ANALYSIS OF POLICIES FOR USE OF MEDICALLY IMPORTANT ANTIBIOTICS IN ANIMALS IN NAMIBIA: IMPLICATIONS FOR ANTIMICROBIAL STEWARDSHIP

Jennifer Kaupitwa[1], Seth Nowaseb[2], Brian Godman[3,4,5], Dan Kibuule[1]*

[1]Department of Pharmacy Practice and Policy, School of Pharmacy, University of Namibia, Box 13301, Windhoek, Namibia.

[2]Department of Pharmaceutical Sciences, School of Pharmacy, University of Namibia, Box 13301, Bach Street, Windhoek, Namibia.

[3]Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow G4 0RE, United Kingdom.

[4]School of Pharmacy, Sefako Makgatho Health Sciences University, Pretoria, South Africa.

[5]School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia

Author of correspondence*

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ABSTRACT

Background: In Namibia, overuse of medically important antibiotics in animals is common and is a considerable driver of antimicrobial resistance. The study aims to analyze policies, resistance patterns and consumption of these antibiotics used in animals in Namibia. *Research design and methods:* A scoping review and retrospective descriptive analysis of policies, resistance patterns and use of these antibiotics in Namibia was conducted, and assessed against the AWaRe (Access, Watch and Reserve) antimicrobial use guidance. *Results*: Of the forty-five antibiotic products registered for use in animals, 77.8% are Access antibiotics, 68.9% are broad-spectrum and 60% are over-the-counter antibiotics– mainly tetracyclines, penicillins and sulfonamides. There is misalignment of antibiotic use policies for animals and humans and no guideline for antibiotic use in animals. Most medically important antibiotics are indicated for control of gastrointestinal (77.7%), musculoskeletal (71.1%) and respiratory (46.7%) infections, and for growth promotion (4.4%). There is high resistance to AWaRe Access antibiotics-sulfonamides (19.5%-100%), tetracyclines (56%-100%) and penicillin (13.5%-100%). *Conclusion:* Whilst Namibia banned the use of antibiotics in farming, current policy frameworks are inconsistent across sectors, and promote overuse of broad-spectrum important antibiotics in animals. A multi-sectoral one health approach is required to harmonize antibiotic use policies and reduce resistance.

Keywords: Antibiotics, antibiotic resistance, antimicrobial stewardship, AWaRe, Namibia, Policies, Veterinary medicine

1. INTRODUCTION

Livestock farming is a significant source of livelihood in sub-Saharan Africa; a region faced with the highest poverty rates, alongside a considerable burden of infectious diseases among animals and humans [1,2]. As a result, farmers in sub-Saharan Africa, routinely use antibiotics to promote animal growth, productivity and health [3–5]. However, the regulation of antibiotic use in animals and humans in most countries in sub-Saharan Africa is typically poor, and antibiotics are readily accessible in informal and licensed medicine outlets without a prescription [6–8]. For instance in Zambia, 100% of community pharmacists contacted sell antibiotics without a prescription with similar high rates among other African countries [9,10]. Alongside this, farmers often self-purchase and administer large volumes of medically important antibiotics (MIA, i.e. antibiotics with therapeutic uses in humans and animals) in animal feeds to prevent a wide-range of bacterial and parasitic infections [11–13], which includes Africa [3]. Published estimates suggest that 73% of antibiotics consumed globally are used in farming, with the greatest rise in consumption among low- and middle-income countries (LMIC), with rates expected to rise unless addressed [14,15]. The World Organization for Animal Health (OIE) identified overuse of MIA in animals as an important barrier to the realization of the Global Action Plan (GAP) against antimicrobial resistance (AMR) [13,16,17]. Currently, the highest consumers of antibiotics globally are China, Brazil, United States of America and India, mainly due their use in intensified farming to meet the increasing demand for food animal production [15,18].

As a strategy to regulate antibiotic use and promote antimicrobial stewardship (AMS), in 2017, the WHO categorized antibiotics into three groups; which were the Access, Watch and Reserve groups (AWaRe) [19–21]. Under the AWaRe classification, the Access group of antibiotics consists of essential antibiotics used as first-line treatments for common infections and they should be readily accessible at all times. Watch antibiotics are those with a high potential for resistance and should be used as second line regimens for selected infections. Reserve antibiotics should restricted for use in treating resistant bacteria [19,20,22]. Despite the AWaRe guidance, there are increasing reports on misuse of access antibiotics in animals in sub-Saharan Africa and Namibia, particularly sulfonamides, tetracyclines and macrolides in animals, which is of public health concern [23–26].These antibiotics are routinely used in farming to

prevent diarrhea caused by *Escherichia coli, Salmonella species* and *Coccidia, as* well as treating secondary bacterial infection during the course of shipping fever [27–29]. There is also increasing use of Watch and Reserve antibiotics in livestock farming across Africa, including beta-lactams, aminoglycosides, glycopeptides and fluoroquinolones [3,23,30]. The high consumption and use of particularly Watch and Reserve in animals has the potential to accelerate multidrug resistance to essential antibiotics and slow progress of actualization of national action plans (NAP) against AMR [23,31–33]. As a result, there is progress among African countries to restrict the use of particularly Reserve antibiotics as seen with colisitin, and such restrictions are likely to grow given increasing rates of AMR across Africa, with sub-Saharan Africa currently having the highest rate of AMR globally [34,35].

However, few studies in sub-Saharan Africa and Namibia have evaluated the appropriateness of antibiotic use policies particularly with regards to the use of MIA in animals, amidst the limited integration of veterinary and medical services in this region. This is a concern given that the development and implementation of NAP is a challenge in Namibia and in most countries in sub-Saharan Africa, [6,36–39]. In Namibia, whilst progress on antimicrobial stewardship (AMS) has been made in medical practice with national treatment guidelines (NTGs), Namibia Essential Medicine List (Nemlist) and monitoring of prescribing of antimicrobials in both ambulatory and hospital care against current guidelines [40–42], little is known in veterinary practice. This is important as there is good compliance to prescribing guidance of antibiotics among physicians in Namibia with the guidelines seen as robust and easy to use [41]. In addition, there is regular monitoring of community pharmacies in Namibia banning the purchasing of antibiotics for humans without a prescription, which appears to be working in practice [6,43].This is unlike the situation with guidelines in other African countries [44–48].

Consequently, the study aims to review and analyze policies, resistance patterns and use of MIA in animals in Namibia in order to identify gaps and provide guidance towards advancing a robust national program. This is in line with the Namibia NAP to reduce AMR.

2. METHODS

2.1 Design and setting

A scoping review and retrospective descriptive situation analysis of antibiotic use policies, resistance patterns and consumption of MIA in animals in Namibia was undertaken. The primary

outcome measure of the study was appropriateness of antibiotic use policies in animals with respect to alignment of antibiotic schedule across the veterinary and medical sectors, antibiotic indications in food animals, restriction of use of Watch and Reserve list of AWaRe antibiotics, and animal disease indication(s) for MIA. The secondary outcomes were to estimate the resistance and consumption rates of MIA in Namibia. Lastly, the study described the product characteristics and disease indications of MIA used in animals in Namibia.

