

# **Global Strategies to Combat Antimicrobial Resistance: A One Health Perspective**

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## Abstract

Background: Antimicrobial resistance (AMR) is a global health challenge that has escalated due to the inappropriate use of antimicrobials in humans, animals, and the environment. Developing and implementing strategies to reduce and combat AMR is critical. Purpose: This study aimed to highlight some global strategies that can be implemented to address AMR using a One Health approach. Methods: This study employed a narrative review design that included studies published from January 2002 to July 2023. The study searched for literature on AMR and antimicrobial stewardship (AMS) in PubMed and Google Scholar using the 2020 PRISMA guidelines. Results: This study reveals that AMR remains a significant global public health problem. Its severity has been markedly exacerbated by inappropriate use of antimicrobials in humans, animals, and the broader ecological environment. Several strategies have been developed to address AMR, including the Global Action Plan (GAP), National Action Plans (NAPs), AMS programs, and implementation of the AWaRe classification of antimicrobials. These strategies also involve strengthening surveillance of antimicrobial consumption and resistance, encouraging the development of new antimicrobials, and enhancing regulations around antimicrobial prescribing, dispensing, and usage. Additional measures include promoting global partnerships, combating substandard and falsified antimicrobials, advocating for vaccinations, sanitation, hygiene and biosecurity, as well as exploring alternatives to antimicrobials. However, the implementation of these strategies faces various challenges. These challenges include low awareness and knowledge of AMR, a shortage of human resources and capacity building for AMR and AMS, in adequate funding for AMR and AMS initiatives, limited laboratory capacities for surveillance, behavioural change issues, and ineffective leadership and multidisciplinary teams. **Conclusion:** In conclusion, this study established that AMR is prevalent among humans, animals, and the environment. Successfully addressing AMR calls for a collaborative, multifaceted One Health approach. Despite this, some gaps remain effectively implementing strategies currently recommended to combat AMR. As a result, it is essential to reinforce the strategies that are deployed to counter AMR across the human, animal, and environmental sectors.

## **Keywords**

Antimicrobial Resistance, Antimicrobial Stewardship, AWaRe Classification, One Health Approach, One Health Perspective, Strategies, Surveillance

## **1. Introduction**

Antimicrobial resistance (AMR) is a public health problem affecting humans, animals, and the environment [1] [2] [3] [4] [5]. This phenomenon occurs when microorganisms resist the lethal effects of antimicrobials [6] [7]. The consequences of AMR include difficulty or impossibility in treating infections and increased morbidity and mortality [8] [9] [10]. If this problem remains unaddressed, then annual deaths due to AMR will be 10 million by the year 2050 [9] [10] [11] [12]. Additionally, it leads to a negative impact on medical costs and the global economy [13] [14] [15] [16]. Furthermore, drug-resistant infections can be difficult, and sometimes impossible to treat [17] [18]. These negative impacts are worsened by the emergence of multidrug-resistant (MDR) pathogens [10] [19] [20] [21] [22]. Due to these global consequences, AMR is now termed a pandemic [23]-[32] and is among the top 10 threats to global public health [33] [34] [35].

It is noted that increases in AMR are driven by a combination of microorganisms being exposed to antimicrobials and natural resistance [36] [37] [38] [39]. Additionally, the drivers of AMR include the overuse and misuse of antimicrobials in humans, animals, and the environment [40]-[49]. These inappropriate practices were also noted during the coronavirus pandemic (COVID-19) pandemic [50]-[57]. Consequently, antimicrobial-resistant organisms can be transmitted across animals and from animals to humans [40] [58] [59] [60] [61], even during animal transportation [62]. This has public health consequences for animals and humans [49].

The increased burden of AMR has necessitated the development and imple-

mentation of strategies to combat this problem globally [24] [63]-[71]. In this paper, we have proposed some strategies that are recommended to address AMR. Globally, the Global Action Plan (GAP) on AMR was developed to address AMR [72]. Additionally, countries across the globe were urged to develop and implement the National Action Plans (NAPs) on AMR to address the problem of antimicrobial-resistant infections [72]. In doing so, these efforts contribute to antimicrobial stewardship (AMS) programmes that are well-coordinated and promote the rational use of antimicrobials and reduce the occurrence of AMR in humans, animals, and the environment [73]. Subsequently, surveillance systems are critical in monitoring AMR across humans, animals, and the environment [74] [75]. Therefore, tackling this problem requires a collaborative multidisciplinary approach involving professionals from human, animal, and environmental health [76] [77] [78]. A strengthened collaborative approach is recommended to promote the rational use of antimicrobials and reduce AMR [79]-[84]. This multifaceted approach to addressing AMR is referred to as a One Health approach [85] [86] [87]. This paper highlights the global strategies and some challenges experienced in combating AMR.

## 2. Materials and Methods

This study utilised a narrative review design, and a literature search was performed using PubMed and Google Scholar databases. We used Boelean operators using key terms "antimicrobial resistance", "antimicrobials", "antibiotics", "animals", "awareness", "environment", "humans", "One Health", "antimicrobial stewardship", "strategies", collaboration", "AWaRe", "drug discovery", "surveillance", "alternatives", "challenges", "drivers", AND "combating antimicrobial resistance". This paper included all publications that were published between January 2002 and July 2023. The paper also included publications that were only published in the English language. All the publications in this paper were included following the 2020 PRISMA guidelines [88]. Abstracts and articles not written in English were excluded from the study. Eight authors independently verified that the selected studies met the inclusion criteria in a blinded manner while any discordances were resolved by the principal author (SM).

# 3. Global Strategies to Combat Antimicrobial Resistance (AMR)

## 3.1. Global Action Plan (GAP) on AMR

The GAP on AMR was established in May 2015 during the World Health Assembly by the WHO in collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE) to address AMR in a "One Health" approach [72]. At this meeting, the leaders agreed and committed to their countries to develop multisectoral national action plans (NAPs) on AMR [72]. Subsequently, countries committed to implementing the NAPs once developed and helped respond to AMR. The GAP on AMR focuses on five (5) objectives to tackle AMR, and these include: 1) to improve the awareness and understanding of AMR through effective communication, education and training; 2) to strengthen the knowledge and evidence base through surveillance and research; 3) to reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures; 4) to optimise the use of antimicrobial medicines in human and animal health; and 5) to develop the economic case for sustainable investment that takes account of the needs of all countries and to increase investment in new medicines, diagnostic tools, vaccines and other interventions [72]. Therefore, there is a need for global collaborations among stakeholders involved in human health, animal health, agriculture, and the environment to monitor AMR, undertake more research, and reduce the spread of AMR [79]. These objectives indicate the need for addressing AMR using a "One Health" approach involving AMR in humans, animals, agriculture, and the environment [72].

