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Current trends on antimicrobial use and emergence of resistance in the animal health sector in Africa: A review covering the period 2013-2023

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Abstract
Increasing prevalence of antimicrobial resistance in the animal health sector in Africa is an issue of great importance to African countries. To understand current trends in antimicrobial resistance and antimicrobial use in the animal health sector in Africa, a review of the latest update was conducted. The review spanned the period 2013 to 2023, covering antimicrobial resistance and associated factors; common practices of antimicrobial use or misuse; antimicrobial testing approaches; measures for delaying emergence of antimicrobials resistance; "One health" approaches for effective management and control of antimicrobial resistance; and "One health" platform. The review outlines the rising antimicrobial resistance, due to irrational use of antimicrobials in human and veterinary medicine and non-compliance with withdrawal periods. The use of antimicrobials without prescription was reported as an important risk factor for the emergence and spread of AMR. Despite diagnostic advances which have contributed to enhancing AMR detection, the lack of standardized testing protocols causes variation in the detected and reported level of AMR between different countries. Challenges persist in integrating AMR surveillance and regulatory enforcement, emphasizing the need for implementation of a "One Health" approach. In addition, the review presents the state of development of AMR National Action Plans. In addition, it presents stewardship programs implementing animal husbandry and bio-security measures intended to diminish the need for antimicrobials. In 2022, a total of 60% (28/47) of African countries undertook monitoring of consumption of antimicrobials in animals. However, this declined to 53% (26/49) of African countries by 2023. Furthermore, only 14% (7/49) African countries undertook routine surveillance for antimicrobial resistance in zoonotic bacterial infections in animals in 2022, while only 16% (8/49) of the African countries did the same in 2023. Only 9% (4/47) of the African countries in 2022 and 15% (7/48) in 2023 undertook surveillance on antimicrobial resistance to identify pathogenic or commensal bacterial species in animals. Such countries were able to systematically collect and disseminate data on antimicrobial resistance from reference laboratories.
In 2022, only 6% (3/47) of African countries had national AMR surveillance systems established. A similar proportion (6%-3/48) was reported in 2023. Only 2% (1/47) of African countries published data on bio-security and good animal husbandry practices in 2022, while only 4% (2/49) did the same in 2023.

Keywords: Current trends, antimicrobial resistance, animal health sector, Africa, 2013-2023

Introduction
Antimicrobial resistance (AMR) is an issue that affects African countries. AMR is a source of concern because it increases the likelihood of treatment failure (Kebede *et al*., 2024) [1]. Development of antimicrobial resistance may be due to misuse in both human disease treatment and in animal husbandry (Hlashwayo *et al*., 2020; Kashoma *et al*., 2015) [2, 3]. In certain instances, farmers disregard the withdrawal periods and recommended dosages, and this leads to AMR (Olabode *et al*., 2017) [4]. In addition, pathogens with resistance can be directly transferred to humans from animals and animal products (Noreen *et al*., 2020) [5]. For example, a significant increase in the prevalence of antimicrobial resistance to *Campylobacter* spp. (29.6-63.1%) from 1990 to 2021 has been reported (Noreen *et al*., 2020) [5]. Antimicrobials are widely used in animal farming as prophylaxis and for growth promotion, which could explain the rising trend in AMR (Mengistu *et al*., 2020; Paintsil *et al*., 2022) [6, 7].

Resistance to antimicrobials, often appears due to its prolonged use that generally supports the growth of resistant bacterial isolates and inhibits the growth of susceptible bacteria. Most times, continuous antibiotic pressure causes resistance not only to antimicrobials in use but towards other antimicrobials from the same class as well (Pulingnam *et al*., 2022) [8].

Globally the health impact of antibiotic resistance is projected to cause 10 million deaths worldwide by year 2050 if the current trend of inappropriate and excessive use of antibiotics continues. Increasing incidence of antimicrobial resistance is likely to potentiate horizontal transmission of the resistant genes. This has been linked to cross-resistance with other antimicrobial families. Antimicrobial resistance due to *Escherichia coli*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*, *Salmonella* spp. and *Staphylococcus aureus* causes significant economic burden (Pulingnam *et al*., 2022) [8].

