harness the power of the One Health approach, constant political commitment, equal funding of the human, animal, and environmental sector, constant investment in innovation in surveillance and diagnostics, and, most importantly, a new approach to health security, which not only includes securing human populations but is a broader concept of security of an interconnected biological system that sustains life in any form, is required.

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