## 3.2. National Action Plan (NAP) on AMR

The NAPs on AMR have been developed by many countries across the globe to address AMR in line with the GAP on AMR [72] [89] [90]. These NAPs have been developed based on the objectives set by the GAP on AMR and are used by countries to monitor AMR using a "One Health" approach [91]. With the GAP on AMR having five (5) objectives, most NAPs on AMR have been developed focusing on the five objectives indicated in the GAP on AMR above.

Some countries developed their NAPs on AMR in line with the GAP on AMR and addressed AMR using a One Health approach [89] [90] [92] [93] [94] [95]. Tentatively, countries that have developed and implemented their NAPs must conduct evaluations to monitor their performance and effectiveness in curbing AMR [93]. So far, countries that have effectively implemented their NAPs on AMR have made good progress in reducing AMR and its consequences. The lack of resources and capacity may cause LMICs to have challenges in implementing their NAPs on AMR [84] [96] [97]. Moreover, despite the availability of NAPs, the response to AMR is considered inadequate [94]. This may be due to poor alignment of the NAPs with GAP, inadequate capacity for implementation or poor awareness of the need for addressing AMR. The level and strength of commitment to NAPs, as well as the capacity of individual countries to develop NAP objectives, is integral to their delivery [94]. Therefore, to harness political engagement and commitment, NAPs need to include objectives that evaluate the economic effect of strategies implemented to optimize antimicrobial use (AMU) in different countries [94].

## 3.3. Antimicrobial Stewardship (AMS) Programmes

Antimicrobial stewardship (AMS) programmes promote the rational use of antimicrobials by emphasising the optimal selection, dose, frequency, and duration of therapy with antimicrobials [98] [99] that leads to the best clinical outcome in infection prevention or treatment and subsequent minimal or no toxicity to the patient and reduction in AMR [100] [101]. AMS programmes are critical in combating AMR [64] [98] [102] [103] [104] [105] [106], and their effective implementation has demonstrated an improvement in AMU and patient treatment outcomes [107] [108] [109] [110] [111]. AMS programmes include public health campaigns or awareness sensitisation, Hospital-based AMS programmes, NAPs, and the GAP [72] [90] [100] [101] [112]-[119].

AMS programmes also raise awareness of AMR through World Antimicrobial Awareness Week (WAAW), previously called World Antibiotic Awareness Week (WAAW), until 2020 [23] [120] [121] [122]. Since 2015, the WAAW has raised awareness of AMR and its consequences globally [120] [122] [123]. The awareness campaigns promote best practices to reduce AMR and its spread across populations, and these campaigns are targeted at the general public, policy-makers, farmers, animal health professionals, and healthcare workers [121] [123]. The WAAW is held annually from the 18<sup>th</sup> to the 24<sup>th</sup> of November [122]. The FAO, OIE, and WHO strongly support the WAAW as it promotes awareness and understanding of AMR [124].

Hospital-based AMS programmes include managing the prudent use of antimicrobials as an instrument in fighting AMR [125] [126] [127]. AMR is a complex issue, and there is no one-size-fits-all approach to creating AMS programmes. These programmes vary based on resources available, local context and setting (primary care, secondary care, or regional level, for example) [126]. These programmes focus on promoting the appropriate use of antimicrobials in hospital settings, including prescribing guidelines, monitoring AMU, and education of HCWs [126]. Alongside this, some outpatient AMS programmes focus on promoting the appropriate use of antibiotics in outpatient settings, including clinics and doctor's offices [128] [129] [130]. These activities typically involve the education of HCWs, patients and the monitoring of antimicrobial prescribing patterns [112] [131] [132].

Community pharmacy-based AMS programmes involve the active participation of pharmacists in promoting the appropriate use of antimicrobials within their communities [133] [134]. By collaborating with healthcare providers, pharmacists can actively engage in interventions such as medication therapy management, patient education, and antibiotic monitoring. Additionally, by leveraging their accessibility and expertise, community pharmacists can guide appropriate antibiotic selection, dosing, and duration to ensure optimal therapy and provide evidence-based recommendations [135]. Implementing a community pharmacy-based antimicrobial stewardship program can significantly contribute to the overall efforts in combating antibiotic resistance and preserving the effectiveness of these life-saving medications [136] [137].

AMS programmes are also implemented in animals globally [82] [138]. For example, at an international level, the GAP on AMR is an international plan that includes measures to address AMR in both human and animal health [72]. It includes promoting responsible use of antimicrobials in animals and developing

alternative treatments for animal diseases [139]. Also, the Animal Disease Prevention and Control Program implemented by the WHO aims to promote the responsible use of antimicrobials in animals to prevent and control the spread of zoonotic diseases [140]. In the US, the Veterinary Feed Directive (VFD) Rule requires veterinary oversight for the use of antimicrobials in animal feed. It aims to reduce the use of antimicrobials for growth promotion in livestock [141] [142]. In the United Kingdom (UK), the Responsible Use of Medicines in Agriculture Alliance (RUMA) promotes the responsible use of antimicrobials in agriculture. It provides guidelines and education to farmers and veterinarians on appropriate antibiotic use [143] [144].

In 2017, the WHO developed a tool known as the Access, Watch, and Reserve (AWaRe) classification of antimicrobials [145]. This categorisation is intended to steer the use of antimicrobials towards a more sustainable and rational usage model and to minimise the development and spread of AMR [146]. The AWaRe framework categorises antimicrobials based on their spectrum of activity and their potential to contribute to antibiotic resistance [146] [147] [148] [149] [150]. The "Access" group contains narrow-spectrum antimicrobials that are effective against a specific type of microorganisms and have a lower potential for causing resistance. These are also antimicrobials that should be widely available, affordable, and quality-assured, given their importance for treating a wide range of common infections [148]. The "Watch" group contains broader-spectrum antimicrobials that have a higher potential for resistance [148]. The use of these antimicrobials should be closely monitored because their overuse and misuse pose significant risks for the emergence and spread of AMR. Lastly, the "Reserve" group includes last-resort antimicrobials that should be used sparingly and selectively for serious infections when all other alternatives have failed [148]. These antimicrobials are crucial for treating multi-drug resistant infections, but their use needs to be limited to preserve their effectiveness for as long as possible [148].

The AWaRe classification is more than just a categorisation; it is a framework to guide appropriate antibiotic use based on the diagnosed condition and the recommended drugs [150] [151]. It can inform policy and practice in AMS programmes, helping to define targets for optimizing the use of antimicrobial medicines. Monitoring antibiotic use in healthcare facilities plays a crucial role in promoting the rational use of these medicines. By ensuring adherence to appropriate prescribing patterns, we can combat the misuse and overuse of antimicrobials, two key drivers of AMR. Adherence to AWaRe classifications could therefore contribute significantly to global efforts to keep antimicrobials effective for future generations [152] [153].

In conclusion, we recommend continuous research that improves the awareness, knowledge, attitudes, and practices of individuals on AMU, AMR, and AMS. Some studies have been conducted to promote these issues [48] [154]-[181]. By doing so, these studies and campaigns will contribute towards the attainment of the objectives set by the GAP and NAPs on AMR.