Burki (2018) [9] estimated loss of capital due to antimicrobial resistance to be approximately $300 billion to $1 trillion by 2050. Likewise, O'neill (2014) [10] projected the cumulative loss of economic output due to antimicrobial resistance within countries of the Organisation for Economic Co-operation and Development (OECD) to amount to approximately $20 to 35 trillion. While, Ventola (2015) [11] estimated the total economic burden in the human health sector in the United States emanating from antimicrobial resistance crisis to be approximately $20 billion and AMR-induced loss of productivity to be approximately $35 billion. The World Bank has estimated that unless urgent action is taken, antimicrobial resistance is likely to increase the level of poverty and cause greater negative impact on the Low-Income countries (Bank, 2017) [12], especially on public health, agricultural systems and socio-economic development. Mshana *et al* (2021) [13] reported that from 2015 to 2019 about 3558 to 4279 tonnes of antimicrobials were used in animals in Africa. Tetracyclines and polypeptides contributed the largest proportion of antimicrobials used. Cattle and poultry production accounted for the largest consumption of antimicrobials.

In animal health, commercialization and intensification in smallholder farms necessitates increased antimicrobial use for prophylaxis and treatment of animals in order to maintain animal health. Antimicrobials are essential for maintaining animal health in livestock production systems, but inappropriate dispensing and dosing, poor quality of drugs, overuse, and self-medication causes antimicrobial resistance (Kemp *et al*., 2021) [14].

Livestock may act as reservoirs for antimicrobial resistant bacteria, with the potential for widespread transmission between humans and animals as a result of close contact, especially along the food chain (Kemp *et al*., 2021) [14]. It is worth noting that nine of the 14 classes of antimicrobials considered "critically important" for human health are used in both human and livestock health. While, three of the 3rd to 5th generation cephalosporins, fluoroquinolones, and polymyxins are considered highest-priority critically important antimicrobials (HPCIAs) for human health (WHO, 2018) [15]. Antimicrobial use in livestock production is predicted to increase by up to 67% by 2030. Increased antimicrobial use is likely to lead to significant negative impacts on animal welfare and food security. Similar strains of antimicrobial resistant bacteria are found in both food animals and humans. Normally, plasmid-mediated resistance in *Escherichia coli* to polymyxins (mcr-1), originates from food animals (Kemp *et al*., 2021) [14].

Antimicrobial Resistance and associated risk factors
Prevalence

Antimicrobial resistance is widespread in the animal health and production sector across African countries (AU-IBAR, 2023) [16]. Reports indicated that resistance occurs predominantly to Tetracycline, Penicillin, Quinolone, Acaricides, Trypanocides, Streptomycin and Sulphonamides. *E. coli*, *Salmonella* spp., *Campylobacter* spp., *Enterococcus* spp. and *Staphyloccoccus aureas* are major pathogens exhibiting resistance. Beef, poultry and dairy constitute major livestock value-chains affected. Furthermore, recent mapping studies on antimicrobial resistance in *E. coli* and non-typhoidal *Salmonella* in farm animals against tetracycline, ampicillin, Sulfamethoxazole-trimethoprim, chloramphenicol, ciprofloxacin, gentamicin and cefoxitin confirmed Southeastern Africa as a hotspot for antimicrobial resistance (Cheng *et al*., 2024) [17].