2.2 Search strategy

Three search strategies were respectively applied to identify published articles, reports and documents on antibiotic use policies, resistance patterns and consumption of MIA in Namibia. The respective key search terms for the policy analysis, resistance patterns and antibiotic consumption were; “antibiotic, policy, Namibia”, “antibiotic, resistance, Namibia”, and “antibiotic, consumption and Namibia”. These were subsequently combined with their synonyms using Boolean operators, and applied in search engines. The primary search engines were PubMed and Scopus. Google scholar with African journals online were used as the secondary search engines. Consequently, a search of gray literature was performed through repositories and websites of universities and libraries in Namibia and South Africa. In addition, antibiotic use policy documents were obtained from focal persons at government ministries and the medicine regulatory authority by means of a snow balling approach. The titles and abstracts of the documents were subsequently screened for relevancy using a PICO (population, intervention, comparator, and outcomes) approach.

2.2 Analysis of policy indications for use of medically important antibiotics in animals

2.2.1 Population and sample

The target population were published policy documents, gazettes, documents and guidelines pertaining to the use of antibiotics in animals in Namibia. The search strategy yielded six documents of which three key reference documents, i.e. Medicine and Related Substance Act, the national medicine policy and veterinary medicine register, were included in the review and analysis [49–51]. In Namibia, medicines used in human and animals are regulated by the Medicines and Related Substances Act, 2003 [51]. The National Medicine Policy on the other hand provides a framework for equitable access to quality, efficacious and safe medicines [52,53]. The veterinary and human medicine registers guide the sale of antibiotics in Namibia and indicate the medicines currently available for use in the country [49]. In addition, the study reviewed the Namibia Essential Medicine List (Nemlist) and National Standard Treatment

guideline (NSTG), to validate that the MIA registered for use in animals are also indicated and recommended for human use [40,41]. Only approved and up-to-date policy documents available at the respective line ministries during the study period, i.e. June – July 2020, were included in the analysis. Outdated policies and the Animal Health Act were excluded from the policy analysis given the timelines of the study and Animal Health focuses on surveillance and control of diseases in animals in Namibia [54].

2.2.2 Procedure

In addition to the search strategy, up-to-date policy documents were obtained from the line ministries including the Ministry of Agriculture Forestry and Water (MoFAW), Ministry of Health and Social Services (MoHSS) and the Namibia Medicines Regulatory Council (NMRC). Subsequently, a list of MIA used in animals in Namibia was generated from the veterinary medicine register in comparison to categorization of MIA by the Food and Drug Administration (FDA) and OIE [16,17].Thereafter, data on the appropriateness and policy indications including medicine scheduling, AWaRe categorization, and indications for use in food animals as well as product characteristics were abstracted from the three reference documents using a standardized tool (Appendix A). The tool was piloted and face-validated by a veterinarian and a pharmacist for completeness and fitness for purpose. In Namibia, medicines are categorized into six schedules (Namibia Schedule, NS0 to NS5), and antibiotics used in animals fall in three categories; NS0 (open market), NS1 (over-the-counter) and NS2 (prescription). The product characteristics included the year of registration, generic name, scheduling status, as well as the AWaRe, pharmacological and WHO Anatomical Therapeutic Classification (ATC) [55]. The WHO ATC system classifies medicines into five levels based on their active pharmaceutical ingredients, with anti-infective included in group J, of which antibiotics are in subgroup J01 [55]. In addition, data on dosage formulation and route of administration, routes of administration, manufacturer, and disease indication were abstracted.

2.3 Analysis of resistance patterns of medically important antibiotics used in animals

2.3.1 Population

The target population were published articles on resistance or susceptibility patterns of MIA used in animals in Namibia. The study only included articles that reported resistance and/or susceptibility patterns to the ATC classes of MIA identified in the policy analysis to pathogenic bacteria known to cause human and bacterial diseases. The main outcome measure was the percentage of bacterial isolates that were resistant to a specific antibiotic. The accessible

population were articles published before 2022, and in English, among journal articles, reports and academic dissertations.

2.3.2 Procedure

A systematic review of resistance patterns of MIA identified in the policy analysis was conducted based on published articles, reports and academic dissertations. The search strategy applied key terms, i.e. “antibiotic OR specific generic name of the antibiotic”, “resistance OR sensitivity” and Namibia”, combined with their synonyms by use of Boolean operators in three search engines, PubMed, Scopus and Google Scholar. Gray literature was searched from the national library as well as repositories of the Universities of Namibia (UNAM) and, Namibia University of Science and Technology (NUST). The search was limited to Namibia, articles written in English, which is the recognized the national language of Namibia and antibiotic resistance involving classes of MIA identified in the policy analysis. Bibliographies of selected papers were searched to identify additional articles. The search returned a total 27 articles, reports and academic dissertations, which were screened for relevancy to the study, and quality. After screening titles and abstracts of the articles for relevancy based on the PICO (population, intervention, comparator and outcome), Nine (9) articles were excluded due to antimicrobial susceptibility testing did not apply to MIA or the study reported general susceptibility rates to an antibiotic across several isolates rather than specific types of bacteria. For instance, Mohulatsi, 2016 only reported the overall susceptibility rates of the antibiotics to all bacterial isolates rather than specific bacteria[56]. We also excluded articles that conducted antimicrobial testing that does not conform to the Clinical and Laboratory Standards Institute (CLSI) and the European Committee for Antimicrobial Susceptibility Testing (EUCAST)recommendations. Consequently, 18 studies were included in the review and the resistance patterns were described as a percentage (%) for each MIA for a specific bacterial isolate.

2.4 **Consumption of medically important animal antibiotics in Namibia**

2.4.1 Population

The target population were published articles regarding the consumption or use of antibiotics in Namibia. We include articles that reported antibiotic consumption rates in Daily Defined Doses (DDD) per inhabitant per day (DIDs), as per the WHO ATC/DDD recommendations. DIDs are recognized internationally for helping to compare utilization patterns across countries.[57–60] We included papers that reported antibiotic use with regards to WHO/INRUD (international network for rational use of medicines) indicator, i.e., the number of outpatient prescriptions with

an antibiotic [38]The study was limited to studies conducted in the public and private sectors in Namibia as well as among animals.

2.4.2 *Procedure*

A scoping review of antibiotic consumption in Namibia was conducted based on published articles and reports. The search strategy applied key terms, i.e. “antibiotic”, “consumption” and Namibia”, combined with their synonyms by use of Boolean operators in three search engines, as described above. The search returned 16 studies of which thirteen met the screening criteria for relevancy; and among these two articles estimated antibiotic consumption in the public and private sectors and eleven articles reported on antibiotic prescribing indicators or compliance to antibiotic guidelines. We excluded qualitative studies that did not quantify consumption or use as DIDs or prescriptions with an antibiotic.