## 3.4. AMU and AMR Surveillance Systems

Surveillance is one of the strategic priorities of the GAP on AMR that helps countries to collect data on the prevalence of AMR and AMU, which is critical in improving patient outcomes, informing policy, identifying people at risk, and recommending interventions [72] [182]. According to surveillance findings, the increased and inappropriate contributes to the emergence and spread of AMR in humans, animals, and the environment [10] [16]. Globally, there has been an increase in AMU, with evidence indicating that there was an increase in AMU expressed as the defined daily (DDD) AMU between 2010 and 2015 by 65% (21.1 - 34.8 billion DDDs) [183]. If this consumption of antimicrobials is not regulated, then by 2030, the AMU would increase to 42 billion DDDs, although an increase of more than 200% was projected compared to the later reported [183].

Surveillance systems are important in monitoring AMR in humans, animals, agriculture and the environment [184] [185]. Well-implemented surveillance systems demonstrate whether there is the presence of AMR or not in a particular population [186]. The surveillance of AMR requires a strengthened multisectoral approach and efficient coordination [186] [187]. Surveillance strategies help monitor AMR in food-producing animals such as cattle, pigs, chickens, goats, and other animal products [188]-[193]. Comprehensive surveillance of AMU is highly recommended to reduce or prevent cases of antibiotic-resistant bacteria and their genes [194] [195]. Finally, surveillance of AMR indicates the size of the problem associated with AMR, the emergence of new AMR, whether the AMR problem is increasing or decreasing, whether there is a spread of a particular resistance, and whether a certain outbreak is due to a particular resistance [196].

A study in South Korea reported a critical need for comprehensive surveillance of third-generation cephalosporin-resistant *E. coli* at all levels of the layer-production pyramid and provided important considerations for controlling infection in large poultry production [197]. In Africa, a study in Egypt reported a need to call for nationwide surveillance programmes to monitor AMR [198].

Accordingly to the WHO, integrated surveillance of AMR in food-borne bacteria must have the following elements; sources of samples, targeted bacteria, sampling design, laboratory testing methodology, data management, validation, analysis and reporting [199]. This has been supported by other published protocols [188] [200] [201]. In addition, an integrated system should have adequate resources, which should come from sustainable investment by governments, prioritisation of which AMR problems to do first, integration into already existing surveillance systems, coordinated activities by different sectors, and available and comparable good quality data [182].

Concerning sample sources, food-producing animals are an important source of AMR that can be transmitted to humans [40]. Samples from food-producing animals should be collected from healthy animals rather than sick ones [199]. Besides, it is recommended to collect one sample per farm, which allows researchers to collect samples from many farms [188]. Samples should be collected from the national level, surveillance area, FAO sector level, and sampling location level using a well-designed sampling plan based on the number of laboratories, sampling sites, target bacteria, available antimicrobials and all necessary resources, and taking into consideration the schedule [188].

According to WHO Global AMR Surveillance System (GLASS), surveillance systems must use recommended indicator microorganisms such as *E. coli*, which is a priority microorganism and *Enterococcus* spp whose presence in samples indicates the resistance patterns of Gram-positive bacteria [199]. This has been supported by other protocols [200] [201]. Other recommended indicator microorganisms for AMR surveillance in food-producing animals like chickens include *Salmonella* spp and *Campylobacter* spp [188]. Therefore, their use as indicator organisms in AMR surveillance in poultry systems is highly recommended. Sampling directly from food-producing animals has been reported to produce reliable inferences that can be made about a particular component of integrated surveillance of AMR in food-borne bacteria [199]. Therefore, the current study focused on sampling from food-producing animals at the farm level so that epidemiological data was also gathered adequately. A sampling at the farm level is very significant as it provides an estimation of the use of antimicrobials in poultry and identifies certain risk factors that can contribute to AMR [199].

The laboratory used for AMR surveillance must have adequate resources for bacterial culture and isolation of target bacteria [188] [202]. This implies that the target bacteria must be isolated and identified using internationally accepted microbiological methods [199]. Therefore, governments must sustainably invest in AMR surveillance by providing adequate human, funding, and laboratory resources [182]. Additionally, antimicrobial susceptibility tests (AST) must be conducted using the European Committee on Antimicrobial Susceptibility Testing (EUCAST) or the Clinical and Laboratories Standards Institute (CLSI) [188] [199]. The WHO has recommended classes of antimicrobials for AMR surveillance in poultry and other food-producing animals [188] [199], and these include aminoglycosides, carbapenems, amphenicols, cephalosporins, macrolides, glycopeptides, quinolones, tetracyclines, oxazolidinones, polymixins, strepto-gramins, penicillins, glycylcyclines, and sulfonamides [188] [203].

The entire process of AMR surveillance should produce good quality data that is available and comparable across sectors and countries [182]. There must be a comprehensive data analysis of all data obtained for AMR surveillance [199]. This should be well coordinated and involve experts so that integrated data analysis, reporting and risk communication are done effectively and efficiently. Epidemiological data should also be entered properly and match the laboratory data [199]. This is important because the findings should be communicated to the stakeholders to help come up with interventions for the risks of AMR. Additionally, there should be adequate databases for data entry, analysis, reporting, and sharing [199].

### 3.4.1. Surveillance of AMR in Humans

Surveillance of antimicrobial resistance (AMR) in humans is crucial for monitoring the development and spread of resistant infections, as well as for informing strategies to combat the problem [30] [72] [204] [205]. The Global Antimicrobial Resistance and Use Surveillance System (GLASS), established in 2015, aims to promote the monitoring of AMR in bacteria that cause common infections in humans and to develop strategies to overcome this problem [201] [206] [207] [208]. Over time, fungal infections, antimicrobial consumption, and a One Health approach have been added to the items monitored by GLASS [193] [201] [206] [209]. GLASS supports the implementation of the GAP on AMR, which seeks to reduce AMU and AMR [201] [206]. As of 2018, 71 countries had registered as GLASS members to share data on AMU and AMR [206] [210]. The number of registered member states increased to 127 countries at the end of 2022 [206], demonstrating a global commitment to sharing information and collaborating with other countries to tackle AMR [206]. However, surveillance of drug-resistant infections can be challenging in low- and middle-income countries (LMICs) where there is a lack of resources and capacity to undertake AMR intervention activities [30] [84] [211] [212]. The overuse and inappropriate use of antimicrobials in humans have contributed to the development of AMR, leading to increased health costs, morbidity, and mortality across the human population [10] [67] [213] [214] [215]. To combat this problem, strategies and interventions coupled with surveillance have been proposed to reduce the transmission of AMR from humans to animals and the environment [63] [216] [217] [218]. Therefore, some countries have developed and implemented NAPs on AMR and surveillance frameworks to monitor AMU and AMR, as guided by the WHO and other stakeholder organizations [30] [89] [90] [93] [94] [219] [220]. These frameworks are critical for tracking the development and spread of AMR and informing effective interventions to combat this global health crisis [72] [82]. However, continued investment in surveillance systems and infrastructure is necessary to ensure that all countries, including LMICs, are equipped to monitor and tackle AMR effectively.