Furthermore, studies conducted on antimicrobial on *Campylobacter* spp. infection revealed prevalence ranging, from 97.2% to 72.9%, 27.1% and 15.1% in Eastern Cape, KwaZulu-Natal, Limpopo and North-West provinces, respectively (Ramatla *et al*., 2022) [18]. The highest prevalence of resistance of *Campylobacter* spp. infection was against clindamycin (Ramatla *et al*., 2022) [19]. Of importance, clindamycin is normally used to treat *Campylobacter* spp. infections in humans (Varela *et al*., 2007) [18] and such resistance would make it ineffective against such infections. Similar results on the prevalence of *Campylobacter* spp. resistance against antimicrobials have been reported elsewhere (Paintsil *et al*., 2022; Hlashwayo *et al*., 2021) [7, 2]. Clinical failures have previously been reported against oxytetracyclines, penicillin-streptomycin and sulfonamides (Hlashwayo *et al*., 2021) [2]. Most prominent treatment failures encountered by farmers were against oxytetracycline. Veterinary professionals attributed such clinical failures associated with oxytetracycline and penicillin-streptomycin to antimicrobial resistance (Hlashwayo *et al*., 2021) [2]. However, veterinary drug distributors lacked sufficient awareness about the existence of resistance to antimicrobials.

Antimicrobial resistance is increasing in pets in Africa (Yaovi *et al*., 2022) [20]. Multidrug resistance has been reported in *E. coli, P. aeruginosa* and *Salmonella* strains. Antimicrobial resistance has been reported in zoonotic strains such as *E. coli*, *Salmonella*, *P. aeruginosa*, *S. pyogenes* and *Staphylococcus*, an issue of public health importance. Moreover, antibiotics used in animals, especially pets, are also used in humans (Yaovi *et al*., 2022) [20].

Staphylococcus aureus resistance to antimicrobials such as nalidixic acid, streptomycin, methicillin, cotrimoxazole, ampicillin, amoxicillin and others has been reported in dogs (Yaovi *et al*., 2022) [20]. Likewise, multidrug resistance has been reported in dogs and humans in Nigeria and in cats in South Africa (Yaovi *et al*., 2022) [20]. Existing evidence indicates that rational use of antibiotics is necessary to prevent transmission of resistant infections from animals to humans, given that several antibiotics used in animals are also used in humans. In addition, good hygienic practices can prevent exchange of pathogens between dogs and their owners. Given the increasing occurrence of multidrug resistance in several bacterial strains, promoting use of medicinal plants in the treatment of bacterial infections in Africa is absolutely necessary (Yaovi *et al*., 2022) [20].

Antimicrobial resistance in *Staphylococci* other than *Staphylococcus aureus* (SOSA) has been reported in animals and humans, with high rates of resistance being against penicillin, tetracycline, fluoroquinolones, linezolid and fusidic acid (Ocloo *et al*., 2022) [21]. Such resistant strains of *Staphylococcus aureas* pose a threat to the livestock industry and public health, given the likely spill-over into the human environment.

Multidrug resistance is increasingly being reported in *staphylococci* isolated from animals in Africa. While, tetracycline resistance has been reported amongst *staphylococci* isolates from mastitic buffalo milk. Elsewhere, resistance to tetracycline, oxacillin and daptomycin has been reported in *staphylococci* isolates from turkeys (Ocloo *et al*., 2022) [21].

Not only do such resistant strains of *Staphylococcus aureus* spill-over to the human environment but also into the natural environment. Subsequently, continuous exchange of virulence and resistance genes takes place amongst strains of *Staphylococcus aureus* within the natural environment. Largely, against antimicrobials used to enhance growth and prevent infection in animals. Consequently, leading to ineffectiveness of preventive measures for *Staphylococcus aureus* infection (Ocloo *et al*., 2022**)** [21].

Environmental studies conducted in South Africa and Algeria have revealed multi-drug resistance in *E. coli*. Moreover, antimicrobial resistance has been reported in animals, humans and the environment (Kimera *et al*., 2020) [22].

Application of sub-therapeutic doses of antimicrobials in animal husbandry causes antimicrobial resistance (Ocloo *et al*., 2022**)** [21]. The threat of antimicrobial resistance is further exacerbated by the exchange of resistance genes between animal pathogens from one farm to another through animal trading and animal husbandry practices (Ocloo *et al*., 2022) [21].