2.4 Data analysis

Data on the appropriateness of antibiotic use policies, resistance patterns and consumption of MIA were entered in Epidata® V3.1 for management and exported to SPSS v25 for quantitative descriptive analysis. The appropriateness of antibiotic use policies were determined using descriptive statistics to include; percentage (%) of schedule NS0 and NS1 (i.e. non-prescription antibiotics), percentage (%) of antibiotic schedules aligned in the veterinary and human medicine registers, % of antibiotics indicated for use in food animals, and % of MIA in the AWaRe Watch or Reserve categories. Consequently, for each MIA identified in the policy analysis, resistance patterns were reported as percentages (%) of bacterial isolates resistant to a specific antibiotic per study. A range of the percentage resistance rate was then reported for each MIA. In this study, resistance rates were categorized as very low (0 to10%), low (11 to 30%), moderate (30–50%) and high (>50%). Lastly, as mentioned, antibiotic consumption rates were reported in DDDs per inhabitant per day (DID), and use as percentage of prescriptions with an antibiotic. In this study, we considered antibiotic consumption rates greater than 22.38 DIDs as high consumers as per the European Surveillance of Antimicrobial Consumption (ESAC) classification 2010[57]. 16.7 DID, and between 16.7-22.38 DID, were regarded as low and moderate consumers of antibiotics. The rate of use of antibiotics was determined by the percentage of prescriptions with an antibiotic, with the accepted target of < 25% in Namibia, lower than the WHO target of <30%[38,42]In addition, we used the compliance to guidelines as an indicator for use of antibiotics in Namibia building on previous studies[42,61]In this scoping

descriptive study, we were unable to make inferences between the appropriateness of antibiotic use policies, antibiotic consumption and resistance patterns in Namibia.

2.5 Ethics

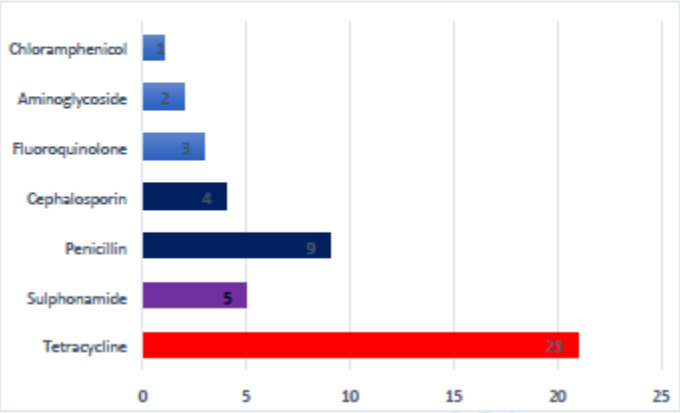
Ethical approval was obtained from the University of Namibia, School of Pharmacy and Ministry of Health and Social Services (MOHSS) research and ethics committees. The study utilized secondary data in policy-documents and published articles, and did not directly deal with persons; consequently, the need for consent was waived. No personal data of reference persons at the line ministries we collected. In addition, brand names, distributors and manufacture of medicines were not included in the analysis. In line with the ATC classification, only the international non-proprietary name (INN) of antibiotics was included.

3. RESULTS

3.1 Characteristics of medically important antibiotics used in animals in Namibia

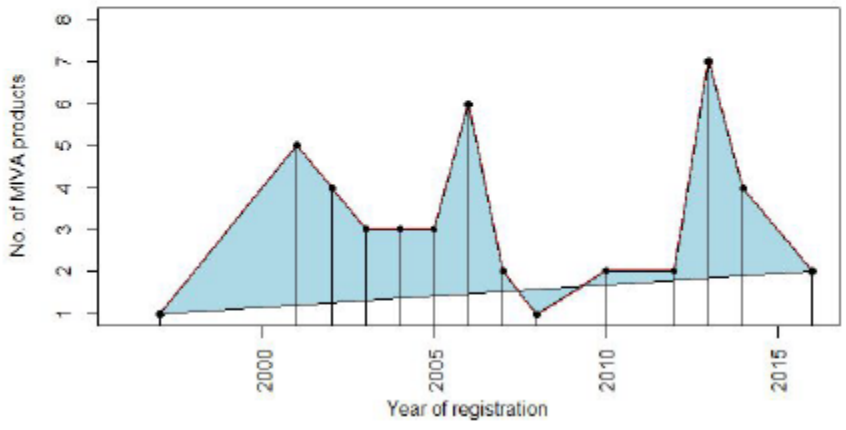
Of the 45 MIA products registered for use in animals in Namibia; 77.8% are of the AWaRe Access category, i.e. first line antibiotics used to treat common infections in humans, mainly tetracyclines, penicillins or sulfonamides (Figure 1), 75% are fixed dose combinations (FDCs), 68.9% are broad spectrum, and all are imported multiple-source products from South Africa (Table 1). With regards to WHO/ATC classification, antibiotic use policies mainly indicated J01A (tetracyclines), J01E (sulfonamides/ trimethoprim) and J01C (penicillins) MIA for use in animals. The ratio of bacteriostatic to bactericidal MIA registered for use in animals in Namibia was 3: 2 (i.e. 27 versus 18). The majority of MIA registered in Namibia are parenteral solutions for treating mastitis and systemic infections (56%) or oral premixes (29%) used as feed additives for growth promotion or control of infections (Figure 2). Other formulations of MIA included oral pastes, topical antibiotics and pessaries.

Figure 1: Classes of medically important antibiotics registered in Namibia *(originally created)*



Of the 45 MIA, 13(28.9%) were registered for use in animals prior to the enactment of the Medicines and Related Substance Act in 2003, and included tetracyclines (n=7/13), penicillins (n=3/13), sulfonamides (n=3/13). The majority of newer antibiotics, i.e. fluoroquinolones, cephalosporins and aminoglycosides, were registered for use in animals after the enactment of the Act (Figure 1 and 2).

Figure 2: Trends in registration of medically important antibiotic used in Animals in Namibia *(originally created)*



3.2 Appropriateness of antibiotic use polices with regards to use of MIA in Namibia

Of the 45 MIA products registered in Namibia, the majority (60%) are schedules as open market medicines (NS0) and can be sold by any person without the need of a prescription and

licensing regulations, or as Over-The-Counter medicines (OTC, NS1) that can be self-purchased without a prescription as in the case of human antibiotics [41] (Table 2).

Table 1: Medically important veterinary antibiotics used in Namibia (n=45) (originally created)