#### 3.4.2. Surveillance of AMR in Food-Producing Animals

Significant work on AMR surveillance has been done in humans compared to food-producing animals [24] [221]. There is substantial use of antimicrobials in food-producing animals which may promote the development of AMR, thereby necessitating surveillance programmes [190] [222] [223]. The surveillance of AMU and AMR in food-producing animals is provided by guidelines from the World Organization for Animal Health (OIE) Terrestrial Animal Health Code [200]. The FAO also supports the development and implementation of AMR surveillance programmes across the globe. Additionally, FAO guidelines recommend that countries develop AMR surveillance systems irrespective of their

capacity to do so [193].

Further, as a food safety priority, FAO encourages monitoring AMR in healthy food-producing animals because people consume them [193]. The FAO guidelines provide detailed guidance on how to design an AMR monitoring and surveillance program, with an emphasis on how sampling and epidemiological data should be collected, laboratory methods to employ, and the management of AMR data [193]. Besides, the guidelines provided detailed information on bacteria to use as indicators in AMR surveillance [193]. Countries can use the provided guidelines to compare the AMR trends across pathogens and report to the OIE for further decision-making [193].

The OIE, FAO, and WHO have provided guidelines on the surveillance of AMR in poultry [188] [193] [200]. Countries need harmonised procedures (data collection, laboratory techniques, data analysis, data management, and data sharing) that will help produce comparable data in AMR surveillance in animal health [224]. Therefore, the surveillance of AMR in food-producing animals should follow laid-down procedures for data collection, laboratory analysis, and data management [188]. Subsequently, there must be heightened regulation and restriction of AMU in food-producing animals [203] [225]. Consequently, this would help to combat AMR [226] [227] [228] [229].

Studies have shown that implementation of AMR surveillance in chickens can help detect antimicrobial-resistant pathogens and inform policy [230] [231]. Through national surveillance, countries would know if the poultry products that humans consume are contaminated with pathogens [230]. In Colombia, a study reported that the surveillance of AMR in poultry was critical as it helped authorities understand the trends in resistance patterns of microorganisms to common antimicrobials used in humans and poultry [202]. Additionally, the surveillance of AMR food-producing animals must be integrated into the national AMR surveillance systems, including the human AMR surveillance system [202]. Therefore, it is recommended to use a One Health approach to effectively conduct AMR surveillance globally [189] [190] [192].

#### 3.4.3. The Roles of Laboratories in AMR Surveillance

Efficient laboratories play a very important role in AMR surveillance through the detection, isolation and monitoring of emerging antimicrobial-resistant pathogens in humans, animals and the environment [185] [232]. Other laboratory activities include antimicrobial susceptibility testing (AST) and molecular characterization using advanced molecular techniques, such as polymerase chain reaction (PCR) and whole-genome sequencing (WGS), to study the genetic basis of AMR [185] [232].

A robust and efficient laboratory network both for diagnostic and public health laboratories is integral to identifying and monitoring AMR in humans, animals and the environment [233] [234]. The routine utilisation of microbiology-based diagnostics in hospital settings has contributed to the containment of AMR by supporting AMS [195] [235] [236]. This, together with the use of public health laboratories, provides data that influence treatment guidelines, and public health

policies and has strengthened laboratory-based AMR surveillance [185] [235].

Systematic evaluation of integrated surveillance for AMU and AMR in One Health paradigms is imperative to ensure the effectiveness of the systems [237] [238]. Laboratory-generated data has driven evidence-based interventions in AMR [234]. To assess progress towards targets of interventions in food and agriculture, FAO developed the Assessment Tool for Laboratories and AMR Surveillance Systems (ATLASS) [83]. Additionally, the standardisation of laboratory methods for culture, identification and sensitivity testing has also helped to generate comparable data across distinctly different settings supported by strong and reliable case definitions [30]. Further, it is highly recommended that whenever necessary, laboratories conduct detailed molecular epidemiology of isolates [239]. Alongside this, standardisation of analysis of antimicrobial susceptibility testing (AST) results, especially using WHONET as recommended by the WHO [44] [45] [240] [241] [242] [243] [244]. Capacity-building for laboratory personnel is also critical in improving surveillance of AMR [245] [246].

## 3.5. Biosecurity and Infection Prevention and Control Practices

Biosecurity is the implementation of measures that serve to prevent the introduction of disease-causing agents and their spread [247] [248] [249]. Some biosecurity measures include isolation of animals (preventing contamination of animals from housing and personal protective equipment, control of traffic (restricting the movement of people, animals, and other products into the farm area where animals are reared), and sanitation (disinfection and cleanliness) [250]. Therefore, biosecurity is a part of the One Health concept that aims to prevent and survey the occurrence of infections across human, animal, and environmental ecological systems [247].

Biosecurity measure recommends the separation of chickens by age and species, *i.e.* keeping livestock animals of different ages in separate houses and not rearing different animal species in the housing environment, *i.e.*, separating ducks from chickens [251]. This is because rearing chickens of different ages and species in the same poultry increases the risk of infection transmission across flocks [252]. Additionally, restriction of entry of people into the poultry houses has also been recommended as a good biosecurity measure that prevents transmission of pathogens from humans to food-producing animals and vice-versa [253].

Commercialisation has added pressure on the livestock industry hence creating increased demand in the production areas to control and regionally eradicate infectious diseases to preserve the marketability of livestock and animal products [254] [255]. Measures have been put in place to reduce the risks of the introduction and transmission of infectious agents, which include bioexclusion and biocontainment [254] [255].

In Belgium, previous studies reported that the implementation of good- quality biosecurity measures led to a reduction in the use of antimicrobials in piggery which resulted in reduced mortality and improved production [256] [257]. Therefore, the implementation of biosecurity is critical in preventing the development of AMR by reducing the use of antimicrobials [249] [258] [259].

To tackle AMR, preventing and controlling the disease of resistant bacteria is of critical importance [260] [261]. Infections Prevention and Control (IPC) practices work to limit the spread of infections and resistant bacteria in congregate settings, healthcare facilities, public spaces and animal farming [262] [263] [264]. Failure of IPC can lead to prolonged illness, increased hospitalisations and increased costs in both healthcare-related needs as well as animal-related foods [265] [266]. One of the main objectives of the GAP on AMR is to reduce or prevent infection through effective wash, sanitation, and hygiene (WASH) [123]. WASH practices must be promoted, especially in hospital environments, schools, universities, markets, and other communities [267] [268] [269] [270]. Therefore, compliance and adherence to hygiene measures are very critical in preventing the occurrence of infections [271] [272].