Risk factors

In many sub-Saharan African countries, there is a paucity of data on antimicrobial resistance. Prudent antimicrobial use is often deterred by inefficient veterinary services, limited regulatory capacities and weak surveillance systems at national, or regional levels (Kemp *et al*., 2021) [14]. Lack of access to proper antimicrobial therapy, poor regulation of antimicrobial use for humans and animals, poor surveillance systems, and scarcity of updated antimicrobial use guidelines constitute factors that exacerbate the situation of antimicrobial resistance in Africa. The situation is further compounded by limited opportunities for prescribers to continue education on antimicrobial use; tendency for animal owners to engage unskilled people to treat livestock; drug abuse by livestock keepers and unregulated disposal of drug waste in the environment (Kimera *et al*., 2020) [22].

The use of antibiotics to inhibit susceptible bacteria and to allow resistant bacteria to survive is known to contribute to antibiotic pressure (Levy and Marshall, 2004) [23]. Such antibiotic pressure is known to activate dormant resistance genes in bacteria. Subsequently, significantly causing emergence of antimicrobial resistance. The thriving bacterial isolates under antibiotic pressure normally spread the resistance gene to other hosts. Prolonged use of antibiotics allows growth of resistant bacteria but inhibits the growth of susceptible ones. Continuous antibiotic pressure causes resistance to both the antibiotics in use and those in the same class (Pulingnam *et al*., 2022) [8]. Worse still, interactions at the human-animal interface increase the risk of transfer of antibiotic resistance from animals to humans.

In Africa, extensive systems are normally used for rearing cattle, poultry and pigs. However, rapid increase in demand for livestock products due to the sprawling growth in human population has led to proliferation of intensive systems for livestock, especially in peri-urban areas. The need to maintain animal health and sustain animal production in such intensive systems has led to enormous misuse of antimicrobials. Resulting into increase in emergence of antimicrobial resistance. Coupled with this, is the emergence and spread of multi-drug resistant organisms in the environment that subsequently contaminate soil, sludge, groundwater, wastewater and surface water.

Furthermore, spillage of waste containing antimicrobials originating from pharmaceutical factories, hospitals and livestock farms into the environment promotes selection of resistomes. Resulting into spill over to animals and humans. *Campylobacter* spp., *Salmonella* spp., *Staphylococcus* spp., *Enterococcus* spp. and ESBL-producing *Enterobacteriaceae* are major pathogens known to circulate in animals, humans and in the environment (Kimera *et al*., 2020) [22].

Common practices of Antimicrobial Use or Misuse

Common practices for accessing antimicrobials in Africa include, procurement from agrovet shops in villages; and provision by field veterinarians during their routine work. This system of accessing antimicrobials is often characterized by farmers buying and stocking antimicrobials without prescription, not respecting withdrawal periods, use of inappropriate dosages, and antimicrobial use being dictated purely by monetary benefit to field veterinarians or to agrovet owners rather than the necessary prudent use of antimicrobials to maintain animal health and animal production of farmer's animals.

Incredible evidence emanating from studies conducted in Kenya (Kemp *et al*., 2021) [14] has confirmed that agrovets sell antimicrobials to farmers without prescription. Customer preference, antimicrobial effectiveness and cost of antimicrobials takes precedence in the sale of antimicrobials to farmers. Farmers are rarely provided with information on the withdrawal periods and dosage instructions. Day-to-day operations of agrovet shops are handled by pharmaceutical technicians but in certain worse situations by unskilled apprentices rather than the veterinarians. Such professionals managing agrovet shops do not have the competence to prescribe antimicrobials though may be capable of selling antimicrobials. Farmers at times may opt to bypass veterinary professionals when treating their animals or to reuse previous prescriptions as a cost-saving measure. Oxytetracycline, penicillin-streptomycin and sulphonamides are the most misused antimicrobials. Farmers easily purchase oxytetracycline from agrovet shops. Only purchase and access to 3rd + generation cephalosporins or fluoroquinolones is restricted.

It has been reported that under such situations in Africa (Kemp *et al*., 2021) [14], where veterinary markets have been liberalized, it incredibly difficult to prevent farmers from administering drugs. Since they take to themselves as a responsibility to maintain their animals healthy.