Antibiotic	AWaRe Classes	Products registered (%)	Label indications of medically important antibiotics
Oxytetracycline*	Access	15(33.3)	**Food animals:** Indicated for food animals (100%, n=15) **Indication:** treatment of secondary bacterial infections; pasteurella, gastroenteritis, scours, respiratory tract infection, urinary tract infection, pneumonia
Cloxacillin/Ampicillin	Access	4(8.9)	**Food animals:** Indicated for food animals (100%, n=4) **Indications:** Mastitis, abscesses, enteritis, septicemia, chronic wounds
Trimethoprim/Sulphamethoxazole*	Access	3(6.7)	**Food animals:** Indicated for food animals (100%, n=3) **Indication:** Mastitis, foot rot, wound infections, phlegmons, cholera
Doxycycline*	Access	3(6.7)	**Growth promotion:** pigs and poultry (33%, n=1/3) **Indication:** Pyoderma, folliculitis, respiratory infections
Cephalexin	Access	3(6.7)	**Indication:** Cutaneous infections (folliculitis, furunculosis, cellulitis)
Procaine Benzylpenicillin	Access	3(6.7)	**Indication:** Metritis, mastitis, tetanus, blackleg
Milbemycin oxime/ Praziquantel	Other	2(4.4)	**Indication:** Hookworms, roundworms, tapeworms
Salinomycin	Other	2(4.4)	**Growth promotion:** pigs, beef cattle
Chlortetracycline*	Access	1(2.2)	**Indication:** Prevention of wound infections, dermatitis, claw/hoof infections
Na-Sulfadimethoxine*	Access	1(2.2)	**Indication:** Pneumonia, calf diphtheria, foot rot, shipping fever complex
Cefquinome sulphate*	Watch	1(2.2)	**Indication:** Mastitis, bulbar necrosis, dermatitis, septicaemia, interdigital necrobacillos
Enrofloxacin*®	Watch	1(2.2)	**Indication:** Skin infections and soft tissue, urinary tract infections in dogs and cats.
Donofloxacin Mesylate*®	Watch	1(2.2)	**Indication:** Respiratory disease by *(Pasteurella haemolytica and P.multocida)*. enteric infections by *E. coli* and *Salmonella spp*.
Gentamycin Sulphate*	Watch	1(2.2)	**Indication:** Arthritis, wound infections, septicaemia, omphalitis, otitis
Kanamycin*	Watch	1(2.2)	**Indication:** Bacterial diarrhea,
Cephalexin/neomycin	Access	1(2.2)	**Indication:** Pneumonia, urinary tract, infections of (ear, skin, bone)
Chloramphenicol*®	Access	1(2.2)	**Indication:** Skin infections, wound infections, bone infections, pneumonia
Sulphadimidine*	Access	1(2.2)	**Indication:** Inflammatory bowel disease, vasculitis
Amoxicillin/Clavulanic acid	Access	1(2.2)	**Indication:** Skin infections, enteritis, respiratory infections, UTI
Marbofloxacin*®	Watch	1(2.2)	**Indications:** lactating dairy cattle, and pigs. Treatment of respiratory diseases, Mastitis Metritis

*=Broad spectrum antibiotics, ® = restricted for use in food producing animals

There are inconsistencies in scheduling of MIA in the human and veterinary medicine registers of Namibia; with 65.9% (n=27/41) of the antibiotics not aligned by schedule. Over 95% (n=43/45) of the MIA used in animals are registered for use in humans as prescription only medicines (95.3%, n=41/43), i.e. medicines that cannot be dispensed without a prescription order from a licensed doctor or veterinarian with laws in Namibia (Table 2). In addition, whilst Namibia has a Nemlist and NSTGs guide use of antibiotics in humans, there is neither for animals (Table 2). In human practice, 26.7% (n=12/45) of the MIA are to be used as prescription only medicines at all levels of care including, primary healthcare clinics and health centers as well as hospitals by qualified healthcare workers; these are categorized as ABC medicines in the Nemlist (Table 2).

Policies indicate six of the AWaRe Watch antibiotics (13.3%, n=6/45) for use in animals. This is a concern as Watch antibiotics have a high potential for resistance development.

Most of the MIA products registered in Namibia are indicated for use in food animals (95.6%, n=43/45) and 7.5% (n=3/45) are restricted by OIE for use in food animals. The main policy indications for use of MIA in animals in Namibia include the prevention and/or treatment of gastrointestinal infections (77.7%, n=35/45), respiratory infections (46.7%, n=21/45) and mastitis (71.1%, n=32/45). In addition, some MIA are indicated for animal growth promotion (4.4%, n=2/45).

Table 2: Medically important veterinary antibiotics used in Namibia (n=45) (originally created)

Antibiotic	AWaRe Classes	Products registered (%)	Label indications of medically important antibiotics
Oxytetracycline*	Access	15(33.3)	**Food animals:** Indicated for food animals (100%, n=15) **Indication:** treatment of secondary bacterial infections; pasteurella, gastroenteritis, scours, respiratory tract infection, urinary tract infection, pneumonia
Cloxacillin/Ampicillin	Access	4(8.9)	**Food animals:** Indicated for food animals (100%, n=4) **Indications:** Mastitis, abscesses, enteritis, septicemia, chronic wounds
Trimethoprim/Sulphamethoxazole*	Access	3(6.7)	**Food animals:** Indicated for food animals (100%, n=3) **Indication:** Mastitis, foot rot, wound infections, phlegmons, cholera
Doxycycline*	Access	3(6.7)	**Growth promotion:** pigs and poultry (33%, n=1/3) **Indication:** Pyoderma, folliculitis, respiratory infections
Cephalexin	Access	3(6.7)	**Indication:** Cutaneous infections (folliculitis, furunculosis, cellulitis)
Procaine Benzylpenicillin	Access	3(6.7)	**Indication:** Metritis, mastitis, tetanus, blackleg
Milbemycin oxime/ Praziquantel	Other	2(4.4)	**Indication:** Hookworms, roundworms, tapeworms
Salinomycin	Other	2(4.4)	**Growth promotion:** pigs, beef cattle
Chlortetracycline*	Access	1(2.2)	**Indication:** Prevention of wound infections, dermatitis, claw/hoof infections
Na-Sulfadimethoxine*	Access	1(2.2)	**Indication:** Pneumonia, calf diphtheria, foot rot, shipping fever complex
Cefquinome sulphate*	Watch	1(2.2)	**Indication:** Mastitis, bulbar necrosis, dermatitis, septicaemia, interdigital necrobacillos
Enrofloxacin*®	Watch	1(2.2)	**Indication:** Skin infections and soft tissue, urinary tract infections in dogs and cats.
Donofloxacin Mesylate*®	Watch	1(2.2)	**Indication:** Respiratory disease by *(Pasteurella haemolytica and P.multocida)*. enteric infections by *E. coli* and *Salmonella spp*.
Gentamycin Sulphate*	Watch	1(2.2)	**Indication:** Arthritis, wound infections, septicaemia, omphalitis, otitis
Kanamycin*	Watch	1(2.2)	**Indication:** Bacterial diarrhea,
Cephalexin/neomycin	Access	1(2.2)	**Indication:** Pneumonia, urinary tract, infections of (ear, skin, bone)
Chloramphenicol*®	Access	1(2.2)	**Indication:** Skin infections, wound infections, bone infections, pneumonia
Sulphadimidine*	Access	1(2.2)	**Indication:** Inflammatory bowel disease, vasculitis
Amoxicillin/Clavulanic acid	Access	1(2.2)	**Indication:** Skin infections, enteritis, respiratory infections, UTI
Marbofloxacin*®	Watch	1(2.2)	**Indications:** lactating dairy cattle, and pigs. Treatment of respiratory diseases, Mastitis Metritis

Source: original , *=Broad spectrum antibiotics, ® = restricted for use in food producing animals

3.3 Resistance patterns of medically important antibiotic used in animals in Namibia

There are high resistance rates (>50%) among a wide range of gram negative and positive bacteria isolates to most AWaRe Access antibiotics in Namibia – particularly tetracyclines, sulfonamides and penicillins (Table 3). The resistance rates are considerably higher among sulfonamides compared to penicillins and tetracyclines **(Table 3)**. On the other hand, most bacterial isolates from the GIT are susceptible to newer antibiotics of the AWaRe Watch antibiotics including the fluoroquinolones and cephalosporins **(Table 3)**. The resistance rates were higher among bacterial isolates from the genitourinary system than respiratory and mucocutaneous sources.