## 3.6. Use of Vaccines in Curbing AMR

Vaccines meant for veterinary use include both attenuated live vaccines and those that are inactivated [273] [274]. Vaccines are capable of providing mucosal immunity thereby protecting animals from severe infection, and limiting the infection caused by live pathogens [274]. Therefore, by preventing the occurrence of infections in animals, vaccines lead to a reduction in the consumption of antimicrobials in animal health [274]. The reduced use of antimicrobials prevents the exposure of microorganisms found in food-producing animals to these medicines leading to reduced risks of AMR development in food-producing animals. For this reason, there is a need to promote the use of vaccines in animal husbandry as a means of preventing the occurrence of infections. Similarly, vaccines are used in humans to prevent or reduce the severity of infections, thereby reducing the use of antimicrobials and preventing the occurrence of AMR in the future [275] [276] [277]. The WHO developed a Framework to reduce AMU and promote vaccinations [278].

## 3.7. One Health Concept for Surveillance and Management of AMR

One Health is an integrated and unified approach aimed at sustainably balancing and optimising the health of humans, animals, and the environment [279]. This approach recognises the interconnection and link between the health of humans, animals, plants, the environment and ecosystems, as shown in **Figure 1** [279]. Therefore, a One Health approach emphasises the need for a holistic, collaborative, transdisciplinary, and multisectoral approach in addressing AMR across humans, animals, and the environment [191] [280] [281] [282] [283].

The concept of one health is central to the global action plan of the WHO on AMR and the Food and Agriculture Organization (FAO)/Organization for Animal Health (OIE)/WHO Tripartite Collaboration on AMR [72]. On a global scale, efforts have been made recently to develop guidance for the integrated Surveillance of AMR, and several systems have been developed worldwide [74]

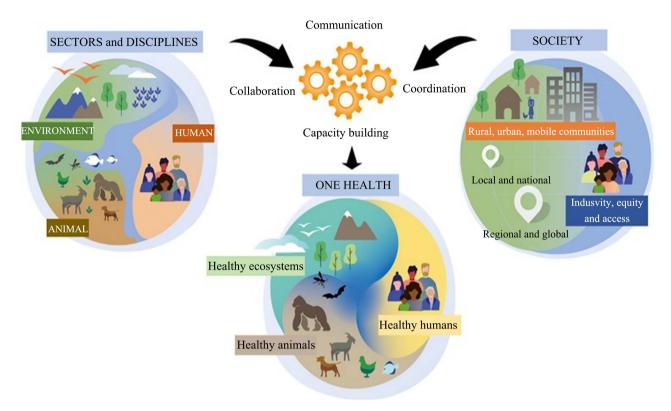


Figure 1. One health approach (Source: [279]).

[199]. The need for new knowledge about the effectiveness and economic efficiency of integrated AMR surveillance systems has been outlined in Canada, where the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARs) has been operational since 2002 [284]. This is a national programme coordinated by the Public Health Agency of Canada (PHAC) which is dedicated to the Collection, Integration, Analysis and Communication of trends in AMU and AMR in selected bacteria from humans, animals and animal- derived food sources in Canada [284]. The program aims at providing an Integrated approach to monitor trends of AMU and AMR in humans and animals, to facilitate the assessment of the public health impact of AM used in human and agricultural sectors, and to allow accurate comparisons with Data from other countries that use similar surveillance systems [284].

According to the United Nations, addressing AMR using a One Health approach may help to achieve sustainable development goals [280]. A One Health approach has been reported to be effective in promoting the rational use of antimicrobials, strengthening AMS programmes [283], and promoting global food safety [285]. In this case, an integrated surveillance system would be necessary as it focuses on AMR in humans, food-producing organisms, and the environment [199].

A One Health approach is recommended in tackling AMR because resistant microbes exist in humans, animals, and the environment [74] [78]. Additionally, the transmission of antimicrobial-resistant pathogens from animals to humans

and vice-versa, from animals to the environment and vice-versa, and from humans to the environment and vice-versa, necessitates the need for a One Health approach to address AMR [91] [286] [287]. Therefore, incorporating AMR programmes in a One Health approach is critical in addressing AMR across humans, animals, and the environment [283] [284].

A One Health approach to report AMR using the Delphi method has been proposed [288]. This Delphi method states that there must be strategic and standardised ways of reporting surveillance data which must be used to monitor AMR, provide interventional measures, and inform policy [288]. There is also a strong emphasis on monitoring antimicrobial consumption in humans and food-producing animals, antimicrobial residues in food-producing animals and the environment [288]. Therefore, a One Health approach is critical in quantifying AMU and AMR through surveillance data collected from humans, animals, and the environment and thus provides points of integration across these sectors [195].

## 3.8. Alternative to Antibiotics

Antimicrobial resistance (AMR) has become a significant public health concern worldwide, mainly due to the overuse and misuse of antibiotics [289]. In combating AMR, the development of alternative approaches to antibiotics is crucial [290]. Various strategies have been proposed, including the use of probiotics, phages, and bacteriocins [291]. Probiotics are beneficial microorganisms that can help restore the gut microbiota and prevent the growth of pathogenic bacteria [292]. Phages are viruses that specifically target and kill bacteria, while bacteriocins are antimicrobial peptides produced by bacteria that can inhibit the growth of other bacteria [293] [294] [295] [296]. These alternative approaches have shown promising results in vitro and animal models. However, more research is needed to assess their efficacy and safety in human populations [297] [298]. Implementing alternative approaches to antibiotics requires a One Health approach, recognizing the interconnectedness of human, animal, and environmental health. Collaboration between human and animal health professionals, as well as researchers in various disciplines, is essential in developing and implementing effective strategies to combat AMR and protect public health [78] [86] [282].

## 3.9. Promoting Access to Quality-Assured Antibiotics

Ensuring access to quality-assured antibiotics is a critical aspect of combating AMR in humans and animals [299]. The lack of access to quality-assured antibiotics can lead to the use of ineffective or even harmful antibiotics, which, in turn, drives excess mortality, particularly in LMICs [300] [301] [302]. Antibiotic shortages can result in the use of suboptimal drug combinations, increasing the risk of treatment failure and the development of resistance [301]. In addition to directly affecting healthcare outcomes, antimicrobial shortages also pose a public

health threat in the form of increased costs [10] [301]. The use of alternative antimicrobials, necessitated by the unavailability of the most appropriate agents, may result in higher expenses and economic losses [9] [13] [301] [303].

Antibiotic shortages may lead to people purchasing substandard and falsified (SF) antibiotics which can exacerbate the spread of resistant bacteria, undermining the One Health approach to addressing AMR [300] [304]. SF antibiotics, which may contain insufficient or incorrect active pharmaceutical ingredients (APIs), can fail to treat infections and promote the development of resistance [302] [305]. A lack of quality control and regulatory oversight contributes to the circulation of SF antibiotics, particularly in low-resource settings [306] [307]. In LMICs, shortages of quality are often due to several factors, such as weak supply chains, inadequate infrastructure, challenges with policy and regulatory processes, and poorly functioning systems of financing and drug pricing [301] [307] [308].