In some countries, insufficient animal professionals or weak veterinary services have made farmers administer treatment to their animals. In other countries, lucrative trade in veterinary drugs through illegal border crossings avails farmers with veterinary drugs with easy in local markets without regulatory controls.

Antimicrobial testing approaches

The main challenge affecting the level of detection and

reporting of antimicrobial resistance in African countries is variation in laboratory-based results. This is attributed to lack of standardized laboratory protocols (Kimera *et al*., 2020) [14]. A recent report indicates that the majority of African countries use antimicrobial susceptibility testing in their national laboratories (AU-IBAR, 2023) [16], with the Disk diffusion test being predominant. Few countries use the Minimum Inhibition Concentration test or both.
Conventionally, antimicrobials testing is performed using either culture-based and molecular-based approaches that are either manual or automated. Either incorporating microscopy-based or spectrometry-based tools for antimicrobials resistance detection (Kaprou *et al*., 2022) [24]. The principle for phenotypic culture-based methods for detecting antimicrobial resistance is evaluating bacterial growth in the presence of antibiotics (Kaprou *et al*., 2022) [24]. This is the approach employed in the antimicrobial susceptibility testing.
Manual tests normally use agar dilution, gradient test, disk diffusion, and broth microdilution when conducting antimicrobial susceptibility testing. While, automated commercial platforms normally employ broth dilution and already-made cartridges (Kaprou *et al*., 2023) [24]. An example is the Sensititre panel method that is normally used in the detection of carbapenem-resistant *Klebsiella pneumoniae* to polymyxins. Monitoring real-time growth of pathogens and analysis of the minimum inhibitory concentration, and generating a comprehensive database for a broad spectrum of organisms is essentially the principle behind such platforms (Kaprou *et al*., 2022) [24].
Molecular-based tests, are nucleic acid amplification-based approaches that are designed to detect specific resistance genes using the polymerase chain reaction (PCR) (Gajic *et al*., 2022) [25]. This involves amplification of nucleic acid sequences that encode resistance to antimicrobials operated as real-time or conventional PCR. Simultaneous testing of multiple genetic determinants in various bacterial species is normally performed using multiplex assays. Especially in case of the identification of cephalosporinase and carbapenemase-encoding genes (Gajic *et al*., 2022) [25].

Measures for delaying emergence of antimicrobial resistance

An efficient system for awareness campaigns on antimicrobial resistance, spelling out the need for its prevention and successful implementation of antimicrobial stewardship programmes could effectively delay emergence of antimicrobial resistance in Africa. Creating awareness amongst field veterinarians and livestock owners about the need to adhere to strict prescription, judicious application of antimicrobials is paramount in either delaying the emergence or mitigating transmission of antimicrobial resistance. In addition, involvement of agrovet staff in antimicrobial stewardship programmes is necessary (Kemp *et al*., 2021) [14]. Prevention of outbreaks of multidrug resistant bacterial infections requires controlled use of antibiotics in health and agricultural sectors (Pulingnam *et al*., 2022) [8]. Furthermore, surveillance and monitoring of antimicrobial use and resistance in the food and agriculture sectors are essential strategies (Kimera *et al*., 2020) [22].

"One health" approach for effective management and control of antimicrobial resistance

The human and animal health sectors, as well as environmental sectors ought to design "One Health" approaches for effective management and control of antimicrobial resistance. This approach has largely been promoted among African countries by the World Health Organization in the fight against antimicrobials resistance (Ramatla *et al*., 2022) [18]. Field challenges in implementation of One Health approach in the surveillance of antimicrobial resistance do exist. This has compelled different sectors (human and animal sectors) to employ different approaches in monitoring antimicrobial use and resistance.
In the animal sector, weak enforcement of the available regulations has largely led to unmonitored production, distribution, handling, storage and sale of veterinary drugs. This limitation could be resolved while African countries review and implement their National One Health Plans for combatting antimicrobial resistance (Kimera *et al*., 2020) [22].