Antibiotic resistance rates for tetracycline ranged from 8.6% to 100%, with highest rates observed among isolates of group A and B *streptococcus*, mainly from the urogenital tracts, as well as with *Haemophilus influenzae* from cerebral spinal fluid. Low resistance rates for tetracycline were observed among isolates from the nasal cavity and cerebral spinal fluid (CSF) of humans as well as *salmonella* isolates from animal feeds and beef (Table 3).

Antibiotic resistance rates against penicillins were high and ranged from 31.4% to 100%; with higher resistance rates among gram negative bacteria from the urogenital system, CSF and respiratory system. Most staphylococcus isolates were resistant to penicillins. Moreover, there was very high rates of resistance to benzyl penicillin, amoxicillin and ampicillin across gram negative and positive bacterial isolates (Table 3).

Very high resistance to sulfonamide/trimethoprim combinations was observed across a wide range of pathogens isolated from humans, but low resistance to *salmonella* obtained from animal feeds and beef (Table 3). There was also high resistance to chloramphenicol among common gram negative and positive isolates, except for *enterococcus*

From the six studies, except for extended spectrum beta-lactamase (ESBL) *Klebsiella*, most gram negative and positive bacteria isolates showed good susceptibility and the least resistance to second and third generation cephalosporins (Table 3). The review also showed high susceptibility rates of isolates to fluoroquinolones and aminoglycosides except with nalidixic acid against *Escherichia coli*, and gentamicin against *enterococcus faecalis* and *staphylococcus epidermidis.*

Table 3: Resistance patterns of medically important antibiotic in Namibia (Key: High resistance ■, Moderate resistance ■, Sensitive ■)

Antibiotic class	Bacterial Isolate	Source	No. of Isolates	Antibiotic: Resistance rate (%)
Tetracyclines	*Streptococcus (Group B)*	Vaginal	117	Tetracycline: 94.8% (Khan, 2016)[62]
			18	Tetracycline: 100% (Haimbodi et al, 2021)[63]; (Haimbodi et al, 2016, CSF n=1)[64]
			12	Tetracycline: 100% (Haimbodi et al, 2021)[63] ; 100% (Festus 2020)[65]
	Streptococcus (Group A)	Vaginal	15	Tetracycline:100% (Vries, 2019)[66]
	Streptococcus	CSF	206	Tetracycline: 13.4% (Mengistu, 2013)[67]
	Streptococcus pneumoniae	CSF	18	Tetracycline: (16.6%) (Haimbodi, 2016)[64]
	Haemophilus influenzae	CSF	2	50% (Haimbodi et al, 2016)[64]
	Staphylococcus aureus	Nasal	352	Tetracycline: 17% (Walter et al, 2020)[68]
		Mixed	600	Tetracycline: 17.4% (lileka et al, 2016)[69]
	Staphylococcus aureus (Coagulase negative)	Nasal	81	Tetracycline: 8.6% (Walter et al, 2020)[68]
	Salmonella serovas	Animal feed	71	Tetracycline: 19.7% (Shilangale, 2012)[70]
		Beef	81	Tetracycline: 3.7% (Shilangale, 2016)[71]
Penicillins	*Streptococcus (group B)*	Vaginal	117	Ampicillin and Benzylpenicillin: 0% (Khan, 2016)[62];
		Urinary	12	Ampicillin and penicillin: 0% (Haimbodi et al, 2021)[63]
	Streptococcus	CSF	170 153 24	Benzylpenicillin: 34.3% (Mengistu, 2013)[67] Oxacillin: 45.1% (Mengistu, 2013)[67] Amoxicillin: 25.0% (Mengistu, 2013)[67]
	Streptococcus pneumoniae	CSF	18	Benzylpenicillin: 70.5% (Haimbodi, 2016)[64]
	Streptococcus (Group A)	Vaginal	15	Benzylpenicillin: 66.7% (Vries, 2019)[66]
	Staphylococcus aureus	CSF Mixed Nasal Mixed	14 600 81 3727	Amoxicillin: 78.6% [68,72] Methicillin:13.5% resistance (lileka et al, 2016)[69] Methicillin: 17.6% (Walter et al., 2020)[68] Methicillin: 13.6% (Festus, et al, 2016)[65]
		Nasal	352	Ampicillin: 96%(Walter et al, 2020)[68]

		mixed	600	Penicillin: 92.4% ; Cloxacillin:13.5% (lileka et al, 2016)[69]
	Staphylococcus aureus (Coagulase negative)	Nasal	81 81	Ampicillin: 66.7% (Walter et al, 2020)[68] Methicillin: 8.6% (Walter et al, 2020)[68]
	Escherichia coli	Urinary	3865 3865 2659 18 668	Amoxicillin: 77% [72]; *78.7% (Jatileni, et al 2015)*[73] ; Oxacillin: 75% and piperacillin:100% (Jatileni, et al 2015)[73] Ampicillin: 77.7% (Haindongo et al, 2022)[74] Amoxicillin: 79.6% (Mengistu et al, 2014)[75]
		Vaginal	31	Ampicillin: 72.2% ; Piperacillin/tazobactam: 2.7%; (n=31), (Nangolo et al, 2018)[76]
		CSF	22	Amoxicillin: 86.4% [68,72]
	Klebsiella pneumoniae	Urinary	390	Ampicillin: 84.9% (Haindongo et al, 2022) [74]
	Klebsiella	Urinary	3226	Amoxicillin: 96.7% (Mengistu et al, 2014)[75]
	Klebsiella ESBL	CSF	7	Amoxicillin: 100% (Mengistu et al, 2013)[67]
		Urinary	390	Ampicillin: 31.4% (Haindongo et al, 2022)[74]
	Proteus marabilis	Urinary	3520	Amoxicillin: 55.9%% (Mengistu et al, 2014)[75] Amoxicillin: 50.3% (Haindongo et al, 2022)[74]
	Vibrio cholerae			0% resistance to ampicillin, amoxicillin /clavulanic acid[77]
	Neisseria meningitidis	CSF	107 2	Penicillin: 15.2% (Mengistu, *et al* 2013)[67]. Penicillin: 0% (Haimbodi, 2016)[64]
Cephalosporins	*Streptococcus agalactiae*	Vaginal	18	Ceftriaxone: 0% (Haimbodi, 2021)[63]
	Streptococcus pneumoniae	CSF	206	Ceftriaxone: 2.2% (Mengistu et al, 2013)[67] Ceftriaxone: 0% (Haimbodi, 2016)[64]
	Staphylococcus aureus	CSF	76	Cefuroxime: 40% (Mengistu et al, 2013)
		Nasal	352	Cefoxitin: 14.5% (Walter et al, 2020)[68]
	Staphylococcus aureus (Coagulase negative)	Nasal	81	Cefoxitin: 8.6% (Walter et al, 2020)[68]
	Escherichia coli	Urinary	18 668	Cephalothin: 33%% (Mengistu et al, 2014)[75]
		Vaginal	31 31	Ciprofloxacin: 2.7% (Nangolo et al, 2018)[76] Nalidixic acid: 2.8% (Nangolo et al, 2018)[76]
		Vaginal	31	Cefuroxime, cefoxitin & ceftazidime: 0% (Nangolo et al, 2018)[76]
	ESBL Klebsiella pneumoniae	CSF	7	Ceftriaxone: 100% (Mengistu, 2013)[67]