Promoting access to quality-assured antibiotics requires a multi-faceted approach that encompasses various strategies. Firstly, it is essential to strengthen regulatory frameworks and enforcement mechanisms to ensure the availability of safe and effective antibiotics [309]. This involves implementing stringent quality control measures, conducting regular inspections of manufacturing facilities, and cracking down on counterfeit and substandard drugs [310] [311]. Additionally, raising awareness among healthcare professionals, patients, and the general public about the appropriate use of antibiotics is crucial. Educational campaigns can emphasize the importance of completing the full course of treatment, the dangers of antibiotic resistance, and the need for responsible prescribing practices [312]. Furthermore, improving healthcare infrastructure and training healthcare workers in proper diagnosis and prescribing practices can contribute to rational antibiotic use [313] [314]. Finally, fostering research and development in new antibiotics, as well as promoting the use of alternative therapies and preventive measures, such as vaccines, can help reduce the reliance on antibiotics and preserve their efficacy for future generations [315] [316]. By employing these strategies, we can strive to ensure that everyone has access to high-quality antibiotics when needed while also addressing the growing threat of antibiotic resistance.

## 3.10. Increasing Investment in the Development of New Antimicrobials

The development of new antimicrobials is a slow and expensive process, taking up to 10 - 15 years and costing billions of dollars to bring a new antibiotic to market [317] [318] [319]. In recent years, there has been a decline in investment in the development of new antibiotics due to factors such as low-profit margins, no new markets, and the perception that AMR is a problem for the future [317] [320] [321]. To ensure the availability of new antibiotics to treat AMR, increased investment in this area is essential, with governments, pharmaceutical companies, and foundations all having a role to play [317] [322] [323]. To encourage companies to produce antibiotics, it is crucial to provide incentives, especially when market forces do not sufficiently drive innovation [323]. Alternative incentive mechanisms can be employed to either push innovation through subsidizing at-risk investments, like government grants or pull innovation by offering rewards, such as guaranteed revenue, for successful outcomes [317] [321] [324] [325]. Other innovative models, such as subscription models (e.g., Netflix models), have been proposed by stakeholders [25]. These models suggest options such as fixed yearly payments for guaranteed supply, incentives to maintain or expand production, and tenders that ensure allocation to multiple suppliers to sustain a healthy market. More recently, several countries, including the UK and Sweden, have started to explore alternative payment models for both new and older antibiotics, indicating a growing interest in finding innovative solutions to address the challenges associated with antibiotic development and access [322] [326]. Such models need to be explored and piloted by LMICs to address the challenges of antibiotic development and ensure a sustainable supply of effective treatments for AMR. Moreover, by prioritizing and increasing investment in the development of new antibiotics, we can address the growing threat of microbial resistance and ensure the availability of effective treatments for future generations [322] [327].

There has been an urge to support and strengthen the discovery of antibiotics from natural sources like traditional medicines [328]-[333]. The rise in resistance to conventional antimicrobials has caused a realisation of the significance of natural products like plants as sources of antimicrobials [322] [334] [335] [336] [337]. Further, the WHO has recommended heightened discovery of antimicrobials from natural sources, and some are undergoing clinical and preclinical development [333].

## 3.11. Strengthening Regulatory Systems and Their Roles in Prudent Use of Antimicrobials

Regulatory systems play an important role in ensuring the quality and safety of medicines. To combat AMR, all antimicrobials must meet international quality standards [302]. Achieving this requires strengthening regulatory systems in all countries and ensuring that antimicrobials are manufactured and distributed following these standards [209] [302]. Collaborative regulatory approval processes through regional harmonisation, such as the ZAZIBONA initiative in the SADC region [338], supported by organizations like the WHO through initiatives such as the prequalification program and the collaborative registration system, have been instrumental in ensuring timely access to quality-assured medicines [302] [339]. These efforts have had a positive impact on public health and cost savings.

In Africa, it is hoped that the establishment of the African Medicines Agency (AMA) can help improve the regulatory environment and harmonize standards across the continent [340] [341]. This, in turn, can have massive impacts on the availability of quality-assured antimicrobials, facilitating a more robust response

to AMR. By streamlining the regulatory process and fostering cooperation among countries, AMA can contribute to the faster approval of new antimicrobials, the elimination of substandard and falsified medicines, and the promotion of best practices in manufacturing and distribution. Ultimately, these efforts can lead to better healthcare outcomes and more effective strategies in combating AMR.

Regulatory authorities play a pivotal role in promoting the prudent use of antimicrobials across various sectors, including human, veterinary, agriculture, and environmental health [313] [342]. Regulatory authorities establish comprehensive guidelines, policies, and regulations to govern the use of antimicrobials. These regulations encompass various aspects such as the sale, distribution, and usage of antimicrobials. They provide the legal framework necessary to enforce appropriate prescribing practices, dosage regulations, and duration of treatment. By ensuring compliance, regulatory authorities aim to curb the indiscriminate use of antimicrobials and limit the emergence of AMR [343] [344].

The approval and oversight of antimicrobial products are essential tasks performed by regulatory authorities. These authorities thoroughly evaluate the safety, efficacy, and quality of antimicrobial agents, including antimicrobials, antivirals, and antifungals. A rigorous assessment of data provided by pharmaceutical companies is conducted to determine whether these products can be marketed and used safely. By approving only those products that meet stringent standards, regulatory authorities contribute to the rational and judicious use of antimicrobials [209].

Regulatory authorities establish surveillance programmes to monitor the sale, distribution, and consumption patterns of antimicrobials. Through systematic data collection, they track antimicrobial consumption in diverse settings such as human healthcare, animal husbandry, and agriculture. This information enables authorities to identify trends, patterns, and potential areas of misuse or overuse. Such surveillance programmes play a crucial role in evaluating the effectiveness of interventions and shaping evidence-based policies to promote the responsible use of antimicrobials [313].

Collaboration with healthcare professionals, veterinarians, and agricultural stakeholders is a key aspect of the role of regulatory authorities [345] [346]. Together, they develop guidelines and educational campaigns to foster responsible use practices. These initiatives aim to raise awareness among healthcare providers, farmers, and the general public about the risks associated with AMR, appropriate prescribing practices, and the importance of considering alternatives to antimicrobials whenever possible. By disseminating accurate information, regulatory authorities actively contribute to changing behaviours and promoting a more cautious approach to AMU [347].

Additionally, regulatory authorities also engage in international collaborations and harmonization efforts to tackle the global challenge of AMR. By working closely with organizations such as the World Health Organization (WHO) and the World Organisation for Animal Health (OIE), regulatory authorities facilitate the development of standardized guidelines, the sharing of data, and the coordination of efforts across borders. These collaborative initiatives enhance global cooperation and enable a more unified response to combat AMR [86] [348] [349].