"One health" platform

One health platforms are necessary for summarizing and integrating current knowledge on antimicrobial resistance from the human and animal sector to strengthen evidence-based surveillance. The platform: resistancebank.org is vital in centralized management of data on antimicrobial resistance, especially involving foodborne and human pathogens. Such online platforms have multiple advantages over individual studies, given their open-access nature. Making it easy to download or upload data or information (Criscuolo *et al*., 2021) [26].

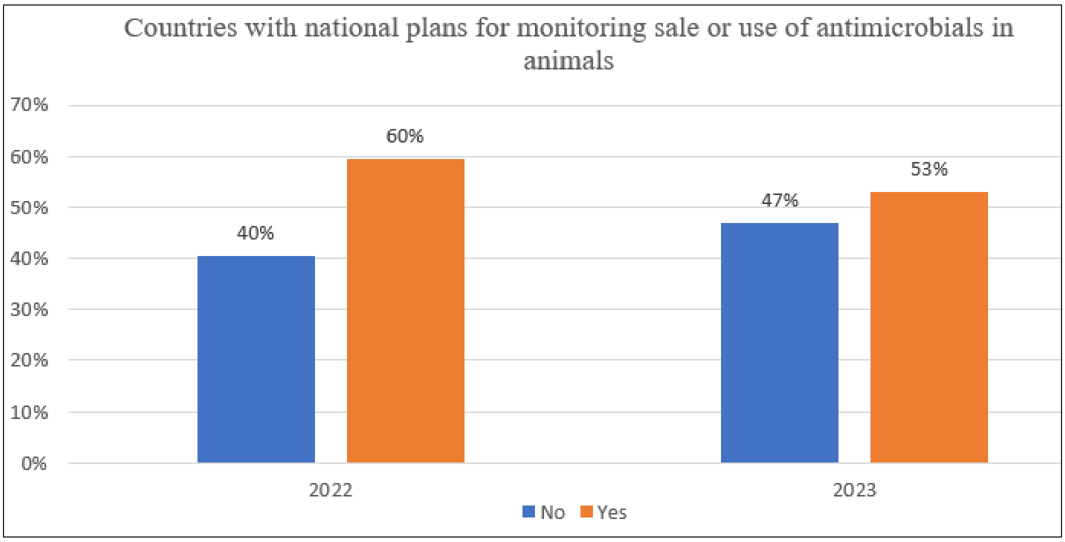

Fig 1: Status of African countries with national plans for monitoring sale or use of antimicrobials in animals

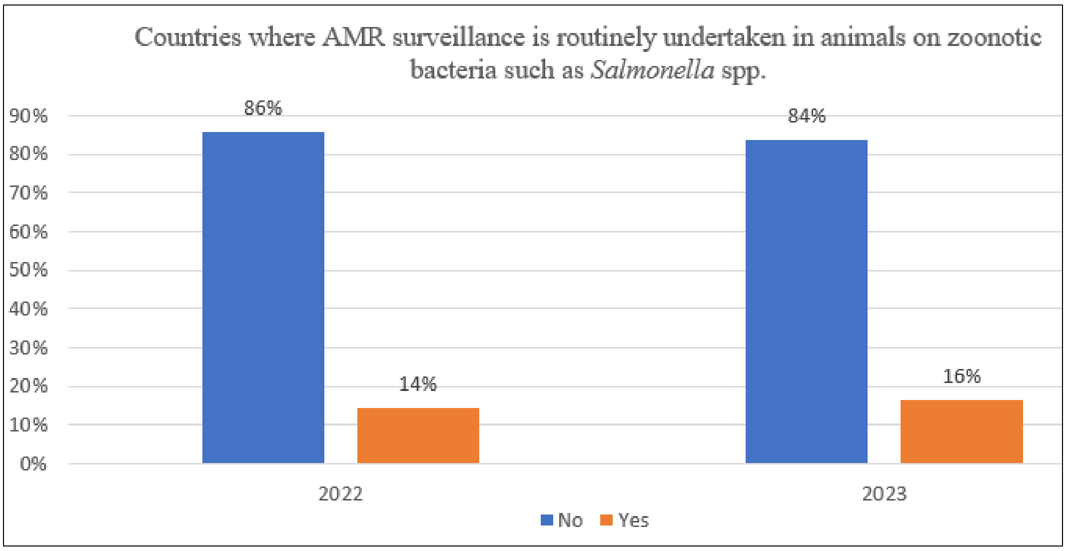

Fig 2: Status of African countries regarding routine AMR surveillance on zoonotic bacteria in animals