	Klebsiella pneumoniae	CSF	7	Ceftriaxone: 28.6% (Mengistu, 2013)[67]
	Vibrio Cholerae	Stool	9	ceftriaxone and ceftazidime: 0% (smith et al. 2008)[77]
	Neisseria gonorrhea	STI	598	Ceftriaxone: 0% (Tobias, et al 2007)[78]
	Haemophilus influenzae	CSF	59 4	Cefuroxime: 25% (Mengistu, 2013)[67] Ceftriaxone: 0% (Haimbodi, 2016)[64]
	Neisseria meningitidis	CSF	3	Ceftriaxone: 0% (Haimbodi, 2016)[64]
Chloramphenicol	*Streptococcus*	CSF	171	Chloramphenicol: 5.3%[67]
	Streptococcus pyogenes	Vaginal	40	Chloramphenicol: 0.9%[63]
	Enterococcus species	Mixed	706	Chloramphenicol: 75% (Jatileni, *et al,* 2015)[73]
	Escherichia coli	CSF	6	Chloramphenicol: 0% (Mengistu, 2013)[67]
	Escherichia coli	Mixed	nd	Chloramphenicol: 82% (Mohulatsi, 2016)
	Haemophilus influenzae	CSF	4 55	Chloramphenicol: 0% (Haimbodi, 2016)[64] Chloramphenicol: 10.9% (Mengistu, 2013)[67]
	Vibrio Cholerae	Stool	9	Chloramphenicol: 0% (Smith et al. 2008)[77]
	Neisseria meningitidis	CSF	2 102	Chloramphenicol: 0% (Haimbodi, 2016)[64] Chloramphenicol: 2.9% (Mengistu, 2013)[67]
Trimethoprim/ Sulfamethoxazole*	*Staphylococcus aureus*	Mixed	600	Cotrimoxazole: 44.9% (lileka, 2012)
	Streptococcus pneumoniae	CSF	16	Cotrimoxazole: 93.7% (Haimbodi, 2016)[64]
	Streptococcus (Group B)	Antenatal	117	Cotrimoxazole: 6% (Khan, 2016)[62]
	Escherichia coli	Vaginal	31	Trimethoprim /Sulfamethoxazole: 61.1% (Nangolo et al, 2018)[76]
		Urinary	3865	Cotrimoxazole: 78.8% *(Jatileni, et al 2015)*[73]
		mixed	1336	sulfamethoxazole-trimethoprim: 77.2% (Haindongo, 2022)[74]
	Klebsiella pneumoniae	mixed	229	sulfamethoxazole-trimethoprim: 60.8% (Haindongo, 2022)[74]
	Vibrio Cholerae	stool	9	Trimethoprim and sulfamethoxazole: 100% (Smith, 2008)[77]
	Haemophilus influenzae	CSF	18	Cotrimoxazole: 66% (Haimbodi, 2016)[64]
	Neisseria meningitidis	CSF	2 107	Cotrimoxazole: 100% (Haimbodi, 2016)[64] Cotrimoxazole: 100% (Mengistu, *et al* 2013)[67]

	Staphylococcus epidermidis	Urinary	569	Gentamicin: 53.9% (Jatileni et al, 2019)[73]

	Proteus mirabilis	mixed	118	sulfamethoxazole-trimethoprim: 58.5% (Haindongo, 2022)[74]
	Salmonella serovas	Beef	81	Cotrimoxazole and sulfisoxazole: 12.4% (Shilangale, 2016)[71]
	Salmonella serovas	Animal feed	71	Cotrimoxazole and sulfisoxazole: 19.7% (Shilangale, 2012)[70]
Fluoroquinolones	*Staphylococcus aureus*	Mixed CSF	600 36	Ciprofloxacin: 4.4% (Iileka, 2016)[69] Ciprofloxacin: 19% (Mengistu, 2013)[67]
		mixed	600	Ciprofloxacin: 4.4% (Iileka et al, 2016)[69]
	Vibrio Cholerae	stool	9	Nalidixic acid and ciprofloxacin: 0% (Smith, 2007)[77]
	Neisseria gonorrhae	STI	118	Ciprofloxacin: 24% (Tobias, et al, 20011[78]
	Streptococcus pneumoniae	CSF	18	Ciprofloxacin: 0% (Haimbodi, 2016)[64] ; 0% (Mengistu, 2013)[67]
	Escherichia coli	CSF	18 668	Nalidixic acid: 33%% (Mengistu et al, 2014)[75]
		Mixed Mixed	982 1744	Ciprofloxacin: 16.3% (Haindongo, 2022)[74] Nalidixic acid: 38.5% (Haindongo, 2022)[74]
	Enterococcus	CSF	9	Ciprofloxacin: 33% (Mengistu, 2013)[67]
	Klebsiella pneumoniae	Mixed Mixed	114 267	Ciprofloxacin: 14.9% (Haindongo, 2022)[74] Nalidixic acid: 21.7% (Haindongo, 2022)[74]
Aminoglycosides	*Staphylococcus aureus*	Nasal CSF	352 17	Gentamicin: 6.8% (Walter, 2020)[68] Gentamicin: 52.9% (Mengistu, 2013)[67]
	Staphylococcus aureus (coagulase negative)	Nasal	81	Gentamicin: 11.1% (Walter, 2020)[68]
	Salmonella	Animal feeds	71	Streptomycin: 19.7% (Shilangale, 2012)[70]
		Animal feeds	178	Gentamicin and kanamycin: 0% (Shilangale, 2016[71]
	Vibrio Cholerae	Stool	9	Streptomycin: 100% (Smith et al, 2008)[77]
	ESBL Klebsiella pneumoniae	CSF	7	Amikacin: 14.3 (Mengistu, 2013)[67]
	Klebsiella pneumoniae	CSF	7	Gentamicin: 16.7 (Mengistu, 2013)[67]
	Escherichia coli	CSF	22	Gentamicin: 17.7 (Mengistu, 2013)[67]
	Enterococcus faecalis	Urinary	706 706	Gentamicin: 66.7% (Jatileni et al, 2019)[73] Amikaicin: 78.3% (Jatileni et al, 2019)[73]

3.4 Antibiotic use and consumption in Namibia

There is limited data on antibiotic consumption and use in Namibia. Two studies have reported on the consumption of antibiotics in Namibia, and both reported high and rising trends in the consumption of antibiotics in both the public and private sectors. On average, the antibiotic consumption rate in the public and private sectors were estimated at 41.8 and 27 DID respectively, and were higher than global target of less than 22.38 DID recommended by European Surveillance of Antimicrobial Consumption (ESAC)**.** Data from the private and public sector indicate high consumption of broad spectrum antibiotics in Namibia, with cephalosporins and penicillins and macrolides the most consumed in the private sector, while sulfonamides and penicillins are the most consumed in the public sector **(Table 4).**