## 3.12. Improving Local Drug Manufacturing

Local drug manufacturing has gained traction as a means to assure supply and access to medicines, especially in response to shortages linked to the COVID-19 pandemic [301] [350]. Government-funded local or regional manufacturing can provide an avenue for improving access to medicines [351] [352] [353]. A portfolio of strategic antimicrobials at risk of shortages could be targeted for manufacturing and supply through such regional hubs. Furthermore, these regional hubs could be developed to facilitate the prioritization and manufacturing of active pharmaceutical ingredients (APIs), where needed [63].

Expanding local and regional production hubs to manufacture and supply APIs can shift the current dominance of API production from China and medicine manufacturing from India [354]. This would prevent the monopolization of manufacturing capacities and could also introduce competitive pricing of APIs, ultimately reducing the cost of goods [355]. Increased public-private partnerships for antimicrobial manufacture and building capacity for public sector manufacture of antimicrobials can further support these efforts [317] [356].

Improving local manufacturing has the potential to reduce the cost of antimicrobials in the future, addressing a barrier to access, particularly in low- and middle-income countries [323] [357]. To improve access to antimicrobials in these countries, it is essential to reduce the cost of these drugs, which can be achieved through the collaborative efforts of governments, pharmaceutical companies, and non-governmental organizations [358]. Enhancing local and regional manufacturing capabilities helps overcome supply chain disruptions and shortages, ensuring a stable and sustainable supply of essential antimicrobials. This contributes to the effective management of infectious diseases and the containment of AMR. This should be accompanied by the allocation of adequate funding for the development of new antimicrobials [359].

## 3.13. Promoting Global Collaborations on AMR

Promoting global collaboration on AMR is crucial in addressing its urgent public health threats [81] [360] [361]. AMR is a global challenge that requires a coordinated effort involving governments, healthcare professionals, researchers, and international organizations. Initiatives like the GLASS and the GAP on AMR provide a framework for monitoring and addressing the issue on a global scale [82] [124] [362]. Additionally, collaborations such as the Fleming Fund and the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) bring together stakeholders from multiple sectors to support research, development, and innovation in combating AMR [363] [364] [365] [366]. These coordinated collaborative efforts foster knowledge sharing, resource allocation, and capacity building, enabling countries worldwide to work together towards effective prevention, surveillance, and control of AMR [187]. By promoting global collaboration, we can collectively tackle AMR and safeguard the effectiveness of antimicrobial drugs for future generations [361] [367].

## 4. Challenges in Implementing Strategies to Address AMR

Addressing AMR is hampered by various challenges. This paper discusses some significant impediments that affect the successful implementation of strategies that address AMR.

## 4.1. The Burden of Disease

The fight against AMRis challenging, especially in resource-limited settings, where the high burden of bacterial infections, poverty, weak governance and frail health systems, and limited awareness of drug-resistant infections pose sub-stantial hurdles [240] [368]-[375]. These issues are particularly prevalent in many LMICs posing major challenges in the fight against AMR [376] [377] [378].

To effectively address these systemic issues, LMICs must strengthen their health systems to address these systems issues, focusing on developing regulatory strategies against unauthorised AMU, AMS programmes, standard treatment guidelines for common infections, and sustainable public awareness campaigns to change health-seeking behaviour [379]. Additionally, heightened investment in research and development of vaccines, newer drugs and improvement in water, sanitation and hygiene to prevent common infections, together with the promotion of diagnostic tests to timely detect and treat infections, are essential to curb the current AMR trends [132] [376].

## 4.2. Human Resource and Inadequate Capacity Building for AMR

One of the major challenges in implementing strategies to address AMR is the need for more human resources, especially in low- and middle-income countries [238] [377] [380]. These countries often have limited resources and insufficient staffing to implement effective AMR programmes and address community infections [381]. Additionally, there is a shortage of trained healthcare professionals who can effectively diagnose and treat AMR infections [89] [382]. The challenges of resources include insufficient financial support for antimicrobial stewardship, a shortage of microbiologists, chemists, and infectious disease specialists, and a lack of technological support for intervention administration [99]. Due to shortage of the human resource, AMR stewardship programmes and infection prevention control (IPC) in NAPs require specialised human resources, which both countries lack [96] [383]. A USA report from the National Department of Health background paper on AMR indicated that AMS and IPC programme knowledge was low [97]. The GAP on AMR recommends prioritising human resources for stewardship programmes to preserve antibiotic efficacy

#### [72] [96].

Lack of healthcare professional capacity building prevents effective AMR surveillance and AMS implementation [384] [385]. Additionally, there has been a global shortage of human resources with the necessary education and training for AMR [384]. These challenges continue to affect the effective implementation of successful strategies to combat AMR.

## 4.3. Funding Challenges for AMR and AMS Costs

Securing sufficient funding for AMR and AMS initiatives often poses a significant challenge [33] [385]. Some governments may not prioritise funding for these initiatives, perceiving them as less urgent compared to other public health concerns [211]. This issue is particularly notable in LMICs, most countries mainly depend on external funding to develop and implement AMR activities [212]. Moreover, the decision to prioritise health in some countries is a political issue [386]. Besides the involvement of multiple government agencies in AMR initiatives can complicate the coordination and monitor spending. The private sector's participation is often limited by a lack of financial incentives to invest in the research and development of new antimicrobials [245]. Finally, despite the need for global coordination and cooperation to address AMR, this can be difficult to achieve due to competing interests and priorities among different countries

#### 4.4. Behavioural Change Issues Concerning Antimicrobial Use

Since humans are the ones that handle and utilize antimicrobials, their behaviour affects every element of AMR, including its prevention [387] [388] [389] [390] [391]. AMR is attributable to the excessive use and misuse of antimicrobials in animal and human health [29] [387], usually due to behavioural issues. Consequently, lack of behaviour change causes humans to continue self- prescription practices which are major contributing drivers to the emergence of antimicrobial-resistance infections [392]-[408]. Changing behaviour is difficult, and it can be challenging to convince people to adopt new practices and habits [409]. Therefore, we believe that the inappropriate prescribing, dispensing, administration, and use of antimicrobials will continue if behavioural change is not addressed.

## 4.5. Laboratory Incapacities and Ineffective Surveillance Systems

LMICs face significant challenges in securing of supply chain and allocating resources for equipment, diagnostics, and reagents [384]. These challenges are compounded by environmental, logistical, and budgetary constraints [30] [410] [411]. Regulatory issues, such as strict regulations for air shipment delivery, can lead to long delays and affect secure cold chain storage.

Laboratory Guidance for the selection, sampling, and transport of specimens is often absent [410]. Leading to a lack of quality assurance and no systematic monitoring of quality indicators [238]. In many LMICs, basic requirements for a functional laboratory infrastructure remain unmet [410].

The lack of high-quality microbiological data, the disconnection between existing data and clinical outcomes, and the unrepresentative nature of available data constitute major obstacles in estimating the global burden of AMR [377]. The quality of data particularly in evaluating bacterial control strains, is another significant issue [412].