Table 1: Status of national surveillance systems for antimicrobial resistance in animals in African countries

Countries with national surveillance systems for antimicrobial resistance (AMR) in animals				
Year	**2022**		**2023**	
Status	**No.**	**%**	**No.**	**%**
A - There are no local or national strategies/plans for generating AMR surveillance data from animals for an AMR surveillance system.	9	19%	9	19%
B - National plan for AMR surveillance in place but laboratory and epidemiology capacities for generating, analysing and reporting data are lacking.	13	28%	13	27%
C - Some AMR data is collected at local levels but a nationally standardized approach is not used. National coordination and/or quality management is lacking.	18	38%	16	33%
D - Priority pathogenic/ commensal bacterial species have been identified for surveillance. Data systematically collected and reported on levels of resistance in at least one of those bacterial species in a reference laboratory	4	9%	7	15%
E - National system of AMR surveillance established for priority animal pathogens, zoonotic and commensal bacterial isolates	3	6%	3	6%
Grand Total	47	100%	48	100%

Table 2: Status of biosecurity and good animal husbandry practices in African countries for reducing the use of antimicrobials and minimizing the development and transmission of AMR in Animals

Countries with biosecurity and good animal husbandry practices to reduce the use of antimicrobials and minimize development and transmission of AMR in animals				
Year	**2022**		**2023**	
Status	**No.**	**Percentage**	**No.**	**Percentage**
A - No systematic efforts to improve good animal husbandry and biosecurity practices	3	6%	3	6%
B - Some activities in place to develop and promote good animal husbandry and biosecurity practices	29	62%	34	69%
C - National plan agreed to ensure good animal husbandry and biosecurity practices in line with international standards	14	30%	10	20%
D - Nationwide implementation of plan to ensure good animal husbandry and biosecurity practices and national guidance published and disseminated.	1	2%	2	4%
Grand Total	47	100%	49	100%

Conclusion

In conclusion**,** the increasing occurrence of antimicrobial resistance is a huge concern in various sectors, including human, animal, agriculture and environmental. Irrational use of antimicrobials in human and veterinary medicine and non-compliance with withdrawal periods is common. The use of antimicrobials without prescription constituted the most important risk factor for the emergence and spread of antimicrobial resistance. Lack of standardized testing protocols for AMR detection hindered efficient diagnosis. Challenges persist in integrated AMR surveillance and regulatory enforcement, emphasizing the need for implementation of One Health approach. In 2022, a total of 60% (28/47) of African countries did monitor consumption and sale antimicrobials in the animal sector. However, this declined to 53% (26/49) of African countries by 2023. Only 14% (7/49) African countries conducted routine AMR surveillance on zoonotic bacteria in animals by 2022 and only 16% (8/49) of the African countries did the same in 2023. Only 9% (4/47) of the African countries conducted surveillance to identify priority pathogenic or commensal bacterial species in animals in 2022 and only 15% (7/48) in 2023. Such countries were able to systematically collect and report data on antimicrobial resistance. Further still, only 6% (3/47) of African countries had national systems to implement surveillance on antimicrobial resistance for important animal pathogens and zoonotic diseases as well isolation of commensal bacterial in 2022. A similar proportion (6%-3/48) was reported in 2023.

Besides, only 2% (1/47) of African countries developed and disseminated national guidelines for animal husbandry and bio-security in 2022. Similarly, only 4% (2/49) did the same in 2023.

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