Several studies conducted in the public sector indicate high rates of antibiotic prescribing in outpatient departments, (>25% of prescriptions with an antibiotic) as high as 78%, and also high self-purchasing of antibiotics for animal but not human use in recent years. Recent published studies in Namibia have shown limited or no self-purchasing of antibiotics with community

pharmacists well aware of the regulations in Namibia [43,79]. This is different to the findings of Pereko *et al* (2015) which showed that 15% of respondents had self-purchased antibiotics (Ref), potential reflecting greater awareness of the regulations among community pharmacists as well as greater monitoring of their behaviour. In addition, there has been sub-optimal compliance to antibiotic treatment guidelines by prescribers, attributed to limited access to guidelines and/or lack of data on susceptibility of pathogens[80]. However, other studies have shown generally good compliance to guidelines in Namibia [40,42].We are not sure of the reasons behind these differences, and may be attributed to variation in implementation of guidelines[81]. In addition, there has been wide spread self-diagnosis and treatment of animal diseases with antibiotics among farmers in Namiba, particularly with oxytetracycline and sulfonamides **(Table 4).**

Table 4: Consumption and use of Medically important antibiotics in animals

Antibiotic Consumption	**Study**	**Rate**	**Antibiotic consumption DID (DDD per 1000 inhabitants per day)** (Consumption rate: ■ High (>22.38 DID), Moderate ■, Low ■)
Public *(Based on distribution data)* **2010-2016**	Nghishekwa, 2018 [82]		Average antibiotic consumption was 41.8 DIDs for the six-year period 2010-2016. • There was a 13.2% increase in antibiotic consumption between 2010 and 2016. • Sulfonamide with trimethoprim: highest consumed antibiotics (51%) • Penicillins: second highest consumed antibiotics (32.7%)
Private Based on sales data **2008-2011**	Pereko *et al*, 2016[83]		Average antibiotic consumption was 26.8 DIDs for the four-year period, 2008-2011 (19, 22.1, 29.1 and 35.4 respectively). • There was a 57% increase in wholesale units of antibiotics from 2008 and 2011 • Penicillins (mainly amoxicillin): highest consumed antibiotics (39% of sales) • Consumption rates: Cephalosporins > macrolides > tetracyclines > quinolones • High sale of broad compared to narrow spectrum antibiotics in the private sector
Antibiotic use	**Study**	**Rate**	**Antibiotic use (% prescriptions with antibiotics) WHO/INRUD indicators** (Prescribing rate key: ■ High (>25%), Moderate ■, Low ■)
Public	Niaz *et al*, 2020 [42]		Antibiotic prescribing rate was 69% in a multicenter study that assessed 1243 out-patient prescriptions.
Public	Kunda *et al*, 2015 [84]		Antibiotic prescribing rate of 78% in a single center study conducted among patients with upper respiratory tract infections.
Community (private)	Pereko *et al*, 2015 [80]		Antibiotic use among the public in the past one-year: 80% of the respondents (n=446) reported to have used antibiotics mainly for colds and flu symptoms. In addition, 15% self-purchased the antibiotics without a prescription.
Public	Lates & Shiyanga, 2001		Reported a national-wide increase in antibiotic use from 39% in 1997 to 51% in 2001

Public	Akpabio *et al*, 2014 [85]		Antibiotic prescribing rate in 2012/2013 was 50% for the 1090 prescription assessed. The compliance rate to guidelines was 26.2%, and 55.1% respectively using a strict and loose criteria.
Community	Kamati et al 2020[79]		Reports that 60% of households used self-medication for acute respiratory infections in children under five-years. However, there was no self-purchasing of antibiotics.
Community (private)	Pereko *et al*, 2015 [80]		Reported that most of the people (85%) in the community used antibiotics prescribed by a recognized professional or institution.
Private	Kibuule et al , 2021[43]		Reports that was typically no change in the utilization of antibiotics in the initial months following the Covid-19 pandemic.
Veterinary	Madzingira et al, 2020[26]		Of the animal medicines frequently used by farmers, 23.7%(n=4/13) are antibiotics. • Oxytetracycline: most commonly used veterinary medicine by farmers • Most farmers (83.3%) use oxytetracycline at sub-therapeutic doses (<1ml/10kg) Most farmers (93.3%) self-diagnose and treat without consulting a veterinarian
Veterinary	Haakuria et al 2020 [25]		Reports overuse of oxytetracycline among farmers: "Farmers in Namibia perceive tetracycline as "vaccines" and refer to tetracyclines as a medicine for all diseases"
Compliance data	**Study**	**Rate**	**Compliance rate (% of prescriptions that complied to guidelines)** (Compliance rate key: ■ High (>25%), Moderate ■, Low ■)
Private	Pereko *et al*, 2015 [80]		Compliance to guidelines among prescribers in private sector :31% (n=44) • First-line antibiotics for upper respiratory infection: amoxicillin with clavulanic acid • First-line antibiotics for urinary tract infections: ciprofloxacin
Public	Nakwatumbwah *et al*, 2017 [40]		Sub-optimal compliance to guidelines (62%). • Penicillins were the most prescribed antibiotics. Antibiotics are mainly prescribed to treat respiratory infections (58%)
Public	Kagoya 2020[86]		Reported that the implementation of the NSTGs in 2012 marginally improved regional but not national trends on medicine use indicators. NSTGs immediately improved regional medicine use, and 53.8% of the regions (n=13) had an immediate decline in antibiotics use.
Public	Niaz *et al*, 2020 [41]		The compliance rate was, 73% among the 1432 prescription that were reviewed.

DDD = defined daily dose per 1 000 inhabitants per day (DID).

4. DISCUSSION

The study aimed to analyse policies, resistance patterns and consumption of (MIA used in animals in Namibia to guide future antimicrobial stewardship efforts in the country. We believe this is the first study of its kind in Namibia and sub-Saharan Africa to help inform future antibiotic use policies and practices across sectors. Our findings show misalignment of antibiotic policies used in the human and animal health sectors, high rates of antimicrobial resistance to, and consumption of, MIA used in animals.

4.1 Policy analysis on use of MIA in animals in Namibia

The study identified policy gaps with regards current regulations of MIA when indicated for medical and veterinary practice There are inconsistences in scheduling of antibiotics used in humans and animals in Namibia, with a considerable number of MIA indicated for use without a prescription in animals as open market or over-the-counter medicines (OTCs). In addition, the antibiotic policies in Namibia were found to be inappropriate given that they indicated MIA in food animals as feed premixes as well as use of AWaRe Watch antibiotics with the majority broad spectrum antimicrobials - particularly sulfonamides, tetracyclines and penicillins **(Figure**

1, Table 1). This is a concern, given that antibiotics are often used in large volumes in animals, which is a well-recognized risk and driver of AMR [3,15]. The misalignment in schedules may promote the use of antibiotics reserved for humans in animals, and vice versa, with a reported increase in the use of ivermectin from veterinary outlets by Namibians as a remedy for Covid-19, similar to the situation in South Africa [87,88]. Among the most indicated AWaRe Access antibiotics in animals was sulfamethoxine/trimethoprim and cloxacillin/ampicillin, which are also first-line antibiotics for treating common outpatient infections in in Namibia [89]. Moreover, current policies indicate the use of these AWaRe Access antibiotics in food animals for the management of a wide range of bacterial infections, including respiratory, gastrointestinal and skin infections **(Table 2).** Similarly, Kibuule et al (2017) reported the non-concurrence of antibiotic policies and national treatment guidelines with regards to use of cotrimoxazole, amoxicillin, and azithromycin as first line antibiotics in Namibia [90].