To accurately assess the burden of AMR, it is crucial to have individual patient data, high-quality microbiological data, representative catchment populations, and a link to clinical outcomes. However, problems with data sharing between institutions and conflicts with ongoing research projects of data custodians often hamper this process [377].

In many low-income countries, there is an inconsistent supply of antimicrobials to the microbiology laboratory which could contribute to data availability bias [385]. Furthermore, the absence of crucial elements such as working relationships, political support, and resources could result in an inability to link data [413].

Reliable surveillance data is crucial for estimating the spread of AMR, identifying its causes, developing targeted control methods, and evaluating the success of implemented strategies. However, many LMICs struggle to obtain representative, high-quality surveillance data [414]. Additionally, there is a paucity of reliable surveillance data in LMIC settings due to the limited application of microbiological diagnostics in clinical practice. It is worsened in settings where culture and sensitivity tests are not done [411] [414]. Further, other challenges such as technical, infrastructural, and behavioural issues also affect the implementation of AMR surveillance data in clinical microbiology [83] [204] [212] [411]. Furthermore, a lack of microbiological diagnostics in patient care guides would negatively affect AMS, IPC practices in healthcare facilities, and laboratorybased AMR surveillance [235]. Of note is the lack of skilled personnel in the microbiology laboratory in many LMICs [415]. This is coupled with a lack of consistent laboratory supplies which may lead to inadequate good data which is required for AMR surveillance [246]. Lack of data management in the laboratory and healthcare system has been shown to affect the overall surveillance of AMR [212] [416]. Lack of government funding will have an impact on AMR surveillance programmes. The political will to combat AMR is a major challenge [385]. Funding for AMR national action plans and surveillance programmes could help efforts to combat AMR [72] [201]. In addition, a lack of awareness among healthcare professionals regarding the significance of reporting may contribute to the inadequate surveillance system [379]. These deficiencies might prevent efforts to monitor and control the spread of AMR, a growing threat to global health.

## 4.6. Development of Natural Resistance and Other Predisposing Factors

The problem of AMR has been worsened by the development of natural resis-

tance to antimicrobials by various microorganisms [36] [39]. Natural or intrinsic resistance is a phenomenon that occurs naturally but has been accelerated by the exposure of microorganisms to antimicrobials [11] [417]. Additionally, a lack of awareness regarding AMR and its consequences among the general public, farmers, healthcare professionals, and policymakers remains a contributing factor to the development of antimicrobial-resistant infections [418]. This has resulted in the inappropriate use of antimicrobials in human, animal, and environmental health sectors [387]. The result has been the emergence of multidrug-resistant infections [419] [420]. Limited availability of new antimicrobials and other antimicrobial agents [211]. Inadequate surveillance systems to monitor the development and spread of AMR [30]. In healthcare facilities, infection prevention and control procedures must be improved. Inadequate written guidelines and processes for maintaining cleanliness contribute to poor healthcare environments. As a result, AMR's emergence and spread are made more accessible [421]. The inaccurately diagnosing of an infection, such as prescribing an antibiotic "just in case" or a broad-spectrum antibiotic, is given to the patient when a specific narrow-spectrum antibiotic may be more appropriate. These conditions increase selective pressure and promote the emergence of AMR [422] [423] [424].

Antimicrobials are widely used in agriculture as growth enhancers and growth boosters for animals worldwide. Animal manure widely disperses antibiotic- resistant bacteria in cattle across the ecosystem and can be hazardous to humans. These bacteria are also easily transmitted to humans through food chains. It could result in complicated, incurable, and chronic infections in people [423] [425] [426] [427].

## 4.7. Data Sharing Challenges

Efficient data sharing necessitates strong collaboration with influential figures across local to international levels, within and beyond the health industry. However, there is a lack of robust laws protecting the privacy of medical and genetic data [428]. In many LMICs, limited resources and a lack of infrastructure result in fragmented and unrepresentative data. This diminishes its usefulness for informing health policymakers and guiding the efficient allocation of financial resources to surveillance programmes designed to combat AMR [211] [212] [238]. The scarcity of high-quality data hinders the monitoring and mapping of resistance spread, early outbreak detection, and the development of national health policies to combat AMR [429]. In LMICs, healthcare providers and institutions often lack the financial and technical resources necessary to effectively collect, manage, and share information [211] [381].

The implementation and maintenance of the infrastructure required for data exchange, such as robust information systems and interoperability standards, can be cost-prohibitive, thereby limiting data sharing [212] [376] [384] [430]. Furthermore, academic institutions often under-share data due to a lack of in-

centives [319]. While these institutions produce vast amounts of research data, funding constraints present major obstacles to disseminating these findings [319]. Addressing these issues is critical for effectively combating AMR and promoting public health.

## 4.8. Ineffective Leadership, Governance, and Coordinated AMS Programmes

The lack of commitment to combat AMR among government leaders is a huge problem [431] [432] [433]. For instance, the implementation of NAPs on AMR requires the involvement of leaders at all levels [204] [385] [434] [435], which is not the case in most healthcare facilities and government units. Further, the implementation of all AMS activities requires commitment from governments, of which if not committed, the fight against AMR fails. Unfortunately, some leaders are not aware of AMS programmes [436]. Hence, this makes the initiation and implementation of AMS activities challenging.

The fight against AMR is affected by uncoordinated or consistently implemented AMS activities [433] [437]. Infective multidisciplinary teams have been reported to be among the hindrances of successful AMS programmes in healthcare facilities [431]. Subsequently, some healthcare facilities do not have functional AMS programmes thereby promoting irrational prescribing, dispensing, and administration of antimicrobials [380] [438]. Some facilities do not have treatment guidelines to guide prescribers on rational prescribing [439] [440]. Consequently, most facilities lack reliable antibiograms for effective surveillance of AMR trends [385] [440].

We believe when these challenges are addressed, it will be easy to combat AMR in sectors and levels of AMU. In this regard, we emphasise the need for more collaborations, leadership commitment, and capacity building to win the fight against AMR.

## **5.** Conclusion

This review paper found that the effective implementation of various strategies to combat AMR is critical in addressing this problem. However, many challenges impede the establishment and implementation of strategies to combat AMR. Some countries still have challenges towards fighting this silent pandemic, including inadequate human resources for AMR, financial challenges, limited surveillance of AMU and AMR, inadequate data sharing resources, lack of awareness and knowledge of AMR, inadequate disease diagnostic resources, behavioural issues concerning prescribing, dispensing, and use of antimicrobials, lack of capacity building and effective AMS. Therefore, there is a need to develop, implement, and strengthen the strategies for combating AMR. Finally, all healthcare facilities should develop and implement sustainable AMS programmes to promote the rational use of antimicrobials and reduce AMR and its consequences in the future.

## **Conflicts of Interest**

All authors declare no conflict of interest.

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