There is also currently misalignment of national policies in terms of use, access, and stewardship, with systems well-regulated on the medical but not the veterinary practice [89,91]. For instance, there are currently no guidelines and essential medicine list with regards to antibiotic use in animals. Secondly, antibiotic policies for animals do not appear currently to be aligned to global developments such as the WHO AWaRe categories and the Veterinary Feed Directives of the OIE and the FDA [17]. Of equal concern is that there is currently no quality control testing of MIA used in animals rather than human in Namibia [52]. On the other hand, antibiotic policies restrict the use of all antibiotics in humans as prescription only medicines [51], which is currently observed in practice and in the findings [43,79]. The current misalignment of antibiotic policies for animal and human healthcare promotes irrational use and undermines national antimicrobial stewardship programmes [6,92–94].

This calls for a one health multi-sectoral approach for the development, harmonization and implementation of antibiotic policies to promote sustainable antimicrobial stewardship, as well as inform the mid-term review of the Namibia NAP against AMR. In particular, encourage the appropriate use of antibiotics in animal feeds. In addition, restrict the use and promotion of growth promoting antibiotics in animals through multidisciplinary collaborative efforts involving medical and veterinary professionals and farmers. We have seen in South Africa that combined strategies including veterinary scientists has restricted the use of colistin to good effect providing guidance to Namibia [35].

4.2 Antimicrobial resistance patterns of MIA used in animals in Namibia

Our findings describe high AMR rates to MIA used in animals in Namibia, especially with sulfonamides, penicillin and tetracycline (Table 3). The high and rising resistance of common respiratory, urogenital and gastrointestinal bacterial isolates to AWaRe Access antibiotics in this study is a considerable threat to future antibiotic use in Namibia **(Table 3)**. Most gram negative and positive isolates were particularly resistant tetracyclines, penicillins and sulfonamides. Nevertheless, most of the isolates were susceptible to newer antibiotics including aminoglycosides, cephalosporins and fluoroquinolones. The WHO identifies the indiscriminate use of broad-spectrum antibiotics, in food animals and humans as a key driver of AMR globally, with its considerable impact globally on morbidity, mortality and cost [6,95–98]. Similar studies in sub-Saharan Africa report growing concerns on the burden of AMR particular with a wide range of bacteria attributed to overuse and inappropriate disposal of veterinary antibiotics [12,16,99]. This is a concern, given that the OIE and FDA identify the animal food chain as an important source of resistant bacteria in humans [27] alongside high and inappropriate prescribing and dispensing of antibiotics for essentially viral infections such as upper respiratory tract infections fueled by the recent COVID-19 pandemic across Africa and wider [100–102]. Moreover, several studies report traces of antibiotics in animal products, such as eggs, meat and milk [11,103]. There is also need for continued surveillance of antimicrobial resistance patterns particularly to MIA included on the EML and STGs within countries including Namibia.

4.3 Antibiotic consumption and use in Namibia

Similarly, we have seen antibiotic consumption rates in Namibia higher than the global target of 22.38 DDD, high prescribing of antibiotics in outpatient departments (i.e., >25% of prescriptions with antibiotics), self-purchasing of antibiotics for animals but not now for human use among community pharmacists, and the wide-use of broad-spectrum AWaRe Access antibiotics among farmers **(Table 4)**. The high consumption of antibiotics greater than 22.38 DID have been documented in both the public and private sectors of Namibia [82,83]. A survey by Pereko *et al*., reported consumption of broad spectrum antibiotics in Namibia's private sector, especially with penicillins (amoxicillin/clavulanate), cephalosporins (cefuroxime) and macrolides (clarithromycin), as well as limited self-purchasing of antibiotics from pharmacies[80]. This is less of an issue within the public healthcare system in Namibia [40,41], and more recent studies have shown limited or no self-purchasing of antibiotics [43,79]. However, there is need to close the gap with unnecessary use of antibiotics throughout the country.

The study reports oxytetracycline as the most empirically used veterinary medicine among farmers in some parts of Namibia [25,26]. Haakuria *et al*. attribute the overuse of oxytetracycline among communal farmers in Namibia to the perception of its broad spectrum activity; consequently, it can be used like “vaccines” to prevent most animal diseases [25]. This is a public health concern with both the OIE and FDA prohibiting the use of MIA as non-prescription medicines and/or feed additives [16,17]. Alongside this, studies report a cross-over use of human antibiotics in animal farming and vice versa, especially among resource limited communities, which is a concern going forward [11,30]. For instance, there was repurposing of veterinary formulations of ivermectin to treat Covid-19 in Namibia when the human formulations were restricted [88,104,105]. This is similar to other African countries, and needs to be avoided due to concerns with its effectiveness in practice to treat patients with COVID-19 [87]. This culture of misuse of the AWaRe Access and Watch antibiotics among farmers in Namibia needs to be addressed and reversed going forward to reduce unnecessary use.

4.4 Limitations

The findings from this study should be interpreted with the following limitations. First, this was a descriptive population-based review, and we are unable to link the resistance patterns in this study to the high antibiotic consumption and incoherence in antibiotic use policies. Second, the interpretation of findings in the analysis of policies is based on current available documents or policies. Third, this review of resistance patterns and consumption of MIA was based on published data, and the actual practice by veterinarians, prescribers and farmers was not determined. Consequently, the resistance patterns and antibiotic use may change overtime and the frequencies may not reflect the current situation. Nevertheless, we believe this is the first study in Namibia and sub-Saharan Africa that analyzes policies for use of medically important antibiotics in animals, and provides preliminary results on the challenges and implications for antimicrobial stewardship under the one health concept. In particular, the study highlights the need for integration of AMS programs for humans and animals at the policy and implementation levels.

4.5 Conclusion and next steps for Namibia

Based on the findings from this study, we conclude that current antibiotic use policies for humans and animals are inconsistent and urgently require harmonization. There is currently high resistance to MIA used in Namibia, exacerbated by high consumption and misuse of broad-spectrum MIA among farmers, prescribers and patients in Namibia. The current antibiotic use

policies may enhance overuse of MIA in animals given that majority of antibiotics used are available on the open market. There is also currently no alignment of antibiotic policies for animals with the global OIE recommendations with regards to prescription medicines and their use as feed additives, with some of these antibiotics licensed for growth promotion. This is a concern as in Namibia there is currently high resistance to commonly used MIA in medical practice, particularly sulfonamides, tetracyclines, and penicillins.

The study therefore recommends the need to align and integrate policies for use of MIA in animals and humans in Namibia. In addition, antibiotic policies in Namibia should be aligned to global AMS efforts including the WHO AWaRe categories and the OIE Veterinary Feed Directives. The non-prescription use of MIA in Namibia should also be restricted building on the colistin example in South Africa. This can be achieved through developing a standard treatment guideline for use in animals at the grassroots level alongside regular monitoring their use, which has proved successful to improve antibiotic utilization in humans. A regulatory framework should incorporate the aspects of rational use, quality control, stewardship and disposal of medically important antibiotics used in animals. We will be researching this in the future.

Lastly, robust antibiotic surveillance systems are required among both health and agricultural sectors to advance rational use of MIA among communal farmers. This will require active multi-professional coalitions, including health, pharmaceutical, agricultural and veterinary professionals, to foster antimicrobial stewardship.

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